Workshop on Environmental Exposure and Health

Jointly sponsored by MRC & NERC
10 & 11 March 2009

Report

Introduction

The increasing pressures on natural resources and the global climate from rapid economic and population growth were identified as one of five treasury grand challenges set out in the Government's announcement of the 2007 Comprehensive Spending Review. NERC led the Research Council response with the launch of 'Living with Environmental Change' (LWEC), an interdisciplinary research and policy partnership involving the Research Councils, Government Departments and Agencies. LWEC aims to implement a research strategy that advances the evidence base for policy development relating to environmental change, including the assessment of links and feedbacks between the natural environment, ecosystem services and human health and well-being, and the protection of human, plant and animal health by predicting how environmental hazards will alter under forthcoming environmental change scenarios.

To fulfil these objectives it is crucial to understand exposure levels and how exposure information can be used to gain a better understanding of the relationship between environmental quality and human/ecosystem health. These relationships should help improve environmental management policies through evidence-based policy decisions.

MRC and NERC jointly sponsored Professor Frank Kelly, on behalf of the MRC/HPA Centre for Environment and Health, to convene a workshop on Environmental Exposure and Health, held in London on 10 and 11 March 2009. The two day meeting was attended by 80 delegates and brought together eminent scientists representing the health and environmental research communities across the UK, policy makers and funders. The workshop aimed to discuss and reach consensus on the key research and policy gaps, needs, and opportunities in order to inform a joint UK funding initiative.

The workshop was structured to address environmental exposure modelling, measurement and effects; the opportunities for biomarker science to contribute to a better understanding of exposure/response relationships; and the potential of exposure research to contribute to the development of evidence-based policies. In an interactive discussion session delegates were asked to address a set of questions to help shape the remit of a proposed call for proposals in the field of exposure and health:

- What are the UK strengths in terms of research or infrastructure and how can we best capitalise on these?
- What are the key research gaps, needs and opportunities that the UK is particularly well placed to address?
- What are the major policy needs and how can we best tackle these?
- Taking account of other national and international activities and funding opportunities what is the niche for a joint MRC/NERC led initiative?

- What are the opportunities for partnerships with other stakeholders?
- Are there training and capacity building needs?

The workshop programme is at Annex 1 and the list of delegates at Annex 2.
Key points raised in the break out groups, as summarised by the rapporteurs, are at Annex 3.
A summary of the exposure grants awarded through the first phase of the NERC-led Environment and Human Health Programme are at Annex4

Outcomes

UK strengths

The workshop highlighted the significant UK strength in **epidemiology and cohort studies**, including the internationally unique collection of birth cohorts and UK Biobank, as well as population health surveys. Plans to enhance the existing cohort infrastructure by a new major birth cohort due to start around 2012 were noted.

The UK health care system was recognised as strength, referring to good primary care networks, and the possibility of linking **routine health data** with population based and environmental studies via the Research Capability Programme**.**

Participants noted the UK's significant research capacity in modern molecular biology, including the **"omics"** technologies, and exploitation of the resulting data through bioinformatics. The UK's traditional strengths in **toxicology** and **ecotoxicology** were also emphasised, although it was recognised that many senior toxicologists were due to retire within the next decade or so and only few young scientists were entering the discipline leading to a capacity problem.

Detection of patterns of pollution through **environmental monitoring** was recognised as a strong point, highlighting the UK's comprehensive atmospheric monitoring programmes, which provide temporally and spatially resolved databases of contaminants and environmental biomarkers. An example is the measurement system for air pollution in London www.londonair.org.uk, which NERC plans to enhance for research purposes through a new initiative on urban atmospheric science.

Delegates also emphasized the good **international links** of UK groups, including the European Prospective Investigation of Cancer (EPIC) and the European Study of Cohorts for Air Pollution Effects (ESCAPE); and the good working relationships and **engagement between the UK research and policy communities.**

Research and policy needs, gaps, and opportunities

High quality exposure information is crucial for scientific advances in environmental epidemiology, including the understanding of exposure-response relationships and gene-environment interactions. It is also essential for the development of evidence-based policies for instance by contributing to the better definition of health risks, the generation of predictive models for cost benefit analyses, and the evaluation of regulation. Although risks are often small, they affect large numbers of people. From a policy perspective, once causation has been accepted or is strongly suspected, usually simple strategies can be introduced to reduce exposure. While there have been significant advances in the determination of genotypes and polymorphisms over recent years, the accurate assessment of environmental exposures remains an unmet

challenge, severely hindering the progress in understanding the impact of environmental exposure on health.

The UK is a world leader in cohort studies. Often extensive genotype and phenotype information and biobanks are available and the value of this resource is going to increase with the opportunities provided through increased linkage of routine health data. The UK's wealth of environmental monitoring data is currently underutilised for environmental health research. There is potential **to capitalise on and enhance the UK's unique cohort studies** through improved exposure measurements or linkage to environmental monitoring information. Protocols for the collection of data and samples and their storage for environmental health research across cohorts are required. Non-invasive sampling is particularly important to ensure high response rates and facilitate repeat measurements.

A key aspect of the proposed initiative in environmental exposure and health should be the analysis of the **connection between environmental exposure, early effects and health outcomes** and the link back to **pollutant source apportionment**. This requires improved methodologies in terms of study design, exposure assessment and data mining as well as an integrated approach across the environmental and health sciences. A summary of the key needs, gaps and opportunities is given below:

There exists a trade off between the large study sizes required for environmental health research and the availability and precision of exposure data. Existing studies can be enhanced with environmental assessments, including for instance the measurement of biomarkers in biological samples, but the amount of material required and cost are often prohibitive. **Innovative study designs, methodologies** and mathematical approaches are needed to address this. These include "mixed designs", based on sub-sampling and calibration, for instance combining small area and individual level data or intensively measured subgroups in larger population studies.

Developments in **modelling and predictive approaches** are important for instance for addressing contaminant mixes, indoor versus outdoor pollution, estimation of life-long exposure in a changing environment, or for providing holistic approaches to policy evaluation linking contaminants to a range of policy drivers under environmental change. The validation and calibration of models is crucial and methodologies are required to do this for instance using survey and monitoring data.

Robust, cheap and easy-to-use **technologies for personal monitoring** are needed that can be applied on a large scale. For example in the case of air pollutants, greater account needs to be taken of indoor as well as outdoor exposures and also interactions between physical activity and exposure and proximity to emissions (in the case of small children). Exciting opportunities exist to build on recent advances in sensor technologies from the engineering sector and to develop instruments for personal monitoring and protocols for their use in cohort and other studies. There are also opportunities to build on and link into the NERC Technology Programme.

Biomarkers provide an important route for connecting exposure and health effects. **Reliable, biologically relevant (bio)markers** are required to address important research questions, such as gene-environment interactions and exposure-response relationships, and to enhance the development of evidence based policies and their evaluation. Markers can also be used to determine bio-accessibility and bio-availability and to monitor and distinguish between exposure sources. The ability to measure the **total burden of exposure** from a variety of sources was considered important.

Markers of human exposure provide information on the internal dose of pollutants rather than ambient concentrations. To better understand biologically active doses, biomarkers of effect including non-genotoxic (oxidative stress) or genotoxic (DNA adducts) are

required. Recent developments in the '**omics' technologies**, including metabonomics, functional genomics, proteomics, and transcriptomics, if used in a targeted way, provide exciting **opportunities for the development of biomarkers of early effect**, which can be used in high throughput processes and be linked to health-related phenotypes. They can also help to identify causal mechanisms, including cellular targets and pathways and, if validated against established toxic endpoints, can significantly enhance risk assessment processes.

More knowledge is needed on individual **susceptibility and resilience** - for instance relating to health status, genetic make up, exposure history, or socioeconomic factors and how this affects the impact of environmental exposure on health outcomes. A better understanding is also required for the differential effects of exposure on **vulnerable subgroups**, such as children, pregnant mothers and the elderly as well as those who are socio-economically deprived. As most diseases develop in mid-life and beyond, early life and childhood are age groups that are important for studying health effects of early life environmental exposures on the emergence of later complex diseases.

Epigenetic modifications provide a plausible link between the environment and alteration in gene expression that might lead to disease phenotypes. Harmful effects can be carried over for several generations. **Epigenomics/epigenetics**, the impact of life course exposure (including later life effects of *in utero* or early life exposure), and trans-generational effects are important areas of research and in which there is real potential to build on the UK's cohort infrastructure in order to address this.

Many health effects are likely to be influenced by the exposure to complex mixtures. More knowledge is needed on the effects of **mixtures of contaminants and multiple stressors and how they may interact,** such as the interaction of air pollution with noise, temperature and diet, the interactions of endocrine disrupting chemicals and pesticides and the impact of urbanisation, climate change and different exposure routes in combination on mixture profiles and human exposures. Methodologies are required to address mixtures and multiple stressors including technology platforms for measuring emissions, methods to estimate and model the effect of multiple exposures, bio-screening systems, and data analysis procedures.

Improved methodologies are needed for the assessment of **long term pollutant exposure** and we need a better understanding of the relative importance of measuring **peaks and troughs versus longer term averages in predicting health impacts.** Effective methodologies for measuring **low level exposure** are also an important requirement.

There is an opportunity to make more use of existing data in a creative way for instance by enhancing **methodologies for the integration of information across different data sets.** This may include linkage of environmental monitoring and health data sets; the integration of information across pollutant sources, such as air pollution, temperature and noise; or meta-analytical techniques to synthesise evidence from a range of studies including animal or other laboratory based studies. Innovative approaches to data mining and capacity in bioinformatics and statistics are needed to make maximum use of increasingly complex data sets.

In contrast to drug development where lower vertebrates are commonly used as model organisms, human environmental toxicology and eco-toxicology have developed largely independently. There are major opportunities to increase the **cross-fertilisation between eco- and human toxicology** and forge links between environmental and human health impact assessments. Information on the effects of pollutants on wild life and domesticated animals for instance relating to mixed stressors or resilience can be extrapolated and interpreted to predict potential health effects in humans or to prioritise research questions. There are significant areas of commonality between the

environmental and health communities which can be exploited through better transfer of knowledge and integration of research for instance relating to the development of biomarkers, understanding bioavailability, the use of sentinel species to predict effects on human health, and the use of epidemiological data to identify contamination hotspots.

There is a need to ensure that **relevant measures** of contaminants are made to understand the eco-epidemiology of disease. For example, understanding the nature of a particle that causes a biological effect, and how the behaviour, speciation and persistence of contaminants in the environment control bioavailability and exposure. The research must be cognisant of the effects of **environmental change**, such as the effects of variable precipitation on chemical fate, behaviour and degradation in the environment, and the potential for direct changes of natural stressors.

Anticipating future health problems from **new materials** and energy policies is a potential gap. For example, there is an opportunity to work with others on emerging effects of nano-technology (e.g. NERC/Defra/Environment Agency funded Environmental Nanoscience Initiative) and radionuclides from nuclear energy generation.

It is important to better understand **the relationship between socioeconomic status and environmental exposures** and their relative impacts on human health. This includes for instance disentangling factors relating to deprivation, such as poor diet, inadequate housing, employment and smoking, from the health effects of environmental pollution and understanding the contribution of social factors to susceptibility. Social science can also make important contributions to the development of environmental health policies based on changes in behaviour.

The **indoor environment** plays a major role in an individual's exposure profile and the significant contribution of indoor pollution in causing health effects is increasingly recognised. However, there is currently relatively little research in this area and the funding responsibilities are not clear. A lot of lessons can be learned from **occupational health research**, where good toxicity information is often available, albeit at much higher concentrations than often experienced in the wider environment. Such data has been of immense value in deriving outdoor air quality standards as undertaken by Defra's Expert Panel:

From a policy perspective improved tools for risk assessment, cost benefit analysis, and health impact assessment were considered valuable. Opportunities were highlighted for the contribution of improved exposure assessment, better knowledge of susceptibility and the interaction between social and environmental factors for the development of more appropriate and targeted evidence based policies. A key requirement is the continued monitoring and **evaluation of environmental policies** and the methodology to achieve this. Source apportionment was also considered an important policy need.

In terms of health priorities relating to environmental exposure, the following areas were considered of particular importance: **cancer, respiratory disease, endocrine disruption, neuro-degeneration and cardiovascular disease.**

Niche for a joint MRC/NERC led initiative and opportunities for partnerships

The workshop reached consensus on the niche for the proposed initiative in supporting **cross-disciplinary research** that cannot be easily supported by individual funders through the existing funding mechanisms. Research should link environmental and health sciences and bring in other disciplines, such as social science or engineering, as appropriate. Participants highlighted the opportunity to create sustainable, multidisciplinary networks of excellence with sufficient critical mass to address real world

problems. Such networks would be expected to be competitive in attracting additional funding from other major funding sources, such as EU programmes. The potential to build on the links and capacity created through the first phase of the NERC-led Environment and Human Health Programme was also noted.

The proposed programme should encourage an **integrated approach** combining expertise in areas such as modelling, epidemiology, eco- and human-toxicology, environmental exposure, social science, risk and health impact assessment to address significant research questions that require collaboration. The **interface between research and policy**, and translation of research results for improved environmental management policies, was considered particularly important.

Delegates emphasized **multiple opportunities for partnerships** involving other Research Councils (ESRC - deprivation, behaviour; BBSRC - domesticated animals; EPSRC - sensors and indoor environment), Government Departments and Agencies (Department of Health, HPA, Environment Agency, Defra, HSE and FSA) and the medical charities including the Wellcome Trust. It is also important to recognise that health issues relating to the environment are cross boundary and should engage the Devolved Administrations in Scotland Wales and Northern Ireland as well as Europe when appropriate.

Participants noted that the beneficial influences of the environment, for instance the impact of green spaces on obesity and mental health, were important research topics. However, these were not covered within the remit of this workshop, given the already broad scope of the workshop and the complexity and distinct expertise required to address this area. Plans for a Wellcome Trust workshop on the influences of the built environment on obesity were noted. Delegates were also informed that pathogens would be the subject of a parallel MRC/NERC led initiative on the environmental and social ecology[1] of human infectious disease.

Training and capacity building

Recognising the opportunities for increased linkage and analysis across different data sets, quantitative skills including **data mining, mathematics, bioinformatics and biostatistics** were highlighted as major training and capacity building needs.

Participants considered it crucial to encourage young researchers into the field and to **train a new generation of scientists that understand the languages of different disciplines** and can apply novel and innovative methods and technologies, for example to modelling, exposure assessment, exposure assignment and evaluation of effects.

Summary of conclusions and recommendations

- There is a major opportunity **to build on the UK's strengths**, including the internationally leading cohort infrastructure, technological advances, such as sensor technologies and 'omics' platforms, and comprehensive biomonitoring data to make a significant difference to our understanding of the environmental impacts on health and improve the development of evidence-based policies.

- The proposed joint UK funding initiative should stimulate **multi-disciplinary and integrated approaches** across disciplines related to the health and environmental sciences and bring in other areas, such as social and engineering

[1] how human activities enable microbes to disseminate and evolve, thereby creating favourable conditions for the diverse manifestations of communicable diseases

as appropriate, to tackle real world problems. It was considered important to **recognise policy needs** and to allow for a balance between blue skies and more applied approaches. NERC and MRC should pro-actively engage other Research Councils (ESRC, EPSRC, BBSRC), Government Departments and Agencies (Department of Health, FSA, HPA, Environment Agency, Defra, HSE) and charities (Wellcome Trust, etc) as potential partners in the initiative.

- The use of **innovative and novel methodologies, study designs**, and technologies for instance addressing exposure modelling and prediction, exposure assessment or the integration of existing datasets should be particularly encouraged.

- **Training and capacity building in quantitative skills** such as data mining, mathematics, bioinformatics and biostatistics and the training of young researchers that can make connections **across disciplines** was considered especially important.

- The proposed initiative should have as a focal point the **relationship between environmental exposure, early effects and health outcomes and the link back to pollutant source apportionment**. Key research and policy gaps, needs and opportunities that might be addressed include:

    - The development, validation and use of novel instruments for **personal monitoring and (bio)markers of exposure and effect**

    - Methodologies to assess the effect of **mixtures, low level or long term exposures**, **and interactions with multiple stressors**, including the prediction of life-long exposure in a changing environment

    - Determining the **appropriate measures to capture environmental influences** on exposure and bioavailability, now and in a changing environment

    - Anticipating prospective monitoring requirements for exposure, effect and health impacts of **new materials**

    - Improved **integration of eco- and human toxicology**

    - **Disentangling social and environmental determinants** of health outcomes

    - Understanding **susceptibility, the impact of early life exposure on later health and inter-generational effects**

    - The contribution of the **indoor environment** to exposure profiles and calibration methods for indoor and outdoor ambient pollutant concentrations

    - The use of improved personal monitoring and/or exposure assessment and biomarkers in multidisciplinary studies to inform **policy development** and **methodologies for policy evaluation**

- Building on the investment in small exploratory and capacity building awards through the first phase of the Environment and Human Health programme, it was considered important to provide **more substantial funding for sustainable networks of excellence**, which bring together a significant critical mass of leading researchers to address real world problems.

Heike Weber, MRC
Caroline Culshaw, NERC
27 April 2009

List of Annexes

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Annex 2 - List of delegates
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Annex 4 – Summary of grants awarded through the Environment and Human Health Programme
Annex 5- Summary of achievements and questions arising from the Environment and Human Health Programme – Discussion document prepared by Professor Mike Moore, Programme Science Co-ordinator

Annex 1

Workshop on Environmental Exposure & Health

Jointly sponsored by MRC & NERC
10th & 11th March 2009

It is becoming increasing clear that pollutant concentrations measured at a single location may not truly represent exposures for humans or ecosystems. It is important to understand exposure levels and how exposure information can be used to gain a better understanding of the relationship between environmental quality and human/ecosystem health. These relationships should help improve environmental management policies through evidence-based policy decisions.

The aim of this workshop is to discuss priorities in order to inform the remit of a proposed call for proposals on the relationship between environmental exposure and health in autumn 2009 and to promote multidisciplinary collaborations in response to the call. The schedule is designed to allow sufficient time for discussion.

Key issues we would like to address include:

- What are the UK strengths in terms of research or infrastructure and how can we best capitalise on these?
- What are the key research gaps, needs and opportunities that the UK is particularly well placed to address?
- What are the major policy needs and how can we best tackle these?
- Taking account of other national and international activities and funding opportunities what is the niche for a joint MRC/NERC led initiative?
- What are the opportunities for partnerships with other stakeholders?
- Are there training and capacity building needs?

Venue: Coin Street Neighbourhood Centre, 108 Stamford Street, London SE1 9NH

Workshop on Environmental Exposure & Health

10th & 11th March 2009

Tuesday 10th March

10.00 – 10.15 Welcome and Introductory Remarks

Professor Frank Kelly, King's College London
Professor Andrew Watkinson, Director, Living with Environment Change
Dr Wendy Ewart, Director of Strategy, Medical Research Council,
Dr Phillip Newton, Director of Science Delivery, Natural Environment Research Council

Session 1 Exposure Estimation and Effects

Chair – Professor Roy Harrison

Exposure science has played an important role in current understanding of the complex relationship between environment and health. Many existing management policies are based on studies that associated pollution concentration with health impacts by inferring that ambient concentrations are equivalent to actual exposures. In future studies, which are needed to underpin improved management strategies, more accurate measures of exposure and a better understanding of exposure-response relationships is needed. This session will overview and identify how new work in this area could progress.

10.15 - 10.45	**Professor Jon Ayres, University of Birmingham** Air pollution as a major factor in determining health; the role of personal exposure monitoring
10.45 – 11.15	**Professor Mike Ashmore, Univeristy of York** The role of modelling in assessing current and future exposure
11.15 - 11.45	**Professor David Briggs, Imperial College London** Advantages of improving exposure assessments in studies of environment-health relationships
11.45 – 12.15	**Dr Diane Benford, Food Standards Agency** Food safety, how do we assess exposure to chemicals?
12.15 – 12.45	**Professor Richard Shore, Centre for Ecology & Hydrology** Long-term risks of environmental stressors (especially contaminating chemicals) for terrestrial ecosystems
12.45 – 1.00	**Concluding Remarks** Led by Professor Harrison
1.00 – 2.15	**LUNCH**

Session 2 Biomarker Science

Chair – Professor Stephen Holgate

Improved biomonitoring can help in a number of ways from the evaluation of exposure trends, identification of susceptible populations, detection of emerging chemical risks, conduct of epidemiological studies, and the evaluation of risk reduction strategies. This session will overview developments in biomarker identification and how they can be used to provide a better understanding of exposure/response relationships. Gaps which are limiting progress in the field of biomonitoring will be discussed.

2.15 - 2.45 Professor Paul Elliott, Imperial College London
Epidemiological approaches to uncover environmental hazards.

2.45 – 3.15 Professor Kevin Jones, Lancaster University
Monitoring, exposure and markers for persistent organic chemicals.

3.15 - 3.45 Professor David Melzer , Peninsula Medical School
Human population biomonitoring: Epidemiological follow-up.

3.45 – 4.15 Professor Paolo Vineis, Imperial College London
New systems biology approaches to assess the impact of environmental exposures.

4.15 – 4.45 Professor Peter Farmer, University of Leicester
Development of sensitive biomarkers to assess pollutant impact.

4.45 – 5.00 Concluding Remarks
Led by Professor Holgate

6.30 DINNER at the RSJ, 33 Coin Street, London SE1 9NR

Wednesday 11th March

Session 3 Update on Policy requirements

Chair – Professor Paul Elliott

There is an urgent need to advance exposure science and its applications to better protect human and ecosystem health. This is a priority area for a number of Government agencies and this session will highlight their individual needs and requirements.

9.00 - 9.15 Dr Louise Newport
Department of Health

9.15 - 9.30 Prof Martin Williams
Department for Environment, Food and Rural Affairs

9.30 - 9.45 Dr Jim Wharfe
Environment Agency

9.45 –10.00 Dr Heather Walton
Health Protection Agency

Session 4 Interactive Session to inform remit of call for proposals

Chair – Professor Frank Kelly

This session will discuss UK strengths, needs, gaps, and opportunities from a research and policy perspective with the aim to inform UK strategy and to advise on the remit of a joint call for proposals on Environmental Exposure and Health.

10.00- 10.10 Funders perspective
Dr Heike Weber

10.10 - 11.10 Breakout Groups: Needs and Opportunities in Exposure Research

Attendees will be split into 4 groups and asked to discuss the following issues:

- What are the UK strengths in terms of research or infrastructure and how can we best capitalise on these?
- What are the key research gaps, needs and opportunities that the UK is particularly well placed to address?
- What are the major policy needs and how can we best tackle these?
- Taking account of other national and international activities and funding opportunities what is the niche for a joint MRC/NERC led initiative?
- What are the opportunities for partnerships with other stakeholders?
- Are there training and capacity building needs?

11.10 – 11.30 COFFEE

11.30 – 12.30 Feedback from Breakout groups

12.30 – 1.00 Synthesis of conclusions

1.00 – 1.15 Concluding Remarks
Led by Professors Harrison & Holgate

1.15 LUNCH & Departure

Annex 2

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Annex 3

Group A Rapporteur's Summary

What are the UK strengths in terms of research or infrastructure and how can we best capitalise on these?
International links/collaborations
Epidemiology, Biostatistics
Toxicology
Human challenge studies
Policy driven research & working relationships Government policy makers
Availability of good quality, routine health data (concern - under threat – data protection)

What are the key research gaps, needs and opportunities that the UK is particularly well placed to address?
Linking existing databases to better characterise where populations are, determine better exposure measures to therefore determine better crf
Children and the environment
Indoor exposures and occupational exposures
Nature and sources of particles
Human data for risk assessment of chemicals (animal models would also be useful)
Issue around energy generation as a whole

What are the major policy needs and how can we best tackle these?
Better risk assessment leading to cost benefit analysis and more appropriate and targeted policies
Focused policies e.g. particle components rather than simple mass measure (PM10)
Target specific chemical compounds

Taking account of other national and international activities and funding opportunities what is the niche for a joint MRC/NERC led initiative?
Integration - exposure assessment to health impact to policy
Integrated approaches to tackle issues where collaboration is required
Chemical environment
Air Pollution
Climate and population change

What are the opportunities for partnerships with other stakeholders?
Government/Agencies/Industry (despite current economic climate)/Research Councils

Are there training and capacity building needs?
Encourage younger researchers into field
Subject is large and diverse and cannot expect everyone to be expert in every field.
Core training program to provide basic skill set
Phd and Masters program to provide this

Group C Rapporteur's Summary

Q1. What are the UK strengths in terms of research or infrastructure and how can we best capitalise on these?

- Parallel infrastructure
  UK Biobank
  UK cohort studies
  Extensive routine data collection

  All underutilised for environmental health research - small investment could have a big impact

- London especially for Air Pollution
  5 million people
  NERC investment in air pollution measures
  Infrastructure- TFL, Oyster cards

- UK links with other countries/studies e.g.
  EPIC
  ESCAPE

Q2. What are the key research gaps, needs and opportunities that the UK is particularly well placed to address?

- Exposure measurement
  Instrumentation that is
  Cheap
  Can be widely used
  Gives information on personal exposure

- Exposure metrics
  Biologically relevant e.g. oxidative stress
  Looking across wildlife and human health effects
  Dealing with mixtures
  Are Peaks or Averages more important
  Susceptibility – who is susceptible?

Q3. What are the major policy needs and how can we best tackle these?

- What do you measure to see if your policy has been effective?

- Cross Links with
  Social scientists – or can't interpret exposures e.g. deprivation or help wtih change in behaviour
  Occupational health researchers

  And cross-links between existing cohorts and environmental scientists.

- Evidence Based policy
  -Use population attributable risk to rank importance of environmental hazards. For some hazards data might not be not available, but can consider extrapolating from occupational and animal health
  -Use evidence to justify step changes e.g. move to remote sensing or move to using biologically relevant measures such as oxidative potential of air pollution
  -Aim for cost reduction while improving outcomes

-Need for continued policy development- monitor health outcomes after policy change, consider using actual biological measure of toxicity, update legislation in some areas e.g. noise legislation based on nuisance not health effects
-Learning from past policy intervention- what worked, what did not (HEI have looked at this for air pollution)

Q4. Taking account of other national and international activities and funding opportunities what is the niche for a joint MRC/NERC led initiative?

Combination of general and specific

GENERAL AREAS

- Exposure refinement
    - Biomarkers- need careful development and usually can't be used without other info. Suite of biomarkers probably more important
    - Source apportionment.
    - Dealing with mixtures.
- Susceptible communities
- Multidisciplinarity across NERC-MRC with an integrated approach e.g. looking across environmental science & wildlife to human health effects, bringing in other research councils as appropriate e.g. BBSRC for domesticated animals, ESRC for social effects, good cross council collaboration is important.
- Stretching science- the difficult areas other funders don't touch e.g. mixtures, methodology, peaks vs. averages

SPECIFIC AREAS

Difficult as each individual will lobby for their specific research interest, which might be as diverse as biomarker, natural air pollution, biobanks, deprivation, cadmium ionising radiation.
PAR approach to rank importance of exposures is helpful but there are gaps in this information

Q5. What are the opportunities for partnerships with other stakeholders?

- Cross council working very important
  BBSRC- domesticated Animals
  ESRC

- Engaging with existing infrastructure
  US and NERC EHH programme mentioned specifically

- Learning from good practice

Q6. Are there training and capacity building needs?

- Build on current EHH programme

- Need to keep bringing together different disciplines e.g. Social science-environment-medicine

- Maintain capacity

- Methodology- especially data mining

- Communication of science- risk communication

Post Hoc TOP TWO PRIORITIES

- Impoverished communities – deprivation – susceptibility. This cross cuts across a lot of areas including mixtures
- Developing methodology-
  - Mixtures
  - Peaks Vs Averages
  - Data Mining
  - Biomarkers

Group D Rapporteur's Summary

Strengths

Existing cohorts (eg ALSPAC)
Existing studies (eg: Biobank, National Diet and Nutrition Survey)
Health care system – with good primary health care networks
Exposure monitoring programmes in place
'omics' technologies

Research gaps

Structural/historical gaps between disciplines, agencies. Lack of joint approaches and collaborative spirit over data sharing

Development across groups of protocols and technologies for

1) cheap personal biomonitoring with high throughput technologies for use in epidemiology
2) protocols for use by epidemiology studies that are currently collecting data on samples to be collected, storage and general approach to biobanking of material NOW

Results from epidemiological studies are synthesised by meta-analytical techniques – can similar aporaches be used to synthesise evidence from studies in animals or other laboratory based studies

Tests that assess 'total burden of exposure', total biological activity of samples (eg for endocrine disruption)

Cross-fertilisation between eco-toxicology and human toxiciology – particularly in field of sentinel species, interpretation of animal studies for human health, understanding resilience

Although 'omics' platforms producing wealth of data, real world interpretation may be difficult, particularly in relation to understanding exposure patterns that produce effects.

Indoor air – in particular who is responsible for funding research in this area

New materials and the influence of environmental change on exposure paterns and on susceptibility to exposure

Mixtures

Policy Needs

Human health relevance
What is the minimal information require on all substances?
Information for cost benefit analysis

Niche for MRC/NERC

To bring together multidisciplinary groups with common overall interst. (?perhaps a qualifying criteria for application)

Opportunities for partnerships

Many
Across agencies, universities
Interest in international collaboration but the need is for development/strengthening o of UK capacity first

Training and capacity

Biostatistics
Exposure assignments

Priorities

Air Pollution
Cancer
Endocrine disruption
Neurodegenerative disorders

Annex 4

Research grants the NERC-led Environment and Human Health Programme

The Environment and Human Health Programme is a £4.4m partnership programme comprising 37 projects that cover a broad field of environmental concerns linked to human health, including inhalation of nanoparticles, long-term exposure to pollution in urban environments, harmful algal toxins, climate change and emerging diseases.

The programme identifies and prioritises research areas where the natural environment and human health interact, and is building a community of scientists in the UK committed to researching this relationship. Their research should improve our ability to identify and predict emerging health concerns, and will also improve the evidence available to support risk assessments and regulation-setting by the government and other policy makers.

The 37 projects all started in 2007 and will be completed in 2008 and 2009. Environment and Human Health is led by the Natural Environment Research Council (NERC) and is a partnership programme supported by the Natural Environment Research Council, the Environment Agency (EA); the Department for Environment, Food and Rural Affairs (Defra); the Ministry of Defence (MOD); the Medical Research Council (MRC); the Welcome Trust; the Economic and Social Research Council (ESRC); the Engineering and Physical Sciences Research Council (EPSRC); the Biotechnology and Biological Sciences Research Council (BBSRC) and the Health Protection Agency (HPA)

Of the 37 projects, 27 have built capacity in the area of environmental exposure and health. These are highlighted in table 1.

Table 1: Awards from the NERC-led Environment and Human Health programme that have built capacity in the area of environmental exposure and health

Begon, University of Liverpool	'Workshop - Predicting Zoonotic Outbreaks: Building on the Plague Threshold Model	Workshop/ Network
Hardy, Central Science Laboratory	'Impacts of climate change on the risks of biological and chemical environmental contaminants from agriculture to human health	Workshop/ Network
Ramsey, University of Sussex	'Multiple Links Towards Integrating Teams for Understanding of Disease and Environment - Multitude	Workshop/ Network
Horwell, Durham University	'A network for the study of the properties and respiratory health effects of natural mineral dust	Workshop/ Network
Cook, Central Science Laboratory	'A UK Network for Environmental and Food Virology	Workshop/ Network
Givens, University of Reading	'Environmental impact on health benefits of organic food production	Workshop/ Network
Collins, University of Reading	'Soil, health and environment network	Workshop/ Network
Davidson, Scottish Association for Marine Science	'Relating harmful phytoplankton to shellfish toxicity and human health	Workshop/ Network
Macdonald, University of Oxford	'Quantifying Biophilia	Working Group
Lai, University College London	'Outdoor airborne pathogens and human health in the UK	Working Group

Banwart, University of Sheffield	'Going Underground: Human Pathogens in The Soil-Water Environment	Working Group
Clough, University of Liverpool	BAMRA: Bayesian Approaches in Microbial Risk Assessment (Working Group)	Working Group
Leake, University of Sheffield	'Grow your own - health risks and benefits of producing and consuming your own food in urban areas	Working Group
Hawkey, University of Birmingham	'The application of clinical microbiological methods to the study of MRSA in the environment (discipline hop)	Discipline Hopping
Thomas, Lancaster University	'Linking environmental fate and behaviour studies with the toxicology and epidemiology of organic pollutants	Discipline Hopping
Harrison, University of Birmingham	Determinants of Oxidative Potential, A Health-Based Metric to Assess Particulate Matter Toxicity	Exploratory Award
Donaldson, University of Edinburgh	A proof of concept study for a structure activity model for the toxicity of nanoparticles	Exploratory Award
Doherty, University of Edinburgh	Impacts of Future Environmental Change on Climate- and Air Pollution-Mediated Human Health	Exploratory Award
Salisbury, University of the West of England	A study of helminths as novel vectors and reservoirs of human pathogens in the environment, using in-vivo real-time imaging systems	Exploratory Award
Kendall, University of Birmingham	Nanotoxicology of Fine PM: The Role of Surfactant and Collectins in Short-Term Health Effects of PM Air Pollution	Exploratory Award
Tyler, University of Stirling	Strategies to manage toxic cyanobacetrial blooms in lakes: remote sensing, modelling and cost benefit analysis	Exploratory Award
Spurgeon, Centre for Ecology and Hydrology	Modelling and measurement of Cd exposure and pathology in human volunteers living in proximity to a smelter source	Exploratory Award
Few, University of East Anglia	Seasonal environmental hazards: a multi-disciplinary approach to the analysis of health risks in lower-income countries	Exploratory Award
Grant, University of East Anglia	Human health risks from contaminated tap water. Can we use microbial ecology to assess the integrity of water distribution systems?	Exploratory Award
Tyrrel, Cranfield University	Endotoxin emissions from commercial composting activities	Exploratory Award
Valsami-Jones, Natural History Museum	Hazards of nanoparticles to the environment and human health	Exploratory Award
Collins, University of Reading	Model human digestive system for the determination of bioaccessibility of environmental pollutants.	Exploratory Award
Matthews, Cardiff University	An exploratory study investigating the physiochemical characteristics of ambient air particles responsible for the dysregulation of pulmonary genes	Exploratory Award

Nieuwenhuijsen, Imperial College London	Born in Bradford: environmental exposure and birth weight	Exploratory Award
Pearson, Durham University	A preliminary assessment of levels of bioavailable anthropogenic platinum-group, lanthanide and high field strength metals in human tissue and DNA.	Exploratory Award
Begon, University of Liverpool	Ljungan Virus - an undetected but dangerous zoonotic agent	Exploratory Award
Gallagher, University of Manchester	Identification and Verification of Ultrafine Particle Affinity Zones in Urban Neighbourhoods / A Proof of Concept Proposal	Exploratory Award
Stone, Edinburgh Napier University	Assessing human exposure, uptake and toxicity of nanoparticles from contaminated environments	Exploratory Award
Atkinson, University of the West of Scotland	Micronutrient deficiency in maternity and child health: scope for agricultural and educational intervention in soil-food-human transfer	Exploratory Award
Mitchell, University of Glasgow	Exploratory award: Multiple environmental classification of areas for researching spatial health inequalities	Exploratory Award
Wang, Centre for Ecology and Hydrology	Plant virus infection as a determinant of pollen allergenicity	Exploratory Award
Stephens, University of St Andrews	Exploring the link between surface structures and toxicity in mineral particles: Case study of induced and intrinsic toxicity in quartz	Exploratory Award

Annex 5

Summary of achievements and questions arising from the Environment and Human Health Programme

Discussion Document for NERC & MRC: - Joint Environment & Human Health Programme – Phase II

Section I –E&HH Programme Achievements & Key Successes to Date

The Joint Environment & Human Health Programme has succeeded in bringing together many scientists from a broad range of environmental and biomedical backgrounds in order to address critical questions on health issues that are linked or believed to be linked to the natural environment. Many of these questions relate to complex issues such as the environmental biology and geochemistry of soils and how these influence the transport, accessibility and bioavailability of chemical pollutants and infectivity of pathogens. The dispersion of harmful particles in the atmosphere is another area of major concern where the E&HH Programme is breaking new ground on how the chemical and physical properties of such particles influence their environmental behaviour and may govern their toxicity and resultant pathological reactions induced following inhalation. Again this has required the formation of interdisciplinary teams of materials scientists, surface and environmental chemists, geochemists, environmental and human toxicologists, food scientists, veterinary scientists, pathologists, epidemiologists, geographers, social scientists, economists and atmospheric modellers. Working groups and workshops have identified potential health problems concerning the transport and emergence of pathogenic human viruses associated with food and water.

Some specific examples are presented below to illustrate why the problems being addressed by this programme, can only be addressed by multi- and interdisciplinary groups of scientists working together in cohesive collaborative projects.

1. Evidence for a specific lung fluid protein causing agglomeration of inhaled ultrafine particles thus modifying their biological behaviour and reactivity in the lungs (NE/E009395/1). This project brings together environmental chemists, material and medical scientists in order to understand how the fluids in the lung can modify the biological reactivity and pathogenesis of airborne nanoparticles.

2. Demonstration of the toxicity of silver nanoparticles in human food-chain model including invertebrates, fish and mammals (NE/E008232/1). The project draws on the combined expertise of environmental chemists, ecotoxicologists, cellular toxicologists and animal and clinical pathologists, as well as health scientists working together to identify the behaviour of nanomaterials in the natural environment and how these may impact on human health through the human food-chain.

3. Demonstration of bacterial endotoxin associated with airborne particles produced by commercial composting, which have detrimental biological effects on an *in vitro* cell-based model of the lung (NE/E008534/1). This project underlines the problem of how coatings of biological origin may affect the harmful biological reactivity of micro- and nano-scale particles. The research involves the physical behaviour of the airborne compost particles, the potential toxicity of biogenic toxins of bacterial and fungal origin and investigation of inflammatory and pathological reactions induced in an *in vitro* experimental model of lung tissue. The project has been dependant on the successful collaboration of environmental scientists (waste management and risk assessment), microbiologists and biomedical scientists.

4. A Report to Defra and HPA on the environmental pathways for exposure to pathogenic viruses and emerging viral problems (e.g., from farm animals and global transport of food products from industrial organic farms in China, Mexico and California). Identification of current knowledge gaps regarding transmission of viruses through the environment and food (NE/E009026/1). This project brought together a wide range of medical and environmental virologists and microbiologists, food and public health scientists, and epidemiologists.

5. Data analysis is currently underway in the UK on soil and blood samples from a field study in Malawi on the effects of micronutrient depleted soils (e.g., selenium) on maternal health and postnatal development. (NE/E008313/1). This is undoubtedly the most logistically challenging project supported by the E&HH programme, involving soil geochemists, healthcare workers and biomedical scientists working together under very difficult social and cultural conditions in central Africa.

6. Development of a robust analytical system for the assessment of the bioaccessibility of arsenic and polycyclic aromatic hydrocarbons (PAHs) in a simulated human gut environment (NE/E008844/1). This has resulted in the development of a patentable test kit. The experimental model of the human digestive tract has provided a novel way of testing the behaviour of harmful toxic environmental contaminants is influenced by the complex interactions between the gut chemistry and microbiology. This project has also demonstrated the detrimental impact of PAHs on the microbial flora from the human gut.

7. Development of screening tests for MRSA in the agricultural environment (NE/E008054/1). MRSA is no longer just a problem in the hospital environment. MRSA and other drug-resistant microbes are present in the natural environment with the attendant concerns about the transfer of the genes conferring drug-resistance to other species of bacteria. This project brought together microbial ecologists and clinical microbiologists in order to address the health risks posed by the widespread presence of MRSA in the environment, where it is associated with pig herds, bovine milk and faeces. Dairy products have also been implicated as reservoirs of MRSA in Europe.

8. Human disease causing bacteria can survive inside nematode worms and are protected from the action of chemical sanitiser treatment (NE/E009085/1). Food-borne diseases are a significant public health problem where pathogens such as *Salmonella* occurring in the soil can interact with other organisms such as free-living helminth worms (nematodes). This project involved the collaborative efforts of epidemiologists, helminthologists, microbiologists and veterinary scientists who have demonstrated that *Salmonella* ingested by the worms can survive and be returned to the environment in a viable and infective state. The inference is that soil nematodes can provide a protective micro-environment for human pathogens with health implications for the persistence of such pathogens in the soil.

9. A book is due to be published in October indicating that the health benefits of organic foods are probably over-rated, and that in some cases they may pose a greater health risk than normal foods (NE/E008399/1). This project dealt with a complicated set of potentially interacting factors including soil science, pesticide toxicology, biogenic fungal toxins and infectious pathogens, as well as the nutritional composition of the foods in question. A two-day International Workshop involving over 80 participants from a wide-range of disciplines, including soil and food science, environmental toxicology and microbiology, nutritional and clinical physiology and public health, specifically addressed these problems.

10. Substantial progress has been achieved towards deriving a summary measure of multiple environmental deprivation at small area level, akin to the measures of multiple socioeconomic deprivation used by health researchers from many disciplinary backgrounds (NE/E0087201). The key achievements have been to i) systematically identify which elements of physical environment should be included in the measure, ii) compile appropriate environmental data for the whole UK, iii) produce several different versions of the measure iv) discover independent associations between the measures and variation in all cause and cause specific mortality, and v) begin to examine the interaction between social and physical environments on health inequalities in the UK. This project involves collaborations between epidemiologists, public health scientists, health geographers and environmental scientists.

Many of the Exploratory Study awards are still ongoing since a number of these did not start until earlier this year. It is anticipated that these will produce exciting new data and insights into many of the issues and gaps identified in **Section II** below. The Network, Working Groups and Workshops have also served to highlight and refine the issues and gaps described below.

The overall research progress has been excellent with many exciting developments highlighting new avenues for future investigation as indicated above. Fortunately, there have been few problems in the implementation of the programme, which given its complexity is perhaps surprising, but nonetheless serves to underline the dedication, skill, ingenuity and resourcefulness of the many scientists involved. Where problems have arisen, they have largely been limited to logistical and staffing issues. The need to await decisions by University Ethics Committees has also resulted in a few delays; but this is understandable given the multi-institutional nature of many of the Projects.

Finally, the establishment of new active research links between many of the projects funded by the Joint E&HH Programme is helping to build a cohesive community of research scientists with both UK and international linkages. Feedback from the researchers themselves has strongly indicated that the interfacial nature of much of the research has resulted in exciting and challenging projects with a lot of intellectual cross-fertilisation and the spawning of new collaborations involving existing and proposed future projects. To try and identify which has been the most successful matching of disciplines is very difficult, and probably impossible at this stage of the Programme, given the huge range of disciplines involved and the very high quality of the research that has been and is being generated.

Section II – Issues and Questions Arising from the E&HH Programme

Exposure to Toxic Contaminants and Pathogens

1. Pathways of exposure – environmental modification of colloids, particles and chemicals – coating of particles with biogenic materials. How does this affect their biological reactivity?

2. Complexity of the soil environmental interfaces – how does this affect the transport and bioaccessibility of contaminant chemicals and pathogens?

3. What is the relative health significance of chemical (including biogenics and novel xenobiotics) and pathogen exposure pathways for food, air, soil and water?

4. Is environmental exposure to toxic contaminants and pathogens – beneficial or harmful? Low level exposures of both chemicals and pathogens may be beneficial by stimulating the body's defensive systems – biphasic effects (hormesis).

Novel Biomarkers

1. Biomarkers of exposure and harmful effect – need to distinguish between complex interactions resulting from exposure to mixtures of chemicals and combinations of chemical, pathogens and physical/nutritional stressors.

2. In biphasic responses, biomarkers of exposure may be expressed during the beneficial non-pathogenic region of the response curve (i.e., hormetic beta-curve). We need to be able to determine whether biomarkers of exposure are indicating pathology or not.

3. Requirement for biomarkers for hormesis – antioxidant defences, heat-shock proteins (*hsp*'s & *hsc*'s, Sirtuin 1 – SIRT 1, etc).

4. Requirement for pathology biomarkers – proteomics?

5. How can we effectively distinguish synergistic and antagonistic interactions in a complex environment?

Gaps Highlighted by the E&HH Programme Projects

1. Improved epidemiological modelling and identification of problems on a geographical scale.

2. How can we quantitatively incorporate uncertainty in assessing hazard and risk?

3. Numerical and Computational Toxicology & Ecotoxicology – conceptual modelling, QSAR modelling, numerical model development and validation, co-evolution of modelling and empirical investigation. How can modelling contribute to evaluation of risk and development of predictive models for impact on human health?

4. Can we interpret stress and disease (including ageing) as a loss of biological complexity? The influence of environmental factors on protein-protein interactions (protein interactomics) and the loss of effective protein-protein interactions and failure to effectively remove damaged proteins and aggregates needs to be assessed since these molecular dysfunctions contribute to ageing and a number of pathologies.

5. How does speciation of chemicals and nano- and micro-particulate material affect their biological reactivity and toxicology?

6. Can QSAR modelling be applied to particulate material?

7. Are interactions between environmental agents and epigenetic processes significant in rapid adaptation to pathogens and toxic materials?

8. Aggregation of particles – how does this affect uptake and toxicity along the foodchain?

9. Do nanoparticles act as Trojan Horses for bringing conventional toxins such as the pesticide Diuron, polycyclic aromatic hydrocarbons (PAHs) and iron into the body (e.g., lungs and digestive tract)? Iron for instance will promote ROS (reactive oxygen species) production.

Gaps highlighted by the Wider Environment & Health Community

1. What are the health consequences of photo-oxidation of biogenic and contaminant chemicals and particles in the natural environment?

2. Can plastic degradation particles concentrate and transport lipophilic contaminants and persistent organic pollutants (POPs)?

3. Are there thresholds or biphasic responses for biological effects of environmental radioactivity?

4. Can we clearly identify environmental reservoirs of contaminants and pathogens?

5. Emergent viral diseases – what is the realistic risk of a human pandemic of bird flu if for example there is transfer of the virulent genes from the H5 strain to the more widespread and H2 and H9 types of the virus which can be contagious in humans?

6. What environmental pathways contribute to the spread of intractable mycobacterial diseases such as tuberculosis?

7. What are the risks from the next generation non-passive nanomaterials – nano-biotech synthetic biological products such as DNA scaffold devices, rosette carbon nanotubes, self-assembling nano-devices including artificial viruses (i.e., replicators), engineered RNA-based cellular computers and supramolecular cellular components (e.g., ribosomes and receptors)?

8. Can some endocrine disruptors (e.g., xenoestrogens, POP's - including brominated flame retardents and bisphenol A) also act as obesogens and possibly trigger type 2 diabetes?

9. Are there more ***prion*** diseases out there in the wildlife and do they pose a threat to humans?

10. Environmental agents acting during pregnancy have been implicated in developmental abnormalities. Do environmental triggers such as exposure to viruses or environmental pollutants apply to conditions such as autism?

11. How widespread in invertebrate Phyla are novel anti-bacterial and anti-viral agents produced by lower organisms (e.g., anti- MRSA, - *Clostridium difficile* and - *E. coli* peptide (s) produced by insect larvae; Prof N Ratcliffe, U. Swansea)?

12. Can lower organisms including invertebrates and fish be used as surrogates for investigating environmental linkages with genetic and epigenetic aspects of human disease processes?

13. Does the oceanic dissolved organic carbon (DOC) of largely viral origin (estimated to be 97-98%) have any biological reactivity and are there health risks or benefits?

Professor Michael N. Moore, Joint E&HH Programme Science Coordinator

20th October 2008