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 will be 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 the evaluation 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 context of their remits, the ESF, EC and WHO would all benefit from a structured exchange of views and the development of common approaches.

In the development of the integrated advice, both the ENHE Steering Committee of the ESF Programme and the EC / ESF / WHO Liaison Group have 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 incorporating the 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 the activities related to research in the field of environment and health at the pan-European level are briefly described.

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 with 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 also recognised. A joint programme for research should be developed involving WHO-EUR, EC and ESF. This joint programme should be 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, in a multidisciplinary approach to address this challenge. An ENHE Steering Committee (see Annex 1) 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 the themes: field reviews and workshops as programme core elements and a designated Programme Co-ordinator to manage its overall development.

To meet the requirements of a coherent European approach the Programme has been developed in a manner complementary to initiatives undertaken by the EC and the WHO. This has been achieved by establishing a EC / ESF / WHO Liaison Group (see Annex 2), which was made responsible for 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 exists a social need better to characterise the impact of the environment on health and well-being, both qualitatively and quantitatively. Better characterisation and linking cause to effect enables proper assessment of risk. 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 trans-boundary 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 the understanding of mechanisms involved in the determination of susceptibility of subgroups of the population, their nature and extent and studies to investigate and elucidate interactions of environmental, socio-economic, psychological and lifestyle factors in determining health status.
For RM, ideally, comparative risk assessment and cost/benefit analysis of preventive measures or interactions should be developed to facilitate policy evaluation,

priority setting, risk perception and risk communication and to stimulate public participation. It is necessary to carry out this process to avoid the inappropriate use of resources.

The ambition of the ENHE Programme is not to cover exhaustively 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, where policy advice is urgently needed, and where there is a reasonable chance of providing this advice based on the best available information.

This integrated report from the ESF/ENHE programme provides the basis for a Consensus Conference to be held in October 1998. During this conference a final document will be prepared in which policy advice on research needs in environment and health will be presented in an agreed priority. The document will serve as a draft 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 aims to bring together life sciences, environmental sciences, physical sciences, technical sciences and social sciences thus stimulating a multidisciplinary approach and allowing a fundamental contribution of these sciences to the Research Programme. The central focus of the Programme will be to investigate the links and steps in the risk assessment process and to define lacunae in research and areas which are particularly amenable to a multidisciplinary approach. Research activities should be directed to stimulate the integration of environmental and health issues into existing policies in order to facilitate the step by step progress towards sustainability. The activities to be undertaken will thus meet the criteria of both European scientific added value and policy relevance to sustainability, especially in its health and quality-of-life domains. Therefore, the research needs depicted are not only focused on basic science questions but also related to the translation of basic science results into policy support and into research needs related to risk management principles.

The Steering Committee deliberately included both sides of the matrix: basic and applied research; in many areas basic science results are the corner

stones for the execution of applied research and for 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 huge and that prioritisation is difficult. Nevertheless, it was considered imperative to aim for priority setting in a balanced manner.

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 including risk assessment in addition to 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 a failure to identify a hazard effectively. There is now a strong case for making the strategic move to develop methods and systems capable of characterising risks quantitatively so 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 issues 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, in the context of epidemiological results.

For the areas identified by the Steering Committee, workshops have been organised and mini-reviews were prepared by the ESF in the years preceding the Ministerial Conference. In addition, results of workshops organised by other organisations were included. The identified areas of research, which are 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)*

During the process of the development of this report the Steering Committee has 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 not having 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 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 of the issues not being considered 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

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

Environment Geographical Information System (HEGIS) as described recently in the WHO 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 official reports, which are annexed.

In considering environmental and health conditions in the countries of Central and Eastern Europe (CCEE) and the Newly Independent States (NIS), one may wonder whether areas 1 to 11 require a research agenda different to the one 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 are 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 the topics which may be the most pertinent to the individual Newly Independent States. A common factor influencing the choice of environment and health research priorities is the difficult socio-economic situation of this part of the European region.
The relevance of research with a pan-European perspective is acknowledged. In particular, the research programme and plans of the European Community are noted as an important factor contributing to collaboration.
The positive impact of international collaboration and funding of environmental health research is emphasised because such programmes have a significant role in the development of national capacities to conduct public health research and to assess environmental health risks in CCEE and NIS.

Specific recommendations for the sections described in the ENHE Programme have been included. It is emphasised 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 for building up information infrastructures for identification and epidemiological analysis of exposure “hot-spots” and clusters of disease related to pollution.
Last, but not least, the development and maintenance of the environmental health research capacity in CCEE and NIS is urgently needed to effectively and efficiently face the environmental threats related to public health.

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) have recently made an inventory of available systems and mechanisms used to initiate and execute environment and health research. They arrive 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 a platform or forum will be instrumental in transforming the identified prioritised research needs into research proposals, to re-evaluate priorities during the process, and to communicate 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 platform, in which the WHO, EC and ESF participate, under whose guidance pan-European interdisciplinary consultation and concerted action should be developed for the areas of research that have been identified.

This interdisciplinary platform may facilitate or be instrumental in:

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

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

– The quality (assurance) and validation of models, statistical measures, uncertainty analysis and scenario analysis.

– The development of research proposals on the basis of the prioritised research needs and the development of further critical research questions on the basis of progress and acquired information.

– The evaluation of the Research Programme and its projects, both at the onset and during the implementation.

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

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

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

The platform developed will ensure that the research needs in the areas 1 to 11 are executed 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, the research needs under B and C generally are the responsibility of the Ministers of Health and/or Environment. However, the interrelation justifies a co-ordinated and integrated approach. Similarly, while basic research questions is in general be 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

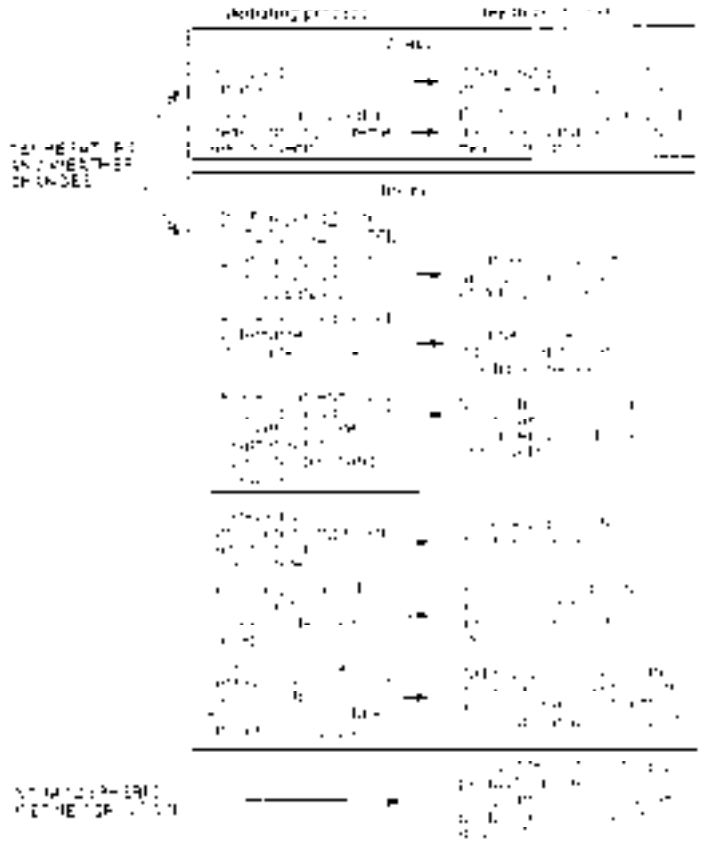
2.1.1 Introduction

The aggregate environmental impact of human economic activity is now sufficiently large to be changing various of 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, cautiously, that the scientific evidence now shows a discernible human influence on the global climate. In light of this strengthening 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, well recognised 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 anticipated 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 alter 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 timeframe of natural variations, and to develop methods of forecasting longer-term health outcomes in response to temporally distant scenarios of environmental change have only begun during 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 is necessarily 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 abovementioned two categories of proposed research. Regional and pan-European geographical information systems (GIS) will enhance the research capacity. There should be a two-way

interplay between formal research (both empirical and forecasting) and the 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 of stratospheric ozone depletion, is important for modelling future changes in the climate system or ultraviolet radiation flux, respectively. That 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.

The role of the "release", in this context, differs from that of the specific release agent 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. Rather, the risks to health are estimated in relation to variations in the consequent environmental exposures (temperature, rainfall, UVR exposure, etc.).

2.1.4 Exposure assessment

Reports of climatic trends (see Annex 4) indicate that Europe has experienced an increase in temperature of about 0.8°C on average during this century. Approximately half that warming 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 was 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. These modelling runs produce 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). The 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 at this regional scale. 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 the late winter-early spring. As for climate change, predictive mathematical models have been used to forecast trajectories in UVR irradiance over the coming century in relation to several scenarios of emissions of ozone-destroying gases (Slaper et al., 1996; Martens 1998).

Because of the several 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 their different strengths of association with mortality, may improve the assessment of health risks – and may also enhance the usefulness of advance warning to populations of upcoming stressful weather conditions. As 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 in indices of UVR exposure. (Such changes will, initially, be very difficult to

detect against the changeable background of other factors also affecting the occurrence of 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 skin cancer incidence, the incidence of 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 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 should provide 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 erythrematosis – and 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 refer predominantly to the future. In this situation, our scientific knowledge and theory must (where possible) be used, via mathematical modelling, to make 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 in the extent). Nevertheless, it is also axiomatic that we cannot directly study the future, nor indeed predict it with any certain precision. The task for scientists, therefore, is to make socially useful forecasts via methods that are amenable to updating and improvement as our knowledge and experience grows. The complexities and uncertainties of the forecasts must be understood and must be 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 of the relatively greater simplicity of the causal relations involved in the latter process (ozone depletion, increased UVR flux, increased risk of UV-induced health effects), it has proven easier to generate quantitative assessments of the future range of changes in skin cancer incidence than it has so far proven to assess the health outomes of climate change.

It is important that this developmental research be supported. With further development, it will acquire a higher resolution that enables 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 the 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 lead onto assessments of the loss of person-years of health and of life, and assessments of the social and economic costs. However, at this stage of research development, much of the empirical research and the 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 such that the sole influence of a projected change in climate or UVR exposure upon the health outcome can be estimated. However, more comprehensive modelling will need to take account of other coexistent, perhaps interacting, projected trends in various deliberate and 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, to underwrite the capacity to do better, more quantitative, research is that of assessing and ensuring the adequacy of information-collection systems and of monitoring (environmental, biological, health) systems in Europe. Techniques of spatial and temporal analysis, including geographic information systems, will enhance the research capacity.

Research Need 5(A)

- **In order to facilitate the early detection of any health impacts of climate change or increased UV radiation exposure in Europe, 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. The 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, 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 as, for example, 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 to be spent in good health. As an example, Finnish men differ in life expectancy at age 25 between basic and high education 6.3 years and in health expectancy between 7.3 and 13.1 years, depending on the morbidity used.

From a policy point of view more insight into the reasons why such inequalities in health occur is of paramount importance since it offers good possibilities to improve the average health status of a population via measures to reduce 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 instead of decreasing. Therefore, several European countries have started 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 approach to find solutions within a relatively short time frame. The development and extension of a pan-European geographical information system (GIS), as currently the case in WHO-ECEH and in an ESF Scientific Programme, will be an important boost to such an approach. In the workshop mentioned above the current state of the art has been discussed and evaluated, and the need for intensified scientific exchange between the various European research groups was confirmed. Moreover, it was concluded that research should be concentrated on scientific explanations rather than on (further) descriptive elaboration. New scientific insights will be the result of 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 making an important and effective link with the ENHE Programme.

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

2.2.2 Overarching issues related to social variances

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

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

It is considered that triggering social inequalities in health may

effectively 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 advanced in order to be able to re-define needs for intervention, thus reducing differences in health expectancy. In the defined research priorities related to effect assessment depicted below, possibilities of cross fertilisation with other issues of research in the ENHE Programme are abundantly available.

Research Need 9(A)

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

Research Need 10(A)

- **The opportunity should be exploited of ongoing longitudinal studies in several European countries to add, 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 consequences of disruption of society, unemployment, homelessness and deteriorating economic situation and its relation to increased violence.

– Living conditions may change due to economic situation changes. This may lead to adverse effects in vulnerable groups (homeless people, unhealthy 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 explained as 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 reversing cognitive effects of toxic substances are assumed to reflect a CNS damage caused by exposure to a high enough level during a long enough 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 explained as a result of a change of the individual's general state (mood, stress, fatigue, arousal etc.) and of the resources available for performing a task. Chemical exposure may also have such effects as a result of intense smell or by evoking fear for the possible consequences of exposure. Noise and heat may have more specific effects on cognitive functions and the presence of irrelevant speech in the environment on certain cognitive processes has been documented.

The environment may also interfere with the performance of cognitive tasks without affecting the cognitive functions involved. 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 deteriorate control of the hand-arm-system during exposure.

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

Research on environmental effects on cognitive functions is done by (1) experimental laboratory studies, (2) quasi-experimental field studies, and (3) epidemiological investigations. Experimental laboratory studies on humans are usually short-term ones at moderate exposure levels, studying acute effects. 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 no models are available.

Quasi-experimental field studies investigate reversible effects in natural (realistic) settings using representative exposed and non (or less) exposed groups. Limitations include the less good control of confounding factors and the difficulty of studying long-term (years) effects. 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. The degree of coping with a situation and the fact that the performance level of a task is well below an individual's maximum level are other problems which interfere with interpretation.

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 large variance of the functions in the normal population. This emphasises the need for studies in large samples, this often only being realised in international collaborative studies. In addition, the development of better and more sensitive tests for impaired cognitive functions, advanced statistical analyses and better research designs is needed. Equally important is the development of ameliorated 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. *Transp-ortation noise and irrelevant speech are the noise sources that have shown* the most replicable cognitive effects. An extension of this research to include more *cognitive* tasks with straight ecological relevance would be valuable taking into consideration 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 get a better understanding of such effects outside the laboratory.

Further research on the indicated effects of a noisy environment on children's cognitive development is of utmost importance. Critical issues include the interaction between noise exposure and stage of cognitive development, 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 the cognitive effects on, for example, reading ability, and the identification of sensitive groups.

As far as heat and cold are concerned, the cognitive effects of thermal stress are primarily a work place and a 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 primarily reflecting central nervous functions. However, there is insufficient ground for conclusions as to which tasks are sensitive to vibration or during which exposure conditions, effects may be expected.

In the report (Annex 6), the available information on environmental effects on cognitive functions is limited and inconclusive. Societal concerns are considerable, indicating the need for development of new techniques, methods and tests for measuring exposure and cognitive functions. Furthermore, there is a need for ameliorated study designs, such as the combination of different basic designs, focus on identified sensitive groups and supranational multi-centre studies. The launching of such studies can only be successful when harmonised, standardised and validated measurements of cognitive functions are available, thus enabling 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 often prevent firm 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:

– The development of designs combining different basic designs such as cross-sectional, between persons designs and longitudinal within person designs with quasi-experimental designs.
– Combination of behavioural functional variables with physiological and neurological parameters.
– Use of animal models related to studies in humans.
– The development of tests as indicators for every day 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 to incorporate 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 in, ideally, quantitative terms. However, risk management is also strongly influenced by risk perception, community tolerance, tolerance development and behavioural attitudes. In relation to this 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 vice versa 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 (Annex 7). Learning, memory, perception and attention play a role in mediating a relationship 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 better, seems warranted. Four areas in which cognitions 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 made available through external channels of information and which, depending on the level and/or duration of exposure, are in principle known to cause health impairment.

– Attribution-based syndromes are related to environmental factors, which have not yet been shown to induce adverse health effects or, based on current knowledge, are unlikely to do so, but which are cognitively linked by sick people to their health impairment as the likely cause.

– 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 the above 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 activating the senses 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 is not yet solved in a widely accepted manner. Some treat annoyance responses as perceptions, others as emotions, and some as attitudes or as rational decisions based on cognitive operations. Despite such conceptual differences, and also despite differences in either assessment mode in terms of one- 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 showed to be highly significant in a statistical sense.

Differences observed between individual and area-centered associations emphasise the importance of person-related factors to modify the annoyance response. Such 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 as developed in 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 complaints about sleep disturbances, headache or gastric symptoms. Self-reported fear of negative health outcome from exposure to industrial odours has been reported to moderate 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 the question if 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, noise and odour longitudinal studies may enable analysis of both the process of the development of certain conditions and the development of physiological and medical symptoms. Inclusion of psycho-physiological measures, 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 to become more person rather than area oriented and for this, closer interactions between the biomedical and social sciences on the one hand and technical disciplines on the other are necessary.

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, traits/styles

of personality) and more specific theories (ecological attitudes, health perception or attribution styles) are needed to explain (indirect) relationships of somatic symptoms to environmental factors.

For SBS as for other environmental syndromes several gaps in knowledge can be identified. These include the identification of population baseline prevalences of somatic symptoms and of "sensitivities", and the clarification of relationships between medically unexplained environmental syndromes and patterns of associations of multiple stressors. Comparative studies of the triggers of environmental syndromes 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 covering "perceptual-cognitive factors" and person-situation interaction is another need as is the development of physiological and sensory methods to be used 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 increases in probability and vice versa. 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 takes place essentially

via attribution. Although physical factors (as with bending, 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 secretion, emphasising the importance of psycho-biological mechanisms interacting with cognitions. It is important to translate knowledge in the area of cognition-regulated pain perception into both preventive interventions as well as into 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 the relationship in a given environment/health interface relative to musculo-skeletal disorders. Insufficient 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 the lack of relaxation ("EMG gaps") for the risk of 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) by way of 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 by long-lasting 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 progression of cancer, 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 in work environment. The fact that the elevation was more pronounced if perceived stress rather than "objective" stress was taken as the variable indicates the importance of cognition as a mediating factor in health effects. Although the earlier mentioned mechanism (chronic overarousal of the HPA axis) may offer a likely explanation, more detailed information concerning biological mechanisms by which psychosocial stress is pathogenic seems necessary. In the occupational setting 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 between 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 axis activation and associated diseases including a profile of pathogenic factors in the psychosocial environment will also provide information for possible intervention measures. Elucidation on 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 dietary habits, 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 laypeople 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 “dread-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. Yet, there are still uncertainties in this approach, particularly at the level of the individual and multiple regression analysis of presumably influential factors 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 as to 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. The question 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. It is advised to perform the research under governance of a platform organisation in order to ensure effective and efficient execution of the research needs in a supranational interdisciplinary way. 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 of physico-chemical factors related to 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 on the one hand and technical disciplines on the other 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. There exists an urgent need to shed more light on many 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

The present knowledge about cognitive functions as mediators of environmental effects on health is as yet largely insufficient to characterise risks in a sufficiently quantitative way. Outcomes of the depicted research may also enable the development of better risk characterisation procedures. 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 process oriented approach for 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 multi(centre)nationally.**

– Aspects to consider include the role of cognitions in treatment and/or prevention, the importance for 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 via 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 estimated that 428,300 children aged up to five die annually due to unintentional injury. Accurate pan-European data are not available but the 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 the 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 the 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 a 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 initiated the 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 the 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 globally.

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

– Severity of injury and impairment of health are independent of national borders. Drawing on the experiences of other states will allow the optimisation of care, both medical and non-medical, following any injuries that do occur.

– Access to a large enough study population to provide conclusions that are statistically robust. This is particularly important for

intervention studies where statistically modest, but clinically important health gains are only demonstrable in large multi-centre studies.

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

When defining research needs in the area of children and accidents several developments are of importance:

– Injury risk may change with new sporting developments and with the extension of activity to a larger proportion of this part of the population - a health objective supported in many countries.

– Increased affluence will increase these pressures and ease of movement in Europe will encourage exploration of new activities.

– Changes are likely to be accelerated in Eastern Europe with its phase of rapid development and this should be closely observed.

– Increased possibilities may become available to familiarise children and the population at large with risks involved, for example by using better and more appropriate risk communication methods. This could be facilitated by the development of a cadre of educators who are trained in objective risk assessment.

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

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

Thus, the development of pan-European interventions to control unintentional childhood injury seems an appropriate and achievable goal. Through multiple approaches based on the varied scientific paradigms of the various stakeholders, tailor-made interventions may become possible and rigorous evaluation will inform prevention policy both within and outside the EC. A pan-European approach should be strengthened by supranational research activities to standardise collection and dissemination of relevant data, and to develop an evidence based European injury prevention policy. Furthermore, it will develop effective means of disseminating the results of effective interventions.

Following the workshop (Annex 8), the following research needs were identified.

2.5.1 Overarching research needs in the area of 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 areas of research. A network organisation will be instrumental in transforming identified priority research needs into quality research proposals, in evaluating progress and priorities during the progress and in communicating information to interested parties on critical issues related to intervention and prevention. More specifically such overarching issues are:

– Standardise collection and dissemination of relevant data at a supranational level to ensure comparability. (This has the highest priority.)

– Develop a pan-European injury prevention network to execute an evidence based pan-European injury prevention policy.

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

– Foster international co-operation and promote development of research skills through enabling interaction between European countries.

– Promote transport related health gain. The development of safe transport policies segregated cycle routes, supervised walking routes and improved, safe public transport systems) will reduce the current trend in Europe for children to be transported by car. This will have benefits both on local environmental pollution and by reducing the emission of greenhouse gasses, 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 support such identification is a necessity to investigate ultimately the possibilities 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 form the basis for standardised methods of recording across Europe to allow robust international comparisons and to identify the most threatening and new hazards.

2.5.3 Exposure assessment

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

Research Need 25(B)

- **Comparative studies of exposure to injury risk in the different regions and countries in 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 seems more common in Southern Europe. Analysis of these and similar risk factors will provide data to set priorities for 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 will foster the development of rules relating to safety across Europe.

2.5.5 Risk Characterisation

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

Research Need 27(A)

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

– Development of systems to quantitatively measure injury rates.

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

– Not only direct costs related to childhood injury but also long-term costs for health and social care and loss of productivity provide information about the economic gain that can be achieved by appropriate prevention and intervention thus enabling appropriate cost/benefit analysis.

Research Need 28(B)

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

– The production of authoritative systematic reviews and, where appropriate, meta-analyses will allow the production of evidence based guidelines. Dissemination of these will facilitate the replication of previous successes.

2.5.6 Risk management

The preceding identified research questions will provide the necessary information for policy-makers to evaluate possibilities for prevention and intervention. These possibilities can only be considered when reasonably realistic numerical data for cost/benefit analyses are available. Prevention of risks by anticipatory actions focused on, for example, product safety, facilities for sport and leisure, farming or transportation may greatly reduce casualties in early life.

Research Need 29(C)

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

– These should include the development of agreed 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 this. Another focal point 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 the 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 and thus all humans are exposed to such particles when breathing air. Air pollution episodes in the past (among others 1930 and 1952) provided evidence 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 daily 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 asthmatic attacks in 2700 children between seven

and eleven per day and to reduce lung function by 10% in 46000 children per day in the same age group.

Although considerable research has been carried out in the field of particulates, the potential severity of the problem, the difficulties in interpretation (in particular problems in attributing the observed effects to specific particle properties and emissions of particles) and the increasing volume of information on acute and chronic health effects warrant a systematic integrated approach in research to effectively counteract the problems by adequate measures. To enable such an integrated research effort a framework is proposed where a multidisciplinary approach involving all necessary disciplines such as atmospheric sciences, epidemiology, toxicology and social sciences will provide the relevant information and link it to the causal chain of human activities and environmental impact.

After a thorough review of the available information an international group of experts identified the most important lacunae in knowledge which, when removed, would provide guidance for policy measures to be taken. The report of this international group of experts is provided in full in Annex 9. The research needs identified to be the most important are described below using the framework of the cause effect chain and the risk assessment paradigm with its interrelated aspects, which in the case of air particulates are described as the following elements: hazard identification, release assessment, exposure assessment, consequence or effect assessment and risk characterisation. Preceding the presentation of these elements some overarching priorities were identified by the group of experts.

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 specialists in the area of research. Such forum or network could be instrumental in transforming the identified prioritised research needs into research proposals, to re-evaluate priorities during the process, to communicate 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:

– The formulation of (possible) working mechanisms of observed health effects related to PM exposure profiles.

2.6.2 Release assessment

Particles can be generated by natural and anthropogenic sources. Annual total amount is estimated at 3,000 million tonnes for natural and 400 million tonnes

for anthropogenic sources. Since the particles from natural sources are mostly coarse, the 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) will also differ strongly due to the processes, conditions and (climatic) variations that govern their production.

While summary information on emissions often exists (yearly national average production of major sources) specific information on the PM, with sufficiently detailed temporal and spatial resolution and 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 enable the linking of exposure to the sources of PM. This includes research on particle sources as well as on dispersion of particles.**

2.6.3 Exposure assessment

Exposure assessment consists of the description and quantification of the relevant conditions and characteristics of human exposure to released particles by a certain source. Exposure to PM is defined as the event when an individual is in contact with a certain concentration during a certain period of time. It may be a micro-environment with a more or less homogeneous concentration but the environment may also have a varying concentration in time and content. PM covers a variety of particles with different properties.

Most widely used is mass-based concentration of PM. Sometimes characterised with a certain size: TSP, BS, PM_{10}, $PM_{2.5}$ (*), 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 the origin, fate or toxicological potential.

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

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 the diversity in sources and composition. In addition, measurement techniques vary throughout Europe, thus making comparison difficult.

Personal exposure measurement experience in Europe is limited, partly due to practical and technical reasons. However, the few studies 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 the different environments (indoor/outdoor) and the 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 the earlier mentioned discrepancies.

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

Research Need 33(A)

- **Characterisation of European air quality according to agreed classification criteria with respect to different measures of particles and their correlation with gaseous pollutants as well as 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 regional basis.

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

– Identification of areas with similar and contrasting PM profiles to optimally use similarity and differences in PM exposure in Europe for design of future studies on e.g. 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-

(*) 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.

environments (home, school, commute, inner-city) and compilation on time-activity data of the European population.

– Measurements of personal exposure of PM in subgroups of the population, 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 assessment or effect assessment

The physical and chemical properties of particulates determine the mechanisms by which they become biologically effective. Whereas the physical properties determine the site of deposition in the respiratory tract, the chemical composition of the particles determine their residence time. Thus together with the physical and chemical properties location, dose, duration and disposition of the particles ultimately determine the response.

Deposition and retention largely depend on the size of the particle. Shape, density, electrical charge and hygroscopicity modifies the deposition pattern to a certain extent, whereas respiratory ventilation and intersubject variability in airway and air space dimensions may modify deposition patterns considerably. Likewise solubility of deposited matters influence retention.

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

Knowledge about the mechanisms by which inhaled particles provoke damage in the lungs is inadequate. Inflammation, cell proliferation, and vascular congestion in the lungs are the most investigated phenomena, usually at high PM concentrations. It is not known what may occur at ambient levels and if adaptation and/or tolerance play an important role. The same holds for the potential effects of inhaled particles on tumour incidence or cardiovascular diseases, or the effect of PM on compromised lungs in animal and man although it is known that human individuals affected by respiratory diseases and elderly are more responsive to inhaled particles.

Thus particulate matter cannot be considered as a single entity but rather as a variety of entities depending on the physical and chemical properties of the particle. The identification of these entities should be the goal of epidemiological and toxicological research to answer the question which specific entities may determine respiratory responses, even at urban air concentrations. Common definitions for and common terminology used by the various disciplines involved is a prerequisite to approaching these questions in a multi-disciplinary context.

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 physico-chemical properties of the particles causing 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.**

In the design of new studies, as well as in the re-analysis or meta-analysis of existing studies, high priority should be given to susceptible populations for different respiratory responses (biological endpoints), and to the issue of co-occurring 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 were compared to established No-Observed-Adverse-Effect-Levels (NOAELs) or sometimes the Lowest-Observed-Adverse-Effect-Levels (LOAELs). The proportion of time that levels were in excess of standards set, which were derived from a NOAEL or LOAEL, defined the impact of exposure. Only recently was it established that associations between fluctuations in 24 hour averages of PM levels and health consequences such as increased daily mortality, hospital admissions, respiratory symptoms and decreased pulmonary functions exist. For instance, in Concern for Europe's Tomorrow it was estimated that in the 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 was strengthened by experimental evidence. This may indicate that concentration-response relations may provide estimations of the quantity of humans in a population or a subgroup of that population, that are affected.

Key issues in such a risk characterisation are biological plausibility, shape of the concentration-response relationship curve and the possibility of extrapolation of the observation of (a number of) specific studies on PM with certain properties to other situations where risk characterisation is desired but not studied. Nevertheless, risk characterisation for PM is complicated since 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 comparison of those effects with supposed benefits linked with emissions of particulates may complicate assessment even more. 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 and the need for aggregation of indicators to ameliorate the comparison of health impacts of various kinds into monetary units that can be added and compared, is discussed. Another aggregation method: Disability Adjusted Life Years (DALY), in which factors are discounted due to the reduction of ability to perform independently daily activities.

Research needs related to risk characterisation of PM 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 avenues for aggregation.

– Surveys and focus group discussions of general public and stakeholders assessment of monetary costs of health effects (e.g. willingness to pay) and reduction of quality of life aspects of various health endpoints.

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

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

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

2.6.6 Risk management

In the preceding sections research needs have been identified which receive a high priority since they provide the information necessary for policy-makers to decide on appropriate measures for abatement. Questions on release and exposure consequences, on effect assessment and on risk characterisation address the information needs of the risk manager.

Nevertheless, there still exists a number of specific questions which do not follow directly from the discussions and results of the elements mentioned. As an example, insufficient is known about the critical fraction, the risk groups and the health effects and their consequences. Epidemiological and experimental studies are needed to be designed to answer these questions and results should be evaluated in a multi-disciplinary context to ensure sufficient input form other disciplines for modelling and validation.

Overarching priorities, which also pertain to risk management aspects, have been discussed in the first part of this ambient air particulates section. From the point of view of risk management the following priorities could be added to the task of the platform; they have consequences for the structure, process and preparation of the research agenda:

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

– To develop a coherent and comprehensive Decision Support System in which results of research can be incorporated and that allows the systematic evaluation of efficiency of abatement policies.

In addition, the following research needs can be added from the risk management perspective:

Research Need 37(C)

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

– Develop and apply concepts like "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.
– Man spends the major part of his time indoors, in particular in developed countries.

The time spent outdoors for most individuals is no more than 5%. Of the remaining time approximately 70% is spent at home and the remainder of the time is spent in other micro-environments such as workplace, school, shops and in transport. In the workshop report "Indoor Air Quality and Health" (Annex 10) the focus has been on the home environment since most time is spent there and many specific sources of air pollution may exist in the home.

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

The indoor environment is characterised by temperature and humidity, which may, when technical and financial means are not available, lead to extremes from which humans may suffer, especially subgroups compromised by diseases which make them susceptible to changes to these variables. Increased energy saving measures in homes leading to less ventilation may enhance this problem. A special physical problem addressed is radon gas emanating from soil and building materials, believed to be a most important environmental cause of lung cancer. Exposure levels vary widely between countries and localities.

Chemical air pollution is evidently abundant in homes and finds its source in non-vented combustion appliances, smoking, furniture, carpets and building materials. Although smoking should not be excluded as an important source, non-vented combustion appliances are important contributors to the sometimes high concentrations of nitrogen dioxide in homes and in addition, depending on the source, carbon monoxide and polycyclic aromatic hydrocarbons. 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). In the same way evaporating building materials such as formaldehyde or other volatile organic components have been thought to provoke chronic irritation, annoyance and produce odour complaints.

Biological pollution may be the most important and least is known about this. Dust mites produce major allergens which are believed to play an important role in 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 (endo)toxins 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 more and more 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 aggravate this situation.

When dealing with indoor air pollution one should be aware of the great influences 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 have been used: (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 in the order of their occurrence in the causality chain.

2.7.1 Overarching priority related to indoor air

– Under 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 limiting of exposure to the sources (see also 32A).**

2.7.3 Exposure assessment

Exposure to harmful indoor environmental factors is inadequately characterised and does not allow a 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 can not be explained adequately. Various indoor air pollutants may be important contributors to or causes for the occurrence. Moreover, 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). Therefore, the relative importance of biological and chemical indoor pollutants in the occurrence of allergy and asthma in human childhood should be investigated.

Research Need 43(A)

- **To establish the role of indoor environments in the causation of allergy and asthma, and to unravel the interactions which (may) exist 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 health and well-being in man (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 an option in the short term. 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 of application of monetary and disability discount factors.

2.7.6 Risk management

In the area of indoor air risk management questions will arise when substantially more information has been gathered. Nevertheless, already today some risk management measures may be opportune. This is especially true for 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 and should be approached in a systematic way rather than the haphazard way practised today:

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, with on the one hand, a great need for water and, on the other hand, a great variety of activities that may cause water pollution.

Micro-biological diseases are still transmitted in certain areas, in particular via drinking water and through exposure to surface water for recreational purposes. Moreover, because of limited resources of ground water 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 like viruses, protozoa and bacteria.

Urban, agricultural and industrial systems interact with the surrounding areas with releases of treated or untreated effluents, gaseous emissions, fertilisers and other agricultural chemicals. Evidently, all these releases may alter the quality of natural water making it less suitable or, indeed, unsuitable for recreation or human 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 necessitate increasingly sophisticated water management, not only at national but also at supranational level. Furthermore, pressure on water resources is complicated by the demand to

maintain aquatic ecosystems of adequate quality, on which other beneficial uses generally depend.

Apart from anthropogenic contamination of water natural conditions may also render water unsuitable for several purposes without extensive and costly treatment. However, such naturally occurring problems, as for example 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 as compared to anthropogenic sources.

In the field of water quality and drinking water ongoing research will also supply fundamental characteristics on the basis of which various technical, economical and managerial instruments may be ameliorated to ensure an effective water management and allocation of resources. However, water management and subsequently research in this water sector has been reactive rather than proactive. It should be emphasised that in the water sector prevention certainly is better than cure since avoidance of potential harm is not only beneficial to human health and well-being but is also beneficial to ecological quality. Furthermore, in most cases it is much more cost effective.

In this section research needs for water quality and drinking water are presented based on the report of a scientific workshop (Annex 11). The research needs are focusing on human health and well-being and usually concern direct links although some needs that are defined are more indirectly related to human health and well-being. The research questions are grouped according to the risk assessment scheme. Nevertheless, some overarching priorities can be depicted, which should be considered as a necessary requirement to answer the research questions posed effectively and efficiently, to avoid unnecessary duplication and to co-ordinate complementary activities in a concerted action.

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

Sustainable improvements in the field of human health and well-being related to water 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 involved 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 the platform (see

Introduction, page 3) would greatly facilitate co-ordination and integration of research on the different elements of the risk assessment scheme: release, exposure and effect assessment, risk characterisation and risk management.

Additonal overarching priorities are:
– Make an inventory of experience in European countries on successful interagency co-operation and inter sector management and implementation of water policies.
– Develop target standards (guidelines) to advise on health risk at each stage of the water cycle and include other necessary compartments in a common, harmonised setting.
– Evaluate the water quality and drinking water programme and its projects at the onset and during its execution.
– Promote a better geographic distribution of research capacity throughout Europe.

2.8.2 Release assessment

Contamination occurs by effluent, waste and deposition of anthropogenic sources and natural sources in surface water and groundwater. Most of these hazardous pollutants arise from a range of varying human sources, both point and non-point, and may reach receptors such as humans and aqueous ecosystems through a variety of different pathways.

Three groups of pollutants are identified: (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 in use in Europe alone. A substantial number (over 2,000) are used in large quantities of over 1,000 tonnes per year. Direct discharges in water or indirect contamination due to interactions of water with other media (polluted soils and air through deposition or through contamination of rain water) are the important means of contamination. Monitoring programmes are currently used in a number of countries. A lack of co-ordination in design of monitoring programmes and in meaningful data acquisition inhibits the production of effective information and realistic modelling exercises.

Research needs in release assessment are:

Research Need 47(A)

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

Research Need 48(B)

- **Design of (risk driven) monitoring programmes with**

the aim to integrate relevant data in order to understand and control releases.

Research Need 49(B)

- **Investigate the possibilities for 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 undertaken to understand pollutant pathways, bottlenecks in knowledge do still exist. In chemical exposure indirect pollutant pathways involving other media (soil, atmosphere) and the food chain are complex and not understood. Compartments previously considered to be terminal sinks are now recognised to be pollutant sources. This is complicated by the large number of pollutants present, the need to understand short and long-term impacts of exposure to individual substances and combinations of chemicals, and our poor ability to predict water pollution problems in the future. Finally, the persistence of many chemicals and their metabolities under aerobic and anaerobic conditions is presently not sufficiently understood. 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 niches for (pathogenic) micro-biological agents onto their vectors. Rapid changes in technology and industry also create new hazards to health, 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 when it concerns regions with poor hygienic conditions or areas where large scale conflicts occur, thus leading to exacerbation of infectious diseases. A large number of microbial agents - bacteria, viruses and protozoa - have been identified as causing disease in man and most of them have been detected in water sources, thus being potential waterborne pathogens. To establish exposure better one needs to address two main issues with priority: (1) quantitative detection of relevant waterborne pathogens, and (2) the development of surveillance systems to guarantee rapid responses to outbreaks and appropriate remedial actions, and to evaluate trends and developments in the occurrence of such pathogens.

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 be of use to risk assessment these methods should yield quantitative information on the occurrence of viable micro-organisms that are infectious to man, and these should be clearly differentiated from non-viable and non-pathogenic ones as well as from strains which do not possess sufficient virulence factors 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 rapid response to outbreak situations and to evaluate occurring trends and new developments.**

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

Research Need 52(A)

- **Research on sources and pathways of chemical pollutants in order to quantitatively predict/model environmental distribution and fate. This should include transmedial and transboundary movements.**

2.8.4 Effect assessment

Chemical and microbial effect assessment methodologies are necessary to enable risk characterisation. Effects of microbial contamination of water are more often 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. To a large extent viruses cause diarrhoeal episodes in children, others affect adults, for example the Small Round Structured viruses (SRV) and hepatitis E viruses. The latter agent has recently been identified as the cause of major outbreaks in South East Africa and in other parts of the world. Bacterial waterborne pathogens may be divided into faecal pathogens among 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 is bacteria which are 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 they are non-infectious to man they may produce toxins which affect health. The most notable example of a 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 protozoa the most important waterborne pathogens in virtually all countries that rely 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 and there are reasons to assume that it is a underreported problem. A cohort study, comparing two groups consuming the same tap water meeting all microbial standards - of which one group received the tap water after ultrafiltration - resulted in an excess of gastroenteritis of 10 to 30% in the group receiving the non-ultrafiltrated tap water. Epidemiological studies may be able to identify the impact of low level transmission. Evidently sound quantitative effect data are not available and do prohibit appropriate quantitative effect assessment and modelling.

The effects of chemical contaminants on health is only known to a limited extent for a limited number of chemicals. Out of the registered number of chemicals approximately 2500 are officially classified as dangerous but limited potential effects to health are known. Experimental data in animals provide some information about potential effects; however, allergies and subtle effects in the endocrine and central nervous system would not be detected with present methodologies.

The general approach to chemicals in setting limit values in order to avoid adverse effects has been proven to be a sensible one for those chemicals that are considered to be threshold chemicals. For the so-called 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 the chemical products, which arise after water disinfection e.g. chlorination. These by-products are usually present at very low concentrations. The by-products trihalomethanes and haloacetic acids are present in the greatest concentration. Numerous epidemiological studies have investigated the possible threat of the occurrence of by-products in chlorinated drinking water. A causal link between diseases (bladder cancer and rectal cancer) has not been established although a meta-analysis study indicated a possible association with relatively small increased risk. It seems unlikely that new studies will provide a definite answer since the levels of by-products have been reduced by improved treatment methodologies.

Finally, insufficient information is at hand about the effect on human health and well-being if the availability of water is limited, or if there is uneven allocation. The growing demand for water, including drinking water, may necessitate 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 disease.**

Research Need 54(B)

- **Research to determine the implications for human health and well-being of the availability of (drinking) water as a result of limited resources, uneven allocations and market forces and research on the implications for human health and well-being if the existing trends of groundwater pollution and deterioration continues.**

2.8.5 Risk characterisation

Risk characterisation is feasible in qualitative terms when exposure data and data on possible health effects are known. For chemicals classically limit values are set to provide "zero effect" levels in order 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 methodologies as well as effect assessment methodologies will thus in future provide a means for appropriate risk characterisation of chemical contamination of water.

Likewise, microbial risk characterisation tries to estimate the possibility of occurrence and, ideally, also the severity of potential adverse health effects in a given population. In such estimates the accuracy of the parameters used is of high importance and uncertainty analysis is a necessity as well as validation of methodologies and models used. In the case of microbial risk characterisation integration of chemical risk characterisation is a necessity and vice versa. Chemical disinfection to reduce the number of microbial pathogens leads to the introduction of toxic chemicals. Integrated risk characterisation may thus define the conditions for optimal treatment of water.

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 applied to 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 in the separate elements of the total risk assessment process will - when translated into research and subsequent results - lead to 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 to develop 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 the control of water abstraction and allocation among stakeholders and users. This may include:**

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

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

– Investigations into interactions between and consequences of increased reliance on market forces to manage 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 the agents of change and the processes occurring in individual and (social) groups?

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

– Which socio-economic tools exist that 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 recreation 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 the 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 critically the data, to summarise the current knowledge on health trends for humans and wildlife and to define research and monitoring recommendations on these issues. Within this context 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. The incidence of testicular cancer has increased quite dramatically in a number of countries, and breast and prostate cancer incidence have increased as well during the past decades. While at least some of the increase can be explained by better reporting and diagnostics it seems that particularly for testicular and breast cancer the increase in incidence is real. Semen quality may have declined and the incidences of undescended testes and hypospadias appear to have increased (there exists a biological association between these disorders and testicular cancer).

The causes of these adverse trends in some aspects of reproductive health are largely unknown. Since the changes occurred in the last two generations and this is parallel to changes in the environment (including lifestyle) the suggestion has been made that

man-made chemicals may be responsible. This suggestion appears to be supported by the findings that some cases exist in the EC area where adverse endocrine effects or reproductive toxicity coincide with high levels of exogenous chemicals, which are known to possess endocrine disrupting properties in certain 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:

– Sufficient evidence is available 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.

– Insufficient data and inadequate studies do not permit an assessment whether changes in female reproductive health other than breast cancer are indeed present.

– Insufficient is known about exposure of humans to possible and proven endocrine disrupting substances.

To unravel possible relationships of environmental and/or naturally occurring EDS with adverse human reproductive health effects the European workshop participants recommended research activities in the field of human epidemiology, mechanism and models, methodology and exposure. The research questions also comprised questions related to wildlife. Below the research questions are depicted in the risk assessment framework; research questions related to wildlife are only included if they have relevance for human health effects.

2.9.2 Release and exposure assessment

An integrated strategy for monitoring of chemicals in the environment focusing on substances displaying ED-potential appears to be a requirement for effective exposure assessment. This should be achieved though integrating human and wildlife epidemiological and/or field studies. Maximum use should be made of currently available data and the development of specimen banks of human and wildlife samples would facilitate the process. The following research questions were formulated:

Research Need 61(A)

- **Conduct effect-driven studies on 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*. The monitoring should include data on effects, external and internal exposure and key pathways. It was advised to include the data 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 on dose-response relationships provide the necessary tools to perform 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 measurement, geographical differences and areas of uncertainties. This may include:**

– Establishment of harmonised standards for measuring relevant endpoints when inter-laboratory comparison indicates that regional comparison cannot be executed.

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, by *in vivo* animal studies and high exposures.

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

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

– Follow-up epidemiological studies after successful activities to reduce 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 humans for 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 such as investigation into similarities in aetiologies of persistent oestrus in rodents and polycystic ovaries in humans; identification of non-hormonal pathways; development of non- or minimal invasive biomarkers associated with endocrine functions and disruption (i.e. testicular and ovarian function) and the 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)

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

Research Need 68(A)

- **Development and validation of *in vitro* assays that predict changes in function, biosynthesis and degradation of hormones 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 model chemicals.

2.9.4 Risk characterisation

Research Need 69(B)

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

2.9.5 Risk management

Research Need 70(C)

- **Studies into the cost and the effectiveness of reductions in exposure to recognised EDS related 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, the respiratory and the alimentary tract that potentially can modulate the immune system. Agents include industrial chemicals, pesticides, air pollutants, natural toxicants and ionising and non-ionising radiation, including UV. Chemicals as such may act as antigens thus provoking immune responses which results in skin, respiratory tract, or alimentary tract allergies. In addition, chemicals may directly affect the function of the immune system thus modulating immune responses to antigens that are not related to chemicals, such as antigens derived from microbial agents.

Chemicals known to modulate immune response through a

variety of mechanisms in animals are among others pesticides, organochlorines, organophosphates, carbamates, dithiocarbamates, pyrethroids, metals, metallic salts and organometals, solvents, halogenated aromatic hydrocarbons, nitrosamines, hormones, polycyclic aromatic hydrocarbons, gases like nitrodioxide and ozone, mycotoxins and addictive substances.

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

In the environment exposure to immuno modulating substances will generally occur at low levels to a mixture by various routes. To investigate possible effects on human health it is of primary importance to have accurate exposure assessment techniques and validated biomarkers. Specifically designed longitudinal epidemiological studies with valid measures of exposure, confounding and health endpoints may answer the question if long-term low level exposure to a mixture of immuno-modulating substances will pose a risk. The most valuable biological measures to study 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 advised.

The symposium report which is attached as Annex 12 stipulates the need for studies as described above to obtain a sufficiently reliable assessment of the potential risk of exposure to environmental immunotoxic substances.

Allergic reactions following exposure to materials/chemicals in the air or in food are common health problems. For contact allergy, predictive models exist in the guinea pig, mouse and humans. There is substantial evidence that these methods, when performed correctly, are adequate for hazard identification. For respiratory allergy, models that will 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 are based upon measurements of immune activation and/or respiratory reactions. However, these tests have not yet been validated on their utility.

There is a need for methods that will permit accurate identification of chemicals and proteins that cause allergic sensitisation of the

respiratory tract. Similarly, such methods should also be developed for oral exposure.

The recommended 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. The 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 to novel antigens, for which insight into determinants is required.**

It is recommemded that in ongoing longitudinal prospective cohort studies in children the occurence of infectious diseases as determined by environmental factors be included.

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 that are not exposed to immunotoxic chemicals with endpoints such as infections, allergies and cancer in addition to function tests such as IgE titres and vaccination titres.

– Results of these studies may indicate the necessity of epidemiological studies in exposed sub-sets of the general population exposed to immunotoxicants.

Research Need 74(A)

- **Multi-centre collaborative studies involving several countries with different exposure patterns to immunotoxic agents such as for example 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 considered of relevance to the ENHE Programme. This section deals with the research needs for the generic issue chemical risk assessment as well as with the 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 has been indicated in the introduction of the ENHE Programme (page 4) quantitative

risk assessment (QRA) is of prime importance to policy makers in that it provides means to quantify risks and to carry out risk prediction. Until recently risk assessment methodologies have been based on conventional toxicity testing involving single compounds given at high doses to experimental animals with the aim to investigate their adverse effects and to establish no observed adverse effect levels (NOAELs).

On the basis of the established NOAEL, acceptable daily intakes for man were calculated by 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 about the nature of effects. Especially the efforts to better assess exposure quantitatively and to establish dose-response relationship for chemicals provide possibilities for improved risk characterisation including quantitative risk characterisation. Key issues to be addressed are described below.

2.11.2 Release and exposure assessment

Chemicals from various sources that are released into the environment are subject to processes such as transport, degradation, metabolism and distribution patterns. Sufficient insight into the environmental fate and distribution of chemicals and into their bioavailability to organisms including man will enable 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 dealt with:

Research Need 75(A)

- **Development of emission scenarios for appropriate categories of substances, where relevant, integrated for different compartments. This may include:**

– Development of predictive tools for the assessment of the fate, interactions and distribution of chemicals in relevant compartments including factors to define 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 are a result of 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). The relationships between tissue dose (internal dose) and the toxic response are described as biodynamics. Physiologically based biodynamic models (PBBD) are much less well developed compared to PBBK, primarily due to the limited understanding that exists of the biochemical mechanisms which link tissue dose with toxic effect. Improvement of PBBD and PBBK models will reduce uncertainties in (quantitative) risk assessment considerably.

Research needs in effect assessment are:

Research Need 77(A)

- **Improvement of the methodologies of chemical effect assessment to reduce uncertainties in quantification of risks.**

– Development of models related to uptake, distribution, metabolism and excretion of chemicals. Such studies should include *in vitro* and *in vivo* comparisons to improve prediction and when possible, reduce the use of animals.

– 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. Thus, results of exposure assessment are related to effect assessment information in order to characterise the probable risk in, ideally, quantitative terms.

Since in the case of chemicals effect assessment predominantly derives from animal experimentation, extrapolation from animal to man is a necessity with uncertainties. However, species extrapolation based on PBBK and PBBD will provide estimates that are superior to conventional methods. In risk characterisation for chemicals a distinction is made between genotoxic and non-genotoxic substances. While for genotoxic the assumption is currently made that its action is a non-threshold phenomenon, the existence of a threshold for non-genotoxic substances is generally accepted. 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 and 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 upon experimental and human data with emphasis also 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 the factors which modify human susceptibility to environmental toxicants and development of methods for measuring susceptibility to chemical exposure, which may lead to the identification of "high risk" groups and sub-populations. Such studies should include the determination of 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 chemicals in the environment is a well developed process. Measures, however, are highly dependent on the risks involved. Therefore, it is imperative that the risks for the environment and for human health are clearly defined. The research needs mentioned above will enable a more accurate risk assessment as the basis for future risk management.

2.11.6 Genetic susceptibility to environmental toxicants

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

Increasingly, information is becoming available that considerable differences may exist in the activity of such physiological processes within a species due to genetic polymorphism. Such a polymorphism modifies the effect of a toxicant and since variant genetic traits are quite common (15 to 50%), it may have an important impact on human health. Although many genetic polymorphisms have been identified, the biological consequences of some of these polymorphisms remain unknown. Similarly, epidemiological studies

to estimate risk associated with specific genotypes or combinations of genotypes are limited.

Most important chronic diseases of modern industrialised societies, including heart disease and cancer, have a multi-factorial origin, and a great number of environmental and genetic risk factors have been identified. Gene-environment interactions are of primary importance in the area of individual susceptibility to the development of specific diseases in their 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 a variety of factors including differences in absorption, distribution, metabolism and excretion of the toxicant, repair of the DNA damage, as well as changes in genes controlling cell growth and differentiation and their expression.

Recent knowledge on the genetic basis for individual differences, metabolism and normal cellular defence presents new possibilities for studies focusing on increased susceptibility for (chronic) diseases like cancer, Alzheimer's disease and neuro-degenerative disorders. Inclusion of information about susceptibility will increase the power of epidemiological studies since the populations can be stratified according to their genotype of enzymes involved in relevant biological processes. Such biomarkers of susceptibility may also contribute significantly to risk assessment methodology since they provide understanding of host factors affecting individual risk and enable accurate estimations of increased risk for certain (exposed) sub-populations.

There are some prerequisites this type of study should meet. Firstly, the role of the phenotype/genotype in modifying human health risks due to environmental exposures can be properly examined only if the population under study has had a well-characterised and documented exposure. Secondly, it is essential to have a biologically plausible hypothesis how the phenotype or genotype may affect the biotransformation or disease processes under study. Thirdly, an understanding of the expression of a genotype at the phenotypic level in the target tissue is warranted. There is a huge research potential for improving the 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 a 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 to allow understanding of the scientific basis of high risk individuals.

– 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 in order to justify epidemiological meta-analysis to estimate population-contributed risk imposed by a specific genotype or a combination of genotypes.**

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

The advent of the antimicrobial era in medicine meant that most diseases of bacterial origin became easily and reliably treatable. It soon became apparent, however, that bacteria could develop mechanisms by which they could resist the antimicrobials to which they were formerly susceptible. Over the 60 years of the antibiotic era the prevalence of resistant strains has increased as has the level of resistance within some strains. For some serious human pathogens the frequency with which isolates are found to be resistant is presently increasing exponentially (78% of Salmonella typhi-murium isolates were resistant to major antibiotic groups in a 1997 French survey). This scenario has led some authorities to speak of a post-antibiotic era, i.e. one in which effective therapy with antibiotics becomes increasingly unavailable. This is already the case in the USA for Vancomycin-resistant Enterococci (VRE). Fortunately,

in Europe VREs remain sensitive to other antibiotics but some other organisms show increasing resistance (e.g. Mycobacterium tuberculosis, Salmonella typhimurium, E.coli, Staphylococcus aureus, Streptococcus pneumoniae).

In addition to those problems, which arose in part due to the frequent use and misuse of antibiotics in human medicine, there is now evidence of a more obscure but maybe much larger threat from the use of antimicrobials in animals, both in therapy and prophylaxis as well as in animal production. The tonnages used annually are often greater in orders of magnitude than in man, e.g. Denmark used 24 kg of Vancomycin in 1994 in humans but 24,000 kg of the related glycopeptide Avoparcin in animals. A survey showed the symptom-free carriage of Vancomycin cross-resistant Enterococci in the animals fed Avoparcin. Denmark, followed by the EC, decided to ban Avoparcin since animal Enterococci may reach man on meat via an unavoidable contamination of carcases with faeces at slaughter. However, it is not known whether Enterococci of animal origin can colonise the human gut or whether in transit they can simply transfer their resistance determinants to commensals already resident in human gut. The 2-8 % VRE carrier prevalence reported in Belgium is claimed to establish the extent to which animal to man transfer has happened. It is believed that, if a VRE carrier becomes a patient who receives Vancomycin, selective pressure operates in favour of the VREs. In consequence they become numerous and can move from the gut to establish systemic infection.

Thus, indirectly, the use of antibiotics in animals can cause microbial disease in man. It is especially noteworthy that this is an effect mechanism which could be quantitatively more important than the classical zoonotic food-borne infections, simply because of the huge numbers of commensals in faeces as compared with pathogens, together with the many opportunities for cross-species transfer of resistance factors.

Dissemination of resistance is known to occur and it is also established that many bacteria can move from one animal species to another, both with disregard for national frontiers. Similarly, it is known that any use of an antimicrobial is accompanied by risk of some induction of or selection for resistance. The former approach to defeat resistance by developing new antimicrobials is claimed no longer to be an available option. 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 the presence of resistance in farm animals in the EC and the mid-October 1997 WHO meeting in the Bgvv in Berlin to discuss "the medical impact of antimicrobial drugs used in food animals". It is also already plain that politicians driven by consumers may act by instituting immediate bans on the mere possibility rather than the substantial proof of danger, as was the case for the animal feed additive antibiotic Avoparcin in April 1997. Antibiotic resistance is now well recognised as an important problem by the public, by politicians and by specific interest groups.

The implications of the resistance question as described above necessitate a multinational approach and this proposal is, therefore, an element of the ENHE Programme. The potential for a research agenda is considerable because little substantial information exists in the matter of the time scale of the waxing and waning of resistance patterns in relation to management strategies such as antibiotic use restrictions. Even the possibility of transfer of resistance from animals to man lacks solid as opposed to indicative evidence and yet risk management action has been taken and more such is sought by some member states.

Furthermore, evidence is now becoming available to suggest that sensitivity does not return other than extremely slowly (perhaps as much as 15 years was suggested in a recent American study) following the cessation of use of an antibiotic. This indicates the need for new molecular means to reverse the resistant state. The rewards could be considerable if, for example, the resistance levels in other European countries could be reduced towards the much lower levels of Denmark, which has long since had a conservative approach towards the availability and use of antibiotics in man and animals.

The most crucial question to be answered is whether and if so, to what extent, the animal resistance pool will get into man and cause disease - research needs 82(A) and 83(B). Should this be the case, more detailed information is necessary about the causation, persistence and elimination of that resistance pool. The resulting information will then be the input for the development of strategies for the future use of antibiotics in animals in a manner which will 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, better to characterise the resistance**

genes, their regulation, their means of expression and the extent of their 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, as a means of infecting humans.

– Screening studies on the fate of resistant Enterococci in carriers on admission to hospital including their subsequent involvement in disease should be performed. 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 in particular 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 involve among others the monitoring of resistance patterns, the subsequent removal of production enhancers and the monitoring of the consequences for resistance.

– The monitoring of use of the production, prophylactic and therapeutic antimicrobials in animals, nationally.

– The investigation of means to enhance the rate of loss of resistance factors and/or means of restoring antimicrobial sensitivity.

– Research into the economic consequences for the production of pigs and poultry 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, paneuropean level

3.1 World Health Organisation

In the Helsinki Declaration on Environment and Health it was 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 consequences for the health and well-being of large numbers of people in Europe resulting from unsatisfactory living, working and recreational environments. 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 the 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 in support of the aims of the Helsinki Declaration.

In the EHAPE it is pointed out that rational management of the environment in relation to health is hampered by gaps in our knowledge of how environmental changes affect health, how they relate quantitatively to health effects, and which population sub-groups (e.g. according to age, sex, genetic predisposition, sensitivity, nutritional conditions, pre-existing diseases) are more vulnerable to this or that change in the environment and to what extent.

According to the EHAPE these gaps can be filled only through well planned and systematic research, especially epidemiological research. This research should aim at defining indicators of exposure and/or early damage due to environmental agents at molecular, cellular and functional levels through laboratory investigations, and at population level through health surveys using *inter alia* the statistical and other data suggested above, suitably broken down geographically. Research should also aim at identifying the environmental factors contributing to the occurrence of unexpected health problems.

Because environmental health management involves more than mere recognition of the need to prevent or mitigate adverse environmental effects on health, research should also be conducted in technological, social and economic fields in order to develop environmental, health-friendly technologies and to reveal

the extent to which their likely higher initial costs, compared with traditional technologies, are offset by gains in health and well-being expressed in monetary terms. Likewise, it would be useful to devise methods to compare detriments and gains that a given activity may simultaneously produce on different aspects of health and well-being in order to ensure a resulting net balance in favour of health.

Thus, in the EHAPE the following objectives are defined:

- To provide 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 the maintenance and development of 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 to health and health effects.
- Assessments of the risks of low-level and complex environmental exposures and of the effects on health 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 methods of exposure measurement 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 to make possible 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 the costs of preventive action achieved through technological advances and other means, and the gains expected in terms of health protection and promotion. This should also include a comparison of the detriments and benefits to health that the same economic activity may simultaneously bring about.

The national NEHAPs have the scope and purpose to develop a programme for improving the health status of the nation by advocating and improving the quality of environments supportive of human health. In the NEHAPs a chapter on "Environmental Health Research" depicting ongoing and future research and priorities is usually included.

During 1997 and 1998 the NEHAPs of a number of countries in West, Central and East Europe have been finalised. These have provided additional input into the process of defining research needs in environment and health and the research needs described in the NEHAPs are complementary to the research needs described in the present document.

A practical determinant of research priorities from the WHO point of view is the need to support WHO guidelines by 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 the translation of results into policy application. Moreover, research data may also enhance the role that WHO plays in the development of methodological guidelines such as in 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 in the framework of 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. On request of ESF/ENHE Steering Committee, WHO/ECEH has 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 have been asked to identify additional priority issues for environmental health research in CCEE and NIS countries. The mini-review of this activity is attached to this document (Annex 3).

Considering the activities related to research in progress in the WHO-EUR Programme the general conclusion can be drawn that they flawlessly fit into and are complementary to the ESF/ENHE Programme.

3.2 European Commission

Environment and health has not been a separately identified issue in the various programmes of the EC. 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) information about the harmful effects on humans from environmental hazards is at present insufficient and that although the relative contribution of environmental hazards to disease in general may be small, (chronic) exposure to unsatisfactory environmental conditions may affect the health of sub-groups of the population such as children, those suffering from 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 is present 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 related to 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 hazards to health from chemicals in the environment (other than in the work place), including methods for exposure prediction and for 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.

- Strengthening the scientific basis underlying risk assessment of environmental chemicals (particularly genotoxic chemicals) through, *inter alia*:
  - Refinement and validation of existing regulatory test methods for new chemicals and increasing their utility in risk assessment.
  - Development of alternative test methods which reduce the numbers of animals required for 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 man, single to multiple and acute to chronic exposures.
  - Identification and improvement of our understanding of the genetic basis for susceptibility of individuals and vulnerable groups to 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 more effectively be translated into practicable and visible results. Through targeting of activities on major EC policies (employment, quality of life and competitiveness) and concentration of efforts on a number of key themes maximisation of impact in relation to resources is sought. For the first time, environment and health receives special attention in a key action on 'Nutrition, environment and health' 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 sound 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, the co-ordination and the links between the environment and health fields. This would contribute to the reduction of potentially negative impacts on health of factors like air pollution, heavy metals, toxic substances, noise, climatic changes and electromagnetic radiation (including those generated by mobile communication systems) and the effect of pollution at the

workplace. To address these issues, the following scientific and technological objectives would be pursued:

- Epidemiological studies: To focus on the application of uniform transnational protocols using large populations in standard-setting to effect public health protection.

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

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

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 the incorporation of health effects into environmental policy and for measuring environmental health benefits and costs; improved techniques to address the issues of environment, health, risk perception and risk communication.

The EC research initiatives are described at a higher hierarchical level compared to the ESF/ENHE Programme research needs. Nevertheless, the two programmes are substantially in accordance with each other, thus enabling a further detailed description at individual project level.

3.3 Global environmental changes and health of human populations

Research concerning global environmental changes is not or only partly covered in the programmes mentioned in this document, the main reason being

that separate task groups at a global level are concerned with this problem. 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) devoted in its second assessment report specific attention to health. In 1996 a comprehensive book on the health impact of climate change was produced by a task group from the WHO, the WMO (World Meteorological Organization) and the UNEP.

The ESF/ENHE Steering Committee recognised that research into the 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 where the research needs on ozone depletion/UVB exposure and climate change in relation to health and well-being are described. This mini-review has already been discussed in this document (see Section 2.1).

3.4 Other specialised agencies

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

References can be found in the appropriate annexes (see Part 2).