An Environment for Better Health

Integrated report of the ESF Environment and Health Programme

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1. Introduction

The ESF Scientific Programme on Environment and Health was launched in July 1996. The Programme proposal describes the main goal of the Programme: to contribute to the development of an overall ESF Research Strategy on Environment and Health and to the development of an integrated document on research needs prepared in close co-operation with the WHO-EUR and the EC. After being adopted at a Consensus Symposium in 1998 this document is now being submitted to the Intergovernmental Conference on Environment and Health in London in 1999 (ICG 1999). The ultimate aim is to provide policy makers with the necessary scientific strategic elements for launching a European-wide research effort in environment and health.

In the field of environment and health a variety of activities have been and are being developed at national and international level. These need to be considered and evaluated. The most important actors at the European level in this evaluation process are the European Commission, the WHO-EUR and the ESF as the umbrella organisation of the National Research Organisations.

In 1996 an EC / ESF / WHO Liaison Group was established in order to facilitate consultation and action in support of the mandate given to the three organisations by the 1994 Helsinki IGC. While pursuing the process of priority setting within the terms of their remits, the ESF, EC and WHO would all benefit from a structured exchange of views and the development of common approaches.

When developing the integrated advisory document, both the ENHE Steering Committee of the ESF Programme and the EC / ESF / WHO Liaison Group played an important role in the co-ordination and preliminary prioritisation of the environment and health research needs. The development of the ENHE Programme is described in Table 1. Chapter 2 describes the ESF/ ENHE Programme on research needs and includes scientific and strategic discussions and recommendations resulting from the workshops organised in close collaboration with the EC and WHO. In Chapter 3 of this document activities related to research in the field of environment and health at the pan-European level are briefly described

References to annexed reports can be found by consulting the ESF home page: http:// www.esf.org/mp/ENHEb.htm.

2. The ESF/ENHE programme

Several events led to the initiative for an ESF Scientific Programme on Environment and Health (see Table 1). In 1994 the European Medical Research Councils (EMRC) identified environment and health (ENHE) as an area in which there was a real need for research to underpin policy and legislative development. In June of the same year the Ministers of Environment and Health of the European countries endorsed a declaration in Helsinki, in which priority environmental health issues were identified. The need for strengthening the scientific basis of actions on some problems of concern was recognised, and a joint programme for research should be developed involving WHO-EUR, EC and ESF. This joint programme is being presented at the next Intergovernmental Conference on Environment and Health in London in 1999.

Table1. Development of the ESF Scientific Programme on Environment and Health Research Needs

	1994	EMRC identifies Environment and Health as an area where research to underpin policy is urgently needed.
June	1994	2nd Conference of Ministers of Environment and Health. Helsinki Declaration: a joint programme for Environment and Health Research involving EC / ESF / WHO.
May	1995	Leicester Meeting on Environment and Health highlighting the main scientific and policy issues and a proposal for a Plan of Action of ESF involving EMRC, LESC and SCSS.
November	1995	The "year zero" proposal prepared by the Advisory Group is submitted to the ESF Council and approved.
January	1996	Appointment of Programme Co-ordinator and ENHE Steering Committee is established.
February	1996	Establishment of EC / ESF / WHO Liaison Group.
June	1996	Proposal for an ESF Scientific Programme on Environment and Health is submitted to the ESF Council and ESF Board, and approved. In this proposal the programme objectives, programme core elements (workshops and mini-reviews) and scientific themes are identified.
During	1996/ 1997/ 1998	Workshops and field reviews are developed and reported. Reports are evaluated and commented on by ENHE Steering Committee. Final reports are prepared.
During	1997/ 1998	Preparation of an Integrated Document on Research Needs and its Priorities to include all reports and reviews.
April	1998	Evaluation and comments of ENHE Steering Committee on Integrated Document. Preliminary adoption of priority setting system.
June	1998	Science driven update meeting to critically discuss Integrated Document on Research Needs and to set priorities.
October	1998	EC / ESF / WHO Consensus Conference to critically discuss the outcome of the update meeting and the supporting Integrated Document, its prioritised research needs and prepare the "Ministerial Document".
February	1999	Submission of the Integrated Document as Background Document and the Ministerial Document to the Pre-Conference Meeting of the 3rd Ministerial Conference on Environment and Health.
June	1999	Background Document on Environment and Health Research Needs in the 3rd Ministerial Conference on Environment and Health and adoption of the Ministerial Document.

The ESF/ENHE Programme forms a substantial part of this programme, and has been developed as an *à la carte* activity by the ESF, using a multidisciplinary approach to address this challenge. An ENHE Steering Committee (http://www.esf.org/mp/ENHEb.htm) guided its development by defining key scientific themes in terms of their priority and tractability in relation to the strategic objectives and by choosing appropriate mechanisms to develop these themes: field reviews and workshops as programme core elements and a designated Programme Co-ordinator to manage its overall development.

To ensure a coherent European approach the Programme has been developed in a manner which complements initiatives undertaken by the EC and the WHO. This has been achieved by establishing a EC / ESF / WHO Liaison Group (http://www.esf.org/mp/ENHEa.htm), which was set up to oversee the development of a mutual framework of priorities in a multi-disciplinary approach including medical, natural and social sciences. The ENHE Steering Committee recognised that there is a social need to have a better understanding of the impact of the environment on health and well-being, both qualitatively and quantitatively. Risk can be properly assessed only when factors and causative associations are understood. Subsequently, identified non-acceptable risks may be reduced by appropriate political measures (risk management). Since a considerable number of environmental problems related to health and well-being are of a multinational or supranational nature, in that they occur at global and/or continental levels, act across borders or occur multifocally, a Europe-wide effort to change the environment for better health is both timely and relevant. In most cases, European/supranational environmental problems can only be tackled efficiently and effectively at the European level.

For the reasons given above the ENHE Steering Committee focused the Programme on research needed to improve tools for environmental health management, particularly the total risk assessment (RA) process (hazard identification, exposure assessment, effect assessment, risk characterisation) and risk management (RM).
In RA, research includes understanding mechanisms which determine the susceptibility of subgroups in the population, their nature and extent, and studies to investigate and elucidate interactions between environmental, socio-economic, psychological and lifestyle factors in determining health status.
For RM, comparative risk assessment and cost/benefit analysis of preventive measures or

interactions should ideally be developed to facilitate policy evaluation, priority setting, risk perception and risk communication and to stimulate public participation. It is necessary to do so in order to avoid inappropriate use of resources.

The ambition of the ENHE Programme is not to detail all possible areas where science-driven advice may be of use but rather to focus on a limited number of issues, in line with the 1994 Helsinki Declaration, in which policy advice is urgently needed, and there is a reasonable chance that this advice can be provided on the best available information.

This integrated report from the ESF/ENHE programme provided the basis for a Consensus Conference held in October 1998. During this conference a final document was prepared in which policy advice on research needs in environment and health was presented as an agreed priority. The document is now serving as a Ministerial Document on Environmental Health Research for Europe. It will be presented to the Ministers of Environment and Health at the Intergovernmental Conference on Environment and Health to be held in London from 16th to 19th June 1999.

Scientific Themes For The Programme

The Programme brought together life sciences, environmental sciences, physical sciences, technical sciences and social sciences as a means of stimulating a multidisciplinary approach and allowing these sciences to make a fundamental contribution to the Research Programme. The central focus of the Programme was to investigate links and steps in the risk assessment process and to define lacunae in research and in areas which are particularly amenable to a multidisciplinary approach.
Research activities were directed to stimulate the integration of environmental and health issues into existing policies in order to facilitate a step by step progress towards sustainability. Activities undertaken thus met the criteria of both European scientific added value and policy relevance to sustainability, especially in its health and quality-of-life domains. The research needs outlined were focused not only on basic science issues but were also related to the translation of basic science results into policy support and research needs within the framework of risk management.

The Steering Committee deliberately included both sides involved: basic and applied research. In many areas data from basic science provide an impetus in the setting up of applied research and the development of risk management principles and tools.

The scientific community can contribute to a large extent to the priority issues identified in the Helsinki Declaration (see page 73). It was also acknowledged that the field of environment and health research is potentially vast and that prioritisation is difficult. Nevertheless, aiming for priority setting in a balanced manner was considered imperative.

It was agreed to focus on a number of problem areas which were felt to be both important and tractable. These problem areas all include generic research issues embracing risk assessment as well as epidemiological methodologies, environmental and public health modelling, cost/benefit analysis and valuation of health gain.

A particularly important generic issue, especially for policy support, is quantitative risk assessment. Failure to assess risk accurately may be just as costly to society as failure to identify a hazard effectively. There is now a strong case for making the strategic move of developing methods and systems capable of characterising risks quantitatively, thereby enabling policy makers to carry out risk benefit analysis. Integration of both exposure and health/well-being effects is of extreme importance. In many areas which are described below, emphasis is put on chemical risk assessment. In a separate Section 2.11, which follows the description of areas of research identified by the ENHE Steering Committee, special attention is given to chemical quantitative risk assessment and its relevance to policy support.

Areas of research in relation to health and well-being identified by the ENHE Steering Committee are listed below. The important areas of diet and health and smoking and health are not included since the Steering Committee did not consider these to be environmental but rather lifestyle issues. However, it was recognised that both areas are important, particularly in relation to chronic disease, causing considerable impairment of health and health expectancy. They are also considered to be important confounders in epidemiological findings and should, therefore, be considered carefully when analysing epidemiological results.

The ESF has organised workshops and prepared minireviews relating to those areas identified by the Steering Committee in the period leading up to the Ministerial Conference. These have incorporated the findings of workshops organised by other organisations. Areas of research identified and listed here in no particular priority order, are:

- Climate Change, Stratospheric Ozone Depletion and Human Health *(mini-review January 1998)*
- Social Variations in Health

Expectancy in Europe *(workshop October 1997 as a joint initiative of the EMRC and the Standing Committee for Social Sciences - SCSS)*

- Environmental Effects on Cognitive Functions *(workshop February 1998)*
- Cognitive Functions as Mediators of Environmental Effects on Health *(workshop September 1997)*
- Children and Accidents *(workshop November 1996)*
- Ambient Air Particulates *(workshop November 1996)*
- Indoor Air Quality and Health *(mini workshop September 1997)*
- Water Quality and Drinking Water *(workshop May 1997)*
- Endocrine Disruptors: A Threat to Human Health? *(European workshop organised by the EC, European Environment Agency, WHO-ECEH, OECD, CEFIC, ECETOC and national authorities of UK, Germany, Sweden and The Netherlands December 1996)*
- Assessment of Human Health Effects of Immunotoxic Agents in the Environment *(Symposium organised by the National Institute of Public Health and the Environment (RIVM), The Netherlands, and co-sponsored by among others the ESF / ENHE Programme, WHO-IPCS and EC November 1997)*
- Chemical Risk Assessment and Related Toxicological Issues *(input from an exploratory workshop on emerging issues in toxicology, organised by ESF)*

When drawing up this report the Steering Committee repeatedly asked the scientific community to identify additional priority areas. In the science driven Update Meeting in June 1998 this question was raised again and a number of key scientists who had not been involved in the process were asked to evaluate it. They concluded that the selected priority issues were indeed the most relevant ones.

Criteria for identifying research needs included relevance in regard to:

- Exposures hazardous to physical and mental health and/or well-being;
- Assessment of the associated risks:
- Mechanisms of cause and effect;
- Feasibility and timeliness;
- Significance for the populations of Europe;
- Environmental impact;
- Social and economic benefit;
- Costs;
- Impact on policy.

All areas identified or included as mentioned above contribute to the priority issues of the Helsinki Declaration, some issues being considered not directly but indirectly as a cross-cutting issue (Table 2). It should be emphasised that many areas also contribute to sustainability (Table 2). In certain areas the use of a Health and Environment Geographical Information System (HEGIS), as described recently in the WHO

Table 2. Activities in relation to the Declaration of Helsinki and the cross-cutting issue of sustainability

ESF topics	Declaration issues							
Declaration issues	Contamination food + water	Ambient indoor	Accidents	Ecology health	Urban health	Occupational health	Armed hostilities	Sustain-ability
1 Climate change, stratospheric ozone depletion and human health	+	+		++	+	+		++
2 Social variations in health expectancy in Europe	+			++	++	++		++
3 Environmental effects on cognitive functions	++	++	+	++	++	++		++
4 Cognitive functions as mediators of environ-mental effects on health	++	++	+	++	++	++		++
5 Children and accidents			++		+	+		+
6 Ambient air particulates		++		+	+	++		+
7 Indoor air quality and health		++		+	+	+		+
8 Water quality and drinking water	++	+		++	+			++
9 Endocrine disruptors	+			++		+		++
10 Assessment of human health effects of immunotoxic agents	+	++		++	+	++		+
11 Chemical risk assess-ment and related toxicological issues	++	++		++	++	++		+

\+ = Relationship ++ = Strong relationship

Regional Publications European Series no. 75 (Atlas of Mortality in Europe; sub-national patterns 1980/1981 and 1990/1991), may facilitate the interpretation of results.

On the following pages the scientific themes (1 to 11) are described in more detail and reference is made to the annexed official reports, (see page 78).

In considering environmental and health conditions in the countries of Central and Eastern Europe (CCEE) and the Newly Independent States (NIS), it may be asked whether areas 1 to 11 require a research agenda different from that most relevant for countries in the Western European region. Since it is the aim of ESF to provide a comprehensive programme, ESF has asked WHO-ECEH to supplement the available ENHE reviews with an evaluation from the CCEE/NIS perspective (see Annex 3).

In general, the topics selected by the ENHE Programme were relevant to the research needs in the CCEE/NIS region. It was mentioned that, while Central and Eastern European countries have similar research priorities, there are major differences among those topics which may be most pertinent to the individual Newly Independent States. A common factor influencing the choice of environment and health research priorities was the difficult socio-economic situation of this part of Europe.

The relevance of research with a pan-European perspective was acknowledged. In particular, the research programme and plans of the European Community were noted to be an important contributory factor in collaboration.

The positive impact of international collaboration and funding of environmental health research was emphasised because such programmes have a significant role in developing national capacities for public health research and assessment of environmental health risks in CCEE and NIS.

Specific recommendations for the sections described in the ENHE Programme have been included. It was stressed that the characteristics of environmental conditions and exposure in CCEE and NIS offer unique opportunities for assessing health effects at relatively higher exposures. Given the limited resolving power of epidemiological studies and difficulties in discrimination and exposure profiles, CCEE and NIS countries should be the first choice for specific questions and should be included in multi-centre studies.

Furthermore, there exists a strong need to set up information infrastructures for identification and epidemiological analysis of exposure “hot-spots” and pollution-related clusters of disease.

Last but not least, development and maintenance of the environmental health research capacity in CCEE and NIS is urgently needed to address environmental threats to public health effectively and efficiently.

Pan-European integration of environment and health research

In most, if not in all workshops organised, pan-European integration of environment and health research was identified as one of the most important issues. Pauli and Häkinen (1996) recently made an inventory of available systems and mechanisms used to initiate and carry out environmental and health research. They arrived at a conclusion similar to that of the scientists in the various workshops, namely that the creation of a platform for interdisciplinary action between specialists would strongly support the anticipated research in environment and health. Such an interagency collaboration would be instrumental in transforming the identified prioritised research needs into research proposals, re-evaluating priorities during the process, and communicating information about critical issues and research needs and outcomes to interested parties. This should be implemented by using available mechanisms and systems.

We, therefore, recommend the creation of an interdisciplinary interagency collaboration, bringing together the WHO, EC and ESF and, under whose guidance pan-European interdisciplinary consultation and concerted action should be developed for earmarked areas of research.

This interdisciplinary interagency collaboration may facilitate or be instrumental in:

– Development of a harmonised common set of definitions for properties and criteria related to health and well-being within the area of research.

– Standardisation, validation and, where appropriate, collection and dissemination of relevant data at supranational level to ensure comparability.

– Quality assurance and validation of models, statistical measures, uncertainty analysis and scenario analysis.

– Development of research proposals based on the prioritised research needs and development of further critical research questions suggested by progress and acquired information.

– Evaluation of the Research Programme and its projects, both at the outset and during implementation.

– Promotion of international co-operation and development of research skills and research capacity through interaction between European countries.

– Development of effective means to disseminate results and added know-how to researchers, policy makers and the population in general.

The creation of this interagency collaboration will facilitate an integrated, multidisciplinary research approach, mobilising available resources in the most effective and efficient way.

The interagency collaboration developed will ensure that research needs in the areas 1 to 11 are implemented in accordance with their assigned priorities.

These research needs are, for practical purposes, divided into three main categories.

A. Basic research needs.
B. Research needs related to the translation of basic science results into policy support.
C. Risk management principles/ research needs, which are directly aimed at facilitating or supporting policy decisions.

Whereas basic research needs are the responsibility of the Ministers of Science, research needs under B and C are generally the responsibility of the Ministers of Health and/or Environment. However, their interrelation justifies a co-ordinated and integrated approach. Similarly, while basic research is in general conducted at the national level, strategic research is more effectively and efficiently conducted at the supranational level.

In the following sections the various scientific themes are described.

2.1 Climate change, stratospheric ozone depletion and human health

2.1.1 Introduction

The aggregate environmental impact of human economic activity is now sufficiently large to be changing some of the Earth's biophysical systems on a global scale. Two of the best known of these global environmental changes are: (1) the accumulation of heat-trapping greenhouse gases (GHG) in the lower atmosphere (troposphere), and (2) the stratospheric ozone depletion caused by ozone-destroying gaseous emissions, in particular chlorofluorocarbons (CFCs). During the 1990s, various authoritative international scientific reviews have described and semi-quantitatively characterised a range of anticipated, mostly adverse, health consequences of these global change processes (IPCC, 1996; UNEP, 1998)*.

The accumulation of greenhouse gases, in particular CO_2, has been documented since the 1950s. However, only recently has the Intergovernmental Panel on Climate Change (IPPC, 1996) concluded, albeit cautiously, that the scientific evidence now shows that humans have a discernible influence on the global climate. In light of this growing evidence, developed countries at the 1997 Kyoto Conference convened under the UN's Framework Convention on Climate Change agreed to curtail greenhouse gas emissions by the year 2012 by an average of 5.2% relative to 1990 emission levels. Stratospheric ozone depletion, a well recognised phenomenon since the mid-1980s, led to collective remedial action by national governments to curb the problem via the Montreal Protocol (1987) and its subsequent amendments in the 1990s (Copenhagen, London).

* References can be found in the appropriate annex (See Part 2).

Fig.1: Major types of impact of climate change and stratospheric ozone depletion on human health

The profile of health hazards arising from these two separate processes, climate change and ozone depletion, is somewhat unfamiliar and complex because the underlying environmental change processes are large-scale, have long time-frames, and – especially in the case of climate change – will predominantly affect human health and well-being by disrupting complex ecological and physical systems. The major categories of potential health impacts of climate change and of ozone depletion are shown in Figure 1. The full review on the subject is attached (Annex 4).

Changes in climate are expected to have both direct and indirect effects. Warmer temperatures would enhance the production of some types of air pollutants (photochemical oxidants); more humid conditions would modify the production of aero-allergens (spores and moulds); more variable climatic patterns would alter the frequency of extreme weather events (heatwaves, floods and droughts). Indirect effects of climate change – relatively less likely to occur in Europe than direct effects – would be mediated by changes in the geographic range and life-cycle dynamics of infectious disease vector organisms and infectious agents, by changes in the productivity in food-producing ecosystems, and in response to the assorted disruptions consequent upon sea-level rise. For stratospheric ozone depletion the anticipated health effects would mostly arise by more direct pathways, entailing ultraviolet radiation-induced damage to various organ systems.

Research into how variations in climate and in ambient UVR influence health risks is currently in an early developmental phase. Systematic attempts to characterise the profile of likely future health consequences of these two environmental change processes, to define the dose-response relationships within the range and time-frame of natural variations, and to develop methods of forecasting longer-term health outcomes in response to temporally distant scenarios of environmental change were started only in the 1990s.

There are two major categories of research needs: (i) empirical studies into the relation between climate/UVR variations and human health outcomes, and (ii) integrated mathematical modelling to assess future health outcomes. The former category serves two purposes – first, extension of the still-incomplete knowledge base about climate/UVR-health relationships and, second, the detection of early health impacts of these environmental change processes within Europe.

2.1.2 Overarching research need priorities in relation to climate change and stratospheric ozone depletion

The complexity of the environmental and ecological changes consequent upon climate change, the diverse types of health outcomes from the two environmental change processes (including infectious and non-infectious diseases), and the modulating influences of population vulnerability and societal responses mean that research within this domain has to be multidisciplinary. Further, much of the research can only be tackled appropriately at supranational or pan-European levels.

There is, in addition, a need for systematic assessment of the adequacy of data collection and monitoring systems within Europe in relation to the two categories of proposed research cited above. Regional and pan-European geographical information systems (GIS) will enhance this research capacity. There should be a two-way interplay between formal research (both empirical and forecasting) and development of these various information-collection systems and spatial-temporal analytic resources.

2.1.3 Release assessment

Assessment of the current and projected gaseous emissions, as the primary cause of climate change or stratospheric ozone depletion, is important for modelling future changes in the climate system or ultraviolet radiation flux. Modelling is carried out by expert climate/atmospheric scientists. The resultant scenarios provide the basis for estimating future health impact via scenario-based health risk assessment.

Release assessment, in this context, differs from evaluation of specific agents released in most other toxicological environmental health problems. The release of GHG and ozone-destroying gases does not itself constitute an environmental "exposure" that affects health. Rather, these gaseous releases cause disruption of atmospheric systems, resulting in environmental/ecological consequences that may then affect health. Hence, studies of climate/UVR-health relationships require no direct reference to gaseous releases. Health risks are, in fact, estimated in relation to variations in the consequent environmental exposures (temperature, rainfall, UVR exposure, etc.).

2.1.4 Exposure assessment

Reports of climatic trends (http://www.esf.org/mp/ENHEb.htm) indicate that Europe has experienced a mean temperature increase of about 0.8°C this century. Approximately half that rise has occurred since the late 1970s. Temperature increases have been greatest in the winter period and minimum daily temperatures have risen more than maximum daily temperatures. Warming has been greatest in Northern/Central European Russia, intermediate in southwestern Europe, and lowest in the Baltic area and Britain. This trend has been accompanied by increased annual precipitation in northern Europe and decreased precipitation in southern-central Europe (IPCC, 1997).

Climatologists, using general circulation models (of increasing sophistication, complexity and validity), conduct simulation "experiments" in relation to the likely scenarios of GHG release. Sequential modelling produces projections of multi-decadal changes in temperature and precipitation at a global level. With gains in model specification and spatial resolution, climatologists are becoming increasingly able to make regional projections (IPCC, 1996). Climate projections over the coming half-century for Europe remain somewhat uncertain (in part because of the specific potential influence of changes in the North Atlantic oceanic circulation). Projections of changes in rainfall are also uncertain on this regional level. Winter precipitation is likely to increase, particularly at higher latitudes; while rainfall during summer may change little.

With respect to UVR, evidence for recent changes in ground-level exposures in European population centres remains sparse – despite clear evidence of increased UV flux through the stratosphere over Europe during late winter-early spring. As for climate change, predictive mathematical models have been used to forecast trajectories in UVR radiation over the coming century based on several ozone-destroying gas emission scenarios (Slaper et al., 1996; Martens 1998).

Because of the various pathways by which climate change can affect human health, "exposures" of various kinds can be defined. For example, the characterisation of air masses by synoptic approaches based on different types of association they have with mortality, may improve the assessment of health risks – and may also enhance the usefulness of advance warning to populations of imminent inclement weather conditions. To give another example: the geographic range and density of vector organisms (e.g. mosquitoes, ticks and sand-flies), which vary in response to climate conditions, and which transmit vector-borne diseases, therefore constitute measures of "exposure" for those diseases.

Research Need 1(A)

- **For both climate change and increased UV exposure, there is a need to improve the modelling of environmental exposure scenarios within Europe, to facilitate better estimations of health impacts, and to enable the modelling of attributable disability-adjusted life years (DALYs) and economic costs.**

2.1.4 Effect assessment

i. Empirical studies

A wide range of health outcomes is anticipated to result directly or indirectly from climate/UVR changes. Improved information about these relationships, especially in relation to short-term trends and fluctuations in exposure, can be gleaned from empirical epidemiological studies conducted in relation to present and recent past exposures.

It will also become increasingly relevant, with the passage of time, to conduct such studies in order to detect early evidence of changes in health risk or in actual health status occurring in response to incipient human-induced changes in climate or in ambient UVR exposure. It is likely that some marginal changes in sensitive health outcomes are already occurring within European populations in response to the documented increases over the past two decades in mean temperature and indices of UVR exposure. (Such changes will, initially, be very difficult to detect against the changeable background of other factors also implicated in those same health outcomes.)

Research Need 2(A)

● **Empirical epidemiological studies of the health impacts of current/recent variations in climate within Europe.**

Studies of particular relevance to European populations would include the assessment of:

- Climatic influences on the production of certain air pollutants (e.g., photochemical oxidants) and aero-allergens.
- Changes in the geographic range and seasonality of vector-borne infections (such as leishmaniasis, Lyme disease and malaria) and environmentally-transmitted infections (e.g., waterborne infections such as cryptosporidiosis, and foodborne infections such as salmonellosis).
- Health impacts (including physical, microbiological and psychosocial) of extreme weather events, such as floods and storms.
- The overall public health (especially mortality) impact of seasonal thermal stresses.

The potential health effects of increased ambient UVR exposure due to stratospheric ozone depletion include increases in the incidence of skin cancers and ocular cataracts, and perhaps immune suppression. These effects are of a direct nature, occurring in response to increases in radiation exposure.

Research Need 3(A)

● **Extension of epidemiological research, with particular emphasis on the quantification of dose-response relationships, into the relationship between ultraviolet radiation and types of skin cancer, ocular cataract, other ocular disorders, and immune system functioning.**

Aspects of particular research interest include:

– Relationship between UVR exposure and cutaneous malignant melanoma is poorly understood with respect to critical age of exposure, dose-response relationship and wavelengths.

– European-wide population level studies comparing: (i) age-specific prevalence rates of cataract and (ii) age-related macular degeneration, by geographic location or preferably in relation to measured geographic gradients in ambient UVR. Such studies should provide: descriptive data enabling the assessment of the disorder with UVR exposure levels and a baseline against which future changes in age-specific prevalence data can be compared.

– Studies on the interaction between UVR exposure and dietary antioxidants in the induction of cataracts.

– Studies on the relationships between indices of immune function and ambient UVR, both within and between populations.

– Studies to determine whether UVR exposure affects vaccine efficacy, especially in childhood.

– Studies into the relationship of various autoimmune diseases - e.g., insulin-dependent diabetes mellitus, multiple sclerosis, disseminated lupus erythematosis – as well as atopic disorders to variations in solar UVR exposure.

ii. Integrated mathematical modelling of health impacts occurring in response to future scenarios of environmental change

Unlike most environmental health hazards, those arising from global environmental changes lie predominantly in the future. In this situation, scientific knowledge and theory must make use of mathematical modelling to produce indicative estimations of likely public health outcomes.

It is axiomatic that this type of scenario-based modelling incorporates uncertainties (as, indeed, does all science - the difference here is the degree of uncertainty). Nevertheless, it is also axiomatic that we cannot directly study the future, nor indeed predict it with certitude or precision. The task for scientists, therefore, is to make socially useful forecasts using methods that can be updated and improved as our knowledge and experience grows. The complexities and uncertainties of forecasting must be understood and communicated appropriately to public and policy-makers.

In recent years, techniques for integrated mathematical modelling of health outcomes of climate change and of stratospheric ozone depletion have been pioneered (see, e.g., Slaper et al., 1996; Martens, 1998). Because the causal relationships involved in the latter process (ozone depletion, increased UVR flux, increased risk of UV-induced health effects) are more straightforward, it has so far proven easier to generate quantitative assessments of the future range of changes in skin cancer incidence than health outcomes of climate change.

It is important that this type of developmental research should be supported. With further development, it will acquire greater exactitude, enabling more satisfactory projections of health impacts to be made at sub-global and, hopefully, at national levels.

Research Need 4(A)

- **Development of methods of integrated mathematical modelling, for the scenario-based assessment of the future health risks of human-induced climate change and of increased exposure to UV radiation consequent upon stratospheric ozone depletion.**

Modelling techniques can be expected to:

– take increasing account of local geographic, demographic and ecological conditions, in order to enable valid down-scaling of forecasts;

– achieve validation against historical and other external data sets;

– improve the handling and communication of inherent uncertainties;

– achieve horizontal integration of the environmental-biological causal chain with social-demographic-economic modulations of that causal process;

– incorporate dynamic adaptive capacity, to take account of human, societal and other adaptations to the health risk at issue;

– provide a basis for the estimation of net social and economic costs (expressed, for example, in loss of healthy life-years and in fully-accounted economic costs).

2.1.5 Risk characterisation

The eventual goal is to quantify the various risks to human health resulting from climate/UVR changes. Such quantitative risk assessment can then be used to produce assessments of the loss of health expectancy and life expectancy, as well as assessments of social and economic costs. However, at this stage of research development, much empirical research and predictive modelling falls short of that level of quantitative precision. Many of the research questions are relatively new, and the primary task, for the moment, is that of effect assessment.

Scenario-based risk assessment, at its simplest, assumes constancy in other health risk factors, thereby allowing estimation of the influence of a projected change in climate or UVR exposure on the health outcome. However, more comprehensive modelling will need to take account of other coexistent, perhaps interacting, projected trends in a number of purposive or inadvertent human interventions (e.g., vaccinations, housing design, life-style changes, etc. that may affect the risks of infectious disease transmission).

A related research need, one which underwrites the ability to do better quantitative research, is that of assessing and ensuring the adequacy of information-collection systems and monitoring (environmental, biological, health) systems in Europe. Techniques of spatial and temporal analysis, including geographic information systems, will enhance this research capacity.

Research Need 5(A)

- **In order to facilitate the early detection of any health impacts related to climate change or increased UV radiation exposure in Europe, and to assess the adequacy of existing information systems, the need for additional monitoring activities, and the feasibility of using such data systems for detecting changes in population health risks or status.**

2.1.6 Risk management

The priority research needs described in the preceding sections will provide important information for policy-makers, relevant to decisions about appropriate measures for reducing emissions of GHG and ozone-destroying gases. Information will also indicate priorities for adaptive reduction of the health impacts of these two global environmental changes within European populations. Because of the unusually far-reaching and potentially serious consequences for human societies of these global environmental change processes, it will be important to have as much information as possible about the likely health consequences of long-term trends in climate change and in stratospheric ozone depletion. Such information will facilitate farsighted and prudent policy-making.

The following research needs may support policy formation for risk management:

Research Need 6(C)

- **Development of integrated predictive health impact assessment combined with demographic, economic, social and technological characterisation as a management tool.**

– Such models should include estimates of resultant loss expressed in DALYs and / or monetary validation units and should be applied to climate change induced health impact, extreme weather conditions, climate change induced changes in VBD transmissible diseases, ozone attributable skin cancer and other disorders.

– Vertical integration modelling (cause-effect chain) and horizontal integration modelling (linking of parallel systems that condition impact and responses) should be combined across disciplines and domains, and will lead to reduction of uncertainties in public health risk assessment.

Research Need 7(C)

- **Development of decision analysis tools, decision support systems and risk communication methods and strategies to improve the management of environmental conditions and public health risks.**

Research Need 8(C)

- **Development of strategies for primary prevention (i.e. actions that prevent changes in climate / UVR), secondary prevention (actions taken in response to early evidence e.g. in disease surveillance) and tertiary prevention (actions taken to lessen morbidity / mortality of newly encountered threat or disease, i.e. by improved disaster response capacity, improved diagnosis and treatment).**

2.2 Social variations in health expectancy in Europe

2.2.1 Introduction

In October 1997 an ESF Exploratory Workshop on Social Variations in Health Expectancy in Europe was held and the workshop report is attached (Annex 5). Socio-economic inequalities in health are found in all countries, both inside and outside Europe, for which data are available. Risks of morbidity and mortality are substantially higher in lower socio-economic groups and health expectancy differs widely as does the average number of years spent in good health. For example, for Finnish men at age 25 there is a difference in life expectancy between basic and high education groups of 6.3 years and in health expectancy of between 7.3 and 13.1 years, depending on the morbidity used.

From a policy stand point more insight why such inequalities in health occur is of paramount importance since it offers a good means of improving the average health status of a population by reducing the burden of health problems in disadvantaged groups. Despite the fact that reduction of health inequalities is a commonly shared goal evidence exists that inequalities have been (and still are) increasing over the past decades rather than decreasing. Several European countries have thereby launched research programmes in this field to describe and explain the phenomenon, and to develop intervention methodologies.

A pan-European co-ordinated multidisciplinary research effort to explain social variations in health expectancy within and between European countries would be an effective way to find solutions within a relatively short time-frame. The development and extension of a pan-European geographical information system (GIS), as currently advocated by WHO-ECEH and an ESF Scientific Programme, will be an important boost to such an approach. This workshop discussed and evaluated the current state of the art, and confirmed the need for intensified scientific exchange between the various European research groups. Moreover, it was concluded that research should be concentrated on scientific explanations rather than on (further) descriptive elaboration. New scientific insights will therefore result from a more co-ordinated application of concepts and tools. This co-ordinated approach should focus on studies of the impact of macro-, meso- and microsocial environment on health, thus forming an important and effective link with the ENHE Programme.

Within this framework a number of research needs were identified; they are described below.

2.2.2 Overarching issues related to social variations

As with other research areas described in this document, pan-European co-ordination will greatly facilitate effective and efficient execution of research related to social variations. The overarching priority is:

– To establish a network of European research centres working with longitudinal data sets, with special emphasis on life course analysis.

Understanding how social inequalities in health are triggered may be achieved by referring to three specific social environments:

(1) the microsocial environment of the family (including - for children - the school); (2) the mesosocial environment of the workplace and the neighbourhood, and (3) the macrosocial environment of society as a whole in a region or country.

In these three defined social environments exposure assessment, resource assessment and health assessment need to be studied in detail in order to be able to re-define needs for intervention, thus reducing differences in health expectancy. There are many possibilities of cross fertilisation with other research issues in the ENHE Programme for those research priorities related to effect assessment.

Research Need 9(A)

- **Studies on health inequalities, investigated particularly through cross national comparisons, focusing on gender, educational, economic, socio-cultural and health policy factors as related to both social and material environment and to cognitive functions.**

Research Need 10(A)

- **The opportunity should be exploited to add to ongoing longitudinal studies in several European countries , using standardised measurements of stressful social environment:**

– Studies following a life course perspective in which links between socio-economic, biological and psychosocial factors in childhood and adolescence and chronic diseases (e.g. ischaemic heart disease, cancers, musculo-skeletal disease) in adults are investigated, applying concepts and measures that have been developed within the framework of "pathway models".

– Studies combining biological and psychosocial approaches in which adverse effects on mortality and morbidity produced by chronic stressful social environments including housing, the workplace and the work / non-work interface, are analysed.

– Special attention needs to be given to the consequences of societal disruption, unemployment, homelessness and deteriorating economic situation and its relation to increased violence.

– Living conditions may change due to altered economic situation. This may lead to adverse effects in vulnerable groups (homeless people, insalubrious building materials, crowded housing).

Research Need 11(A)

- **Studies focusing on the broader environment, in which contextual effects on inequalities in health produced by economic, socio-cultural and health policy factors are explored.**

2.3 Environmental effects on cognitive functions

2.3.1 Introduction

The physical and chemical environment may interfere with cognitive functions in several ways. Broadly speaking, the cognitive effects of chemical substances have been thought to be the results of toxic effects on the central nervous system, whereas the effects of physical environmental factors have been interpreted within a psychological theoretical framework. However, in both cases it is conceivable that the environment affects a specific cognitive function or that it has a more specific effect on the individual's state.

For chemical substances, such as industrial solvents and metals, the irreversible or slowly reversible cognitive effects of toxic substances are assumed to reflect CNS damage caused by exposure to a high sufficiently level during a sufficiently long period of time. The effect and the critical exposure dose may depend on the individual's cognitive development when exposure occurs.

The cognitive effects of physical environmental factors during or shortly after exposure are also thought to be a result of a change in the individual's general state (mood, stress, fatigue, arousal etc.) and resources available for performing a task. Chemical exposure may also have such effects, e.g. through intense smell or fear about the possible consequences of exposure. Noise and heat may have more specific effects on cognitive functions.

The environment may also interfere with the performance of cognitive tasks without the cognitive functions involved being affected. Peripheral sensory and motor functions may be impaired in a way that impedes the intake of information or the execution of responses. For example, noise may mask important acoustic information, and whole-body vibration may impair control of the hand-arm-system during exposure.

A large amount of research into environmental effects on cognitive functions has dealt with effects during and immediately after exposure. Broadly speaking, this applies to research on physical factors, whereas research on the effects of the chemical environment has mostly focused on long-lasting effects that are considered irreversible or only very slowly reversible. Industrial solvents are the only group of chemical substances for which both types of effects have been investigated extensively.

Research into environmental effects on cognitive functions takes three approaches: (1) experimental laboratory studies, (2) quasi-experimental field studies, and (3) epidemiological investigations. Experimental laboratory studies on humans are usually short-term studies of acute effects at moderate exposure levels. Longer-term studies are considered to be impractical and unethical; instead quasi-experimental field studies are often performed. Animal studies are important when long-lasting behavioural neurotoxic effects are involved but they are hampered by the fact that many human cognitive functions cannot be studied since models are lacking.

Quasi-experimental field studies investigate reversible effects in natural (realistic) settings using representative exposed and non (or less) exposed groups. Limitations include poorer control of confounding factors and the difficulty of studying long-term effects (years). Such long-term effects are generally studied in cross-sectional and longitudinal epidemiological studies. However, it is very often difficult to obtain valid estimates of exposure. When investigating experimental effects on cognitive functions several problems may arise. For example, performance for certain functions may be influenced by many factors, of which environment is only one. Interpretation is also hampered by the way individuals cope with a situation and the fact that the performance level of a task may be well below an individual's peak.

Chemical agents known to cause effects in cognitive functions include metals (lead, mercury, aluminium, manganese) and organic solvents. In many cases, however, studies of chemical substances show rather inconsistent results, which may in part be due to a wide variation in these functions in the normal population. Hence the need for studies with large sample populations, something which can often be achieved only in international collaborative studies. In addition, better and more sensitive tests for impaired cognitive functions, advanced statistical analyses and better research designs need to be developed. Equally important is the development of improved methods for exposure assessment (see Section 2.11).

Physical environmental factors, which may affect cognitive functions, include noise, heat and cold, vibration and light conditions. Noise is distracting and reduces concentration or performance. Chronic cognitive effects are impairment of learning ability and memory. However, it is not possible at present to draw simple, general conclusions about how noise interferes with the performance of different cognitive tasks. Different types of noise are likely to have different effects and adaptation to work in a noisy environment varies between persons and situations. Transportation noise and irrelevant speech are the noise sources that have shown the most replicable cognitive effects. Extending research to include more cognitive tasks of clear ecological relevance would be valuable, given that transportation noise and irrelevant speech are serious problems in many schools and work places.

After-effects of work in noise have been demonstrated in many laboratory studies. It would be of great interest to obtain a better understanding of such effects outside the laboratory.

Further research on the effects of a noisy environment on children's cognitive development is of utmost importance. Critical issues include the interaction between noise exposure and cognitive developmental stage, and also between noise exposure and other physical and social environmental conditions, including the effects of a noisy environment on the behaviour of teachers and other adults. Other important questions relate to the mechanisms mediating cognitive effects on, for example, reading ability, and the identification of sensitive groups.

The cognitive effects of thermal stress are primarily a workplace and school problem. Several studies of school children have found acute effects on the performance of school tasks. Few studies have related performance changes to the individual's thermo-regulatory state. Individual adjustment patterns and the role of making an effort are of equal importance in the research on thermal stress in noise research.

Vibration may impair performance in tasks involving central nervous functions. However, there are not enough data to be able to pinpoint which tasks are sensitive to vibration or which exposure conditions are likely to produce effects.

In the report (http://www.esf.org/mp/ENHEb.htm), information on environmental effects on cognitive functions is limited and inconclusive. Societal concerns are considerable, indicating that there is a need to develop new techniques, methods and tests for measuring exposure and cognitive functions. Furthermore, there is a need to improve study designs, such as combining different basic designs, focussing on target groups at risk and organising supranational multi-centre studies. Launching such studies can only be successful when harmonised, standardised and validated measurements of cognitive functions are available, thereby allowing adequate comparison of international and national data and results.

2.3.2 Exposure assessment

Reliable exposure data are generally scarce, especially in cross-sectional epidemiological studies. Here, as elsewhere in this report, there is a need to focus on exposure assessment methodology (see Section 2.11).

The following priority research needs are defined:

Research Need 12(A)

- **Development of reliable exposure measurement methodology and modelling in order to improve exposure**

assessment (see Section 2.11). This should include:

– Chemical, physical and stress factors in the field and in the occupational setting, under conditions differing in space and time.

– Improvement of personal monitoring and development of non-invasive measures in critical organs.

2.3.3 Effect assessment

Many studies performed to investigate possible relations between the environment and cognitive functioning have not given clear answers, although there are some exceptions. It is recognised that poor methodologies usually hinder reliable conclusions. Specific designs in epidemiological studies may also facilitate future research on the impact of environmental factors on cognitive functions. In the field of effect assessment many priority research needs focus on methodological issues such as:

– Development of study methodologies based on a combination of different basic designs such as cross-sectional, between-person and longitudinal within-person designs along with quasi-experimental designs.
– Combination of behavioural functional variables with physiological and neurological parameters.
– Use of animal models in addition to studies in humans.
– Development of tests as indicators for everyday functions.

Research needs in effect assessment are:

Research Need 13(A)

- **Environmental effects on mental and cognitive function. There is a need for more research networks and incorporation of relevant outcomes into existing or planned studies.**

2.3.4 Risk Characterisation

Risks can only be characterised quantitatively when exposure measures and effect measures are sufficiently reliable. In addition, the nature and severity of cognitive function effects should be defined. Specific research needs in this area are:

Research Need 14(B)

- **Studies should be undertaken to define:**

– The nature and severity of cognitive function effects.

– The impact of combined effects.

– The attribution of individual factors to the process.

– The stability of certain effects and the possibilities of establishing thresholds.

2.3.5 Risk management

Risk management decisions can only be made when risks related to certain environmental factors are sufficiently characterised, ideally in quantitative terms. However, risk management is also strongly influenced by risk perception, community tolerance, tolerance development and behavioural attitudes. Corresponding research needs are:

Research Need 15(C)

- **Investigations to define the role of cognitive functions in risk perception and risk communication. This may include:**

– Research on (in)tolerance and tolerance development.

– Development of comparative risk strategies.

– Research into trends in behavioural attitudes, their impact on risk perception and communication, and conversely the impact of risk perception and communication on behavioural attitudes.

2.4 Cognitive functions as mediators of environmental effects on health

2.4.1 Introduction

Cognitive functions are those psychological functions by which humans acquire and use knowledge about their environment (http://www.esf.org/mp/ENHEb.htm). Learning, memory, perception and attention mediate between environmental influences and health outcomes. Closer and more systematic attention to this mediating role is necessary in order to understand better the relations between human well-being and aspects of the contemporary environment. Four areas in which cognitive functions may have a mediatory role can be distinguished:

– Sensation-based perceptions. This area deals with those adverse physico-chemical aspects of the environment (odour, noise) capable of activating the senses and which, in so doing, may have negatively arousing properties associated with potentially adverse health effects.

– Information-based perceptions refer to those physico-chemical aspects of the environment which do not induce sensory activation (e.g. ionising radiation), but are cognitively registered through external channels of information and which, depending on the level and/or duration of exposure, may in principle cause health impairment.

– Attribution-based syndromes are environmental factors which have not yet been shown to induce adverse health effects or which current knowledge suggests are unlikely to do so, but which are nonetheless cognitively imputed by sick people to the onset of their health impairment.

– The psycho-social environment, as distinct from the physico-chemical environment has also been shown to affect health and well-being, but is also likely to interact with the above-mentioned areas in an additive or even synergistic way in terms of health impairment.

In discussing these areas of interest further, particular attention will be paid to gaps in knowledge and the identification of research needs for the general environment and for occupational settings.

2.4.2 Sensory environment, cognitive functions and health

Adverse physico-chemical aspects of the environment like crowding, heat, odour and noise are capable of sensory activation and have negatively arousing properties, associated with potentially adverse health effects, including annoyance responses and somatic as well as social/ behavioural symptoms.

The precise meaning of annoyance is not fully understood, definitions vary and integration into broader theoretical constructs has not yet been accomplished in a widely accepted manner. Some treat annoyance responses as perceptions, others as emotions, and some as attitudes or rational decisions based on cognitive operations. Despite such conceptual differences, and despite differences in assessment mode in terms of uni- or multidimensional measures of annoyance on the one hand, or of environmental load (exposure) on the other, the empirical data base is consistent.

Clear-cut relationships between environmental load (i.e. sound pressure levels for noise or odour concentrations or frequency of odour events) and degree of annoyance have been established in population-based studies. These associations are typically somewhat higher for noise than for odour annoyance, probably due to a more precise exposure assessment, but for both environmental stressors such correlations always been shown to be highly statistically significant.

Differences observed between individual and area-centered associations emphasise the importance of person-related factors in modifying the annoyance response. Factors acting as intervening variables (mediators, moderators, or process-oriented variables) include cognitive constructs such as perceived health, perceived noise/ odour sensitivity, fear of health impairment as well as appraisal and coping processes. These constructs have emerged from transactional stress models.

Although typically treated as an endpoint in both odour and noise studies, annoyance has also been shown to be a cognitive mediator for somatic symptoms such as sleep disturbances, headache or gastric discomfort. Self-reported fear of negative health outcome from exposure to industrial odours has been reported to modify effectively the degree of annoyance and associated health complaints. There is also some evidence that vascular responses to traffic noise are mediated by both actual and long-term retrospective annoyance, and that self-reported noise sensitivity influences heart-rate acceleration and vaso-constrictive responses following experimental noise exposure.

In view of such observations closer attention needs to be paid to whether and to what extent cognitive attitudes like annoyance or self-reported environmental sensitivity affect the association between traffic noise exposure and prevalence of cardiovascular diseases. Furthermore, longitudinal studies on noise and odour may enable analysis of the development of certain conditions as well as of physiological and medical symptoms. Inclusion of psycho-physiological variables, such as stress hormones or indicators of immune-system dysfunction in such studies seems warranted.

Finally, exposure assessment for both odours and noise should be improved so as to become more person- rather than area-oriented. This requires closer interactions between the biomedical and social sciences on the one hand and technical disciplines on the other.

2.4.3 Cognition and environmental syndromes

Reporting of somatic symptoms in the context of environmental syndromes is prevalent in the general population. Values as high as 40% have been reported for symptoms like fatigue and headache in representative population-based studies.

Like other so-called environmental syndromes such as chronic fatigue syndrome, multiple chemical sensitivity, or amalgamism, the so-called sick building syndrome (SBS) is characterised by symptoms rather than by identified causative factors in the environment. Since a high proportion of somatic complaints in the context of environmental syndromes remains unexplained by conventional medical and psychiatric categories, the term "medically unexplained syndromes" is increasingly being used as a descriptor.

Symptoms related to environmental syndromes while exhibiting some specificity, show more uniformity across the various syndromes. However, conventional psychiatric diagnostic categories are insufficient to explain the prevalence of somatic symptoms. It seems that in addition to psychiatric disorders such as depression, anxiety and somatisation disorder, psychological theories (childhood experience, occupational stress, conditioning models, personality traits/modes) and more specific theories (ecological attitudes, health perception or attribution modes) are needed to explain (indirect) relationships of somatic symptoms to environmental factors.

For SBS as for other environmental syndromes there are several identifiable gaps in our knowledge. These include the identification of baseline population prevalences of somatic symptoms and "sensitivities", and the clarification of relationships between medically unexplained environmental syndromes and association patterns for multiple stressors. Comparative studies of environmental syndrome triggers such as SBS may address these issues, and may stimulate adequate perceptual characterisation of the individual's physical and social environment. The development of good diagnostic tools for environmental syndromes in terms of "perceptual-cognitive factors" and person-situation interaction is another need, as is the development of physiological and sensory methods for provocation tests.

2.4.4 Cognition and pain perception

Attribution based syndromes such as musculo-skeletal disorders (pain in the neck, shoulders and the lower back) are the most common and costly health problems in Europe and North America today. Cognitions are central for an understanding of pain perception and resulting behaviour. Three models have been developed to characterise the role of cognitions in pain perception:

i. The Gate Control Theory. In this model, in which afferent or efferent neuronal activity is modulated by activity in other sensory/motor fibres or CNS activity, cognitive factors like attributions, expectations, attention and coping are given a central role. Pain is seen as a multi-dimensional experience with sensory, affective and evaluative components.

ii. The second model emphasises three systems, namely physiological activity, cognitive and behavioural aspects of pain. Physiological activity is experienced both as a sensation and an unpleasant emotion. Behaviour serves to communicate or to relieve the pain.

iii. The third model integrates parts of the other two models and focuses on the importance of cognitive processes in relation to learning: behaviour that reduces pain is more likely to be adopted and conversely. In general, a number of cognitive processes like attribution, beliefs, fear-regulated avoidance behaviour, and coping have been studied in relation to pain perception and pain regulation.

The role of the work environment in back pain is essentially attributive. Although physical factors (such as bending and lifting) do play a certain role, psychosocial factors in the work environment like stress, poor job satisfaction or social relations (to superiors or peers) seem more important risk factors.

In addition, psychological processes in pain perception are associated with (or result in) physiological changes such as muscle tension or catecholamine release, emphasising the importance of the interaction of psycho-biological mechanisms with cognitions. It is important to translate knowledge in the area of cognition-regulated pain perception into both preventive interventions and treatment programmes. Research is also necessary to unravel the intercorrelations and interactions between cognitive processes involved in pain perception. For example, there is a need to clarify how cognitive processes influence this relationship in a given environment/health interface, e.g. in relation to musculo-skeletal disorders. Not enough is known about whether mental and physical demands have synergistic or additive affects on muscle tension, or if physical demands under certain conditions can mask the influence of cognitive demands. It is also necessary to study the role of frequent or intense muscle activation versus absent relaxation ("EMG gaps") as a risk for developing muscular disorders. Very little is known about the background of inter-individual differences in "vulnerability" and whether susceptibility to musculo-skeletal disorders is associated with differences in personality, coping behaviour or biochemical parameters. Finally, it has to be determined whether muscle tension is part of a generalised psycho-physiological stress response, or specifically related to certain environmental conditions.

2.4.5 Cognition, environmental stress and chronic diseases

Since the early days of Selye, stress is frequently taken as an objective or measurable set of conditions exerting some sort of pressure on organisms surpassing their reserve capacity or coping potential. This "physicalistic" view, based on animal studies, is incomplete or insufficient to account for stress effects in human beings since similar external conditions may be perceived differently by different individuals. Research into the effects of psycho-social stress (occupational or environmental) on chronic disease has to consider both objective as well as "perceived" aspects.

Stressful psychosocial conditions may have an impact on human health by two not necessarily distinct mechanisms, (1) through an unhealthy lifestyle, and (2) by over-activation of the autonomic nervous system (ANS) as mediated by the hypothalamic-pituitary-adrenal axis (HPA). HPA-activation due to long-standing psychosocial stress has been found to be associated with precursors of cardiovascular disease, such as arteriosclerotic changes in arterial walls and hypertension, but also with down-regulation of the immune system. Stress-related immune suppression as indicated by decreased natural killer cell activity (NKCA) may be involved in cancer progression, chronic viral infection and auto-immune disease.

Elevated odds-ratios for cardiovascular disease (CVD) have been reported for stress-related versus non-stressful conditions in general and at work. The fact that the elevation was more pronounced if perceived rather than "objective" stress was taken as the variable indicates the importance of cognition as a mediating factor in health effects. Although the above-mentioned mechanism (chronic over-activation of the HPA axis) may offer a likely explanation, more detailed data on how biological mechanisms render psychosocial stress pathogenic are required. In the work environment, studies into interaction between physico-chemical and psychosocial conditions may provide useful information, and quantification of the relative contribution of (psychosocial) workplace conditions may explain social differences in health and disease within Europe (see also Social Variations, Section 2.2).

Detailed investigation into the mechanisms of stress-related long-term effects on immuno-suppression and other organ systems (nervous system, musculo-skeletal system, reproduction etc.) may provide tools for preventive measures. Pan-European studies on HPA-activation and associated diseases including a profile of pathogenic factors in the psychosocial environment will also provide information for possible intervention measures. Determining which cognitive functions make individuals attribute their health problems to environmental factors and how individuals with environmental health problems differ from psychosomatic patients in terms of perceived health and biological stress indicators are other relevant issues.

2.4.6 Cognitive determinants of perceived risk

Risk is an important issue in modern societies and refers to the probability of harm associated with a given hazard. Psychologically, it is common to differentiate between "lifestyle risks" and "environmental risks". Whereas lifestyle risks like smoking, unhealthy diet, sports, etc., are typically under direct personal control ("voluntary"), this is not true for ("involuntary") environmental risks (nuclear power, chemical pollution).

Since the seminal work of Slovic and co-workers the term "risk perception" has been used to describe attitudes and intuitive judgments of lay people about risks. It was found that people tend to underestimate risk associated with natural or lifestyle hazards whereas they tend to overestimate risks from societal-technical hazards. Over- and underestimation refers to the "true" or statistical risks.

The methodological tool in such studies was the so-called psychometric approach based on ratings of a set of hazardous activities, substances or technologies. Multivariate analyses (i.e. factor analysis) revealed two main dimensions of such ratings, namely a "dreads-risk-factor" (i.e. severity, lack of controllability, dreadfulness) and an "unknown risk-factor" (observable, known or new risk). Only the dread factor exhibited substantial correlation with perceived risk. Findings as revealed by the psychometric approach have been confirmed in many different countries and contexts. However, there are still uncertainties in this approach, particularly at the individual level, and multiple regression analysis of factors which may be influential such as control, familiarity, voluntariness and dread have produced only moderate contributions to explain perceived risk.

Beyond the psychometric approach other cognitive factors such as knowledge, belief-structures, judgmental heuristics, attitudes, framing and effect have been studied in terms of their effect on risk perception. In most instances, results have not been very consistent and effects, if present at all, have been found to be rather weak. It should also be pointed out that although health outcome is a frequently used criterion in risk perception studies, research directly relating variability of risk perception to health indicators in terms of symptoms, complaints or biological stress indicators, does not seem to exist. The focus of research in risk perception should shift from a structural to a more process-oriented approach to follow the judgmental stages from information acquisition and processing to the final risk judgment. Whether variables like knowledge, attitudes or affect are able to shape the judgmental process underlying risk perception should also be addressed as well as the social dynamics in which risk perception takes place, namely trust, credibility and social risk amplification.

2.4.7 Overarching priority related to cognitive functions as mediators of environmental effects on health

In the preceding paragraphs several aspects have been depicted which need further investigation. In the general environment as well as the occupational environment knowledge gaps and resulting research needs have been identified and evaluated for relevance, feasibility, multi-disciplinarity, supranational aspects and potential for policy support. Research should be carried out under the governance of a platform organisation in order to ensure effective and efficient execution of the research needs in a supranational and interdisciplinary manner. The priority research needs are discussed within the framework of the risk analysis scheme.

2.4.8 Exposure assessment

Research Need 16(A)

- **Improvement of exposure assessment methodologies (see also Section 2.11 on physico-chemical factors related to the senses (noise, odours, crowding) and its applicability should become more person- than area-oriented and, in addition, should be validated against psycho-biological effects**

– Is frequency of noise events a more valid exposure measure than the time-weighted average?

– To achieve this a closer interaction between biomedical and social sciences and technical disciplines is necessary.

2.4.9 Effect assessment

Research needs in the area of effect assessment encompass the whole area of methodology, mechanism, pathways, susceptibility and resilience. It is pertinent that more effort should be given to understanding the various aspects of sensation-, information- and attribution-based perceptions and their mediating properties to (adverse) health effects.

Research Need 17(A)

- **Development of measures of perceived exposures, health beliefs and their influence on health outcomes.**
- **Psycho-biological mechanisms of symptom formation.**
- **Prevalence, impact, attributions and outcome of unexplained symptoms and syndromes in a cross-national perspective.**

Research Need 18(A)

- **Studies into the role of coping in the relationships between occupational environment and health, including feelings of control and coping strategies over time.**

2.4.10 Risk characterisation and risk management

Current understanding of cognitive functions as mediators of environmental effects on health is not yet refined enough to characterise risks in a sufficiently quantitative way. Outcomes of putative research may also allow better risk characterisation procedures to be developed. This also pertains to risk management principles. With respect to risk perception the following research needs may have priority:

Research Need 19(B)

- **Development of methods for a process-oriented approach to risk perception.**

Research Need 20(B)

- **Assessment of links between risk perception and symptom**

vulnerability, including potentials for appropriate intervention.

Research Need 21(C)

- **Where appropriate the possible effects of treatment or intervention should be investigated, nationally and internationally in multicentre studies.**

– Aspects to consider include the role of cognitions in treatment and/or prevention, their importance in policy support and whether effects can be applied at the individual, interpersonal or organisational level.

Research Need 22(C)

- **Improved risk management strategies for environmental incidents using systematic reviews of best psychosocial management.**

2.5 Children and accidents

Unintentional childhood injury is a major cause of morbidity and mortality. Globally, it is thought that 428,300 children aged up to five die annually due to unintentional injury. Accurate pan-European data are not available but WHO estimates for the developed world indicate that European rates for unintentional injury cause approximately 250 deaths per 10^6 children less than five years of age. This represents more than 15% of total deaths in that age group.

According to the European Commission, injuries in the EC are "*the leading cause of death at all ages between 1 and 34. This concentration in the youngest age groups makes injury a disproportionate cause of potential life years lost.*" In the United Kingdom a total of 5.8 x 10^6 home and leisure accidents are expected to occur annually, of which 800,000 (14%) will affect those aged under five and 2.3 million (40%) affect those aged under fifteen. Children are particularly vulnerable to unintentional injuries because of their physical, psychological and behavioural characteristics.

The term unintentional injury, rather than accidents, is increasingly being used in the international literature. This reflects the recognition that accidents are not simply random events but are influenced by a number of predisposing factors including the physical environment in which a child lives, learns and plays. Other influences include the age/gender of the child, and psychosocial characteristics of the family. The relative importance and impact of environment, education, enforcement/legislation and evidence based practice on the prevention of unintentional injuries is also a complex issue.

The Melbourne Declaration (1996) sets a global agenda for injury prevention through world-wide partnership. An important statement in the Declaration is:

"*Improving the availability of accessible and linked data (which includes the cause of injury) and information on effective interventions, and increasing research which supports the design of new interventions.*"

There exist strong arguments to define research needs which will identify the most appropriate prevention strategies. To achieve this, a twin approach at both national and pan-European level is necessary for the following reasons:

– Exposure to accident risks varies greatly across Europe allowing ecological studies of the actual hazards associated with particular risks.

– Adequate expertise to tackle the research agenda exists across Europe and supranational collaboration, drawing on familiarity with different patterns of injury, will strengthen this considerably. Apart from the work already done by the ESF in the ENHE Programme, the European Evaluation of Children's and Adolescent's Accident Preventive Policies (EURECAAPP) survey has already set the way for development of formal links between researchers across the EC. An international network, the International Society of Child and Adolescent Injury Prevention (ISCAIP), was formed three years ago and there is scope for strengthening links between European members and extending membership within the EC.

– Improved communication between the child safety research community and manufacturers, both with individual states and across Europe, may lead to safer products and environment. This will support the development of enforceable European product and environment standards.

– The development of broadly similar, rigorously evaluated education and awareness programmes, tailored to the risk profiles and health care systems at the national/regional level, will be applicable to many other countries worldwide.

– Exchanging experience will allow countries with higher injury rates to apply lessons learnt by those countries that have had greater success in lowering their childhood injury rates. For example, child resistant containers and packages are of proven benefit in reducing poisoning but are not used universally.

– Injury severity and health impairment are independent of national borders. Drawing on the experiences of other states will allow optimisation of care, both medical and non-medical, should injuries occur.

– Access to an adequate study population in order to provide statistically robust conclusions. This is particularly important for intervention studies where statistically modest, but clinically important health gains are demonstrable only in large multi-centre studies.

– The cost of performing large multi-centre studies and trials can be considerable. Spreading cost across several states will make adequate funding more accessible and ensure that work is carried out to a high scientific standard.

When defining research needs in relation to accidents among children several developments are of importance:

– Injury risk may change with new sporting developments and with increasing activity among a larger proportion of this sub-population - a health objective supported in many countries.

– Increased affluence will step up these pressures and ease of movement in Europe encourage uptake of new activities.

– Changes are likely to be accelerated in Eastern Europe which is undergoing rapid development; this should be closely observed.

– More means of familiarising children and the general population with risks involved, may become available e.g. by using better and more appropriate risk communication methods. This could be facilitated by developing a cadre of educators trained in objective risk assessment.

– An initiative has been taken by the European Commission for a prevention programme on accidental injuries in the framework of public health activities.

– Agricultural injuries are an important cause of occupational fatalities. Among them injuries to farm children are a considerable health hazard.

Development of pan-European interventions to control unintentional childhood injury therefore seems an appropriate and achievable goal. Using different approaches based on the various scientific paradigms of those involved, it should become possible to intervene in a purposeful way. Prevention policy both within and outside the EC should be informed by rigorous evaluation. A pan-European approach should be reinforced by setting up supranational research activities to standardise collection and dissemination of relevant data, and by developing an evidence-based European injury prevention policy. This will also provide an effective means of disseminating the results of successful interventions.

Following the workshop (http://www.esf.org/mp/ENHEb.htm), the following research needs were identified.

2.5.1 Overarching research needs in relation to children and accidents

The scientific community strongly supports the creation of an interdisciplinary platform/network organisation to facilitate interaction between specialists involved in the various research areas. A network organisation will be instrumental in transforming targeted priority research needs into quality research proposals, evaluating progress and priorities and communicating information to interested parties on critical issues related to intervention and prevention. More specifically, such overarching issues are:

– To standardise collection and dissemination of relevant data at a supranational level in order to ensure comparability. (This is the top priority.)

– To develop a pan-European injury prevention network in order to implement an evidence-based pan-European injury prevention policy.

– To develop a pan-European intervention programme to control unintentional childhood injury.

– To foster international co-operation and promote the development of research skills by enabling European countries to interact.

– To promote transport-related health gain. Developing safe transport policies (segregated cycle routes, supervised walking routes and improved public transport systems) will reduce the current trend in Europe for children to be transported by car. This will reduce local environmental pollution and the emission of greenhouse gases, thus supporting sustainable development.

2.5.2 Hazard identification

In the area of children and accidents the hazard is not always adequately identified. Research to identify such hazards is required in order to determine the ultimate feasibility of prevention and intervention:

Research Need 23(A)

- **Assessment of injury severity in a standardised classification system.**

– Standardisation of both diagnostic categories (perhaps based on ICD 10) and injury severity scores is a prerequisite for pan-European research co-operation and injury reduction.

Research Need 24(B)

- **Collection and dissemination of data.**

– Data from physicians / general (family) practitioners, schools, emergency room attendance, hospital admission and death certificates may serve as a basis for standardised methods of recording across Europe in order to allow robust international comparisons and identify the most threatening or new hazards.

2.5.3 Exposure assessment

Cultural and lifestyle differences across Europe with accordingly different customs and habits influence the pattern of injuries. Analysis of such patterns will provide tools for prevention and intervention in the regions and countries of Europe.

Research Need 25(B)

- **Comparative studies of exposure to injury risk in the different regions and countries of Europe.**

– Patterns of injury may vary across Europe due to a variety of risk factors. Whereas burns due to domestic heating appliances are common in the Northern part of Europe, drowning in swimming pools and recreational water areas seems more common in Southern Europe. Analysis of these and similar risk factors will provide data for priority-setting in intervention and prevention strategies.

2.5.4 Effect assessment

Research Need 26(A)

● **Cross-cultural studies of causation.**

– Qualitative and, where possible, (semi)quantitative techniques will allow examination of different approaches to parenting and foster development of safety guidelines across Europe.

2.5.5 Risk Characterisation

The identification of risk-related injury patterns and the measurement of health and economic loss and gain will enable a more precise characterisation of risks in terms of incidence and severity, thus providing decision-making tools for priority-setting in prevention and intervention methods.

Research Need 27(A)

● **Measurement of health gain and economic benefits.**

– Development of systems to measure injury rates quantitatively.

– Estimation of potential health and economic benefits. This will enable priority-setting in effective prevention strategies.

– Long-term costs of health and social care and lost productivity can be used in addition to direct costs to provide information about the likely economic gain achievable through appropriate prevention and intervention i.e. allowing appropriate cost/benefit analysis.

Research Need 28(B)

● **Production of systematic reviews and meta-analyses.**

– Authoritative systematic reviews and, where appropriate, meta-analyses can be used to produce evidence based guidelines. Dissemination of these guidelines will reinforce previous successes.

2.5.6 Risk management

The research issues targeted above should provide policy-makers with the information required to evaluate the feasibility of prevention and intervention, something which can be done only when reasonably realistic numerical data for cost/benefit analyses are available. Risk prevention by pro-active measures focused on, for example, product safety, sport and leisure facilities, farming or transportation may greatly reduce casualties in early life.

Research Need 29(C)

● **Assessment of a hazard-orientated approach to product safety.**

– This should include developing acceptable common safety criteria and test methods for domestic products as well as guidelines for improving environmental safety, both inside and outside the home.

Research Need 30(C)

● **Prevention of sports and leisure injuries.**

– The primary focus should be on playgrounds and cycling injuries. For example, evaluation of bicycle helmet use and, if appropriate, strategies to increase its use. Another issue which should be considered is drowning.

Research Need 31(C)

● **Pan-European intervention studies to prevent unintentional injuries to children and adolescents.**

– Appropriate methodologies for injury research with particular emphasis on controlled evaluations of injury prevention programmes for pre-school children and adolescents. Multiple approaches should be used including systematic reviews of interventions, comparative studies of exposure risk, and statistical methods to compare injury surveillance data in the different regions and countries in Europe. A WHO working group is currently developing a standardised classification of external causes of injury. Outcome data may be obtained from physicians, general (family) practitioners, schools, emergency room attendance, hospital admission and death certificates.

– Measurement of health gain and economic benefits. Outcomes will include an assessment of the societal costs and psycho-social consequences of injuries and cost benefits of injury prevention programmes. The latter will include direct and indirect costs of childhood injury and information about the economic gain that can be achieved by appropriate intervention.

2.6 Ambient air particulates

Particles are ubiquitous constituents of the outdoor and indoor environment; all humans are exposed to such particles when breathing air. Episodes of air pollution in the past (notably 1930 and 1952) showed that air pollutants of anthropogenic origin can have significant acute consequences for health. Environmental policy measures to lower air pollution levels were taken in many areas in Europe and North America but even at the current low levels of particulates in urban areas associations have been found between daily exposures to mass concentrations of particles and mortality and morbidity.

Brief periods of exposure to particulate matter (PM10) has been estimated (The Netherlands) to accelerate mortality by 50 persons per day, to increase hospital admissions by 73 persons per day, to cause 2700 asthmatic attacks per day in children aged between seven and eleven and to reduce lung function by 10% in 46000 children per day in the same age group.

Although considerable research has been carried out into particulates, the potential severity of the problem, interpretative difficulties (in particular problems in attributing observed effects to specific particle properties and emissions) and the increasing volume of information on acute and chronic health effects warrant a systematic integrated research approach to counteract them effectively with adequate measures. A proposed framework for such an integrated research effort requires a multidisciplinary approach involving all key disciplines such as atmospheric sciences, epidemiology, toxicology and social sciences; only this approach will provide the relevant information and link it to the causal chain of human activities and environmental effects.

After a thorough review of existing information an international group of experts identified crucial gaps in our knowledge; once this situation is rectified, policy-makers will be better informed about measures to take. The report of this international expert group is provided in full on the ESF home page http://www.esf.org. Research needs identified as the most important are described below in terms of the cause effect chain and risk assessment paradigm with its interrelated aspects, which in the case of air particulates are as follows: hazard identification, release assessment, exposure assessment, consequence or effect assessment and risk characterisation. Before presenting these aspects, the expert group highlighted some overarching priorities.

2.6.1 Overarching priorities in the field of air particulates

As in most identified research areas the scientific community strongly supports the creation of a platform/network for interdisciplinary interaction between research specialists. Such a forum or network could be instrumental in transforming prioritised research needs into research proposals, in reevaluating priorities during the process, and in communicating information about critical issues and research to interested parties. In addition to the overarching priorities depicted in the Introduction, the priority in the field of particulate air is:

– Formulating (possible) working mechanisms for observed health effects related to PM exposure profiles.

2.6.2 Release assessment

Particles can be generated by natural and anthropogenic sources. The estimated annual total amount is 3,000 million tonnes for the former and 400 million tonnes for the latter. Since particles from natural sources are mostly coarse, anthropogenic sources contribute approximately 60% of the total fine atmospheric particle burden, which is of most concern in relation to health.
In Europe, substantial differences exist in primary emissions (both natural and anthropogenic). However, secondary emissions (as a consequence of a gas-to-particle conversion process) are also subject to marked differences due to the processes, conditions and

(climatic) variations that govern their production.

While summary information on emissions often exists (mean annual national production of major sources) specific information on PM, with sufficiently detailed temporal and spatial resolution, specific to size and chemical and physical perspective, is hard to come by. This latter information is needed to predict exposure and effect adequately.

Research needs on release assessment are:

Research Need 32(A)

- **Development of appropriate source apportionment of PM in indoor and outdoor air to allow exposure to be linked to PM sources. This includes research on particle sources as well as on dispersion.**

2.6.3 Exposure assessment

Exposure assessment consists of describing and quantifiying the relevant conditions and characteristics of human exposure to released particles from a given source. Exposure to PM is defined as the event in which an individual remains in contact with a specific concentration for a certain period of time. This may involve a micro-environment with a more or less homogeneous concentration or one where the concentration varies in time and content. PM covers a variety of particles with different properties.

Most widely used is mass-based concentration of PM. Sometimes characterised in terms of size; TSP, BS, PM_{10}, $PM_{2.5}$ (*), it is commonly expressed in mg/m^3 over time. Further refinement may be achieved by subdividing particles into fractions according to chemical or biological properties in order to specify their origin, fate or toxicological potential.

Although the technical means are available to measure particles in number, size and surface concentration there is a lack of historical data or source-related information in Europe. Moreover, there are still technical problems: control of size, selective cut-off, artefacts due to condensation/ evaporation of material on or from filters on which PM is collected or interference with the filter material itself.

Exposure in Europe mainly concerns time-series of 24 hours average mass-based concentrations of TSP, BS, PM_{10} or $PM_{2.5}$ (*) from fixed-site monitoring networks usually operating for regulatory purposes. These data provide insufficient information about diversity in terms of sources and composition. In addition, measurement techniques vary throughout Europe, thus making comparison difficult.

Personal exposure measurement experience in Europe is limited, partly for practical and technical reasons. However, the few studies

(*) TSP = Total suspended particulate matter without particle size selection, e.g. as measured by high volume samplers.

BS = Black smoke or British smoke; measurement based on filter reflection by which particles of aerodynamic size diameter of < 4.5 mm are collected.

PM_{10} = Particles are measured which pass through a size selective inlet with a 50% cut-off at 10 mm aerodynamics diameter.

$PM_{2.5}$ = Particles are measured which pass through a size selective inlet with a 50% cut-off at 2.5 mm aerodynamics diameter.

that have been reported indicate that personal exposure measures deviate substantially from measures derived from fixed-site monitoring networks. The length of time spent in different environments (indoor/outdoor) and differences in PM levels are the major reasons for this discrepancy. Currently, a first multi-centre EC-funded study (EXPOLIS) aims to generate personal indoor and outdoor PM exposures in selected adult urban populations; and the results to date confirm discrepancies mentioned above.

Exposure assessment-related PM research needs concern technical, mathematical, epidemiological and experimental toxicological disciplines. They include development and application of measurement and modelling techniques to determine population exposure to the relevant exposure profiles and PM properties. In addition to these generic research needs in exposure assessment (Section 2.11) an additional research need involving air particulates is:

Research Need 33(A)

- **Characterisation of European air quality according to agreed classification criteria with respect to different particle types, their correlation with gaseous pollutants, and characterisation of personal exposure to PM. This may be implemented by:**

– Interdisciplinary expert consultation to develop criteria.

– Classification of reported mass-based PM concentration on a regional basis.

– Identification of areas with similar and contrasting PM profiles to optimise similarities and differences in PM exposure in Europe when comparing existing study results (e.g. APHEA or similar local studies).

– Identification of areas with similar and contrasting PM profiles to optimise similarity and differences in PM exposure in Europe for design of future studies, e.g. on source apportionment, measurement and modelling techniques, and for new health studies.

– Monitoring size, mass, number and surface, chemical composition, spatial and temporal distribution of PM indicators like PM_{10}, PM_{25}, PM_{1} and BS.

– Compilation of databases on PM concentrations in different micro-environments (home, school, commute, inner-city) and compilation on time-activity data of the European population.

– Measurements of personal exposure of PM in population subgroups, e.g. children, adults, elderly, cardiovascular disease (CVD) and chronic obstructive pulmonary disease (COPD) patients.

– Improvement of models for the indoor environment, in particular to model outdoor/ indoor penetration of PM and the role of personal behaviour in PM exposure.

– Determination of the relationship between personal exposure and ambient concentrations at fixed-site monitoring stations.

2.6.4 Consequence or effect assessment

The physical and chemical properties of particulates determine the mechanisms by which they become biologically active. Whereas their physical properties determine the site of deposition in the respiratory tract, their chemical composition determines their mean residence time. Response is ultimately determined by physical and chemical properties such as particle location, dose, duration and disposition.

Deposition and retention largely depend on particle size. Shape, density, electrical charge and hygroscopicity modify the deposition pattern to some degree, whereas respiratory ventilation and intersubject variability in airway and air space dimensions may modify deposition patterns considerably. Likewise, the solubility of deposited matter influences retention.

How these effects act on health and the specific PM properties involved are poorly understood. A large epidemiological database consistently describing PM effects (i.e. mortality, hospital admission, medications used, aggravation of respiratory symptoms, asthma and pulmonary function) does exist, and no alternative causal agents have been identified to explain these effects.

Knowledge of the mechanisms by which inhaled particles cause lung damage is inadequate. Pulmonary inflammation, cell proliferation, and vascular congestion are the most investigated phenomena, usually at high PM concentrations. It is not known what occurs at ambient levels or whether adaptation and/or tolerance play an important role. The same holds for the potential effects of inhaled particles on tumour incidence or cardiovascular diseases, and PM effects on compromised lungs in animals and humans; although it is known that the elderly and those with respiratory diseases are more susceptible to inhaled particles.

Particulate matter cannot therefore be considered to be a single entity but rather as a variety of entities which depend on the physical and chemical properties of the particle. Identification of these entities should be the goal of epidemiological and toxicological research, i.e. determining which specific entities cause a respiratory response, even at urban air concentrations. A set of common definitions and terminology for the various disciplines involved is a prerequisite to a multi-disciplinary approach to these questions.

Research questions defined for effect assessment are:

Research Need 34(A)

- **Application of toxicological and clinical research tools to**

study acute and chronic respiratory and cardiovascular responses to inhaled ambient particles.

– Identification of those physico-chemical properties of the particles which cause detrimental respiratory and cardiovascular responses.

– Determination of dose-response relationships for inhaled ambient particles.

Research Need 35(A)

- **Epidemiological studies on effects of long-term exposure to respirable particulate matter including prospective studies with precise assessment of exposures and health outcomes as well as retrospective studies with estimation of past exposures.**

When designing new studies, or when proceeding with re-analysis or meta-analysis of existing studies, high priority should be given to susceptible populations for different respiratory responses (biological endpoints), and to concurrent pollutants.

2.6.5 Risk characterisation

Risk characterisation aims to describe the nature and magnitude of the problem and to determine how many people are affected by specific health effects due to PM exposure. Classically, ambient levels have been compared to established No-Observed-Adverse-Effect-Levels (NOAELs) or sometimes Lowest-Observed-Adverse-Effect-Levels (LOAELs). Impact of exposure was defined by the length of time that levels were in excess of a set of standards derived from a NOAEL or LOAEL. It was however been established only recently that 24-hour mean PM level fluctuations are associated with health consequences such as increased daily mortality, hospital admissions, respiratory symptoms and decreased pulmonary function. For instance, in Concern for Europe's Tomorrow it was estimated that in European cities for which TSP data were available 29 million people (95%) experienced levels exceeding 120 mg/m^3 (24 hours average), at which level 30 to 50% increases in morbidity can be expected. The biological plausibility of some of these health consequences has been reinforced by experimental evidence, indicating that concentration-response relations may provide estimations of the number of affected humans in a population or subgroup of that population.

Key issues in such risk characterisation are biological plausibility, shape of the concentration-response curve and whether it is possible to extrapolate observations from some studies on PM ith certain properties to other situations where risk characterisation is desired but not studied. However, risk characterisation for PM is complicated: PM cannot be considered a single pollutant with well-defined sources; it is a complex mixture of particles with different physical and/or chemical properties originating from natural or anthropogenic sources.

Furthermore, adverse effects cover a variety of reversible and irreversible effects. In addition to these complications comparison of various health effects may be cumbersome and assessment complicated even more if these effects are compared to supposed benefits linked to emissions of particulates. An approach to this problem is described in the Risk Management section, in which aspects like quality-of-life reduction or loss of healthy life-years are discussed along with the need for aggregating indicators to improve the comparison of different types of health impacts in quantifiable monetary units. Another aggregation method is that of Disability Adjusted Life Years (DALY), in which factors are discounted due a reduced ability to perform daily activities independently.

Research needs related to PM risk characterisation are:

Research Need 36(B)

- **Formulation of a set of policy scenarios for PM and its public health impact for public evaluation. This may include:**

– Design and application of databases of specific exposure-response relationships for source-specific PM exposures and specific health endpoints.

– Formulation of a core set of meaningful health impact indicators and estimation of these indicators using existing information.

– Design and application of aggregation protocols for diverse health effects of PM.

– Consultations and Delphi studies to address possible aggregation approaches.

– Surveys and focus group discussions of public and stakeholders' assessments of the monetary costs of health effects (e.g. willingness to pay) and reduced quality-of-life aspects of various health endpoints.

– Application of monetary and disability-discount factors to the PM information base and one or more other environmental stress factors.

– Concerted action of experts and policy makers to develop PM environmental policy scenarios with their potential costs and potential benefits.

– Surveys and focus group discussions to evaluate dimensions and determinants of acceptability for different scenarios.

2.6.6 Risk management

High priority has been given to research needs identified in the preceding sections since they provide the information needed by policy-makers when deciding on appropriate measures for abatement. The information needs of the risk manager are met by questions on release and exposure consequences, effect assessment and risk characterisation.

Nevertheless, there are still some specific questions which do not follow directly from the discussions and findings mentioned above. For example, not enough is known about the critical fraction, risk groups, health effects and their consequences. Epidemiological and experimental studies need to be designed to answer these question; results should be evaluated in a multi-disciplinary context in order to ensure sufficient input from other disciplines for modelling and validation.

Overarching priorities, which are also pertinent in risk management were discussed in the first part of this section on ambient air particulates. In terms of risk management the following priorities ought to be added to the platform; they have consequences for the structure, process and preparation of the research agenda:

– To ensure optimal compatibility of various research activities regarding release, exposure, effect assessment and risk characterisation.

– To develop a coherent and comprehensive Decision Support System incorporating research findings and allowing systematic evaluation of the efficiency of abatement policies.

In addition, a risk management perspective should include the following research needs:

Research Need 37(C)

● **Formulate a meaningful set of health impact indicators for describing the scope/extent of the PM problem. This set should ideally also be used to describe, compare and prioritise other environment and health problems:**

– Develop and apply concepts such as "disability-adjusted-life-years" (DALY) for environmental health impacts.

– Develop and apply monetary validation of health impact indicators.

– Develop cost-benefit analyses to compare cost-effectiveness of abatement policies.

Research Need 38(C)

● **Evaluate efficacy of previous and current regulatory approaches in terms of public health gain.**

Research Need 39(C)

● **Evaluate risk management in different economic growth scenarios for cost-benefit and public health gain.**

2.7 Indoor air quality and health

Indoor air quality is an important public health issue.

– Indoor pollution may lead to high exposures.
– Pollutants exclusively generated outdoors may significantly contribute to indoor exposure.
– Individuals spend the major part of their time indoors, in particular in developed countries.

Time spent outdoors for most individuals is no more than 5%. Of the remaining time approximately 70% is spent at home; the rest is spent in other micro-environments such as workplace, school, shops and transport. The workshop report "Indoor Air Quality and Health" (http://www.esf.org/mp/ENHEb.htm) focussed on the home environment since most time is spent there and many specific sources of air pollution may be found there.

Problems associated with the home environment arise from physical, chemical or biological agents. Many reports and publications have reviewed health problems associated with indoor pollution.

The specific features of the indoor environment are temperature and humidity. When technical and financial means are inadequate humans may suffer from extremes of either, especially subgroups compromised by diseases which make them susceptible to changes in these variables. Increased energy-saving measures in homes with reduced ventilation may make this problem more acute. A special physical problem is that of radon gas emanating from soil and building materials, and thought to be a significant environmental cause of lung cancer. Exposure levels vary widely between countries and localities.

Chemical air pollution is evidently abundant in homes and originates from non-vented combustion appliances, smoking, furniture, carpets and building materials. Although smoking should not be overlooked as an important source, non-vented combustion appliances are major contributors to the sometimes high concentrations of nitrogen dioxide and, depending on the source, carbon monoxide and polycyclic aromatic hydrocarbons found in homes. Environmental tobacco smoke (ETS) has been implicated in several health problems such as lung cancer, respiratory diseases, cardiovascular diseases, reduced lung function in children and the Sudden Infant Death Syndrome (SIDS). Similarly, evaporating building materials such as formaldehyde or other volatile organic components may produce chronic irritation, annoyance and complaints about odour.

Biological pollution may be the most important factor; it is the least understood. Dust mites produce major allergens thought to play an important role in the causation and aggravation of asthma. For fungi and bacteria no convincing association has been established between exposure and (respiratory) diseases. The possible role of mould cell wall components (glucans) and bacterial endotoxins as inflammatory agents and adjuvant factors in the aggravation of mite allergy-induced asthma has yet to be elucidated.

House dampness, an increasing problem due to the tendency to build increasingly airtight homes may worsen biological pollution.

The role of house pets in biological pollution is not sufficiently understood. Increasing pet ownership in the future may worsen this problem.

When dealing with indoor air pollution one should be aware of the major influence lifestyle and cultural and psychological factors play in the occurrence of indoor-related diseases. This has become specifically apparent in the gradients found in Eastern and Western European countries.

For priority setting of research needs for indoor air pollution the following criteria were applied: (1) proportion of the population affected, (2) severity of the problem, (3) contribution to sustainable solutions of the problem, (4) pan-European added value, and (5) interdisciplinary approach.

The research needs are stated below as they occur in the causality chain.

2.7.1 Overarching priority related to indoor air

– Under the guidance of the network organisation (see Introduction, page 11) a European interdisciplinary consultation and concerted action should be implemented

2.7.2 Release assessment

The major sources of indoor environmental pollution have been insufficiently quantified.

Research Need 40(A)

- **Development of quantitative methods or models for apportionment of sources in indoor and outdoor air to enable exposure to be limited to sources (see also 32A).**

2.7.3 Exposure assessment

Exposure to harmful indoor environmental factors is inadequately characterised and does not allow reliable health risk assessment.

Research Need 41(A)

- **Characterisation of indoor air factors associated with prioritised health risks through a European wide monitoring network. This may include:**

– Development and standardisation of methods for exposure assessment in the indoor air.

– Development of monitoring technologies and protocols.

Research Need 42(A)

- **Development of proxy exposure variables and innovative strategies aimed at collecting reliable exposure information on chemical and physical factors, bearing in mind that each home constitutes to a certain extent a unique environment.**

2.7.4 Effect assessment

The increasing prevalence of childhood allergy and asthma in many European regions is of great concern and cannot be explained adequately. Various indoor air pollutants may be important contributing factors or causes. Moreover, the health risks of indoor exposure to volatile and semi- or non-volatile organic solvents are poorly defined (i.e. complexity of mixtures and physical or psychological effects on the central nervous system). The relative importance of biological and chemical indoor pollutants in the occurrence of allergy and asthma in human childhood ought therefore to be investigated.

Research Need 43(A)

- **To establish the role of indoor environments in the causation of allergy and asthma, and to elucidate possible interactions between individual susceptibility and exposure to indoor pollutants in relation to allergy including asthma.**

Research Need 44(A)

- **To establish the impact of mould exposure on health problems through non-allergic mechanisms.**

Research Need 45(A)

- **To establish the impact of chemical indoor air pollutants and physical factors on human health and well-being (i.e. whether effects seen in laboratory experiments can be reproduced in field studies).**

2.7.5 Risk characterisation

Since exposure assessment and effect assessment in indoor air quality is as yet poorly developed, risk characterisation is not a short-term option. However, when information becomes available in the years to come, the overarching network organisation may define research needs in order to facilitate risk characterisation, particularly quantitatively, and to integrate risk characterisation in a general framework for applying monetary and disability discount factors.

2.7.6 Risk management

In the area of indoor air risk management greater information-gathering is likely to produce many more questions. Nevertheless, some risk management measures may already be opportune. This applies particularly to new housing developments and renovation cycles for housing stock in Europe. Renovation and new house construction offer ample opportunities for the creation of healthier indoor environments: measures should be implemented systematically rather than haphazardly as is presently the case:

Research Need 46(C)

- **To develop an integrated system by which existing and newly generated knowledge about indoor environmental problems and their solutions are included in building, construction and renovation codes and practices in Europe.**

2.8 Water quality and drinking water

It is well recognised that availability of water in quantity and of sufficient quality is a necessity for human survival, health protection, and social and economic development. Europe is one of the most populated regions in the world, having a great need for water as well as being a source of many activities that may cause water pollution.

Micro-biological diseases are still transmitted in certain areas, in particular via drinking water and on recreational exposure to surface water. Moreover, because of limited ground water resources the use of surface water is bound to increase in the production of drinking water. This will lead to increased infectious pressure from micro-biological contaminants such as viruses, protozoa and bacteria.

Urban, agricultural and industrial systems interact with their immediate environment and may involve the release of treated or untreated effluents, gaseous emissions, fertilisers and other agricultural chemicals. All these substances may potentially alter the quality of natural water making it less suitable or, indeed, unsuitable for recreational use or consumption.

The need for water, particularly in a densely populated continent like Europe, is expected to increase, leading to pressures on water resources and their allocation. Competing demand will require increasingly sophisticated water management, not only at a national but also at supranational level. Furthermore, pressure on water resources interacts with the need to maintain aquatic ecosystems of adequate quality, a prerequisite for beneficial use.

Apart from anthropogenic contamination of water natural conditions may also make water unsuitable for different uses without extensive and costly treatment. However, such naturally occurring problems, e.g. ground water contamination with high levels of arsenic in the border area of Hungary and Romania, are of regional importance and affect a relatively limited population compared to anthropogenic sources.

In the field of water quality and drinking water ongoing research will also supply key data which will serve as a basis for improving various technical, economical and managerial instruments in order to ensure effective water management and resource allocation. However, water management and by implication water sector research has been reactive rather than proactive. It is important to note that water sector prevention is undoubtedly better than cure, since avoidance of potential harm is beneficial not only for human health and well-being but also for ecological quality. In most cases it is also much more cost-effective.

This section describes research needs for water quality and drinking water on the basis of the report of a scientific workshop (http://www.esf.org/mp/ENHEb.htm). Research needs are centred on human health and well-being, and usually concern direct links although some are more indirectly related to human health and well-being. Research questions are grouped according to the risk assessment scheme. Nevertheless, some overarching priorities can be outlined, and should be considered a prerequisite for an effective and efficient response to research questions, avoiding unnecessary duplication and coordinating complementary activities in a concerted manner.

2.8.1 Overarching research needs priorities in the area of water quality and drinking water

Water-related sustainable improvements in the field of human health and well-being can only be made through a multi-disciplinary integrated approach designed to ensure an integrated resource and quality management policy in a sustainable environment. Likewise, significant progress in research can only be made through interdisciplinary interaction between specialists in the different scientific fields with a role in water quality and drinking water. The creation of an interdisciplinary network organisation of European researchers and policy-makers on water quality and drinking water under this platform (see Introduction, page 3) would greatly facilitate co-ordination and integration of research into the various facets of the risk assessment scheme: release, exposure and effect assessment, risk characterisation and risk management.

Additonal overarching priorities are:
– To produce an inventory of experience in European countries on successful interagency co-operation and inter-sector water policy management and implementation.
– To develop target standards (guidelines) in a common, harmonised setting which characterise the health risk at each stage of the water cycle and include other key compartments.
– To evaluate the water quality and drinking water programme and its projects before and during execution.
– To promote a better geographic distribution of research capacity throughout Europe.

2.8.2 Release assessment

Contamination occurs due to effluent, waste and deposition of anthropogenic sources and natural sources in surface water and groundwater. Most of these hazardous pollutants arise from various human sources, both point and non-point, and may reach receptors such as humans and aqueous ecosystems in different ways.

There are three known groups of pollutants: (micro)biological, chemical and physical pollutants, of which the latter are relatively unimportant. Chemical pollutants originate from the use of chemicals of which over 100,000 are marketed and used in Europe alone. A substantial number (over 2,000) are used in large quantities of over 1,000 tonnes per year. Direct discharge into water or indirect contamination due to interactions of water with other media (polluted soils and air through deposition or contamination of rain water) are the main routes of contamination. Monitoring programmes are currently in operation in a number of countries. A lack of co-ordination in their design and in meaningful data acquisition prohibits effective data gathering and realistic modelling exercises.

Research needs in release assessment are:

Research Need 47(A)

- **Development of tools which are better able to identify the importance of different sources, both quantitatively and qualitatively, using cross-sectional model linkage tools which can demonstrate anthropogenic, biotic and abiotic catchment influences.**

Research Need 48(B)

- **Design of risk-driven monitoring programmes for integration of relevant data in order to understand and control releases.**

Research Need 49(B)

- **Investigate the potential use of economically efficient closed systems in direct or indirect recycling of water and domestic wastes within and around human settlements.**

2.8.3 Exposure assessment

Although a considerable research effort has been devoted to understanding pollutant pathways, there are still gaps in our knowledge. In chemical exposure, indirect pollutant pathways involving other media (soil, atmosphere) and the food chain are complex and poorly understood. Compartments previously considered to be terminal sinks are now recognised to be pollutant sources. This is complicated by the large number of pollutants, the need to understand short- and long-term impacts of exposure to individual substances and chemical combinations, and our poor ability to predict water pollution problems in the future. Finally, persistence of many chemicals and their metabolites under aerobic and anaerobic conditions is not adequately understood at present. Estimation methodologies such as quantitative structure activity relationship (QSAR) biokinetics and biodynamic data may provide tools for estimating effect levels more precisely.

Exposure to micro-biological agents is the major human health problem. Ecological changes have created new vector niches for (pathogenic) micro-biological agents. Rapid changes in technology and industry also create new health hazards, through possible contamination with microbes entering the aquatic systems. Human behaviour and transport of foods and people are major reasons for the spread of infectious diseases, especially in regions with poor hygienic conditions or subject to large-scale conflicts. A large number of microbial agents including bacteria, viruses and protozoa have been identified as causing disease in man; most have been detected in water sources and are thus potential waterborne pathogens. Two priority issues have been addressed to understand exposure better: (1) quantitative detection of relevant waterborne pathogens, and (2) development of surveillance systems in order to guarantee rapid responses to outbreaks and appropriate remedial actions, and also to evaluate trends and developments in pathogen occurrence.

In addition to generic research needs in chemical exposure assessment as mentioned in Section 2.11, research needs on exposure assessment are:

Research Need 50(A)

- **Development of quantitative detection methods for all relevant waterborne pathogens.**

– To help in risk assessment these methods should yield quantitative information on the occurrence of viable micro-organisms that are infectious in humans; they should be clearly differentiated from non-viable and non-pathogenic strains and from strains of insufficient virulence to affect humans.

Research Need 51(A)

- **Development of predictive models of microbial pollution at local levels and development of adequate surveillance systems to enable a rapid response to outbreak and evaluation of trends and new developments.**

– Such activities should be integrated within broad infectious disease surveillance systems.

Research Need 52(A)

- **Research on sources and pathways of chemical pollutants in order to allow quantitative prediction or modelling of environmental distribution and fate. This should include transmedial and transboundary movements.**

2.8.4 Effect assessment

Chemical and microbial effect assessment methodologies are required for risk characterisation. Effects of microbial contamination of water are usually correctly identified, especially in regions where hygienic measures fail due to political and economic instability. Recent outbreaks of cholera in Eastern Europe, typhoid in Tadzjikistan, dysentery and infectious hepatitis in large parts of Europe and Russia as well as the continuous threat of Giardia lamblia to drinking water safety in many industrialised countries are a few examples.

Many newly recognised waterborne pathogens such as viruses and protozoa continue to be a threat to health. Viruses mainly cause diarrhoeal episodes in children, although others affect adults, e.g. the Small Round-Structured viruses (SRV) and hepatitis E viruses. The latter has recently been identified as the cause of major outbreaks in south-east Africa and other parts of the world. Bacterial waterborne pathogens may be divided into faecal pathogens of which Campylobacter jejuni is the most important: 10 to 20% of all cases of gastroenteritis in Europe are attributable to this organism, and water-based outbreaks are frequently recorded. Another group of bacteria is able to multiply in drinking water after treatment, e.g. Legionella. A third group is that of the cyanobacteria, which can be found in well water. Though non-infectious in humans, they may produce harmful toxins. The most notable protozoan is Cryptosporichium parvum which has caused outbreaks of illness in Europe and the USA. The high resistance of protozoa to natural inactivation and disinfection makes them the most important waterborne pathogens in virtually all countries relying on piped supplies.

The impact of waterborne pathogens on public health is difficult to establish. Outbreaks are usually only detected once they are relatively large. There are also reasons for assuming that the problem is underreported. A cohort study of two comparative groups receiving the same tap water which met all microbial standards, in which one group received the tap water after ultrafiltration, showed a 10 to 30% rise in gastroenteritis in the group receiving the non-ultrafiltrated tap water. Epidemiological studies may be able to quantify the impact of low level transmission. Solid quantitative effect data are not available and prohibit appropriate quantitative effect assessment and modelling.

The effects of chemical contaminants on health is known to a limited extent for a limited number of chemicals. Approximately 2500 chemicals among those officially registered are classified as dangerous but this potential harm is insufficiently known. Experimental data in animals provide some information about potential effects, although allergic and more subtle endocrine and central nervous system effects would not be detectable with present methodologies.

The general approach when setting limit values for avoidance of adverse chemical effects has been shown to be appropriate. For "non-threshold" chemicals (in general mutagenic chemicals and genotoxic carcinogens) quantitative low-dose extrapolations are used to establish levels of no appreciable risk.

Particular attention has been given to the possible health effects of chemical products which are produced following water disinfection e.g. chlorination. These by-products are usually present at very low concentrations. Trihalomethane and haloacetic acids are by-products present in the greatest concentration. Numerous epidemiological studies have investigated whether by-products in chlorinated drinking water are a threat to health. No causal link with disease (bladder and rectal cancer) has been established although a meta-analysis indicated a possible association, with a relatively small increased risk. It seems unlikely that new studies will provide a definite answer since by-product levels have been reduced by improved treatment methods.

Finally, not enough is known about the effect on human health and well-being if water availability is limited, or allocation unequal. The growing demand for water, including drinking water, may require research in this area.

In addition to generic research needs (see Section 2.11), research needs on effect assessment related to water quality and drinking water may include:

Research Need 53(A)

- **Epidemiological studies to identify the impact of background transmission of water-borne pathogens on health in order to establish the role of water in the general transmission of infectious diseases.**

Research Need 54(B)

- **Research to determine the implications for human health and well-being of drinking water availability as a result of limited resources, unequal allocation and market forces, and research on the implications for human health and well-being if the current trend of groundwater pollution and deterioration continues.**

2.8.5 Risk characterisation

Risk characterisation is feasible in qualitative terms when exposure and possible health effect data are known. For chemicals, limit values are usually established to provide "zero effect" levels and to avoid adverse effects. However, quantitative risk characterisation for chemicals can only be made when reliable quantitative exposure data and quantitative effect data are available. Development of exposure assessment and effect assessment methods will therefore provide a future means for appropriate risk characterisation in relation to chemical contamination of water.

Likewise, the aim of microbial risk characterisation is to estimate the likelihood and, ideally, severity of potential adverse health effects in a given population. The accuracy of the parameters used in such an estimate is of key importance, along with uncertainty analysis and validation of methodologies and models used. Chemical risk characterisation has to be taken into account in microbial risk characterisation and vice versa. Chemical disinfection to reduce the number of microbial pathogens may introduce toxic chemicals. Integrated risk characterisation may therefore define the conditions for optimal water treatment.

In addition to generic research needs on chemical risk characterisation, a research need in risk characterisation related to water quality and drinking water is:

Research Need 55(B)

- **Development of quantitative risk characterisation methodologies for infectious agents and algal toxins by improving uncertainty analysis and probability distributions using appropriate mathematical and statistical methods.**

2.8.6 Risk management

Research questions raised as separate aspects of the total risk assessment process will - when translated into research and findings - provide opportunities for policy-makers to consider prevention and intervention management. Sound management principles can only be applied if based on reliable data. Several research questions are depicted which provide policy support. Answers to these questions will enable preventive and/or remedial actions to improve the quality of surface, ground and drinking water and development of appropriate decision support systems.

Research needs in risk management:

Research Need 56(C)

- **An inventory of existing systems and their principal characteristics should be made for control of water abstraction and allocation among stakeholders and users. This may include:**

– Trends and changes in these systems in Europe should be evaluated. Long-term alternatives and implications for human health and well-being should be assessed.

– Can health concerns and evaluation of well-being be integrated into an overall scheme or system for aquatic ecosystem protection?

– Investigations into interactions between and consequences of increased reliance on market forces for management of drinking water supply and water resource systems.

– How can we increase understanding of the processes underlying behavioural changes in “affected” and “target” groups, addressing both agents of change and processes occurring in individual and (social) groups?

– Measures and actions that may facilitate and encourage adoption of improved agricultural and agronomical practices.

– Which existing socio-economic tools could encourage more efficient and careful use of water?

Research Need 57(C)

- **Investigate the possibility of integrating *a priori* resource and source protection, thereby limiting current and potential risks in the absence of environmental and health outcome data.**

Research Need 58(C)

- **Development of models for microbial water quality as a management tool.**

– Setting microbial standards for recreational water, shellfish water and irrigation: what is their potential effect on public health, and what are the costs to society?

Research Need 59(C)

- **Development of alternatives to the use of water bodies as vehicles for waste transport, "treatment" and disposal and consequences of their use.**

Research Need 60(C)

- **Development of real-time and predictive data acquisition systems for direct management.**

2.9 Endocrine disruptors: a threat to human health?

2.9.1 Introduction

In the early 1990s considerable concern arose about the possible threat of environmental man-made chemicals due to their endocrine disrupting properties. An endocrine disrupting substance (EDS) can be defined as an exogenous substance that causes adverse health effects in an intact organism or its progeny, as a consequence of changes in endocrine functions. Several national agencies have reviewed the issue in recent years, and in December 1996 a European workshop was organised by the European Commission, the European Environment Agency, WHO-ECEH, OECD, national departments of the UK, Germany, Sweden, the Industrial Chemical Industry Council (CEFIC) and the Institute for Environment and Health (Leicester, UK) (European Workshop on the Impact of Endocrine Disruptors on Human Health and Wildlife. Report Proceedings, 2-4 December 1996, Weybridge, UK). The aim was to examine data critically, to summarise current knowledge on health trends for humans and wildlife and to define research and monitoring recommendations on these issues. Xenoestrogens considered were synthetic hormones, phytoestrogens, organochlorine pesticides, poly-chlorinated biphenyls, dioxins, alkylphenols, polyethoxylates and other chemical classes of concern.

Adverse health trends affecting the reproductive organs of both men and women have been observed. In the past decades the incidence of testicular cancer has increased quite dramatically in a number of countries, as has the incidence of breast and prostate cancer. While at least some of the increase can be explained by improved reporting and diagnosis it seems – particularly for testicular and breast cancer – that there is a genuine rise in incidence. Semen quality may have declined, and the incidence of undescended testes and hypospadias appears to have increased (there is a biological association between these disorders and testicular cancer).

The causes of these adverse trends affecting aspects of reproductive health are largely unknown. Since they have occurred in the last two generations, parallel to changes in the environment (including lifestyle), it has been suggested that man-made chemicals might be responsible. This suggestion finds some support from findings which indicate that some cases occur in areas of Europe where adverse endocrine effects or reproductive toxicity coincide with high levels of exogenous chemicals known to have endocrine disrupting properties in specific test systems.

However, our present knowledge of environmental chemicals in relation to reproduction is limited and there is a need for further exploration. On the basis of the available data the European workshop concluded that:

– There is sufficient to indicate that the increase in human testicular cancer is real.

– The apparent decline in sperm counts in some areas is not easily explained by known (confounding) variables.

– Data and studies are inadequate do not allow assessment of whether changes in female reproductive health other than breast cancer are indeed occurring.

– Not enough is known about the exposure of humans to possible and known endocrine disrupting substances.

To determine whether there may be a relationship between environmental and/or naturally occurring EDS and adverse human reproductive health effects, the European workshop participants recommended research activities in the field of human epidemiology, including mechanisms and models, methodology and exposure. Outstanding research questions also relate to wildlife. Research questions in the risk assessment framework are described below; those relating to wildlife are only included if they are relevant to human health effects.

2.9.2 Release and exposure assessment

An integrated strategy for monitoring of chemicals in the environment which concentrates on substances with an ED-potential is a prerequisite for effective exposure assessment. This could be achieved though integrating human and wildlife epidemiological and/or field studies. Currently available data should be put to optimal use. Development of specimen banks of human and wildlife samples would facilitate the process. The following research questions were formulated:

Research Need 61(A)

- **To conduct effect-driven studies into exposure assessment in humans comprising epidemiological (including case control) studies linked to evaluation of exposure and other lifestyle factors at critical life stages. This may include:**

– Development of biomarkers which predict the impact on reproductive effectiveness.

Research Need 62(B)

- **Development of a European-wide strategy for monitoring EDS.**

– Focus should be put on substances known to be active *in vivo.* Monitoring should include data on effects, external and internal exposure and key pathways. Data should be harmonised and included in a uniform database such as the International Uniform Chemical Information Database (IUCLID).

2.9.3 Effect assessment

Hazard identification as well as increased knowledge about dose-response relationships are the tools required for effect assessment. Research into this area may comprise epidemiological, animal models, mechanistic studies and methodology.

Research needs in the area of human epidemiology are:

Research Need 63(A)

- **Continuation of current (pan-European) investigations into known changes in reproductive health, focusing on the establishment of baseline measurements, geographical differences and areas of uncertainty. This may include:**

– Establishment of harmonised standards for measuring relevant endpoints when inter-laboratory studies indicate that regional comparison cannot be conducted.

Research Need 64(A)

- **Cohort studies on reproductive health in cohorts with different general exposure to pollutants, industrial chemicals and/or naturally occurring EDS.**

– Lifestyle-related factors, including dietary and socio-cultural differences should be included.

– Focus should be on established EDS, using *in vivo* animal studies and high exposures.

– Pre- and post-natal exposure effects should be considered for readily measurable endpoints.

– Collection of body fluid and tissue samples should be considered for current and future analysis.

– Follow-up epidemiological studies to examine the effects of reduction of exposure to EDS expected to be relevant to human reproductive health.

Research needs in animal models and mechanistic studies are:

Research Need 65(A)

- **Development and validation of animal models relevant to human testicular cancer and testicular descent. Validation of current animal models with particular focus on human relevance.**

Research Need 66(A)

- **Extension of basic knowledge of hormonal systems and their role in pathophysiological conditions. This may include:**

– Basic research into mechanisms of testicular descent, hypospadias and polycystic ovaries in humans e.g. investigating the similar aetiology of persistent oestrus in rodents and polycystic ovaries in humans; identification of non-hormonal pathways; development of non- or minimally-invasive biomarkers associated with endocrine functions and disruption (i.e. testicular and ovarian function) and establishment of their cross-species consistency and predictability.

– Development of techniques to study neuro-developmental and / or neuro-behavioural effects in animal and human systems.

Methodological research needs:

Research Need 67(A)

- **To prioritise and integrate structure activity relationship (SAR) development in association with new data acquisition.**

Research Need 68(A)

- **To develop and validate *in vitro* assays predictive of changes in hormone function, biosynthesis and degradation in whole organisms. This may include:**

– Investigations into the predictive value of measurements in exposed parents for neonates and weanlings.

– Investigations into the existence of a hierarchy of sensitivities for relevant biomarkers in mammals, birds, fish and invertebrates for a set of relevant standard chemicals.

2.9.4 Risk characterisation

Research Need 69(B)

- **Improvement of risk assessment methodology taking into account possible interactive effects of multiple exposures.**

2.9.5 Risk management

Research Need 70(C)

- **Studies into the cost and effectiveness of reducing exposure to recognised EDS in relation to health / quality of life gain.**

2.10 Assessment of human health effects of immunotoxic agents in the environment

2.10.1 Introduction

Humans are exposed to a variety of agents in the environment through the skin, respiratory system and alimentary tract that can potentially modulate the immune system. Agents include industrial chemicals, pesticides, air pollutants, natural toxicants and ionising and non-ionising radiation, including UV. Chemicals may act as antigens, causing an immune response which triggers skin, respiratory tract, or alimentary tract allergies. In addition, chemicals may directly affect immune system function thereby modulating immune responses to antigens unrelated to chemicals, such as antigens derived from microbial agents.

Chemicals known to modulate the immune response through various mechanisms in animals include pesticides, organochlorines, organophosphates, carbamates, dithiocarbamates, pyrethroids, metals, metallic salts and organometals, solvents, halogenated aromatic hydrocarbons, nitrosamines, hormones, polycyclic aromatic hydrocarbons, gases such as nitrodioxide and ozone, mycotoxins and addictive substances.

In addition, a number of immuno-suppressants such as anti-inflammatory agents, antibiotics, tranquillisers, anti-depressents, analgesics and anti-epileptics are known to share these properties.

In the environment, exposure to immune modulating substances generally occurs at low levels, and involves mixed susbtances and different routes of entry. To investigate possible effects on human health it is of prime importance that accurate exposure assessment techniques and validated biomarkers are available. Specifically designed longitudinal epidemiological studies with valid measures of exposure, confounding and health endpoints may determine whether long-term low-level exposure to a mixture of immuno-modulating substances poses a risk. The most valuable biological measures when studying the effects of exposure on hypersensitivity responses are the skin prick test, the antigen-specific IgE enzyme-linked immuno-sorbent assay (ELISA) and the radio-allergo-sorbent test (RAST). For changes in immune function measurement of vaccination responses to a neo-antigen may be useful.

The symposium report which can be consulted at http://www.esf.org states that studies as described above are required in order to obtain a sufficiently reliable assessment of the potential risk of exposure to environmental immunotoxic substances.

Allergic reactions following exposure to airborne or alimentary materials/chemicals are common health problems. Predictive models of contact allergy exist in the guinea pig, mouse and humans. There is substantial evidence that these methods, when performed correctly, are adequate for hazard identification. Models of respiratory allergy that identify protein allergens are less well-defined and are usually based on assessment of anaphylactic antibody induction. Predictive tests for the identification of chemical respiratory allergens have been proposed and rely on measurement of immune activation and/or respiratory reactions. However, the utility of these tests have not yet been validated.

There is a need for methods that will allow accurate identification of chemicals and proteins causing allergic sensitisation of the respiratory tract. Similar methods should also be developed for oral exposure.

The proposed research needs are described below.

2.10.2 Research needs

Research Need 71(A)

- **Development of methods to assess the allergenicity of chemicals and genetically modified foods by the inhalational and oral routes. Development of a European consensus, based on such methods, for assessing the allergenicity of genetically modified foods.**

Research Need 72(A)

- **Development of biomarkers of immunotoxicity (stimulation or suppression). Such biomarkers may include vaccination titres against new antigens, where prior knowledge of determinants is required.**

It is recommemded that ongoing longitudinal prospective cohort studies in children should include infectious diseases triggered by environmental factors.

Research Need 73(A)

- **Occupational cohort studies to defined mixtures of immunotoxicants.**

– Such studies may include comparisons of groups occupationally exposed to immuno-toxicants, and similar occupational groups not exposed to immunotoxic chemicals using endpoints such as infections, allergies and cancer in addition to function tests such as IgE titres and vaccination titres.

– Results of these studies may show that epidemiological studies are required in exposed sub-sets of the general population exposed to immunotoxicants.

Research Need 74(A)

- **Multi-centre collaborative studies in several countries with different exposure patterns to immunotoxic agents such as mycotoxins.**

– Studies should involve Western European countries as well as CCEE and NIS countries.

2.11 Chemical risk assessment and related toxicological issues

2.11.1 Introduction

In an exploratory workshop on Emerging Issues in Toxicology organised by the ESF a number of research priorities were proposed which are relevant to the ENHE Programme. This section deals with research needs for generic issue chemical risk assessment as well as with prioritised research needs for the following two specific issues: (1) genetic susceptibility to environmental contaminants, and (2) the containment of the spread of resistance to microbials.

As indicated in the introduction to the ENHE Programme (page 4) quantitative risk assessment (QRA) is of prime importance to policy makers since it provides a means of quantifying risks and allowing risk prediction. Until recently, risk assessment methodologies were based on conventional toxicity testing with single compounds given at high doses to experimental animals in order to provoke adverse effects and establish no observed adverse effect levels (NOAELs).

On the basis of the established NOAEL, acceptable human daily intakes were calculated using a safety/uncertainty factor in a worst-case approach, assuming that humans may be approximately 100 times more sensitive than experimental animals. Exposure levels for humans should be below the calculated ADI.

In recent years, more detailed information has become available about on-site exposure and the nature of effects. Improved efforts to assess exposure quantitatively and establish dose-response relationships for chemicals have been especially important in finetuning risk characterisation including quantitative risk characterisation. Key issues to be addressed are outlined below.

2.11.2 Release and exposure assessment

Chemicals from various sources released into the environment are subject to transport, degradation, metabolism and distribution patterns. Proper understanding of the environmental fate and distribution of chemicals and their bioavailability in organisms including humans should allow appropriate quantitative exposure assessment. Accurate, high-quality exposure data are the keystone for scientifically based QRA.

To achieve this goal the following aspects have to be addressed:

Research Need 75(A)

- **Development of emission scenarios for appropriate substance categories with integration, where relevant, of different compartments. This may include:**

– Development of predictive tools for assessing the fate, interactions and distribution of chemicals in relevant compartments including determinants of bioavailability and duration of exposure.

Research Need 76(A)

- **Improvement of external and internal exposure assessment including modelling.**

– Research should include better characterisation of actual exposures, bioavailability and duration of exposure. This will be dependent upon the development of biomarkers of exposure.

2.11.3 Effect assessment

Adverse effects induced by substances or their metabolites result from the absorption, distribution, metabolism and excretion (ADME) of such substances. Advanced techniques to predict absorption and distribution have been developed. Such models attempt to provide an accurate description of the distribution of the substance and/or its metabolites in the body and to determine the internal dose at the target organ or tissue. Best known are the physiologically based biokinetic models (PBBK). Relationships between tissue dose (internal dose) and toxic response are described as biodynamics. Physiologically based biodynamic models (PBBD) are much less well developed than PBBK, primarily due to the limited understanding of the biochemical mechanisms which link tissue dose to toxic effect. Improvement of PBBD and PBBK models will considerably reduce uncertainties in quantitative risk assessment.

Research needs in effect assessment are:

Research Need 77(A)

- **To improve the methodologies of chemical effect assessment in order to reduce uncertainties in risk quantification.**

– Development of models on uptake, distribution, metabolism and excretion of chemicals. Such studies should include *in vitro* and *in vivo* comparisons to improve prediction and, where possible, reduce animal use.

– Development of biomarkers of effect (such as mutation spectra) for defined endpoints.

– Understanding of the mechanisms which lead to detrimental effects.

2.11.4 Risk characterisation

Risk characterisation aims to describe the nature and magnitude of adverse effects, and to determine in quantitative terms how many humans will be affected at a given exposure. Results of exposure assessment are therefore correlated to effect assessment data in order to characterise probable risk, ideally in quantitative terms.

Since effect assessment for chemicals predominantly derives from animal experimentation, data has to be extrapolated to humans. This is accompanied by a degree of uncertainty. However, species extrapolation based on PBBK and PBBD will provide estimates that are better than conventional methods. In risk characterisation for chemicals a distinction is made between genotoxic and non-genotoxic substances. While it is currently assumed for genotoxic substances that their action is a non-threshold phenomenon, it is generally agreed that there is a threshold for non-genotoxic substances. For genotoxic substances mathematical models (one hit, multi-hit, multi-stage) are used to extrapolate to low doses. For non-genotoxic substances quantitative information should be derived from dose-response relationships with appropriate species-to-species extrapolation.

In this field of risk characterisation research needs are:

Research Need 78(B)

- **Development of quantitative chemical risk characterisation based on experimental and human data with emphasis on estimating human variability in response to chemical exposure.**

– Improvement in species-to-species extrapolation, including dose-response derived quantitative estimation of the relationship between effect and exposure.

– Mechanistic studies into "potential" thresholds of activity.

– Identification of factors which modify human susceptibility to environmental toxicants and development of methods for measuring susceptibility to chemical exposure, which may help to identify "high risk" groups and sub-populations. Such studies should include determining the polymorphic distribution of proteins in multi-centre studies.

– Improved design and analysis of epidemiological studies taking into account the above factors.

2.11.5 Risk management

Risk management for environmental chemicals is a well-developed process. However, measures are highly dependent on risks involved. It is therefore imperative that risks for the environment and human health are clearly defined. The research needs mentioned above will allow more accurate risk assessment as a basis for future risk management.

2.11.6 Genetic susceptibility to environmental toxicants

Environmental toxicants play an important role in the aetiology of many chronic diseases by influencing important physiological processes or modifying genetic information. The biological effect of a toxicant depends on the concentration of active metabolite in the target tissues. This concentration is in part determined by the activity of biotransformation enzymes, e.g. members of the cytochrome P_{450} and glutathione S-transferase families.

Increasingly, data suggests that there may be considerable inter-species differences in the activity of such physiological processes due to genetic polymorphism. Polymorphism modifies toxicant effects and since variant genetic traits are quite common (15 to 50%), this may have an important impact on human health. Although many genetic polymorphisms have been identified, the biological consequences of some remain unknown. Similarly, epidemiological studies to estimate risk associated with specific or combined genotypes are limited.

Most important chronic diseases of modern industrialised societies, including heart disease and cancer, are multi-factorial in origin: many environmental and genetic risk factors have been identified. Gene-environment interactions are of prime importance in individual susceptibility to developing specific diseases in response to environmental hazards. A large number of interacting factors contribute to an individual's risk for disease: among others, environmental exposures, genetic factors, diet, socio-economic status, age and gender. The intrinsic susceptibility of an individual can be altered by many factors including differences in absorption, distribution, metabolism and excretion of toxicants, repair of DNA damage, and changes in genes controlling cell growth and differentiation and their expression.

Recent understanding of the genetic basis of individual differences, metabolism and normal cellular defence raises new possibilities for studies into increased susceptibility to chronic conditions like cancer, Alzheimer's disease and neuro-degenerative disorders. Inclusion of susceptibility data will increase the power of epidemiological studies since populations can be stratified for genotypes of enzymes involved in relevant biological processes. Biomarkers of susceptibility may also contribute significantly to risk assessment methodology since they provide an understanding of the host factors which modify individual risk, and allow accurate estimations of increased risk for specific sub-populations.

This type of study should meet certain conditions. Firstly, the role of the phenotype/genotype in modifying human health risks resulting from environmental exposure can be properly assessed only if the population under study has been exposed in a well-characterised and documented way. Secondly, a biologically plausible hypothesis of how the phenotype or genotype may affect the biotransformation or disease processes under study is required. Thirdly, an understanding of how a genotype express itself at the phenotypic level in the target tissue is needed. There is a huge research potential for improving our understanding of gene-environment interactions and their role in human diseases.

Research needs in this specific area are:

Research Need 79(A)

- **Development of methodologies for the identification of "high risk" groups or sub-populations. This may include:**

– Establishment of criteria for proper study design and adequate methods of statistical analysis.

– Identification of sub-groups with different susceptibility, e.g. early onset of disease or especially sensitive to low exposure levels.

– Epidemiological studies of gene / gene and gene / environment interaction.

– Application of genetic markers for exposure and susceptibility.

– Determination of polymorphic distribution of proteins in multi-centre studies involving different European populations. To estimate population contributed risk imposed by a specific genotype or combination of genotypes.

Research Need 80(A)

- **Identification of the genetic basis for phenotypical expression of enzymes involved in the detoxification of environmental toxicants or in the protection of cells against endogenous or exogenous stress.**

– Model systems to understand toxic response, e.g. transgenic animal models.

– Functional significance of allelic variants in allowing an understanding of high risk individuals in the scientific context.

– Identification of new candidate genes - genetic models, linkage analysis.

Research Need 81(B)

- **Determination of polymorphic distribution of proteins in multi-centre studies involving different European populations as a means of justifying epidemiological meta-analysis for estimation of population-contributed risk imposed by a specific genotype or combination of genotypes.**

2.11.7 The need for a strategy to contain the spread of resistance to anti-microbial drugs

The advent of the antimicrobial era in medicine made most diseases of bacterial origin easily and reliably treatable. It soon became apparent, however, that bacteria could develop mechanisms of resistance against the antimicrobials to which they were formerly susceptible. Over the past 60 years the prevalence of resistant strains has increased, as has the level of resistance within some strains. The frequency with which resistant isolates are found in some serious human pathogens is presently increasing exponentially (78% of Salmonella typhimurium isolates were resistant to major antibiotic groups in a 1997 French survey). This phenomenon has led some authorities to speak of a postantibiotic era, i.e. one in which effective therapy with antibiotics is increasingly not an option. This is already the case in the USA with Vancomycin-resistant Enterococci (VRE). In Europe, VREs fortunately remain sensitive to other antibiotics, but some other organisms are showing increasing resistance (e.g. Mycobacterium tuberculosis, Salmonella typhimurium, E.coli, Staphylococcus aureus, Streptococcus pneumoniae).

In addition to those problems, which have arisen in part due to the frequent use and misuse of antibiotics in human medicine, there is now evidence of a more obscure but possibly more significant threat from the use of antimicrobials in animals, both in veterinary therapy and prophylaxis and in animal production. Annual tonnages used are often greater by several orders of magnitude than amounts used in humans, e.g. in 1994 Denmark used 24 kg of Vancomycin in humans compared to 24,000 kg of the related glycopeptide Avoparcin in animals. A study showed the symptom-free carriage of Vancomycin cross-resistant enterococci into the animals fed Avoparcin. Avoparcin in meat was banned just in Denmark, and then in the EC, since humans may acquire enterococci due to unavoidable faecal contamination of carcases at slaughter. However, it is not known whether enterococci of animal origin colonise the human gut or whether as a transit species, are able to transfer their resistance factors to commensals already resident in human gut. It is thought that the 2-8 % VRE carrier prevalence reported in Belgium is an indicator of the extent to which animal-to-humans transfer has already occurred. It is believed that, if a VRE carrier becomes a patient receiving Vancomycin, selective pressure operates in favour of the VREs. As a result, they multiply and migrate from the gut causing systemic infection.

The use of antibiotics in animals can therefore cause indirect microbial disease in man. It is of special note that this is an effect mechanism which could be quantitatively more important than the classic zoonotic food-borne infections, simply because of the huge numbers of faecal commensals as compared to pathogens, together with the many opportunities for cross-species transfer of resistance factors.

Spread of resistance is known to occur and many bacteria can move from one animal species to another. These phenomena are not regulated by national frontiers. Similarly, any use of an antimicrobial is accompanied by at least some risk of resistance induction or selection. The former option of overcoming resistance by developing new antimicrobials is no longer so straightforward. The development of new antimicrobials is believed to be less likely in the future than it was in the past. All these reasons indicate the need for supranational corrective measures.

In Europe many initiatives are already under discussion or development, e.g. a systematic survey of resistance in farm animals in the EC, and the mid-October 1997 WHO meeting in the Bgvv in Berlin which discussed “the medical impact of antimicrobial drugs used in food animals”. It is also apparent that under consumer pressure, politicians may act by instituting immediate bans on mere suspicion rather than substantive proof of danger, as was the case for the animal feed additive antibiotic Avoparcin in April 1997. Antibiotic resistance is now well recognised to be an important problem by the public, politicians and specific interest groups.

The implications of the resistance issue as described above require a multinational approach, a proposal which is therefore an element of the ENHE Programme. The potential for a research agenda is considerable: there is little substantial information about the time scale of how resistance patterns rise and fall depending on management strategies such as restricted antibiotic use. Even the likelihood of resistance transfer from animals to humans lacks solid evidence even though risk management actions have been taken and more are proposed by some member states.

Furthermore, evidence now suggests that sensitivity takes a long time to return (perhaps as much as 15 years according to a recent American study) once antibiotic use has been stopped. This indicates the need for new molecules to combat resistance. The rewards could be considerable if, for example, resistance levels in other European countries could be reduced towards the much lower levels of Denmark, which has long had a conservative approach towards the availability and use of antibiotics in humans and animals.

The most crucial question to be answered is whether and, to what extent, the pool of animal resistance will transfer to humans and cause disease: research needs 82(A) and 83(B). Should this indeed be occurring, more detailed information is required on the causation, persistence and elimination of this resistance pool. The resulting data could be used for developing strategies for the future antibiotics use in animals in a way likely to remove the threat to human health: research need 84(C).

Suggested areas of research are:

2.11.8 Release and exposure assessment

Research Need 82(A)

- **Studies to allow better characterisation of resistance genes, their regulation, means**

of expression and degree of dissemination.

– Studies should include the inter-species transferability of resistance to relevant antibiotics and subsequent survival of commensals such as enterococci in the digestive tract.

– Studies involving the prevalence of relevant resistance carriage in the enteric microflora of man and production animals on a country-by-country basis.

– Studies to evaluate the role of faecal contamination of uncooked vegetables in the possible delivery of resistance-carrying enteric microflora to man.

2.11.9 Effect assessment

Research Need 83(B)

● **Studies into the possible epidemiological relationship between the use of relevant antibiotics and resistance prevalence in man and animals on a country-by-country basis in health and in disease.**

– Studies should include the role of carcass contamination in surface-to-surface contamination with resistant enteric organisms, e.g. enterococci, in human infection.

– Screening studies should examine the fate of resistant enterococci in carriers on admission to hospital including their subsequent disease history. In addition, treatment failures with antimicrobial drugs should be characterised and quantified through an accessible monitoring programme.

2.11.10 Risk management

Research Need 84(C)

● **Development of strategies which will minimise the rate at which resistance might emerge, in particular in the case of "last-resort" or "reserve" antibiotics.**

– Such strategies should be focused on intensive animal production (pigs and poultry) where antimicrobials are extensively used to increase production at continuous low-level exposures, conditions known to be favourable to the creation of microbial resistance.

– Studies will include monitoring for resistance patterns, with subsequent removal of production enhancers and monitoring of the consequences for resistance.

– Monitoring of national use of the prophylactic and therapeutic antimicrobials in production animals.

– Finding ways to enhance the rate of loss of resistance factors and/or to restore antimicrobial sensitivity.

– Research into economic consequences for pig and poultry production in the absence of antimicrobials.

– The development of guidelines for all uses of antimicrobial drugs.

3. Activities in the field of environment and health at the international, pan-European level

3.1 World Health Organisation

The Helsinki Declaration on Environment and Health concluded that both the CET and the Pan-European State of the Environment for Europe process had highlighted issues requiring preventive and remedial action to reduce the serious effects of unsatisfactory living, working and recreational environments on the health and well-being of large numbers of people in Europe. Priority issues identified were:

- Contaminated food and water
- Ambient and indoor air pollution
- Death and injuries from all forms of accidents (including nuclear emergencies)
- Ecology and health
- Urban health
- Occupational health
- Consequences of armed hostilities

Following the Helsinki Conference, development of the Environmental Health Action Plan for Europe (EHAPE) and the subsequent National Environment and Health Action Plans (NEHAPs) in the European region have been important activities underpinning the aims of the Helsinki Declaration.

EHAPE points out that rational management of the environment in relation to health is hindered by gaps in our understanding of how environmental changes affect health, how they relate quantitatively to health effects, and how and why certain population sub-groups (e.g. based on age, sex, genetic predisposition, sensitivity, nutritional conditions, pre-existing diseases) are more vulnerable to given environmental changes.

EHAPE suggests that these gaps can be filled only by well-planned, systematic research, especially of an epidemiological kind. It should aim at defining indicators of exposure and/or early damage due to environmental agents at molecular, cellular and functional levels using laboratory tests, and at a population level through health surveys based on statistical and other data as suggested above, with appropriate geographical breakdown. Research should also aim to identify environmental factors implicated in the onset of unexpected health problems.

Because environmental health management involves more than just recognising that there is a need to prevent or mitigate adverse environmental effects on health, research should also be conducted in the technological, social and economic fields in order to develop environmental, health-friendly technologies and to show how their higher initial costs, as compared to traditional technologies, are likely to be offset by monetary gains in health and well-being. Likewise, it would be useful to devise methods able to compare concurrent loss and gain for a given activity in terms of different aspects of health and well-being, sharing a resulting net balance in favour of health.

EHAPE therefore defines the following objectives:

- To lay down the scientific basis for policies aimed at identifying environmental hazards, assessing risks and reducing or preventing environmental effects on health.
- To provide appropriate technology and other tools for maintening and developing an environment that is conducive to health and well-being.

To achieve these objectives, research is needed in the following fields:

- Identification of environmental health indicators.
- Development or improvement of methods for hazard identification and risk assessment.
- Determination of quantitative dose-response relationships between exposures to recognised environmental hazards and health and health effects.
- Assessments of the risks of low-level and complex environmental exposures and health effects of interactions between socio-economic and lifestyle factors and environmental agents.
- Identification of groups that are particularly vulnerable to exposure to certain environmental hazards.
- Identification of damage-causing mechanisms in the general population and in vulnerable groups.
- Improvement of exposure measurement methods and modelling to give a realistic picture of the actual exposure of selected individuals and populations, and identification of molecular, cellular and functional markers of early effects.
- Encouragement of technological research and development in order to show energy-efficient waste minimisation, re-use and recycling and provision of low-cost methods of monitoring food, air and water quality and product safety.
- Development of methods for comparing costs of preventive action achieved through technological advances and other means, and expected gains in terms of health protection and promotion, as well as comparison of concurrent detriments and benefits to health resulting from the same economic activity.

The scope and purpose of national NEHAPs embrace development of a programme for improving the health status by advocating and improving the quality of environments supportive of human health. The NEHAPs usually include a chapter on “Environmental Health Research” outlining ongoing and future research and priorities.

During the last three years, the NEHAPs of many West, Central and East Europe countries were finalised. These have also helped to define the process of defining research needs in regard to environment and health, and those described in the NEHAPs complement the research needs described in the present document.

A practical determinant of WHO's research priorities is the need to support its guidelines with solid research data. In particular, WHO Air Quality Guidelines, Drinking Water Quality Guidelines and several Environmental Health Criteria documents may profit from research and facilitate translation of results into policy application. Moreover, research data may also enhance the role WHO plays in the development of methodological guidelines such as exposure assessment, monitoring strategies and risk assessment. Early in 1996 WHO-EUR and the European Environment Agency (EEA) published a monograph "Environment and Health 1", which was presented at the Sofia Conference of European Environment Ministers in October 1995. Significant environment and health issues identified were:

- Pollution of air with suspended particles.
- Microbial contamination of drinking water.
- Road traffic accidents.

WHO/ECEH has also contributed to a number of mini-reviews organised within the framework of the ESF/ENHE programme. In particular, the meetings on Climate Change and Stratosphere Ozone Depletion, Children and Accidents, Research Needs on Water, Environment and Health in Europe were developed in close collaboration with WHO scientists. At the request of ESF/ENHE Steering Committee, WHO/ECEH reviewed the relevance of topics identified by the ESF/ENHE Programme, particularly from the perspective of countries in Central and Eastern Europe (CCEE) and newly independent states (NIS). In a mini-workshop, participants were asked to identify additional priority issues for environmental health research in CCEE and NIS countries. The mini-review of this activity can be found on the ESF's home page (http://www.esf.org).

Considering the ongoing research-related activities in the WHO-EUR Programme it can be generally concluded that they match and are complementary to the ESF/ENHE Programme.

3.2 European Commission

Environment and health has not been identified as a separate issue in the various EC programmes. Nevertheless, attention is devoted to this issue in various documents related to either health or environment.

In the report from the Commission to the European Parliament on the state of health in the European Union it is concluded that quantitative data on the harmful effects of environmental hazards on humans is at present insufficient, and that although environmental hazards may have a relatively small role in disease in general, chronic exposure to unsatisfactory environmental conditions may affect the health of population sub-groups such as children, those with other diseases and pregnant women. Relevant issues mentioned in this report are:

- Housing (basic sanitary facilities and indoor air).
- Homelessness (overcrowding, stress, etc.).
- Transport (accidents and environmental pollution).
- Access (physical disabilities in relation to access) to public transport and buildings.
- Noise.
- Air (pollution with emphasis on particulates).
- Water (chemical contamination due to agricultural chemicals).
- Waste and sewage.
- Radiation (UV-B, medical X-rays and Radon).
- Biodiversity.

In the Framework Programme 1994-1998 of the European Commission, environment and health-related research feature in both the Biomed and the Environment and Climate Programme. While the main focus in the Biomed Programme is on occupational and environmental risks to health such as cancer and other diseases, the focus in the Environment and Climate programme is on methods of estimating and managing risks to human health. In particular, the following research tasks have been identified:

- Improvement of exposure assessment methods for health hazards resulting from environmental chemicals (other than in the workplace), including methods for exposure prediction and early indicators of exposure.
- Development and validation of health effect assessment methodologies with emphasis on early indicators of adverse effects resulting from exposure to environmental pollutants, especially air pollution including particulates.
- Reinforcement of the scientific basis underpinning the risk assessment of environmental chemicals (particularly genotoxic chemicals) by:
  – Refinement and validation of existing regulatory test methods

for new chemicals with enhanced utility for risk assessment.
– Development of alternative test methods which reduce the need for animals in the testing of new chemicals.
– Development and use of quantitative structure-activity relationships (QSARs) for priority setting.
– Validation of assumptions used in risk assessment of new and existing chemicals, particularly in extrapolations from appropriate models to humans, single to multiple and acute to chronic exposures.
– Identification and improvement of the understanding of the genetic basis for susceptibility in individuals and vulnerable groups to the adverse effects of environmental chemicals.
– Immunotoxicological, neurotoxicological and endocrine disrupting effects of chemicals.
– Development of methods to integrate chemical toxicological endpoints in the risk assessment process.

Framework Programme V (1998-2002) is another milestone in the EC's contribution to research; the Programme has been redesigned to ensure that research efforts will be translated more effectively into useful and visible results. It attempts to maximise impact in terms of resources by targeting activities on major EC policies (employment, quality of life and competitiveness) and concentrating efforts on key themes. For the first time, environment and health receive special attention as a key action in the Life Sciences Programme.

The high level of social awareness of environmental risk factors throughout Europe (social demand), the need for sustainable economic development and the common belief that solid basic information will greatly facilitate environmental regulation and policy making - not only within the EC but also at the pan-European level - is the rationale behind the key action.

The overall goal of this key action is to improve the knowledge base, and co-ordination and links between the environment and health fields. This would contribute to the reduction of the potentially negative health effects of factors like air pollution, heavy metals, toxic substances, noise, climatic changes and electromagnetic radiation (including those generated by mobile communication systems), and pollution at the workplace. To address these issues, the following scientific and technological objectives will be pursued:

- Epidemiological studies: Focussed on the application of uniform transnational protocols using large populations in standard-setting in order to implement public health protection.

RTD priorities: Analysis and quantification of the impact of environmental factors on human health; assessment of the relative importance of and interactions between factors affecting on health; improved understanding of interrelations between environmental and public health indicators; assessment of climatic effects and other global changes on human health.

- The development of new methods of diagnosis, risk assessment and prevention. The objective would be to enhance identification of groups vulnerable to environmental exposure.

RTD priorities: Biomarkers of exposure, effect and/or susceptibility to environmental agents including mixed exposures and cumulative effects; improvement of predictive toxicity testing and mechanism-based risk assessment aiming at eventual reduction, refinement and replacement of animal testing; improved methods and technologies for both long- and short-term exposure and effect assessment.

- The development of processes to reduce causes and harmful health effects; focus to be placed on quality of indoor and outdoor air, on quality of water and soil, on wastes as well as regional manifestations of climate change and other global changes.

RTD priorities: Improved understanding of the mechanisms of action for the identification and control of environmental risk factors; methods for incorporating health effects into environmental policy and measuring environmental health benefits and costs; improved techniques addressing issues of environment, health, risk perception and risk communication.

EC research initiatives take a higher hierarchical level compared to the ESF/ENHE Programme research needs. Nevertheless, both programmes are substantially in concordance, thus enabling a further detailed description at the individual project level.

3.3 Global environmental changes and health of human populations

Research into global environmental changes is not or only partly covered in the programmes mentioned in this document, mainly because separate task groups are concerned with this problem at a global level. Nevertheless, global environmental changes may have a considerable impact on human health, particularly in the field of climate change and stratospheric ozone depletion.

The Intergovernmental Program on Climate Change (IPCC) specifically looked at health in its second assessment report. In 1996, a comprehensive book on the health impact of climate change was produced by a task group from the WHO, WMO (World

Meteorological Organization) and UNEP.

The ESF/ENHE Steering Committee recognises that research into health impacts of global change has received substantial attention in recent years. However, to ensure that certain research needs in this particular area are not overlooked, the ESF / ENHE Steering Committee has asked one of the members of the IPCC, Prof. Dr. T. McMichael, to prepare a mini-review describing research needs on ozone depletion/UVB exposure and climate change in relation to health and well-being. This mini-review has already been discussed in this document (see Section 2.1).

3.4 Other specialised agencies

Among national and international institutions active in specialised areas relevant to environment and health at a European level, the WHO International Agency for Research on Cancer (IARC) has developed several systemic programmes, which include multinational epidemiological studies on the evaluation of carcinogenic hazards related to environmental agents, particularly in the European context, and programmes on epidemiological and statistical methods for environmental cancer epidemiology.

References to annexed reports can be found by consulting the ESF home page: http://www.esf.org/mp/ENHEb.htm