

**Aanvraag tot erkenning en betoelaging als steunpunt voor
beleidsrelevant onderzoek voor het thema**

Milieu & Gezondheid

**Deel III
Meerjarenprogramma**

Consortium

**Vrije Universiteit Brussel
Universiteit Gent
Katholieke Universiteit Leuven
Universiteit Antwerpen
Vlaamse Instelling voor Technologisch Onderzoek
Provinciaal Instituut voor Hygiëne**

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I. GENERAL INTRODUCTION

Environment and Health is an important policy topic for the Flemish Government as reflected by the governmental agreement, chapter XII, Environment, section D, Environment and Health, and the Policy Document, Environment and Nature 2004-2009. It goes beyond the individual policy scopes of environment and health, what makes it a good example of integrated policy.

The 2007-2011 program is on one hand a continuation of the 2001-2006 program: especially the human biomonitoring, including risk communication and the Action Plan, is given a still more central role, but the information desk, models of participation and social involvement and research about endocrine disruptors were yet present in the former program. On the other hand, new topics are the research on fine dust and nanoparticles, on social inequality versus health and environment and the inclusion of new chemicals.

1. General Coordination

This part defines the task description and functioning of the coordination cell and the different committees (executive committee, fieldwork coordinators committee, ...) inside the Flemish Center of Expertise on Environment and Health. Furthermore it defines important issues and their conditions as:

- the quality assurance aimed for in the activities of the Center
- the communication within the center, as well as external information and communication.
- The management of the working budget
- The ownership of and rights on foreground knowledge
- Publications and active distribution of information to a broad public
- Authorship of publications

2. Human biomonitoring:

Human biomonitoring is one of the most direct methods to measure the impact of pollutants in men. Biomarkers of exposure and biomarkers of effect will be monitored. The first type of biomarkers gives information on exposure over time by various routes and also on the resulting internal dose. For a limited number of pollutants the internal dose can be compared to international standards. The second type of biomarkers allow to measure in an integrated way biological and health effects due to combined exposures including also unidentified substances and taking antagonistic and synergetic effects into account.

Several members of the Center have been involved in previous Flemish biomonitoring programs (1999, 2001-2006) and have acquired a very good expertise. The biomonitoring program will consist of several related sub-projects:

- (1) A surveillance program with identification of high risk groups. This program will be linked to the forthcoming European Project on Human Biomonitoring (it is expected that it will start early 2007) that is prepared via the EU-ESBIO Project. The surveillance program will include classical pollutants such as toxic metals and persistent organochlorine pollutants (POPs), but also new emerging chemicals in order to obtain some insight in the exposure levels of these new substances in the Flemish population. In total we estimate that about 600 participants will be recruited to establish a reference database for these

- biomarkers. Non-environmental exposure routes such as nutrition and smoking will be assessed via questionnaires.
- (2) There will be a follow-up of relevant cases observed in previous biomonitoring projects: candidates are POPs in rural Flanders, Antwerp and the Albert Canal area or modern pesticides in the Fruit production area. The Action Plan of the 2001-2006 biomonitoring exercise will guide us in the selection of cases.
 - (3) The effect of hot spots (strong polluting point sources) on the health status of residents living in the vicinity of the hot spot will be studied. Possibly a gradient approach (the point source is the center) for the recruitment of participants will be adopted. A transparent and deliberative procedure for the selection of the hot spot(s) will be developed and tested;
 - (4) The design of the Action Plan consists of 3 phases (see Figure 2 in the description of the project). For each of those phases, a practical cycle is developed with the different procedural steps, actors and roles. The practical cycle is made up of cyclic steps to be taken during each phase of the Action Plan. It is clear, however, that the consortium is not sufficiently equipped for the day-to-day implementation of the Action Plan, but it will guide and process the internal and external process and research steps.
 - (5) External communication of biomonitoring results will be elaborated on the basis of scientific insights present in risk communication literature and the expertise acquired during previous biomonitoring campaigns (2001-2006). Initiatives for participation are a logical outcome too of the scientific insights in contemporary risk communication literature.

3. The information desk:

The information desk will operate very similarly as in the previous 2001-2006 programme. Several governmental services and policy making institutions need information on health damaging properties of substances (common ones and also recently developed ones), radiations, environmental factors,... To cope with these needs, the information desk will develop 2 main types of activity: (1) provide answers to precise questions from the authorities using the available large stock of library information and (2) make systematic in depth studies of important environmental health issues including the danger of new chemicals.

4. Research projects on the health and environment

4.1. Effects of fine particulate air pollution and nanoparticles:

This topic includes 5 sub-projects: (1) small particulate air pollution and markers of inflammation and hemostasis in a panel study of elderly patients with COPD and persons at higher cardiovascular risk; (2) a cross-sectional analysis of markers of inflammation and hemostasis in association with fine particulate air pollution in adolescents; (3) time series on the association between preterm delivery and fine particulate air pollution; (4) association between markers of genotoxicity and indicators of traffic related air pollution; (5) Validation and development of biomarkers for individual exposure to particulate matter.

Part of the study will be co- financed by a federal grant (BELSPO). The content en financing of the different subparts will be described in detail in an agreement between the partners concerned.

4.2. Research projects on the health effects of endocrine disruptors:

This topic includes 3 sub-projects: (1) a case control study in patients with male sub fertility, (2) a case control study in patients with female sub fertility, (3) a study of the relation between exposure to endocrine disruptors and biological effect.

4.3. Support research related to participation and to social inequality:

The social scientific expertise related to participation is integrated in different integrated research topics of the consortium. The policy relevance of risk surveillance and environment-health research will be significantly higher when contemporary social scientific insights on risk assessment, knowledge production, interdisciplinary and transdisciplinary interaction, and risk communication are taken into account. The role of social sciences in such settings is also a valuable research topic in itself.

To get better insight in the relation between social inequality and environmental health factors, social status information will be included in biomonitoring exercises. However, before that a check of literature and research findings is recommended before developing additional questions on social class.

4.4. Asthma and allergy (newborns)

There will be a follow-up research study including the children who participated as newborns in the biomonitoring project 2001-2006. Updated information about health, school results, length and weight,... will be asked to the parents. In addition, a more detailed study about nutrition, exposure to fine dust, allergies and neurological development will be performed on a sub-group. Part of the study will be co- financed by a federal grant (DWTC program). The content en financing of the different subparts will be described in detail in an agreement between the partners concerned.

4.5. Additional morbidity and mortality information about adult participants involved in the pilot study (1999) and the biomonitoring program (2001-2006) will be gathered via consultation of databases and local administrations.

For all the tasks described here above, objectives, methodologies and valorization will be described.

II. PROGRAM

1. General Coordination of the Center

1.1 Promotor-coordinator and promotor-spokesperson

Prof. W. Baeyens (VUB) is the project promotor-coordinator and responsible for the management of the program with respect to costs and the planned milestones. The promotor-coordinator will also be responsible for the interface with the administrations of the Flemish Government, as for the submission of technical and financial reports. The promotor-coordinator will also be responsible for the coordination between all participants and for the follow-up of the project plan, including the issue of the progress reports, management reports and the output of the deliverables. For this purpose the promotor-coordinator will be assisted by a management assistant. The coordinator will also chair the executive committee (dagelijks bestuur) board and organize all necessary meetings. He will also be in charge of annual and final reporting, to which all promoters and partners are expected to contribute.

Prof. N. van Larebeke (UGent) is the promotor-spokesman (promotor-woordvoerder) of the Flemish Center of Expertise for Environment and Health. He will act as the interface between the Center and the Flemish Government and its administrations as to medical and health-related issues and is also the spokesperson of the Center towards the public and the stakeholders. The content of the messages will be discussed and approved beforehand by the executive committee. For external communication the promotor-spokesman will be assisted by specialized research teams.

1.2 Executive Committee (Dagelijks Bestuur)

The executive committee consists of the following promoters and representatives of VITO and PIH¹ of the Flemish Center of Expertise for Environment and Health:

- Prof. Willy Baeyens (VUB)
- Prof. Nik Van Larebeke (UGent)
- Prof. Benoit Nemery de Bellevaux (KULeuven)
- Prof. Ilse Loots (UA)
- Prof. Greet Schoeters (VITO)
- Dr. Vera Nelen (PIH)

The executive committee will also include one representative of the scientific candidates for the doctorate, chosen by the scientific co-workers, paid on credits of the Center.

The executive committee will at least meet on a two-monthly basis and will be chaired by the promotor-coordinator Prof. Willy Baeyens. In his absence the chairmanship will be assumed by the promoter-spokesman Prof. Nik Van Larebeke. In absence of both the promotor-coordinator and the promotor-spokesman, the eldest promotor will chair the executive committee. Absent promoters will look for replacement and their absence can not be an argument to postpone decisions. A delegation of the executive committee will

¹ Since VITO and PIH are co-initiators of the second generation Center of Expertise for Environment and Health, the Center considers the status of their representatives as equal to those of the promoters.

accompany the promoter-coordinator and promoter-spokesman, depending on the agenda points, to the meetings with the steering group.

The executive committee will, based on the submitted long-range plan, establish a detailed project plan and quality assurance plan for the information desk, human biomonitoring and research activities. The plan will describe the organization and different phases of the activities of the Center, detail the tasks carried out by each partner, describe outputs to be produced. The quality assurance plan will describe the functional organization of the research activities and the methods used to manage these activities, such as the methods of investigation and the methods for result analysis, adhering to Good Laboratory Practices. The executive committee will evaluate the progress of the project and will compare the obtained achievements with the milestones and project deliverables. The executive committee will also approve the management and financial reports of the coordinator and decide on strategic modification to the project or to its organization, should this be necessary.

A document ‘Spelregels’ will be designed in the first months of 2007 and will be submitted for agreement to the Flemish government. This document describes in a general way the rules for external communication of the research results and comprise agreements made between executive committee and the Flemish government, which then will form the basis for the communication strategy and plans.

The executive committee is the forum on which external communication will be tested; before it is communicated externally.

The executive committee will develop a systematic interaction with other Centers of policy relevant research, such as the Center of Expertise for Well-being, Health and Family (Steunpunt Welzijn, Gezondheid en Gezin), The Center of Expertise for Mobility and Public Works (Steunpunt Mobiliteit en Openbare Werken), The Center of Expertise for Space and Living (Steunpunt Ruimte en Wonen), The Center of Expertise for Sustainable Development (Steunpunt Duurzame Ontwikkeling).

1.3 The Strategic Objectives Committee (SOC)

For specific items such as the Field Coordinators Committee (see 1.4) a SOC can be established.

1.4 The Field Coordinators Committee (FCC)

The biomonitoring program will be executed by the field coordinators committee. This committee will be headed by Prof. G. Schoeters, Dr. V. Nelen and Prof. N. Van Larebeke. Prof. G. Schoeters (chairman) will be responsible for the coordination. The FCC consists further of the representatives of the different disciplines necessary for the realization of the program. The FCC will at least meet on a monthly basis. Delegations of the Flemish government can be invited for specific points on the agenda. The chairman invites, in name of the management of the FCC, the participants and is responsible for the agenda and reports of the meetings.

The FCC works out the details of the biomonitoring program, described in the long-range plan and monitors the progress of the program in function of the objectives and the time schedule. It assures optimal integration of all biomonitoring activities of the

Center including those foreseen in the research projects. It decides on scientific aspects such as the sampling strategy, selection of appropriate biomarkers for the biomonitoring areas as under investigation. It will develop a strategy for biomonitoring in hot spots and specific cases that were selected by policy makers after consulting stakeholders. The choices for biomarkers and target groups will be described in the annual plan and submitted to the executive committee and steering group for final approval. The FCC designs the statistical analysis of the data.

Decisions in the FCC are made in consensus. Cases, in which no consensus can be reached, will be presented to the executive committee for a final decision.

The results will be interpreted acknowledging the input of the different disciplines. They will be reported to the executive committee. The minority's point of view will be also reported in case no consensus can be reached. After approval by the executive committee – under the responsibility of Prof. Baeyens (promotor-coordinator), Prof. Schoeters (coordinator of the FCC), Prof. Van Larebeke (promotor-spokesman) and Prof. Nemery - the results will be reported to the steering group and to the stakeholders according to the “Spelregels” document.

The VITO team will be responsible for the organization, the chairmanship and the coordination of the different tasks of the FCC and for smoothly proceeding of the program. The VITO team will collect the data from toxicological and biochemical analyses and organize the quality control.

The fieldwork will be headed by Dr. V. Nelen of the PIH. Dr. Nelen will be responsible for the use of the data following the rules of ethics and privacy. She will be responsible for submitting the scenarios for biomonitoring to the committees for Ethics and Protection of The Personal Atmosphere of Life. The PIH team will be responsible for the recruitment of the survey participants and for the communication with the survey participants in cooperation with Dr. N. Van Larebeke.

The University of Hasselt partner, Prof. G.Molenberghs, will be responsible for the Statistical data processing with respect to sampling strategy and data analysis.

The research group of Prof. Dehenauw (University Ghent) will be responsible for the analysis of data on nourishment and use of local food with respect to biomonitoring outcomes.

The toxicological analyses carried out under the responsibility of Prof. W.Baeyens, Prof. N. Van Larebeke and Prof. G. Schoeters.

The communication strategy will be designed by the social scientists of the University of Antwerp under the responsibility of Prof. I. Loots and Prof. L. Goorden.

Prof. N. Van Larebeke (promotor-spokesman) is responsible for the external communication to the authorities and the public concerning the biomonitoring program. The spokesman will be assisted in external communication by the involved experts of the participating research teams.

1.5 The International Scientific Committee (ISC)

The coordination cell of the Center will also ensure the contact between the Center and the ISC. This committee serves as advisory body and sounding board for the ISC guards quality control procedures and assures that the activities are in line with the international developments. The committee is composed of internationally well-known experts. The following experts will be asked to be members of the committee:

- Chairman: Dr. P. Lefèvre-Witier (Toulouse, Fr.)
- Cancer: Dr. S. Bonassi (Genova, It.)
- Embryo toxicity: Dr. C.V. Howard (Liverpool, UK.)
- Endocrine disruptors: Dr. J. Koppe (Amsterdam, NL), Dr. J. Oleo (Madrid, Sp.)
- Epidemiology: Dr. A. Saso (Lyon, Fr.), Dr. G. Winneke (Dusseldorf, D.)
- Screening technology: Dr. B. Brouwer (Amsterdam, NL)
- Genetic toxicology: Dr. Jos Kleinjans (Maastricht, NL.)
- Policy instruments: Dr. R. Van Leeuwen (Bilthoven, NL.),

This basic Group of experts can be complemented by ad hoc and thematic experts, if necessary. Consultation will be electronically on ad hoc basis.

In case an expert refuses to be a member of the ISC, the Center will look for replacement.

1.6 Quality Assurance

The quality assurance aimed for in the activities of the Flemish Center of Expertise for Environment and Health is based in the first place on the research plan itself: it is important that the proposal is written and structured in a very clear way. The responsibilities and tasks of the participating research groups are well defined in the project.

The following tasks will be executed:

- Establishing the critical points of the projects and the subprojects in collaboration with the research leaders and scientists;
- Verifying those critical points by using a control program;
- Reporting possible aberrations to the research leaders and the management;
- Approving the research report by means of a QA-statement

The promoters and partners are responsible for the elaboration of a clear research program including the “mile stones” and the intermediate evaluation of the research plan. In order to guarantee the quality of the research plan measures are taken to manage and to control the complete “primary process”. The primary process starts with sampling and ends with reporting of the results. At each step or level, a number of quality aspects have to be dealt with:

Sampling, transport and storage samples

- Sampling plan with instructions to collect samples in a representative and statistically correct way
- Sample identification
- Manner of packaging and measures preventing (cross-) contamination

- Conservation conditions and periods, taking into account the stability of the sample
- Measures preventing loss, contamination

Analyses

- Method validation (accuracy, reproducibility, matrix effects, linearity, LOD, LOQ, robustness)
- Quality control: first line control and the use of control charts
- Use of certified reference materials
- Ring tests

Data Treatment

- Used statistical methods
- Verification of raw data and calculations, preferentially by an independent person

Reporting

- Defining the internal and external communication lines and the way to elaborate, to verify and to approve work reports
- Verification of the content of a report
- Approval

1.7 Communication

1.7.1 Communication within the Center

For all meetings a secretary will be appointed, who will be in charge of reporting of the meeting and distributing all necessary documents or reports to all partners. In addition to meetings, information exchange will be made by e-mail, telephone, fax and mail.

1.7.2 External information and communication

External information does not contain results of the study or does not refer to them unless there is a mutual agreement on the external communication between the Center of Expertise for Environment and Health and the responsible ministers and their administrations. The guideline governing external communication is the document “Spelregels”, that that will be developed in the first months of 2007 and will be discussed with the Flemish government.

The following instruments will be used for external messages and communications:

- a) A website will inform about the aims, activities, reports and publications of the Center and will also contain an interactive compound to collect and reply, when possible, to questions and comments
- b) A brochure of the results of the different biomonitoring studies for extended distribution
- c) A by e-letter Environment and Health (the Biomonitor)

1.8 Management working budget en personnel

The working budget of the Center will be paid on the bank account of the Free University of Brussels. In the cooperation contract (samenwerkingsovereenkomst) will be described in detail how this budget will be further divided between the promoters/partners, following the global budget overview of table 1:

Year	2007	2008	2009	2010	2011
W. Baeyens (VUB)	185.000	185.000	185.000	185.000	185.000
N. Van Larebeke (UGent)	175.000	175.000	175.000	175.000	175.000
B. Nemery (KULeuven)	100.000	100.000	100.000	100.000	100.000
I. Loots (UA)	85.000	85.000	85.000	85.000	85.000
G. Schoeters (VITO)	220.000	220.000	220.000	220.000	220.000
V. Nelen (PIH)	85.000	85.000	85.000	85.000	85.000
S. Dehenauw (UGent)	35.000	35.000	35.000	35.000	35.000
G. Molenberghs (UHasselt)	10.000	10.000	10.000	10.000	10.000
Endocrine Expert Committee (EEC)	30.000	30.000	30.000	30.000	30.000
Totaal	925.000	925.000	925.000	925.000	925.000

Table 1: Global budget overview. The amounts are in euro.

Once-only funding for the realization of the complete action plan 2007-2008 regarding the human biomonitoring results gathered in the scope of the first generation Centre of Expertise for Environment and Health (2002-2006) (*Onderzoek naar de invloed van het voorkomen van milieugevaarlijke stoffen in het milieu op de mens en naar de oorzaken daarvan in opvolging van de groepsresultaten van de biomonitoringcampagne (fasenplan)*)

Year	2007-2008
VITO, PIH and UA	€ 220.000

The financial departments of each of these promotors/partners will manage the specific costs for the Center. The staff services of the promotors/partners are responsible for the handling of all the personnel activities going from contract, salary states, tax states, social security etc.

The complete accountancy and personnel handling of the Center will be organized in line with the Belgian fiscal and social security rights. The accounts are supervised by the governmental commissioners of each university and will afterwards be presented to the Rekenhof.

1.9 Foreground Knowledge - Ownership and User Rights

In accordance with article 44 of the Beheersovereenkomst, the Foreground Knowledge will be owned by the initiating institutions (Initiators) as defined in the Beheersovereenkomst. User rights will be granted to the Flemish Government in accordance with the conditions as defined in the Beheersovereenkomst.

Notwithstanding the above-mentioned, the parties agree that the collected data, results and knowledge of the biomonitoring program will be co-owned by the initiating institutions and their partners, represented by the promotors Prof. Willy Baeyens, Prof. Nik Van Larebeke, Prof. Benoit Nemery de Bellevaux, Prof. Ilse Loots, Prof. Lieve Goorden, Prof. Greet Schoeters, Prof. Vera Nelen. These results are entirely and permanently at the disposal of the initiating institutions, their partners and the Flemish Government. For the application of these results determinations concerning publications and authorship, as the guidelines concerning privacy and ethics (see point 2.11) will be observed.

During the steunpunt period (2007-2011) and also after 2011, the Flemish government has permanent, free, complete and unlimited user rights of the data and the results of the human biomonitoring.

A copy of the datasets of the human biomonitoring will at the end of the steunpunt be transferred to the “opdrachtgever”, the administrations of the to involved ministers.

Commercializing of data of the humane biomonitoring program by any initiator, partner or third approved user is strictly forbidden.

1.10 Publications and active distribution of information to a broad public

The researchers of the Center have the right to publish theirs results and perceptions that arise from the research financed by the Flemish Government as part of the Flemish Center for Environment and Health. These publications, however, have first to be presented to the responsible Minister(s) (functioneel bevoegde minister(s)) who can

delay the submission of the publication by three months, starting from the day the Cabinet received the publication.

Press conferences, press releases and other active distribution to a broad public will only be organized by the Center in co-operation with the responsible Minister(s), the steering group and only with the approval of the responsible Minister(s). The study results will first of all be presented to the steering group and the responsible ministers.

- Individual researchers reserve – within the framework of the academic freedom - the right to give their own opinion about the research results or insights to the public, but need to inform the steering group and responsible Minister(s) about the content of their communications. The Minister can enforce a moratorium of three months.

- In collaboration with the steering Group and with agreement of the responsible Minister(s), the Center enhances public awareness by announcing and publishing research activities in vulgarized way on the website of the Center.

During and after the ending of the Center the website of the Initiators has to announce the by the Center delivered research activities.

1.11 Authorship of publications

Concerning the authorship of publications two items are of special importance. First, the publishing of scientific articles needs to be made easier. Second, the legitimate interests of the concerned scientist must be guarded. The following procedure needs to be followed:

1. When a researcher of the Center wishes to write an article that contains data which were generated within the framework of the Center, he/she needs to present a short description and a list of authors (from within or outside the Center) to the executive committee. With regard to the biomonitoring especially a small group of researchers will be composed within the frame work of the field coordinators committee, who will write an article together. As first author the researcher will be presented who writes the larger part of the article. Co-authors can also be scientists who do not belong to the Flemish Center of Expertise on Environment and Health. The coordinator of the FCC needs to present to the executive committee a short description of the article and a list of authors.
2. The application will be formally presented at the meeting of the executive committee. The executive committee takes the final decision concerning the authorship and co-authorship and motivates this decision to the applicant of the field coordinators committee.
3. The authors are responsible for the content of the article.
4. Each publication will be presented to the executive committee and will be announced to the steering group.
5. This procedure does not need to be followed in case of abstracts and publications in other than scientific or professional magazines or books. However the concerned texts will be presented to the steering group.
6. The origin and the financing source of the used data need to be clearly announced in every publication. The acknowledgement, is the following: “The study was

commissioned, financed and steered by the Flemish government (Department of Science, Department of Public Health and Environment, Nature and Energy Department).“

2. Biomonitoring: a programme for environmental health surveillance and research

2.1 Introduction

Human biomonitoring is one of the most direct methods to measure the impact of pollutants in men. It takes into account exposure over time by various routes, and reflects the internal dose which is toxicologically relevant for interpretation of health effects.

This proposal aims for the further establishment of a human biomonitoring network which has to become an important tool for policy support in the domains of environment and environmental health. The biomonitoring network will also contribute to research projects elaborating on the relationship between environment and health. In the proposed program we will mainly focus on the assessment of reference values for the Flemish population as to internal exposure to a series of pollutants and on research about endocrine disruptors, fine dust, and interference of social factors and environmental health.

Since several members of the consortium have been involved in the Flemish biomonitoring pilot project (1999) and in the three past Flemish biomonitoring campaigns (newborns and mothers, adolescents and older adults 2001-2006) we will build on the available knowledge, fill in the gaps and improve the approach. Since members of the consortium are also involved in the preparation of a European pilot project on biomonitoring, we also attempt to integrate the Flemish proposal optimally into the European initiative.

One of the new aims will be to obtain reference values for the Flemish population, not only for traditional pollutants but also for newer emerging chemicals. The reference values will be the basis for comparison with data from international studies, and for the comparison with data from high risk populations e.g. residents of specific locations (hot spots) within Flanders or specific subgroups in the population which may be vulnerable due to specific diets, habits, social behavior, health status etc.

A framework for decision making will be established which will allow the different stakeholders (authorities, scientists, advisory groups, the public, etc.) to be consulted to define and prioritize the needs for specific tailored studies. Selection of biomarkers, study population and number of participants will be tailored in response to these specific study demands.

Transparency in the communication on objectives, methodology and results to stakeholders and participants, ethical and privacy issues are major aspects of the presented program.

2.2. Analysis of the needs on the relation between environment and health

Concerning the relation between environment and health in Flanders the needs can be resumed in a number of questions. Some of these questions are very general, other more precise as previous research already provides some information and offers certain opportunities.

1. Does environmental pollution actually lead to health effects and to what extent (this question was considered the most important in the relevant resolution of the Flemish Parliament)

2. To what extent is the Flemish population exposed to endocrine disrupting substances? Are biological or health effects observable?
3. To what extent are biological or health effects associated with exposure to fine particles?
4. Do environmental factors contribute to social inequalities in health?
5. To what extent is the Flemish population internally exposed to more recently introduced pollutants?
6. Is exposure to these pollutants in the Flemish population associated with biological or health effects?
7. To what extent are the associations between exposure and biological or health effects that were observed during previous biomonitoring campaigns reproducible and what is their strength?
 - Lead and DNA effects (comet assay)
 - Lead and mutation frequency
 - Lead and sexual maturation in girls
 - Persistent chlorinated substances and need of fertility treatment
 - Persistent chlorinated substances and sexual maturation in boys
 - Cadmium/lead and asthma
8. Are levels of pollutants in cord blood (as measured during the biomonitoring campaign on neonates) associated with neurobehavioral effects, allergy, growth and differences in general development at a later age?

2.3 General objectives

Surveillance of exposure to environmental chemicals is the most important objective of this proposal. This surveillance is translated into determination of Flemish reference values and into a tailored response concerning hot spots, risk regions and risk groups. Next to biomarkers of exposure this proposal includes determination of biomarkers of effect. Since only a fraction of environmental chemicals can be measured –because of analytical and financial limits-, and synergetic effects may occur; measuring effects gives an idea on a total impact on an organ system and adds information to the general picture of environmental hazards.

Next to surveillance the biomonitoring program offers the opportunity to answer research questions and to improve knowledge.

The biomonitoring program presented here combines both surveillance and research aspects in a series of biomonitoring projects which are focused on providing answers to the above mentioned needs and questions.

We consider that defining all of these projects in detail in this first description of our monitoring program is not optimal, as the results of measurements on pooled blood and urine samples collected during the actual biomonitoring program (2001-2006) and the results of the biomonitoring on adults should also be taken into account, and as input from Flemish authorities, experts on emissions and possibly from certain population groups is also needed. To that last end we will provide a framework for decision making as to the selection of specific surveillance programs and for the linkage of the results to policy programs. We are of the opinion that the choice of specific geographical areas should to a large part be based on available local emission and immission data, and also on societal considerations.

A first series of objectives, more related to surveillance, are:

- To establish a reference base for the presence of environmental chemicals in the Flemish population which will be a bench mark for further spatial and temporal analysis.
- To link the Flemish biomonitoring program to the European biomonitoring initiative
- To identify and characterize high risk subpopulations

A second series of objectives, including besides surveillance also research perspectives, will focus on several of the above-mentioned questions. Taking into account budgetary limitations, it is not possible to address all of the above mentioned research questions. The aim is to contribute to answer to as many questions as possible. To this end we will, where possible, take advantage of observations that were made in the past and that offer opportunities to extend knowledge efficiently. For instance: making additional observations on children that took part in previous biomonitoring campaigns.

On the basis of the research questions identified above, of considerations concerning opportunities (e.g. existence of data on groups of persons that participated in previous biomonitoring campaigns) and of information presently available to us we consider that the following objectives are prior:

- To study health effects of fine particulate air pollution.
- To study the relationship between endocrine disruptors and male sub fertility
- To study the relationship between endocrine disruptors and female sub fertility
- To study health effects of exposure to fine particles
- To follow up exposures and health effects in Flemish regions where previous biomonitoring showed there was some reason for concern
- To study internal exposure and biological and health effects in the immediate surroundings of an important point source in relation to distance from the source and in relation to local immission values. Due attention will be paid to the social status of residents in relation to distance from the point source, internal exposure and biological and health effects.
- To study exposure and effects related to presently used pesticides in the "fruit" region
- To follow up neurobehavioral and puberty development, prevalence of asthma and respiratory function in children who participated as babies in the 2001-2002 biomonitoring.
- To collect data on mortality and cancer incidence for the persons for whom tumor associated proteins were measured during previous biomonitoring campaigns.

Transparency and early communication of results is an important point of attention in this proposal. Timing of communication may be different for different aspects of biomonitoring. Research questions require more in depth analysis and discussions and therefore a more extended timing. Surveillance questions can be analyzed, taking into account relevant confounding factors in relatively limited time. Distinguishing these two aspects of biomonitoring offers the opportunity to improve timing of communication of readily available results and to guarantee quality by taking time for thorough analysis of more demanding research questions. When external communication is planned, the government will be informed beforehand about timing

and content of the information distributed, so they are able to prepare an appropriate answer.

2.4 Biomonitoring – surveillance program / identification of high risk groups

2.4.1 Aims of the surveillance program

In 2001 the first cycle of the Flemish human biomonitoring program started. The aim was to establish a biomonitoring network for surveillance of environmental health which is able to detect in the population early warning signals of increased environmental exposure to pollutants.

The program is actually running (2001-2006) and tests the hypothesis whether living in different geographical areas results in differences in exposure and early biological effects. It is based on the measurement of biomarkers of exposure² and biomarkers of effect³ in residents from 8 geographical areas with expected differences in pollution loads. In each geographical area, three age groups were systematically recruited: mother – newborn pairs, 14-15 years old adolescents, older adolescents between 50 and 65 years. In total about 4800 persons were included in the campaign. From the results that are already available it can be concluded that 1) a wide variety of environmental pollutants can be measured in the Flemish population, 2) significant differences in biomarkers of exposure and effects can be detected in residents from different areas and 3) although the levels of pollutants that were measured are low and are supposed not to pose immediate health concerns, several associations were observed between some of the exposure markers and effect markers, suggesting the potential increased health risk of some of the measured pollutants even at levels that are currently present in the environment.

Taking into account ethical and privacy issues, the results of the program have been communicated in full transparency to the participants of the campaigns, to the policy makers and to the public, and the results are currently translated into publications in internationally recognized scientific journals. The results are available on the web site www.milieu-en-gezondheid.be. In order to render the results useful for policy makers, a program has been initiated to translate the results into policy supporting information.

The current proposal aims to continue and build further on the program which has been accepted and referred to by the Flemish and Belgian policy makers (Budapest conference), the public, the press, local authorities and health professionals and by the international scientific community (see involvement in the SCALE program, EU implementation group for human biomonitoring, EU ESBIO and EU INTARESE program⁴).

For the new program we propose also some improvements with respect to the current program:

² Biomarkers of exposure: an exogenous substance or its metabolite or the product of an interaction between a xenobiotic agent and some target molecule or cell that is measured in a compartment within an organism (IPCS, Env Health Criteria 155,1993)

³ Biomarkers of effect: a measurable biochemical, physiological, behavioural or other alteration within an organism that, depending upon the magnitude, can be recognized as associated with an established or possible health impairment or disease (IPCS, Env Health Criteria 155,1993)

⁴ SCALE: A European Environment & Health Strategy; ESBIO: Expert team to Support BIOmonitoring in Europe, Policy oriented research; INTARESE: Integrated assessment of health risks from environmental stressors in Europe

- (i) a different approach for establishing reference values and reference ranges for the whole of the Flemish region instead of deducing these values from measurements in specific geographical areas.
- (ii) a more flexible approach for identification and characterization of high risk subpopulations.
- (iii) inclusion of new and emerging compounds in the human biomonitoring program in order to obtain some first insights in the exposure levels of the newer pollutants in the population.

Establishing reference values

Monitoring the general population in the whole of the Flemish region should allow to calculate population mean values and ranges of biomarkers which are more representative for the population living in the whole of Flanders. These values can then be compared (1) with corresponding values of specific *a priori* defined high risk groups (selected groups within the Flemish region), (2) with biomarker values from other EU Member states or (3) with biomarker values collected at different time points. The approach followed until now in the Flemish campaign, is that monitoring occurred in 8 *a priori* defined areas of interest. These areas all together covered about 20 % of the Flemish area and its population. A strategy for representative sampling in these 8 areas has been designed and as a consequence the obtained “Flemish reference values”⁵ were obtained from data representing about 20% of the population. In the new program we would argue to build up reference values which are really representative for residence in the global Flemish area.

These reference values can be obtained from a limited number of samples per age group. Sample size calculation will precede the monitoring campaigns (see 3.4.2.1).

Monitoring the general population will allow policy makers to have reference values:

- (i) a time based and Flemish based reference value for evaluation of environmental health policies;
- (ii) be able to compare Flemish reference values with data from other EU member states.

Identification and characterization of high risk groups

Reference values for the general population may be interesting for policy makers to follow time trends and to evaluate the further needs or efficacy of environmental measures. Defining and characterizing the exposure levels among high risk groups may be even of higher priority. High risk groups may be subpopulations living in areas with elevated environmental exposure e.g. industrial areas, vicinity of waste sites, historically polluted areas (Nouwen et al, 2001), or they may be populations belonging to specific social classes (Rotko et al, 2000), with specific dietary habits e.g. fish eaters (Sjodin et al, 2000) or with a specific home environment (Raw et al, 2004).

⁵ “Flemish reference values” for each biomarker were calculated based on the geometric mean and P90 of all data obtained in each campaign, they were weighed for the population size in each area

High risk subjects may be a high interest group for surveillance, as they are the most likely target to benefit from policy changes. Also, high risk groups may be the first to show an impact from an intervention, much before it reflects on the general population, providing a *role as indicators*. Another advantage of including high risk groups is that high risk subjects are likely to provide most informative links with exposure. As a consequence it may be *easier to link biomonitoring (of high risk subpopulations) with environmental and health data*. They are likely to signal sources of high exposure or behaviors that lead to high exposure and disease events.

The new proposal aims to identify and characterize high risk populations but based on *a priori* identified interests and criteria. Specific biomarkers should be studied in these groups, sampling methods and proper specific study powering is needed, in order to produce a meaningful analysis. The biomonitoring Field Coordinators Committee (FCC) will come up with an appropriate study design tailored for testing the hypothesis that a specific subpopulation has a higher exposure than the general population and for characterizing that subpopulation.

It is unlikely that high risk groups can be identified and characterized in general population sampling unless they are very frequent. This would in general require large sample sizes depending on the frequency of the high risk subjects in the population. High risk subjects are likely to be under-represented in a general population sampling for proper characterization. Moreover, identification and characterization of high risk groups from a general population sampling effort would require *a posteriori* comparisons which are less powerful, sensitive to bias from multiple comparisons and to inappropriate consideration of confounding factors. From the current biomonitoring campaign there is also the experience that elevated biomarker values may exist in subsets of the sampled population but that they are easily diluted if mean values or P₉₀ values are calculated from a large dataset. As an example, the current monitoring program showed that biomarker data from adolescents living in the vicinity of a household waste incinerator had no statistically significant elevated biomarker levels if the data were expressed for all 6 sites together. If the data were expressed per individual site and compared with a post hoc comparison test, statistical significant differences for specific biomarkers values were observed e.g. habitants of Menen (next to the French border) showed significantly higher mean values for PCBs and HCB. Also a recent study by Nawrot et al. (2006), showed that elevated exposure and health effects may be very local.

Including specific high risk populations in the monitoring program will allow policy makers:

- to evaluate needs and efficacy of local environmental measures;
- to investigate and objectivate local or specific concerns with respect to environmental exposure;
- to evaluate how policies directed to reduce general population exposure have also an impact on highly exposed groups;
- to evaluate how highly exposed groups signal exposure levels and exposure levels changes in the general population.

Monitoring of newer chemicals

The present program focuses on classical pollutants such as lead and cadmium, and persistent chlorinated hydrocarbons such as PCBs, dioxins, DDE and hexachlorobenzene. These compounds have well known toxic properties Adverse

health effects are expected in populations with elevated concentrations of these biomarkers above certain health based guidance values or at intake limits which are not far above the intake values that are expected to occur in the general population (small safety margin)(Lars, 2003; Feely and Brouwer, 2000; Pohl and Tylanda, 2000). From a health based point of view monitoring of these compounds is relevant, definitely since they were not included earlier in a systematic large scale biomonitoring program in Flanders. In addition, a lot of policy measures have been directed to control emissions and immissions of these compounds. It was obvious to start the biomonitoring program by obtaining information on the levels of these well known pollutants in the population. The last decades new chemicals have entered the environment. New technologies and new products may bring benefits to society but they may also pose some unknown health risks. Especially persistent or even bioaccumulating substances with long half-lives in humans are of concern, because such substances were found to have, on the long term, toxic properties that remained undetected for decades in the face of intensive use and considerable human exposure. For some of the new compounds the exposure and health risks are still largely unknown. We propose to include new and emerging compounds in the human biomonitoring program in order to obtain some first insights in the exposure levels of the newer pollutants in the population. This will be further elaborated under section 2.4.2.2.

In conclusion: the new program that we propose should allow to:

- establish reference values and identifying reference ranges for specific biomarkers;
- gather information on exposure to newer chemicals in the general population;
- compare the differences in mean biomarker values among groups with the reference values and ranges: e.g., selected groups within the Flemish region, the so called “hot spots” or “cases”, but also values from EU Member States;
- focus on well defined “hot spots” or “cases”.

2.4.2 Design of the biomonitoring surveillance program

A scenario is proposed in which general population sampling is alternated with sampling of high risk groups (see table).

2.4.2.1 Study population and sampling unit:

Reference values

To establish reference values the recruitment area will include the general population representative of the whole of Flanders.

Geographical resolution

In contrast to the previous campaigns in which the sampling areas represented only 20 % of the Flemish region, we propose to include now the whole of the Flemish area as a target area for recruitment. The sampling protocol should reflect the geographical distribution of exposure. Recruitment will be stratified by geographical areas. As such a minimum of samples will be collected from each region. As currently proposed for the EU pilot project on human biomonitoring (ESBIO) we will select at minimum 1 in 50

000 participants recruited from the different districts of Flanders (arrondissementen) proportional to their population size.

Inclusion/exclusion criteria

Age, Gender

Ideally sampling protocols should reflect the general population including all ages and gender. The present Flemish campaign includes three age groups: newborns and their mothers, adolescents of 14 -15 years of age, older adults between 50 and 65 years. This enables to have an overview of exposures in different important stages of life, similar to e.g. the campaign from the CDC in the US (Pirkle et al, 2005; CDC, 2005).

Sampling **women in childbearing age** serves three purposes: (1) measuring biomarker levels in women and by this determining exposure of the developing child which is especially vulnerable (Selevan et al, 2000; Tamburlini et al, 2002), (2) getting insight in biomarker levels of a population group in which prevention may be very efficient, and (3) awareness rising in young households. In the current campaign, the willingness to participate in this age group was 98%. However recruitment of women at childbearing age may be logistically complicated and not very cost effective as shown by the current campaign and by the WHO POPs campaigns (measuring persistent organic pollutants in human breast milk). In the present campaign they were recruited at the maternities at delivery. This enabled to obtain information on the newborn baby and cord blood was obtained which was useful for the analysis of biomarkers requiring large sample volumes of blood such as persistent chlorinated hydrocarbons. Because of the health relevance we suggest to include this population group at least for establishing reference values.

Sampling in **adolescents** has the advantage of providing information (1) on a vulnerable stage of life (puberty development) (Den Hond and Schoeters, 2005), and (2) on exposure and effects in subjects that will soon become fathers and mothers, (3) Internal concentrations in adolescents reflect, more than those in older persons, recent exposures, (4) adolescents have a specific life style and often come into contact with a lot of consumer products (Bolt, 2002; Valent et al, 2004; Neri et al, 2006), (5) adolescents are not yet professionally exposed, and show less exposure to traffic outside their region of residence, (6) recruitment of adolescents can be organized through the school system which may enable the school teachers to pick up the message and further sensibilise the adolescents for environmental health care, (7) data on sexual maturation and general development are gathered by CLB and can be most valuable for the interpretation of biomarker data, as was clearly demonstrated in the current biomonitoring project. (8) A biomonitoring campaign by the World Wide Fund for Nature suggested that the highest concentrations of some substances that were only more recently introduced into widespread use were found in adolescents, indicating a more intensive exposure of adolescents when the long half-life of these substances is taken into account. (9) Adolescents are old enough to have accumulated a significant proportion of the mutations they will incur during their life.

Recruitment logistics are far easier than for newborns and their mothers and recruitment has been successfully accomplished during the current campaigns of human biomonitoring in Flanders. However the participation degree may be somewhat lower in this age group. In the current campaign between 58 and 86 %

of the students that were invited effectively participated in the program. We propose to include this age group preferentially in the monitoring campaigns for establishing reference values and for specific campaigns addressing high risk exposure populations.

Older adults were selected in the current program to reflect exposure and effects that may accumulate over life time e.g. persistent pollutants (Vaclavik et al, 2006; Batáriová et al, 2006), DNA damage (Moller, 2006). The results of this campaign are not yet available. This study population can be successfully contacted through the national register of residents. Although of interest, we consider monitoring of the older population of less priority from a public health standpoint view compared to monitoring in the younger age groups.

To establish reference values we propose to monitor at least two age groups: newborns and mothers (18-40), adolescents (14-15). Priority will be given to complying with the European project on reference values. It might be interesting to include also the active male population (18-40) for the study of fertility and the older population (50-65), in order to obtain a complete overview of the impact of environmental pollutants in different age classes, however budgetary limitations might force us to make choices.

Based on initial sample size calculations (and to be further modified based on more extended calculations) we envisage that 150 to 200 participants per age group will be needed to obtain reference values for a biomarker. Not necessarily all age groups will be monitored for each biomarker. We need to indicate the appropriate age group e.g. cadmium in urine will be measured in the active population and in the older population; dioxins, PCBs, bromated flame retardants and lead are more relevant in the newborn-mother cohorts since the developing child is the most vulnerable subgroup in the population. If relevant for the age group, biomarkers will be preferentially measured in adolescents since they can be most efficiently recruited by the school system. If a region is very small or scattered, the approach used for regions around waste incinerators that has proved successful in the previous biomonitoring program will be used.

In total we estimate that up to 600 participants will be recruited to establish a reference database for biomarkers.

Other inclusion/ exclusion criteria:

In the present campaign everyone could participate if they were selected by the randomized sampling scheme, if they resided in the area for at least five years and if they were able to fill in a Dutch questionnaire. Residence for five years in the area was thought to reflect the exposure of the area well enough, although one should be aware that including residents with longer and shorter residence times and documenting this would inform about the strength of the impact of the environmental status on the biomarker levels. However this would require enlarging the sample size substantially. The requirement of being able to fill in a Dutch questionnaire was due to practical considerations, not having the manpower to translate the questionnaires in different languages. Smoking behavior was not considered as exclusion criteria, because smoking may interfere with effects from other environmental pollution (Burkart, 2001). However, it might be better to exclude smokers because active smoking is not an environmental hazard and because comparison of the general population with a study group exposed to a high risk environment might be hampered by the inclusion of

smokers into the sample of the general population. Also health status was not an exclusion criteria, since we cannot exclude that health problems can be related to environmental pressure or that diseased people have higher exposure levels. Documentation of smoking and health status by questionnaire information will allow correct identification and classification.

Exclusion/inclusion will be discussed for the different biomonitoring actions. Inclusion or exclusion of smoking will be a point of attention in this discussion. The criteria will be finalized taking into account the approaches proposed by the European pilot project.

Statistical analysis program and treatment of the data

Prior to the start of the program a plan for statistical analysis of the data will be designed and approved by the fieldwork coordinators committee after consultation of the steering group. The plan will explicitly state the hypothesis to be tested; it will be designed to match the objectives of the program and will define clearly the outcomes of the campaign. Important hypotheses and corresponding statistical tests will be defined previous to the sample size determinations. The data from the study will be collected in one data base which will be the basis for the further statistical analysis. The format, content and logbook of the databases will be discussed in the fieldwork coordinators committee and the steering group.

Sample size

Calculations of sample size will precede the study population definition and the sampling design. The sample size is one of the most determining aspects of the costs and timeline, it determines the power/precision of the estimates and the potential analysis and interpretation that will result from the campaign. Sample size calculations will be performed for all biomarkers considered. The biomarker with the highest population variance or lowest exposure prevalence will limit the minimum sample size requirements. If the difference between the sample size requirements among the selected biomarkers is significant, then a scenario where not all samples need to be processed for the most precise biomarkers may be considered. Sample size calculations will be based on the standard deviations of the biomarker data from each age group from the previous campaigns in Flanders. It can be calculated that for e.g. levels of lead in blood of adolescents and adults respectively 110 and 161 samples are needed to detect a minimal difference of 20 % with a statistical power of 80% and a statistical significance level of 0.05. This means that if differences in mean biomarker values are 20 %, statistical significant differences ($p < 0.05$) can be detected in 8 of the 10 studies.

For biomarkers for which no measurements in the Flemish population are available, sample size calculations will be done based on studies reported in the international literature.

Sampling strategy

A sampling strategy will be developed taking care to assure that sampling methods allow the identification and selection of any subject within the defined age range with equal probability (or, at least, a measured probability). Stratification will be based on *a priori* agreed criteria such as inclusion of age groups, gender and geographical resolution. To recruit participants either for the general population study or for studying specific high risk populations, following information systems can be used: registries of residence, school registries, or primary care registries, use of populations identified from well conducted other studies or surveys in the Flemish area. The Steering Committee will be asked to support the administrative requirements to obtain the

necessary data. Selection bias will be controlled by non-responder analysis. Representativity will be assessed by comparing the characteristics of the recruited population with population characteristics from the general population which can be obtained from national registers.

Questionnaires

To appropriately characterize the study population and to be able to discriminate between other factors but environmental factors which may influence the biomarker levels the participants will be asked to provide information based on questionnaire data. The questionnaire should give information on health status and disease, actual and previous residence, occupation, exposure by personal hobbies and activities e.g. farming, painting..., exposure to traffic, home environment, dietary habits, the origin of food items, social class and composition of the household.

An extended questionnaire has been developed in the current program. This questionnaire can be filled out by the participants without assistance and will be used again. Some questions which have not been found adequate enough will be revised and if possible the questionnaire will be shortened. In function of new chemicals that will be measured, specific new questions may be introduced e.g. exposure to consumer products. Since the consumption of locally grown food items has been identified as an important co variable for the biomarker values in the present campaigns, more attention will be paid to the exact role and contribution of these locally grown foods enabling a better quantification of the intake.

Questionnaires will be tested in advance on their performance in selected target groups. This will allow us to evaluate the time required to fill out the questionnaire and whether the questions are well fit to provide the information that is required.

2.4.2.2 Selection of biomarkers:

In the previous campaign, biomarkers were selected based on their well known toxic potency, their abundance in the environment and the existence of well established health based guidance values or intake limit values. In the new campaign we propose to extend this and include also newer emerging pollutants that are more recently introduced in the environment and for which almost no information on exposure is available.

Next to exposure biomarkers we propose to include also some effect markers. Since not all potential pollutants can be monitored individually, effect markers may overcome this limitation since they integrate the effects from toxicants with the same mode of action and may thus have a signaling function. Effect markers are early biological changes which are the result of the presence of a combination of toxicants, in this way they are much closer to health endpoints and have more health relevance than exposure markers. Combining the measurement of both exposure and effect markers in the same individual may allow to get some more insight in the causal exposure-effect relation chain, provided that possible confounders and covariates have been taken into account appropriately.

Based on distinct selection criteria following biomarkers are retained for the new program:

- Health relevance: this implies that adverse health effects are well known and that health based guidance values are established, e.g.
 - lead in blood (children) (Lanphear et al, 2005),
 - Cadmium in urine (adults) (WHO, 1992; Bernard, 2004).

- A small margin of safety between expected actual exposure level and the levels which cause adverse effects, e.g.
 - Dioxins in serum fat or milk fat (WHO, 1998)
 - PCBs in serum fat or milk fat (EFSA, 2005)
 - Arsenic (urine) (WHO, 2001)
 - Methyl mercury (hair) (EFSA, 2004)
- Chemicals⁶ from which we know that they recently entered the environment, e.g.
 - o Brominated flame retardants PBDE (serum fat) (Birnbaum and Staskal, 2004)
 - o Phthalates (DEHP and MEHP) (urine- adolescents) (Schettler, 2006; Duty et al, 2005)
 - o Bisphenol A (serum) (Fromme et al, 2002) (Von Sahl, 2005)
 - o Perfluoralkylated compounds (FFOS, PFOSA, PFNA – serum) (Kannan et al, 2004)
 - o Personal care products (Liebig et al, 2006)
 - o Pesticides in present use (e.g. chloorpiryfos, chlorophenoxypesticides, pyrethroids) (CDC, 2005)
- Biomarkers for combined exposure and for early response to the presence of chemicals in the body
 - o Effect markers for which reference values can be established are e.g. comet assay and micronuclei in peripheral blood cells of adolescents or adults (Moller, 2006; Neri et al, 2006). Data on occurrence of asthma and allergy (Basagaña et al, 2004), on fertility (Evers, 2002), on puberty development (Tanner and Whitehouse, 1976) can be obtained from questionnaires or from already registered medical health data.
 - o New biomarkers for combined exposures to endocrine disruptors (estrogen like compounds, anti-androgens, thyroid like compounds, aromatized inhibitors) are to be expected in the near future. Different international research groups (Hamers et al, 2006) and Flemish research groups (Van der Ven et al, 2005; Van den Belt et al, 2004; Christiaens et al, 2005) are currently developing such markers. If they become available as validated measurements, they may be introduced in the new biomonitoring program.
 - o Also new non invasive biomarkers are under development e.g. for measurements in exhaled air there are new promising non invasive alternatives for effect biomonitoring. Exhaled air measurements are easily applicable even in children. Markers in exhaled breath condensate and in the gaseous phase may signal changes in the airways that are related to respiratory toxicity in relation to air pollution (Montuschi, 2002). These markers are not yet validated, but it is envisaged that if they are validated, they may be introduced and applied in the new biomonitoring program.

The link with the REACH program will be a point of attention in the selection of biomarkers.

2.4.2.3 Linkage with the European biomonitoring initiative:

⁶ A number of the chemicals are measured in pooled samples from the current biomonitoring campaign, the results are to be expected in the fall 2006. Based on these results we will have a rough estimate of which chemicals will be possibly elevated in the Flemish population in comparison with reported values in the literature.

Background

As a first note, it is important to notice that the European Biomonitoring project (HBM) is still under development, and the information presented here may potentially be updated in the future. We aim to maximally integrate the Flemish human biomonitoring program into the EU initiative without fundamentally changing the objectives of the presented program.

The ESBIO Project (Expert team to Support Biomonitoring) is a two year program that is funded by the European Commission (DG Research) and focuses on the preparation of the framework for a coordinated EU approach with integrated quality control, communication strategies and the use of HBM for policy making. ESBIO has made a number of recommendations to the “Consultative Forum on Environment and Health”, and it is expected that the European Pilot Project on Human Biomonitoring will start in early 2007.

As one of the promoters of the current proposal is member of the ESBIO group and work package leader (VITO under the person of Greet Schoeters), we will be able to contribute in shaping the EU HBM pilot project and establishing close links between the Flemish and EU wide initiatives. The following is mainly based on the second Recommendation of the ESBIO group to the Consultative Forum of March 2006, and following discussions.

Proposal of pollutants

After repeated consultation with stakeholders and Member States, a twofold approach to pollutant choice was suggested by the ESBIO project

- Basic Scenario:
 - Lead in whole blood: target group is women in childbearing age and children
 - Methyl mercury in scalp hair: target group is women of childbearing age
 - Cadmium in urine: target group is women of childbearing age
 - Cotinine in urine: target group is women in childbearing age and children
- Extended Scenario:
 - This is not a fixed list, but an ad-hoc list that can be extended as long as five different member states agree on incorporating a pollutant. Based on Member State comments, PAHs, Phthalates and Brominated Flame Retardants are expected to be part of this extended scenario list. However, there is no obligation to measure these compounds.

The Basic Scenario aims at establishing a harmonized and unified sampling, analysis and reporting framework within Europe (“Learning by doing”), aiming at providing comparable data for all different Member States and broadening the scope and scale of HBM in Europe. The extended scenario also implies that Flanders would be able to propose a number of biomarkers of exposure and/or effects themselves (and potentially get European funding as well). Especially for biomarkers like dioxins/CALUX or new chemicals (PFOS/PFOA, BFRs), there might be enough support from other Member States to establish Flemish Reference Values within the European HBM context.

Sampling procedures

It is assumed that either mother/child cohorts or children will be the main target group for the ESBIO project. The age classes have not been fixed yet, but will probably be relatively wide (3-15 years). The adolescent's population as was defined in the previous Steunpunt, should normally fit this description.

The number of samples that will be collected in the European pilot project obviously depends on the financing received. Normally, this should be a "1 for 1" financing from the European Commission and Member States. It was suggested that one sample for every 50.000 inhabitants should be taken, which would mean about 150 samples for Flanders.

Because it is the specific aim of the European Pilot Project on Human Biomonitoring to generate an overview of pollutant concentrations throughout Europe using a harmonized and standardized methodology, there will be a preference in collecting data per administrative sector. Probably, the NUTS2 or NUTS3 classification will be followed, which implies for Flanders that samples need to be gathered at the level of respectively "Provinces" or "Arrondissementen". The following map gives an overview of what this would mean for the 22 identified arrondissementen in Flanders in terms of the number of samples (Source: NIS, situation on 01/01/2005).



For now, it remains questionable whether it is desirable to have only 1 sample for regions like Veurne or Diksmuide, although mathematical techniques to mitigate this are available (e.g. Bayesian statistics). Furthermore, this sampling should be seen as an effort to detect differences in pollutant exposure patterns among more than 200 regions in Europe, not as an effort to compare different regions within Flanders. However, this sampling strategy would be very efficient to obtain region- and population-representative reference values for contaminants for Flanders.

Links with environment and health

Part of the European Pilot Project on HBM will focus on integrating the biomarker data with data on environmental concentrations of pollutants (e.g. data on air quality) and health outcomes (e.g. data from cancer registers). The integration of these "lines of evidence" will happen through a GIS environment (Geographical Information System) and will present spatially explicit data on contaminant distribution in different environmental compartments, in human tissues and on health outcomes. This will facilitate the identification of hot-spots (at a European level), where areas with high exposure or high disease prevalence can easily be identified. Also in the Flanders region

there has been an interest to aggregate environmental and biomonitoring data into a geographical environment using GIS; a pilot program was conducted in the previous steunpunt. This GIS data base on health and environment is currently under supervision of the health administration. We have the intention, also for the current biomonitoring proposal, to operate in cooperation with them. Modalities of cooperation can be established.

2.4.3. Monitoring of high risk population or of the impact of specific exposures.

Supplementary to the development of reference values for the general population, a number of high risk populations '*hot spots*' or '*selected groups*' will be studied. It is this study that can really contribute to our knowledge of the impact of environmental pollutants on human health. Sufficient emphasis has thus to be given to this activity. Since the budget is limited we are also limited in the number of high risk groups that can be studied. A framework for consultation on the selection of these subgroups has been developed in this proposal (see 2.6). For studies of specific subpopulations, the same strategy and principles as for establishing the reference values mentioned above will be followed, but the selection of the study population and sampling design will be tailored towards the hypothesis to be tested.

Based on their previous experiences the researchers are well aware of possible relevant study groups. They have been listed below but prioritization according to point 2.6 and further inclusion of other studies based on the input of other stakeholders is needed.

Possible high risk populations or specific exposures to be studied in the program 2007-2011 are the following:

- (1) needs of the government:
 - to what extent does social class influence environmental exposure
 - fine dust: biomonitoring in high traffic areas
 - ...
- (2) public concerns:
 - heavy metals in 'De Noorderkempen'
 - heavy metals in Genk
 - POPs in eel consumers
 - - intensive use of pesticides in fruit production
 - ...
- (3) conclusions of the biomonitoring program 2002-2006:
 - POPs elevated in 'rural Flanders area'
 - Follow up of residents of the Antwerp and/or Albertkanaal area's...

Following studies are considered priority:

2.4.3.1. Health effects of Small particulate air pollution

These aspects will be treated under 4.1, under studies on the health effects of fine particulate air pollution.

2.4.3.2. Study of the association between internal exposure to pollutants and male fertility

These aspects will be treated under 4.2, Studies on the health effects of endocrine disruptors.

2.4.3.3 Study of the association between internal exposure to pollutants and female fertility

These aspects will be treated under 4.2, Studies on the health effects of endocrine disruptors.

2.4.3.4 Continuation of the area-specific biomonitoring concentrating on area's with exposures of special relevance or where the existence of special problems was suggested through previous studies.

This study will be carried out on 200 adolescents per area. Areas of most interest are:

- The region of Antwerp
- The Albertkanaal area
- The area of intensive fruit cultivation
- Rural Flanders

The definitive choice will be made in function of budgetary possibilities and could include a "Selection procedure for hot spots" as described hereunder.

Besides some classical pollutants more recently introduced pollutants will be measured. Biomarkers of effect including psychomotor and attention-measurements will be included. Special attention will be paid to sexual maturation.

Biomarkers of effect could include:

- Hormone levels (in males)
- Comet assay for DNA damage
- Micronucleus test
- Neuropsychic tests, both computerized and based on paper
- Lung function tests
- Measurements of genetic expression on lymphocytes in vitro

Reporting and communication: The surveillance aspects, that are the internal exposure of the groups of participants and, as far as technically possible, possible regional differences in hormone levels, genotoxic tests or lung function tests, will be reported and communicated a short time after the measurements will be completed. Differences in neuropsychic tests, possible exposure-effect relationships and more complex relations between measured parameters and data obtained through questionnaires will be reported and communicated after a more profound analysis.

2.4.3.5. Study of exposure and biological and health effects associated with residence near a point source.

First part of the study: Study of 3 to 5 point sources in order to select relevant point sources for human biomonitoring.

The prospection of the point sources should be organized in collaboration with the relevant Flemish public organizations (such as OVAM, VMM, LNE, ToVo). They are important stakeholders in this matter and can have an input of data collected under their supervision. In listing potentially interesting point sources information from interested groups from the public should be taken into account. The final choice will be made based on objective data from measurements on environmental samples, on size and characteristics of the exposed population and on the results of the "Selection procedure for hot spots". The study on environmental samples should be carried out in collaboration with the relevant Flemish public organizations (such as OVAM, VMM, LNE, ToVo). Minimally they can contribute by providing access to their data, if possible these organizations can participate with extra measurements of pollutants in

relevant environmental compartments. Contacts will be made with the relevant organizations in time, to discuss if they can include new measurements in their measurement programs for the following year. Measurements on environmental samples concerning:

- Heavy metals
- Dioxin-like activity
- PCB and chlorine pesticides
- Perfluorinated substances

can be performed by the Steunpunt itself.

Possibly these measurements, using classical techniques, could be replaced or supplemented by a high number of measurements based on new electronic techniques.

Integration of HBM activities with existing environmental measurement networks was the topic of a pilot program (Afstemmen van milieumeetnetten en –strategiën op het biomonitoringprogramma – OL200200238, financed by Dienst Milieu & Gezondheid, Environment, Nature and Energy Departement). The outcome of this program will be structurally implemented into the steunpunt so there will be maximal use of the data.

Second part of the study: biomonitoring on 400 persons (adolescents or adults, depending on the case) residing around the selected point source.

Participants would include persons residing at different distances from the point source, taking into account the results of measurements (of relevant pollutants) on environmental samples. So participants would be selected to show exposures of different intensity to the point source. Exclusion/inclusion will be discussed for the different biomonitoring actions. Inclusion or exclusion of smoking will be a point of attention in this discussion.

Smoking behavior may interfere with effects from other environmental pollution and therefore this group may better be included (Burkart, 2001). On the other hand, it might be better to exclude smokers because active smoking is not an environmental hazard and because comparison of the general population with a study group exposed to a high risk environment might be hampered by the inclusion of smokers into the sample of the general population. The inclusion of smokers will diminish the power of a biomonitoring study to detect internal exposures or biological effects due to environmental exposures. This might be offset by an increase in the number of participants, but this again increases the financial costs. In any case social status, smoking habits, occupation of the participants will be recorded with due attention.

Biomarkers of exposure and effect will be selected on the basis of the point source under study and could include:

- Heavy metals:
- Dioxin-like activity possibly making a distinction between dioxins and PCBs: PCBs, chlorine pesticides
- Other pesticides or their metabolites in blood or urine
- Perfluorinated substances
- tt-muconic acid in urine
- 1-hydroxypyrene in urine:

Tests for biological effects:

- Hormones in males
- Sperm quality
- Comet assay for DNA damage

- Micronucleus test:
- Tumor associated proteins
- Neuropsychic tests
- Long function tests
- Measurements of genetic expression on lymphocytes in vitro

Reporting and communication: The surveillance aspects, that are the internal exposure of the groups of participants and, as far as technically possible, possible regional differences in hormone levels, genotoxic tests lung function tests, sperm quality or tumour associated protein levels will be reported and communicated a short time after the measurements will be completed. Differences in neuropsychic tests, possible exposure-effect relationships and more complex relations between measured parameters and data obtained through questionnaires will be reported and communicated after a more profound analysis.

2.4.3.6 Continuation of the follow-up study on neuropsychic development, asthma and allergy of the biomonitoring campaign 2001-2006

These aspects will be treated under 4.5

2.4.3.7. Collection of data on morbidity and mortality for adult participants to previous biomonitoring campaigns

These aspects will be treated under 4.6

2.4.4 Ethics and privacy issues:

The scenario of the biomonitoring program will be documented in detail describing the aims of the campaign, the sampling strategy, the population to be recruited, the informed consent, the handling of questionnaire data and of samples according to ethical and privacy rules, treatment and communication of the results. This scenario will be submitted for approval to an ethical commission and to the privacy commission. We aim to communicate the individual results to the participants and give them an interpretation in terms of situating the individual result in comparison with the overall results of the campaign and if possible in terms of the health impact. We will ask permission, and collect enough information, that would allow for new rounds for monitoring or questionnaires in later years. The medical doctor responsible for the field work is the sole responsible for contacting the participants and linking the identity of the participants with the records. All other involved laboratories will work with anonymised data.

2.4.5 Quality control program:

An extensive quality control program will be part of the program. The quality control system of the European pilot program will be taken into consideration. Quality control of the biomonitoring will be at different levels:

Data base construction and quality control of imported data: Questionnaires will be scanned automatically; input from open questions will be manually. For open questions, a double manual data-entry will be done.

Data from toxicological and biochemical analysis will be subject to quality control in the providing laboratories. Outliers will be checked by contacting the labs and checking

questionnaire information. The cleaned database will be constructed in one center and will be the unique source for further statistical analysis.

Handling of samples: Standard operating procedures are available or will be established for the sampling procedures for transport and storage of the samples. Sample recipients will be controlled for interference with the analytical outcome. Status of the samples will be recorded, making tracking of the samples possible at all times. Personnel will be trained in advance.

Toxicological, clinical and biochemical analysis: All chemical analysis will be subject to rigorous control procedures. Laboratories which are candidates for the analysis should be able to demonstrate that they work according to the principles of Good Laboratory Practices. Preferentially they should have accreditation according to DIN EN 45001, ISO/IEC 17025 or equivalent although this is not very common (widely spread) in the field of human biomonitoring. The laboratories should show that the analytical method that they will use is suitable for the analytical task. They should document the limits of detection and of quantification, the accuracy of the method, its reproducibility at the level of interest. They should also provide evidence of participation in round robin tests for the analysis of the compound in the matrix of interest and at the level of interest. If such external quality control programs do not exist, they should document the internal quality procedures.

Samples with high levels of analytes will be analyzed twice, 5% of the samples will be analyzed in a different laboratory as a supplementary external control.

All documentation on quality control will be made available by the laboratories upon request from the responsible of the biomonitoring program.

An invitation to participate in the program will be sent out to different laboratories, this invitation will include the above described requirements. The offers will be evaluated based on price / quality criteria.

2.4.6 Activities and task distribution 2007-2011

The biomonitoring program will be executed by the field coordinators committee. This committee will be headed by Prof. G. Schoeters, Dr. V. Nelen and Prof. N. Van Larebeke. Prof. G. Schoeters (chairman) will be responsible for the coordination. The FCC consists further of the representatives of the different disciplines necessary for the realization of the program. The FCC will at least meet on a monthly basis. Delegations of the Flemish government can be invited for specific points on the agenda. The chairman invites, in name of the management of the FCC, the participants and is responsible for the agenda and reports of the meetings.

The FCC works out the details of the biomonitoring program, described in the long-range plan and monitors the progress of the program in function of the objectives and the time schedule. It assures optimal integration of all biomonitoring activities of the Center including those foreseen in the research projects. It decides on scientific aspects such as the sampling strategy, selection of appropriate biomarkers and proper age groups for the biomonitoring areas as under investigation. It will develop a strategy for biomonitoring in hot spots and specific cases that were selected by policy makers after consulting stakeholders. The choices for pollutants and target groups will be described in the annual plan and submitted to the Executive committee and steering group for final approval. The FCC designs the statistical analysis of the data.

Decisions in the FCC are made in consensus. Cases, in which no consensus can be reached, will be presented to the executive committee for a final decision.

The results will be interpreted acknowledging the input of the different disciplines. They will be reported to the executive committee. The minority's point of view will be also reported in case no consensus can be reached. After approval by the executive committee – under the responsibility of Prof. Baeyens (promotor-coordinator), Prof. Schoeters (coordinator of the FCC), Prof. Van Larebeke (promotor-spokesman) and Prof. Nemery - the results will be reported to the steering group and to the stakeholders according to the “Spelregels” document.

The VITO team will be responsible for the organization, the chairmanship and the coordination of the different tasks of the FCC and for smoothly proceeding of the program. The VITO team will collect the data from toxicological and biochemical analyses and organize the quality control.

The fieldwork will be headed by Dr. V. Nelen of the PIH. Dr. Nelen will be responsible for the use of the data following the rules of ethics and privacy. She will be responsible for submitting the scenarios for biomonitoring to the committees for Ethics and Protection of The Personal Atmosphere of Life. The PIH team will be responsible for the recruitment of the survey participants and for the communication with the survey participants in cooperation with Dr. N. Van Larebeke.

The University of Hasselt partner, Prof. G.Molenberghs, will be responsible for the Statistical data processing with respect to sampling strategy and data analysis.

The research group of Prof. Dehenauw (University Ghent) will be responsible for the analysis of data on nourishment and use of local food with respect to biomonitoring outcomes.

The toxicological analyses carried out under the responsibility of Prof. W.Baeyens, Prof. N. Van Larebeke and Prof. G. Schoeters.

The communication strategy will be designed by the social scientists of the University of Antwerp under the responsibility of Prof. I. Loots and Prof. L. Goorden.

Prof. N. Van Larebeke (promotor-spokesman) is responsible for the external communication to the authorities and the public concerning the biomonitoring program. The spokesman will be assisted in external communication by the involved experts of the participating research teams.

Overview of tasks:

Surveillance program / identification and characterization of high risk populations					
Year	Activities	Target population	Estimated number of participants	Milestone	Deliverable
2007	Preparation biomonitoring protocol- reference values and ranges			Approval of scenario by ethics and privacy commission	-List of selected biomarkers -Scenario for surveillance
	Development of decision making framework for prioritization of studies on high risk populations (hot spots)			Composition of steering group with relevant stakeholders	-Scenario for practice cycle “green paper” -List of relevant stakeholders -List with assessment criteria for monitoring high risk populations
2008	Field work biomonitoring: reference values and ranges Cd, Pb, PCBs, CALUX, DDE/DTT, HCB and emerging pollutants	Mother newborn pairs	150	Recruitment of participants	
		Children/ adolescents	150	Recruitment of participants	
		adults ⁷	300	Recruitment of participants	

⁷ Selection of participants (age group) in function of the selection of biomarkers and in agreement with the selection of the EU wide biomonitoring program

Surveillance program / identification and characterization of high risk populations					
Year	Activities	Target population	Estimated number of participants	Milestone	Deliverable
	Prioritization/selection of first 2 high risk groups for inclusion in biomonitoring (hot spots)			Approval of protocol -Selection of the first 2 “high risk groups“ to monitor	-Protocol for prioritization - Description of selected high risk groups and rational for choice
	Study design for monitoring high risk groups (hot spots)			Approval of scenario by ethics and privacy commission	Scenario for biomonitoring“ high risk groups”
2009	Biomonitoring of 2 high risk populations “hot spots “ or “specific cases”	Adolescents if indicated as population of choice ⁸	400	Recruitment of participants	
	Prioritization/selection of another 2 high risk groups for inclusion in biomonitoring (hot spots)			-Approval of protocol -Selection of the 2 “high risk groups“ to monitor	-Protocol for prioritization - Description of selected high risk groups and rational for choice

⁸ Final selection will depend on the monitoring question that has to be addressed, and may change in function of the pollutants to monitor . Preferentially adolescents will be recruited

Surveillance program / identification and characterization of high risk populations					
Year	Activities	Target population	Estimated number of participants	Milestone	Deliverable
	Communication of biomonitoring reference ranges for all age groups			Approval of results by management team and steering group	Report on internet and publication (Dutch and English)
	Evaluation and modification of action plan (early 2009)			Approved protocol after modification based on current experience	-Review of current action plan -Protocol for modified action plan
2010	Biomonitoring of high risk populations “hot spots“ or “specific cases”	adolescents if indicated as population of choice ⁹	400	Recruitment of participants	
	Start action plan (beginning of 2010)			-Desk research -Stake holder consultation	Synthesis from experts Communication of results
2011	Communication of biomonitoring results – results from “ high risk ”			Approval of results by management team and steering group	Report on internet and publication (Dutch and English)

⁹ Final selection will depend on the monitoring question that has to be addressed, and may change in function of the pollutants to monitor. Preferentially adolescents will be recruited

Surveillance program / identification and characterization of high risk populations					
Year	Activities	Target population	Estimated number of participants	Milestone	Deliverable
	groups” monitoring				
	Continuation action plan			Desk research Stake holder consultation	Synthesis from experts Communication of results

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2.5. Action plan (Fasenplan)

2.5.1 Aim of an ‘Action Plan’

The outcome of surveillance, as detailed before in this proposal, is not ready to be directly translated into policy supporting actions. Human biomonitoring helps to look more closely to the health impact of environmental exposure to humans by direct measurements in the human body. However no legal framework exists for the interpretation of the biomonitoring data and for transferring them into policy measures. Results are expressed with a degree of uncertainty. As soon as the data are communicated to participants, to the larger public and to stakeholders, they raise further concern. Two main issues arise (1) the health significance of the data and (2) the origin and pathways of the pollutants from the environment into the body. These aspects are relevant and human biomonitoring programs require from the start a strategy to take these concerns into account.

The ultimate goal of human biomonitoring is to prevent in the most efficient way further exposure and to take the most efficient measures to reduce exposure. This implies that human biomonitoring should only be seen as a starting point for further actions. It gives the opportunity to orient environmental measures to the most sensitive and vulnerable areas or populations.

We will take the challenge and the opportunity to take the biomonitoring results a step further and elaborate a framework to make the results useful for preventive policy with regard to environmental health care.

In 2004-2005 an interdisciplinary and transdisciplinary working group already developed an action-plan to deal with a large amount of biomonitoring data of the past campaigns (2002-2006, the measurements of pollutants and health effects in more than 4000 inhabitants of Flanders). Part of the development process was the growing awareness of the limits of scientific interpretation and the lack of an existing legal framework for interpretation of the data. Social scientists introduced a decision making procedure in which the use of scientific interpretation and ‘societal’ insights complement one another in order to assess policy priority options. A concept of flow chart has been developed which allows further interpretation of the data and decision making according to predefined criteria and consultation rounds. Both scientists and policy makers agreed on this (conceptual) action plan. This action plan has been initiated in 2006. The first and second phases of the action plan are currently running as a follow up of the first biomonitoring campaign with mother-newborn pairs. Modifications of the concept are possible and are still needed as we experienced in practice.

Parts of the procedure are an expert round and a jury debate, which both give advice to the authorities. One of the methods still to be elaborated for the jury deliberations is a multi criteria analysis. We will discuss this procedure below, its development process, perspective for the future, in combination with the task division for 2007-2011. For its social scientific background and bibliography (action or interactive research, boundary work between science and policy, transdisciplinarity, inclusiveness), and also its innovative character and the challenges we refer to point 2.5.3 in this application.

2.5.2. The design of the Action Plan: phased evaluation (see figure 1)

In a **pre-phase** the biomonitoring results are compared to existing data and available guidelines. Only with regard to lead and cadmium (international) health based guidance values for the general public do exist. For the other exposure and effect parameters other strategies have to be followed in order to proceed with the data interpretation. In the previous Flemish biomonitoring programme reference values (geometric mean and P₉₀) were calculated based on the biomarker data obtained in all the study areas of the whole campaign. These reference values serve as an internal standard to which geometric means and P₉₀ values from individual monitoring areas are compared. Even if the reference values are exceeded in one or more of the studied areas, this does not automatically imply serious health concerns and immediate action. To elaborate this further a comparison is made the data with research outcomes from other (international) biomonitoring studies.

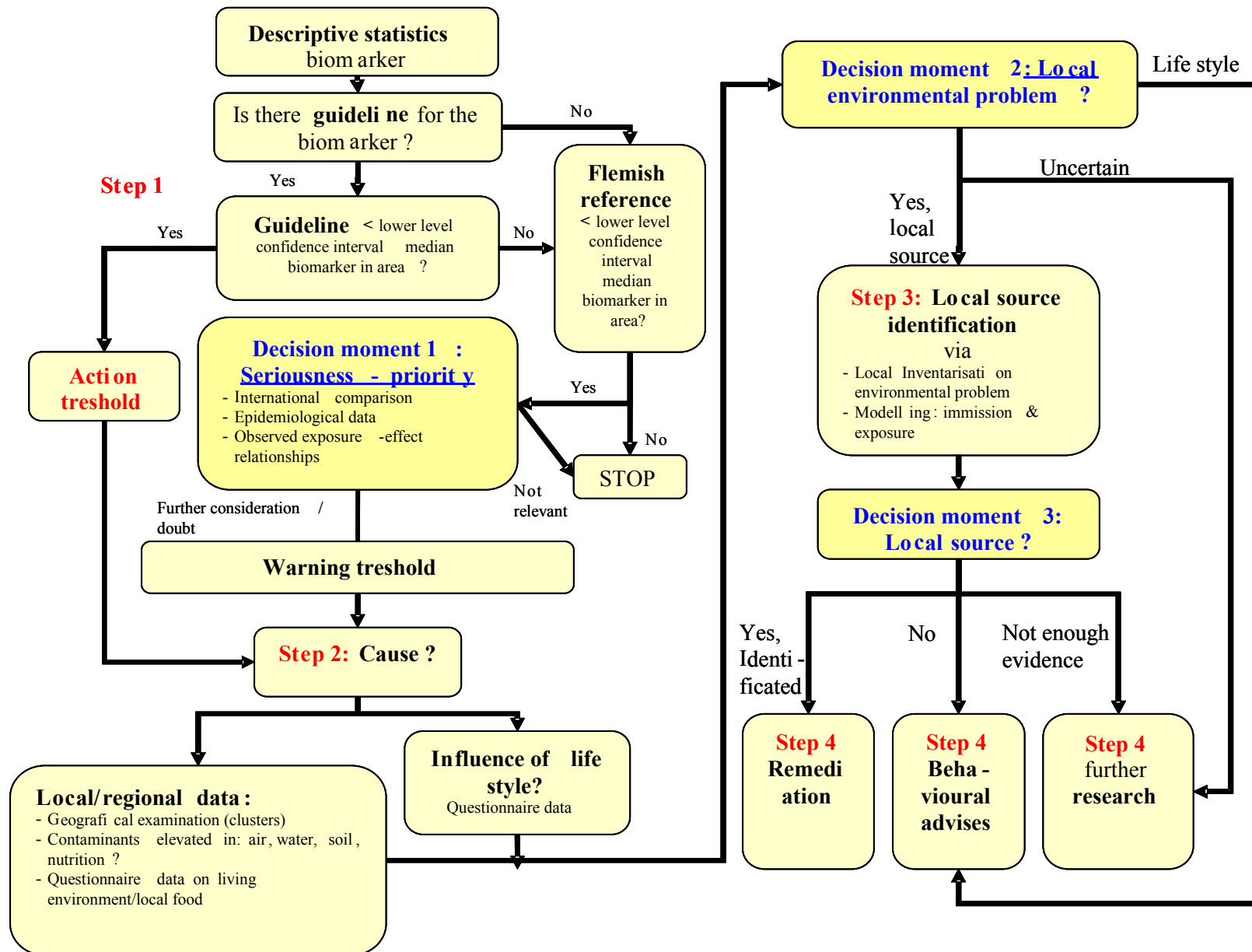
The **first phase** then focuses on the question: how *severe* are specific results with regard to public health risks? Is this measured level of concern? To a large extent the discussion focuses on reference values for interpretation of the data. This is quite problematic since few internationally accepted values are available. Biological effect data, available health data of the same study area - either at the individual level or aggregated level-, associations between exposure and effect data and historical data are taken into account to set priorities for further action. Furthermore societal and policy aspects are taken into account.

The **second phase** identifies whether individual life style factors or environmental quality of the study area is linked to the elevated biomarker concentrations. In this stage it is important to gather all possible information on environment and health which is available from the area, and to analyse questionnaire data of the participants in depth. Also at this stage relevant societal and policy aspects will be taken into account.

If environment is acknowledged as a determinant of the elevated biomarker levels in the study area a **third phase** is needed which is oriented towards identification of local sources.

Progress through the action plan depends on the advice given by a panel of experts and the advice of a jury. At first the action plan was considered as a merely scientific quest: with the right group of experts the interpretation with regard to policy priorities will follow automatically. While trying to build bridges towards policy interpretation, limitations of an exclusively scientific endeavour became clear: no scientist or group of scientists was able to claim the necessary and overarching knowledge for answering difficult questions. Questions e.g. on policy priorities when also other than (health and environmental) factors had to be taken into account (economics, social preferences, feasibility of policy measures; issues introduced by the social scientists). Therefore the formation of a jury was proposed that would judge relevant data and knowledge in order to give advice to the authorities. Furthermore the need for a procedure ‘from data-interpretation to decision making’ was obvious as well as the involvement of central and local stakeholders, next to experts.

Figure 1. The main steps in further data interpretation



2.5.3 Practice cycle of the Action Plan

Each phase of the action plan is furthermore split in several steps, all together called a practice cycle. This prescribed cycle allows to organize the process and to identify the actors that should be involved. Such practice cycle consists of different procedural steps, actors and roles from assessment to decision making. The practice cycle is made up of cyclic steps, to be taken during each phase of the action-plan:

- **Step 1:** Deciding how to operate and which actors to involve during the process
- **Step 2:** Desk research on the bio monitoring results and expert consultation
- **Step 3:** Confronting a jury with a synthesis of the desk research and expert consultation; main focus is on recommending priorities for further steps
- **Step 4:** Synthesis of desk research, expert consultation and jury advice for the administration
- **Step 5:** The administration translates a synthesis of the above into policy options
- **Step 6:** The authorities decide on next steps
- **Step 0-7:** External communication

Two steps need some further explanation:

Step 2: Desk research and expert consultation

Desk research is needed in each phase of the action plan and consists of environmental and health information and information on societal and policy aspects. The interdisciplinary synthesis of desk research information and corresponding check list, tailored for the expert consultation, is the deliverable after each phase (see figure 2).

In the **first phase**: internationally established health based guideline values are collected as well as data on biomarkers from studies from abroad. Health based guideline values exist for a limited number of compounds. Comparison of biomarker data from different studies should be carried out carefully since this is hampered by lack of harmonization on how data should be presented in different studies and on lack of information in the reported studies on analytical uncertainties, on how to deal with non-detects, on choice of confounders and correction for confounders.

The other approach to evaluate the *seriousness* of the biomonitoring data is to collect biological effect data or health data from the same study population, either at the individual level or aggregated level. Appropriate health data are needed to put biomarker data in a health perspective. Individual data e.g. health parameters of newborns, are often available, but ethical and privacy issues should be carefully considered if these data are collected. Aggregated data are often not complete and are difficult to collect. Linking exposure biomarkers with effect biomarkers at the individual level will also increase knowledge on potential health significance of the exposure levels that have been measured.

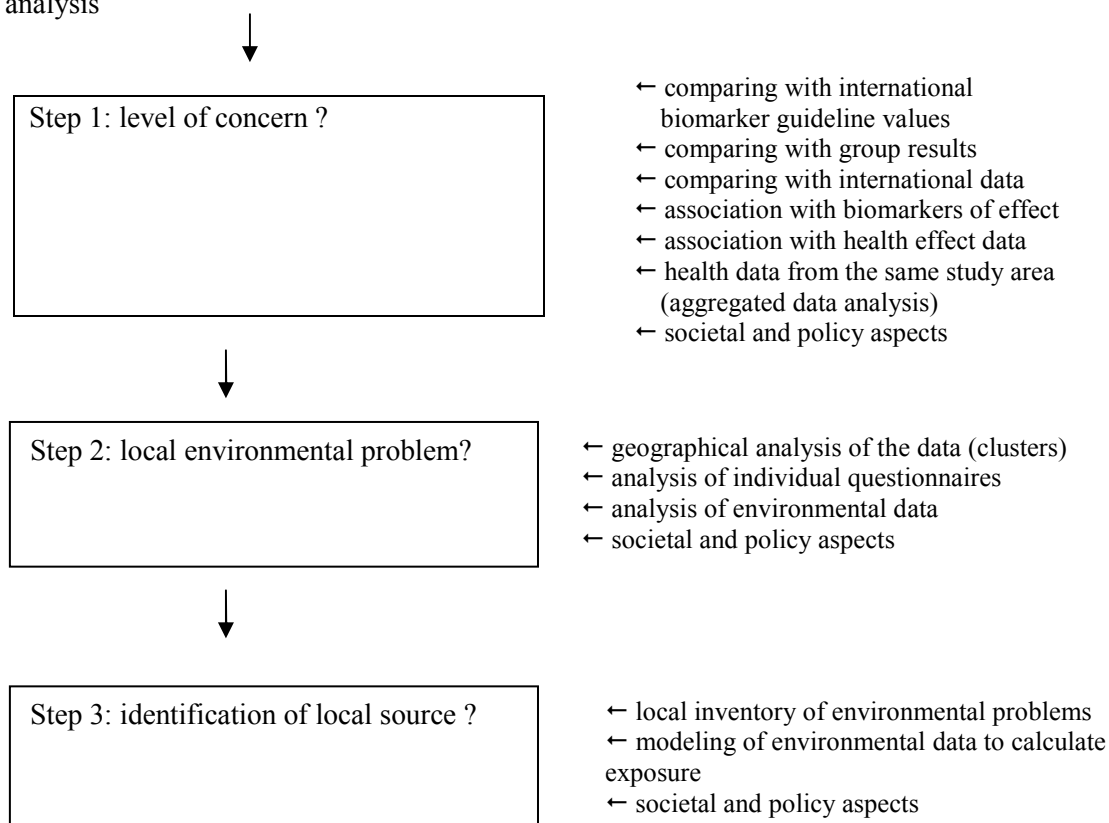
Furthermore societal aspects and policy aspects are taken into account. Societal aspects relate to public perception of the issues at stake and public debate: the degree of public concern and comparison with other aspects such as economic aspects. Also public support for relevant policy measures is investigated. Policy aspects relate to policy priorities with regard to environment and health as well to opportunities for policy intervention with regard to the issues at stake.

The **second phase** identifies whether individual life style factors or environmental quality of the study area is linked to the elevated biomarker concentrations. A detailed statistical analysis of the questionnaire data is performed and additional environmental monitoring data (soil, water, air, biota) and relevant health data are collected. Also in this phase relevant societal aspects and policy aspects are taken into account.

The **third phase** tries to identify local sources in the environment if in phase 2 local environment is identified as a determinant for elevated biomarker concentrations. Environmental data are needed to link biomarker measurements to environmental sources. A lot of environmental monitoring data exist. But metrics and sampling sites are not always optimal for estimating the exposure of the population. Knowledge on kinetics of compounds in the body is essential for linking biomarker data to environmental data. Finally mainly local social and policy aspects will be considered.

Figure 2. Key steps for desk research

Prefase: Data descriptors & statistical data analysis



Step 3: Jury and Multi Criteria Analysis

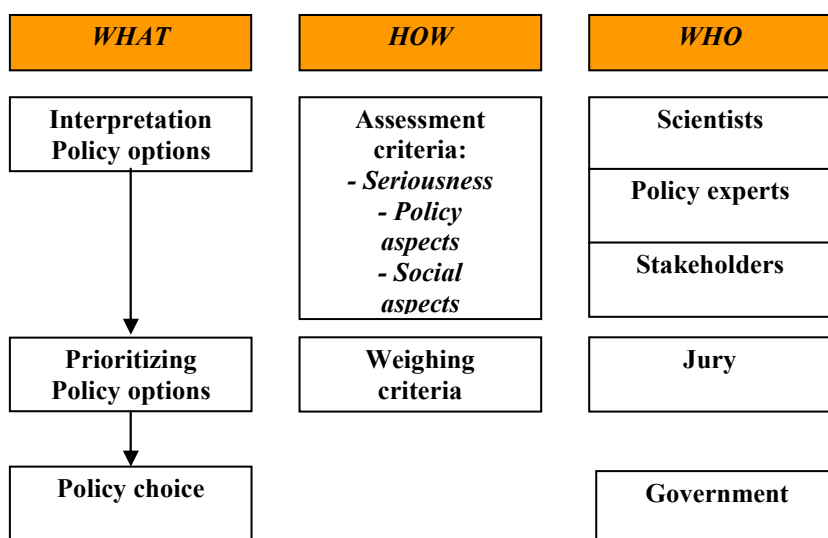
The fact that no scientist or group of scientists could claim the necessary and overarching knowledge for answering all difficult questions, formed the occasion for the social scientists to propose to work with a jury. The jury will be made up of experts,

stakeholders and (other) citizens. The reservoir of potentially relevant actors will form the basis for selecting candidates.

For the jury in the first phase of the action-plan, we are developing a multi criteria analysis. The three main (groups of) criteria are: seriousness of environmental & health risks, feasibility of policy measures and societal aspects. The information for these three criteria is obtained from the desk research and expert consultation. In the multi criteria analysis the jury will discuss the relative importance (weight) of each criterion. The outcome will be more than merely a numeric ranking of policy priorities though. The jury process will be a group discussion in which participants can learn from each other and where views, arguments and concerns will be exchanged and monitored. The multi criteria analysis functions as a method for structuring discussions and for supporting reflection during the deliberations. Transparency and practical employability therefore are essential features. In case consensus is impossible, minority viewpoints are detailed and considered.

Deliberations of the jury result in policy advices offered to policy administration. Afterwards decisions may differ but authorities are committed to transparency. Governmental decision makers will inform civil society about the final decisions and, the arguments behind it and will respond to suggestions, arguments and concerns raised during the process.

Figure 3. Multi Criteria Analysis



2.5.4 Action Plan in policy practice

The action-plan was accorded by both the Centre of Expertise for Health and Environment 2001-2006 and policy representatives, and was adopted by the government in 2005. With regard to the first wave of biomonitoring results (new born babies) a first pilot project started in 2006. It is impossible to foretell how this action-plan will work out in practice. Promising is the engagement of government to test the procedure in practice. Moreover the Flemish experience will be of inspiration for a European Union pilot project with regard to biomonitoring.

2.5.5. Activities Action Plan and task division 2007-2011

Three main research needs can be distinguished: (i) evaluation and reflection of the action plan, (ii) recommendations for implementation for the biomonitoring results of 2007-2011, (iii) implementation of the action plan.

They can be treated in a logical order, although the biomonitoring practice will cause serial and tailored implementation, for different goals and cases.

The partners involved in the different steps of the action plan are the following:

- Step 1: Deciding how to operate and which actors to involve during the process: *Steering Group, preparations by the Core Group*
- Step 2: Desk research on the biomonitoring results and expert consultation: *VITO, UA, PIH*
- Step 3: Confronting a jury with a synthesis of the desk research and expert consultation; main focus on recommendation of priorities for further steps: *VITO, UA*
- Step 4: Synthesis of desk research, expert consultation and jury advice for the administration: *VITO, UA, UG, VUB*
- Step 5: The administration translates a synthesis of the above into policy options
- Step 6: The government decides on next steps
- Step 0-7: External communication: *Core Group*

2.5.5.1 Reflection on the conclusions of the evaluation and adjustment of the action plan

In 2006 a practice cycle was tried out for a case study “DDE elevations in newborns of two regions in Flanders, are there environmental indications for higher pollution (= phase 2)”. In this case study, phase 1 of the action-plan - considering the seriousness of the elevated levels above the reference values – was jumped over. Proceeding directly with phase 2, made it possible to proceed more quickly into a time span of three quarter of a year to more detailed research of one biomarker result. Main aim was also to gradually build-up experience in practice with one real case and to further adjust and develop the structure of the action plan on the basis of practical experiences. A part of this is the development of a multi-criteria analysis methodology and of the adjusted structure of the action plan. The coordinated outcome of these different subparts of the action plan of 2006, as mentioned above, will be handed over to the political government for adoption.

As a next step, a complete action-plan regarding the human biomonitoring results gathered in the scope of the first generation Centre of Expertise for Environment and Health (2002-2006) (*Onderzoek naar de invloed van het voorkomen van milieugevaarlijke stoffen in het milieu op de mens en naar de oorzaken daarvan in opvolging van de groepsresultaten van de biomonitoringcampagne (fasenplan)*) will be put into practice in 2007-2008. It will be funded by an once-only funding of 220.000€.

Additionally, this action plan will be internally evaluated by the Steering Group Action Plan. The final results of this evaluation are expected at the end of 2008.

With respect to the human biomonitoring results which will be gathered in the scope of the second generation Flemish Centre of Expertise for Environment and Health (2007-2011), a first research activity will be to draw conclusions (early 2009) from the

evaluation of the action plan (as mentioned above) for the continuation of the Action Plan. This is a necessary step as the presented new human biomonitoring program has a somehow different set-up including a new surveillance and research context. The focus will remain on surveillance outcomes, but as demonstrated in other parts of the application, these data result from surveillance of reference values for Flanders (recruitment in 2008). More specific cases will be investigated in order to deliver comparable outputs (markers of exposure and health effects for specific regions, for specific target groups, for new pollutants).

The conclusions and the intention to adjust or differentiate the practice cycle of the action plan have to be based on a consensus within the Steering Group. Next, the upgraded Action Plan(s) has/have to be accorded at governmental level in order to apply the Action Plan for the first results that come out in 2008.

2.5.5.2 Recommendations for implementing the Action Plan for specific surveillance and hotspot results

The former paragraph reports about the procedure, the concept or ‘the improved’ Action Plan, and how this will be updated. Another question is how to cope with the autonomous cycle of new results coming up during the period 2007-2011. A major ambition is to enable fluent throughput through the procedure but providing transparency and keeping essential consultation rounds. The research teams of VITO and the University of Antwerp will prepare the scenario for putting into place the Action Plan on a specific empirical context of results or group of results. The goals, the level of complexity, rough time table, stakes, tasks and means for the practice cycle will become clearer and discussed with the general Steering Group. This is like a quick scan of the steps in the practice cycle. Included will be a recommendation on the composition of the Core Group (scientists and policy representatives most actively involved in the project). It will be clear that the complexity of the issue will imply the collaboration of different public (and also private) stakeholders. The Action Plan is a Flemish initiative, but implementation will engage multi-level and multi-sector networking.

2.5.5.3 Applying the Action Plan for specific surveillance and hotspot results

Once the Steering Group has decided to implement the Action Plan for a specific result (or a group of results), decisions on the distribution of tasks and additional costs have to be made and agreed upon. It is clear that the consortium is not sufficiently equipped for the day to day implementation of the new developed and accorded Action Plan in 2009-2011. Depending on the engagement of responsible authorities and the available means, the research teams of VITO and the University of Antwerp and policy representatives (in the Core Group) will guide and process the necessary internal and external process and research steps as described in the practice cycle (see also above for the task division within the consortium). Collaboration with PIH for additional fieldwork and with the co-ordinator of the consortium is envisaged if appropriate. The improved ‘scenario’, will be translated into a more tailored programme.

2.6 A Selection Procedure for hot spots

2.6.1. Aim of the selection procedure

Aim is to **develop and test a transparent and deliberative procedure for the selection of ‘hot spots’ (cases)** for human biomonitoring surveillance during the period 2007-2011.

A unique set of reference values for biomarkers of exposure and effect in different age groups will be provided by the regular human biomonitoring surveillance campaigns. This offers the opportunity to evaluate environmental exposure in specific settings (high risk groups, hot spots or specific cases) and to compare the results of these specific campaigns or studies with the reference values that are obtained in the regular surveillance programme. Many specific cases can be envisaged e.g. areas with high population density, areas around industries, areas with documented high environmental loads, areas of previous concern following an earlier biomonitoring study, areas with perceived health concerns, Due to time and budget constraints choices have to be made. To make these choices a procedure will be developed based on two starting points:

- 1) transparency of the selection procedure to stakeholders and
- 2) participation of stakeholders in the selection process, consultation on their viewpoints and arguments.

A procedure will be developed and tested in a pilot phase. If the pilots on these cases are successful, integration within the Action Plan (see point 2.5) can be taken into consideration.

Consultation on selection can support the need for justification of choices made within the environmental health surveillance, as decision making on research priorities deals with a certain amount of uncertainty. In principle, ‘health relevance’ should guide prioritisation, but direct health impact of environmental loads (well known health effects – despite combined exposure conditions) is difficult to demonstrate unequivocally. For some pollutants such as lead and cadmium health based reference values exist, surpassing these is generally agreed to pose an increased health risk. In most cases selection of ‘monitoring cases or areas’ will be based on societal arguments related to documented environmental data and perceived health concerns. Experiences with the existing biomonitoring program clearly demonstrated the strategic value of choices of ‘biomarkers’ and ‘regions’. Prerogatives need to be identified, explained and argued. The consortium also recognises the opportunities of a selection procedure for an increasing awareness for environmental health issues and enhanced trust of involved partners and the public in general as a positive impact. Instead of inviting the civic society for its opinion on environment and health in general, pilot cases on selection will have practical relevance and involve specific cooperation with several actors. The social scientific justification and bibliography for this approach is described in point 4.3.2.4 of this application. Here we will focus on the specific program and task division.

2.6.2 The design of a procedure

The Action Plan that was elaborated during the former Steunpunt M&G starts where results come out of the surveillance system and need to be interpreted in order translate them into policy action(s). The Selection Procedure should identify and argue the

choices, made for specific surveillance activities and linked scientific research. The philosophy behind the selection procedure however, is similar to that of the Action Plan: complementary to the expert opinion, a round of stakeholder consultation and deliberation complements the decision making, in casu on **research priorities**. Its objective is to select cases, by giving structure to a process and taking into account the reflections made. Flemish advisory groups can be invited to comment the final concept of this procedure. A Steering Group will involve the relevant consortium representatives, other experts and authorities. A Core Research Group will implement the necessary research steps.

The operational design and methodology for surveillance and further research remain the responsibility of the - multidisciplinary – team of scientists within the consortium (environmental and medical scientists, toxicologists, social scientists and biostatisticians). Aspects of transparency on this study design and processing are explained in point 3.7. The consortium has a pragmatic perspective: where no objectives can be guaranteed no vague promises should be made. The Action Plan and this new initiative on case selection already are promising prerogatives, realised in the co-production perspective of knowledge and policy advising.

2.6.3. Activities and task division 2007-2011

The following tasks have to be done in 2007-2011: (i) establishment of consultation procedure for selection of ‘hot spots’, (ii) selection of pilot cases of ‘hot spots’, (iii) integration of ‘hot spot’ biomonitoring data into full action plan.

2.6.3.1 Identification of basic structural aspects of the consultation procedure

In a first year, the basic structures of the Selection Procedure(s) will be elaborated. The outcome should be a Green Paper on the process: practice cycle (cfr text in the Action-plan), assessment criteria (for definition of potential cases and for assessment of relative priority and selection), relevant central, regional and local stakeholders. Examples of relevant stakeholders are: environmental and health experts, trade unions, companies and their organisations, environmental groups, local resident’s organisations... Examples of assessment criteria are: the size of the potentially exposed target groups, existing environmental data which indicate potential exposure risks, information from previous biomonitoring campaigns, the vulnerability of target groups such as children or socially vulnerable inhabitants in polluted areas and reflections on environmental justice, scientific feasibility of the research, costs, ethical considerations, policy needs for follow up of environmental measures, policy perspectives for taking actions, political or public controversy, ...

Knowledge on stakeholder consultation and experience with international human biomonitoring will be taken in mind: as elaborated in the EU-TRUSTNET programme, EU-AIRNET, EU-PINCHE programme, EU-ESBIO and the SCALE initiative¹⁰. Also

¹⁰ TRUSTNET-in-action (TIA): Inclusive governance of hazardous activities (1997-2003) and (2003-2006)

EU-AIRNET: policy interpretation network on air pollution and health (2002-2004)

PINCHE: policy interpretation network on children’s health and environment (2002-2006)

SCALE: A European Environment & Health Strategy

ESBIO: Policy oriented research, scientific support to policies, Expert team to Support BIOmonitoring in Europe

developments within (the screening and scoping stage of) Strategic Impact Assessment will be taken into account.

This identification phase is treated as a co-production process. A Core Research Group will do the main research activities and a Steering Group (with a diversity of relevant experts such as scientists of the Flemish Centre for Health and Environment, government representatives, experts from public institutions, MMK's (Medisch Milieukundigen), (local) stakeholders) will be used for input and reflection. A first report is made on the basis of discussion with the Steering Group, existing view points, position papers of stakeholder organisations, headlines within research programmes, policy plans and documents of concerned stakeholders or advisory councils and can be realised by discussions with the Steering Group and desk research. The final concept can be reviewed by an existing Advisory group with a composition that reflects main and representative stakeholders at the Flemish level such as the MiNa-Raad, the Vlaamse Gezondheidsraad and the network of MMK and will be open to further consultation for stakeholders and the public. The final outcome will be submitted to the steering group of the Center for approval.

2.6.3.2. Selection of pilot cases

First results of this pilot should be available before the third year, so that the research design can be worked out in time within the Field Work Committee of the consortium. During the second year, the try out of the procedure can be prepared and started up. One full time researcher cannot accomplish all mentioned social scientific tasks at once and consultations should anyway respect the consultation life cycle.

If argued in the first stage of the planning (see point 2.7.3.1) and feasible within the time frame, collaboration with viWTA will be solicited for this pilot. viWTA is a TA-institute, attached to and at the service of the Flemish parliament, and advises parliament with state of the art reports and with public consultation and deliberation on controversial issues, linked up to science and technology in society. The biomonitoring can be considered as an innovative scientific methodology with a societal impact (defining risks) and addressed to policy makers.

The reflections, made about the cases for surveillance and research priorities can be considered as a White Paper. The scientific team commits to transparency on the final choices made on the case(s). But as the described steps rely on stakeholder consultation and collaboration, results of the negotiations can not yet be predicted in this application. The objective is to set up and to test the procedure and to gain support for the final selection made. Justification, particularities of and bibliography for this approach (of action research) are to be found in point 4.3.2 of this application.

3.6.3.3 Integration within the Action Plan?

The results of the selected complementary cases will potentially be candidate data for the Action-plan run for all regions and biomarkers, which where elevated compared to reference/guideline values. Whether they will be treated together with the main surveillance results and on an equal basis will have to be worked out later.

2.7. Integrated communication and initiatives for participation

The **external communication** of the results will be elaborated on the basis of scientific insights presented in risk communication literature and the insights, acquired during experiences with external communication in former biomonitoring campaigns (2002-2006). Content-related, procedural and institutional requirements will be used as prerequisites for adequate communication (see point 4.3.2.4 and included bibliography of this proposal). At the organisational level, the external communication follows the time frame of the biomonitoring. In this point, only derived characteristics of the external communication will be discussed. Also envisaged tasks are listed up.

Initiatives for participation are a logical outcome too of the scientific insights in risk communication literature. In other parts of this proposal, specific initiatives are already announced and detailed (Selection Procedure; Action Plan; Risk perception research) and will not be repeated here.

2.7.1 Golden rules for external communication in a context of risk

The external communication is linked up to the following conditions and *rules*:

- researchers and government should provide transparency on the research design and methodological background to individual participants and to intermediaries and not only on the research results;
- scientific controversies and uncertainties are normal, both as a consequence of the complex character of environmental – and health research and as a consequence of the social construction of knowledge. Lack of unambiguous conclusions about environmental factors and health effects and scientific uncertainties will, to a large extent, continue to dominate the debate on environment and health, so application of adequate communication procedures will be necessary;
- experts, citizens, authorities and producers perceive risks in different ways; every perspective is valuable (different problem definitions, different solutions to be taken into account). The strategy to fill the gap between objective and perceived risks by merely trying to convince the public of the expert view (the traditional one way-risk communication by means of merely informing the public) is not adequate. Persistent controversies about the environment and health are energy-consuming for all actors involved. Moreover, these definitions and risk perceptions are dynamic: they evolve;
- the Center and the government representatives agree on the way the external communication will be organised; in case of controversy on the distribution and interpretation of the information every actor acts in line with his professional guidelines and role and these different positions are clearly communicated;
- within the external communication of biomonitoring results (surveillance) priority (in timing) will be given to the participants in the campaign and to identified intermediary authorities and actors;
- the interpretation of the biomonitoring data needs full attention and should be encouraged, for future policy formulation: an Action Plan (developed during 2004-2005 by a Steering Group of consortium-members and governmental representatives and to be continued) will accompany deliberation and decision making on interpretation for action. The biomonitoring data are not a goal in itself but should lead to an improvement of environmental health;

- researchers and government will provide information on the focal points for questions from participants, intermediary organisations, authorities and the general public in line with the open ended interpretation of results;
- scientific valorisation is evident and of relevance to the national and the international scientific community and the valorisation of Flemish policy oriented research abroad;
- the results of the biomonitoring are of interest and relevance to the public at large.

These rules or appointments reflect an open perspective: they will support interaction with societal actors. Participation is considered fruitful for the development of knowledge in complex issues, fruitful for the support to define problems and solutions of Environment & Health-issues and fruitful for gaining trust between the parties. The Action Plan and the Selection Procedure for the research topics are both examples of an interactive and deliberative or argumentative approach, of participation facilities for stakeholders, normally kept external to the scientific research, but in our approach integrated to the surveillance and research activities (see detail in points 2.6 and 2.7). Discussion rounds with different types of actors (experts, policy makers, private stakeholders) are included.

2.7.2 Organisation of communication and task division 2007-2011

The *organisational conditions* for external communication are:

- in line with the general principle of integrated social scientific research (see point 4.3.2. of the proposal) only **integrated communication initiatives** will be organised. This means that in principle, external communication activities will be organised internal to the biomonitoring activities and research programme. Strategies will be developed on the basis of contemporary insights, but implemented in the specific context of the consortium results. Interdisciplinary collaboration (involvement of different scientific disciplines) is necessary.
- **shared external communication** means that the responsibility and the work load for the external communication are discussed and agreed on within the Field Work Committee and with the Spokesman and the Co-ordinator of the Centre of Expertise for Environment and Health. The members of the Field Work Committee are all considered as main stakeholders (the social scientific team included; not to be perceived as the communication cell of the consortium). This is due to the complexity of environment and health issues (insufficient scientific knowledge, no one-dimensional interpretation). As transparency and risk dialogue become crucial, the scientists enter in open communication and are open to ‘frequently asked’ questions on the methodology, design and stages of the scientific research, the results and their interpretation, uncertainties and controversies.

The social scientific team specifies the following tasks and initiatives during the biomonitoring and specific research activities (case studies) in order to support the goals and conditions mentioned, with transparency as a key condition as it is of importance for all concerned parties and initiatives. For the Action Plan and the Selection Procedure for hot spots (as initiatives for participation) we refer to the points 2.6 and 2.7.

- upgrade and consolidation of the ‘**Spelregels**’ for the new Center of Expertise for Environment and Health and the collaboration with the Steering Committee of the Flemish government. The basic principles, quality standards and rules in these Spelregels should guarantee a transparent and open external communication of the results of the consortium, focussed at trust of all parties;
- discussion on the **common communication strategy** on the biomonitoring results and their first interpretation, to be agreed in the Field Work Committee, the Consortium Management Team and with the Steering Committee. Also the MMK-network will be invited to comment the strategy. This communication strategy is based, in the first place, on the agreed Spelregels. A **communication plan** will prevail more detailed information on the implementation:
 - o the goals or functionalities of the external communication (in order to start from a common perspective and common expectations, prior to ex post evaluation activities)
 - o individual steps or initiatives, detailing ‘what/how, why, who and when’. The who-question will include attention to the different roles in risk communication, participants in the study, policy makers, experts and medical and environmental professionals as practitioners and MMK, stakeholders and the public in general.
 - o the internal operational aspects, responsables and task division
 - o mode of ex post evaluation
- responsible for the evaluation of past (external) communication;
- advising aid for the design and updating of the Steunpunt-website (evaluation initiatives included);
- advising aid on the design and updates of the BioMONITOR, a frequently e-mailed newsletter of the Consortium and involved administrations environment and health (as a member of the Editorial Board; evaluation initiatives included).

2.8 Risk perception research

2.8.1 Aim and relevance of risk perception research

Comparable to the former biomonitoring campaigns, questionnaires will **include questions on the perception of environment and health risks and trust** in sources of information and responsables for solutions for environmental health problems. Complementary questions (and resulting data) on socio-demographic and socio-economic characteristics and social network of the participants will allow to assess awareness, opinions and attitudes of Flemish inhabitants and residents of specific regions (hot spots), with relevance to risk communication and risk management. The need to map risk perceptions is also expressed in the Flemish MINA-plan 3 (2003, also other references are to be found in the bibliography of point 4.3),

Risk perception research is useful for several reasons. One obvious reason is that purely technical or quantitative research methods cannot explain why people perceive and accept risks as they do: technical or quantitative research methods are limited because of blind spots. Moreover, understanding risk perception is valuable for risk management (Renn and Rohrman 2000). An important tool in risk management, risk communication, needs to take into account risk perception. In order to tackle complex

problems such as environmental health problems, it is necessary to incorporate different forms of knowledge of these problems as well as respect for the fact that professionals and non-professionals, for example, may perceive problems quite differently.

One of the main problems in risk communication is negligence of the fact that different perceptions are relevant and should be respected. Overcoming the gap between science and the public is still one of the biggest challenges of risk communication. Mutual understanding is necessary to create trust in order to solve problems that are both scientifically and socially complex. Risk communication is no panacea though, but will result in fewer misunderstandings and ‘better’ (informed) conflicts (Drijver and Woudenberg 1999). From the perspective of perception management moreover, in order to achieve social change, taking perceptions seriously is a prerequisite. Finally an important reason for taking into account lay knowledge is simply the fact that science itself suffers from many uncertainties and unknowns. Lay knowledge may contribute to the better understanding of problems. A social scientific perspective on risks thus broadens the horizon and offers other ways of understanding and describing reality and the way people socially construct their own realities (Renn and Rohrman 2000).

2.8.2 Methodology of risk perception research

Public health risks related to environmental pollution are scientifically very complex. This is not the only reason why environmental policymaking is difficult. Apart from the lack of unambiguous scientific knowledge, risks are socially complex: they are interwoven with our way of life, with our norms and values. Different perceptions of risk are related to many factors. Next to scientific factors, also social factors are very influential (Covello 1991, Slovic 1998, Renn and Rohrman 2000) e.g. whether people are voluntarily exposed to risks, and the distribution of costs and benefits of risk-generating activities such as industry. Next to this, the amount of trust people have in individuals or organisations that are responsible for risk management is of great importance (Wynne 1996; Renn and Levine 1991). Wynne (1992) also stresses that risk perception is not purely an individual matter. It is part of and shaped by the interaction between people.

When Wynne (1992) discusses risk perceptions as part of a social process, he refers to the concept of social learning. In discussion with other people, the ideas and values that are of importance to the perception of risks are exchanged and tested. People learn from other people’s viewpoints. Such a process of social learning can also be understood as negotiation. In discussion between different viewpoints, the problem definition, the meaning, or a problem solution strategy can be constructed by mutual learning and negotiating.

Risk perceptions can also be complex because of apparent paradoxes. In a consultation of residents in a neighbourhood next to a heavily polluting factory for example, there seemed to be little unrest about the health risks (Keune et al 2002, Keune 2003). Further research showed that lack of individual opportunities to change the problematic situation, or for residents to move to another residential area, caused people to be more or less resigned to their fate.

The idea to combine perception research **with biomonitoring** mainly resulted from cooperation between social scientists and the environmental and health experts within the framework of the Centre for Health and Environment. The opportunity of linking perception research with questionnaires to several thousands of participants (in three

campaigns over 4000 people) combined with the interest of investigating public perceptions of environment and health issues formed the basis, although perception research by way of questionnaires has serious disadvantages. These disadvantages refer to the static character of surveys while perceptions are dynamic as social constructs, the possible bias due to closed questions, the lack of information for further interpretation of the individual and group results. But the fact that the biomonitoring is likely to be repeated (and even sometimes longitudinal), offers the possibility of monitoring perceptions over time. And last but not least, data on the perception of participants in the study can be of extra value within the Action Plan (desk research).

The opportunity to work on integration of different perspectives and forms of expertise, different scientific disciplines and lay knowledge and perceptions, is of great importance for bridging the gap between science and society. Of course this is a step-by-step process. It is a rather complex process: different spheres with different vocabularies cannot be expected to ‘understand’ each other easily. Moreover some division of labour will of course remain. It does not mean that scientific specialised expertise is no longer needed. On the contrary, the complexity of the issues at hand necessitates a combined effort. Based on this research we hope to come up with some indications and hypotheses for further work and research on both perceptions and integration of different perspectives.

2.8.3 Activities and task division risk perception 2007-2011

- **recommendations on indicators in questionnaires** for perception and social determinants, taking into account European and Flemish public opinion surveys on environmental awareness, nuisance, attitudes and behaviour. Complementing this with indicators such as residence status, employment, social class, social capital. As the former three human biomonitoring campaigns focussed on the regional level, comparison with tested surveys at the Flemish level will make even more sense with the Flemish (reference values oriented) biomonitoring. As described in point 4.3.1., specific attention will go to information on social class, in line with the other statistical analyses. An extra argument for this and further research on social differentiation can be found in the striking differences within a region, in contrast to the regional differences (see results of former biomonitoring campaigns 2002-2006, www.milieu-en-gezondheid.be).
- **adjustment of the perception survey** to the context of Flemish reference value monitoring, not aimed to assess regional differences within Flanders but still sufficiently tailored to detect individual and regional or other context factors.
- **adjustment of the perception survey to the context of hot spot surveillance** (aimed to compare with Flemish references)
- **analysis** the collected information of a campaign (with the advice of the statistical team involved in the consortium). As mentioned in the text on social inequality (point 4.3.1, extra cross-sectional information can be involved in the analysis. For hot spots, the analysis of the perception survey depends on the capacity and feasibility in time.
- **active participation in the Field Work Committee** for surveillance
- **reporting on the results**, in line with the time schedule of the biomonitoring campaigns and the internal and external communication of the results;
- including of results for the desk research in the Action Plan
- we also refer to the text on ‘Selection procedure’ as the identification of criteria for the selection and ranking of cases also reveal risk perceptions.

3. The information desk (vraagbaak)

3.1 Context

There are thousands of toxic chemicals in the environment, each in low to very low concentrations (Huff & Hoel, 1992; Huff, 1993; Lewtas, 1993). Biological and health effects stem often from exposure to complex mixtures. Exposure to Ionizing radiation and non-ionizing radiation are ubiquitous. Interactions between these many agents are probably important (Deman & van Larebeke, 2001). Uncertainties are huge (Finkel, 1995). There exists, among scientists and in the public, concern as to the health effects associated with fine particles (air pollution) and new agents, in particular endocrine disrupting substances wireless telephony, and nano-particles.

3.2 Analysis of the needs

Several governmental services and policy making institutions need:

- quickly available information on health damaging properties of substances, radiations, processes and procedures.
- information on new developments and new insights concerning health damaging effects of environmental factors
- information on the health effects of substances, radiations, processes or procedures that were recently introduced or that could be introduced in the near future.
- to be able to correctly assess risks from environmental exposures that include many agents in low doses and numerous interactions.

3.3 Aims

To answer questions of the authorities on:

- the danger associated with a particular agent
- the risk associated with a particular exposure
- the possibility of an association between a particular situation entailing exposures and the incidence or prevalence of a particular disease.
- the possibility of a causal link between a particular situation entailing exposures and the incidence or prevalence of a particular disease.

To inform the authorities and to give them advice on:

- the risks of low dose exposures, in particular those occurring in the environment
- the effects of interactions and exposure to complex mixtures in general
- the effects of receptor binding and hormone disturbing chemicals. In particular in the very low dose range.
- the biological and health effects of the main polluting chemicals
- the biological and health effects of non-ionizing radiation and nano particles

3.4 Methodology

The information desk will develop two main types of activity:

- Provide answers to precise questions posed by the authorities (25% of FTE)
- Make a systematic and in depth study of some important aspects and of new developments in environmental health (50% FTE)

Furthermore the information desk will also provide:

- information needed for the policy response (action plan) to findings from the biomonitoring (15% FTE)
- information needed for the writing of articles on the biomonitoring results (10% FTE)

3.4.1 Providing answers to precise questions posed by the authorities

- The information desk will be situated in the University of Ghent or in the secretariat of the consortium. The questions must be addressed to the secretariat of the consortium.
- If the question is not urgent (the answer may wait for 1 month or more) the question is distributed to:
 - 1° The scientists responsible for the "Information Desk". These determine which scientists in the consortium, with special expertise in the field, will have to answer the question (within three weeks)
 - 2° All scientists involved in the consortium. Each of them can forward her/his advice to the "Information Desk". Every scientist in the consortium can require the organization of a meeting on the question, provided he/her assists at that meeting.

The scientific collaborator linked to the toxicological cell will consult the international databases: Tomes, OSHA, medline en Toxline plus and if possible EMIC. To the extent of what is possible the most important original articles will be gathered and consulted. As far as financially possible electronic access to important scientific articles will be purchased. The data retrieved will be transmitted to the scientists responsible for the "Information Desk" and to the experts belonging to the consortium who were designated.

Finally the scientists responsible for the "Information Desk" will give an answer taking into account all information obtained. The final report is send to all the scientists in the consortium before being sent to the authorities in order to ask for reactions. Two scientists in the consortium with relevant experience will have a special responsibility in review the report, this will be acknowledged. If opinions diverge within the consortium, both the majority view and the views of minorities will be included in the answer given to the authorities.
- If the question is urgent (answer required within less than one month):

The question will be send to the scientist responsible of the "Information Desk" and to all scientists participating in the project with mention of the deadline (date and time) for their advice. If the scientist responsible of the "Information Desk" is absent, another scientist, known to the secretariat of the Expertise Centre, will assume his responsibilities.

The scientific collaborator working for the information desk will consult the international data bases: Tomes, OSHA, medline en Toxline plus and, if possible, EMIC. The data retrieved will be transmitted as soon as possible to the scientists responsible for the "Information Desk". The scientists responsible for the "Information Desk" draw up an answer taking into account all available information and advice. If opinions diverge within the consortium, both the majority view and the views of minorities will be included in the answer given to the authorities.

3.4.2 Systematic and in depth study of some important aspects and of new developments in environmental health

- A search in "Toxline Plus" and medline on the main polluting chemicals, which will be repeated annually
- A continuous search in "Toxline Plus" and medline on a series of topics that are central to the "Low Dose" and "synergism" problems, with special attention paid to mechanistic and quantitative aspects.
- As far as possible, a regular screening of the websites of international organisations and some important institutions will be performed to monitor new developments such as new projects and emerging issues concerning environment and health. The whole of the expertise centre will introduce relevant information concerning new research programs and research findings on an intranet site to which the authorities have access.
- As far as financially possible electronic access to important scientific articles will be purchased
- Data retrieved from the scientific literature will be organized in a specially structured Filemaker Pro data base offering easy access.
- The scientists responsible for the follow-up of the literature will keep in touch with all the specialists involved in the present project "Steunpunt Milieu en Gezondheid".

3.5 Expected results Communication and valorization.

The language used in reports will be adapted to the target group.

3.5.1 As to answers to precise questions posed by the authorities

Reports offering the authorities a reliable and well founded advice on:

- | |
|--|
| <ul style="list-style-type: none">- the danger associated with a particular agent- the risk associated with a particular exposure- the incidence or prevalence of a particular disease in a particular area of Flanders- the possibility of an association between a particular situation entailing exposures and the incidence or prevalence of a particular disease.- the possibility of a causal link between a particular situation entailing exposures and the incidence or prevalence of a particular disease. |
|--|

Furthermore the information desk will also provide information needed for the policy response to findings from the biomonitoring

Each year several reports will be sent to the authorities and will be put on the website (www.milieu-en-gezondheid.be) of the consortium

3.5.2 Systematic and in depth study of some important aspects and of new developments in environmental health.

Review-type studies will be written on several topics.

Although the precise list will depend on future developments and the input of the steering group and the Flemish government, a preliminary tentative list is presented below

2007:

- a report on the dose-effect relationship for receptor binding substances.
- an article on the importance of epigenetic mechanisms in the induction of cancer will be presented to the "Tijdschrift voor Geneeskunde".
- a contribution will be made to at least one article on biomonitoring results that will be presented for publication to an international scientific journal.
- a report on the health effects of some "new" endocrine disrupters.

2008

- a report on the health effects of non-ionizing radiations.
- a report on the possible effects of nanoparticles.
- an article on the health effects of some "new" endocrine disrupters will be presented to the "Tijdschrift voor Geneeskunde".
- a contribution will be made to at least one article on biomonitoring results that will be presented for publication to an international scientific journal.

2009

- a report on receptor-ligand interactions: the importance of interactions between different receptors and of differences in effects on gene expression in function of the ligand binding to the receptor.
- a contribution will be made to at least one article on biomonitoring results that will be presented for publication to an international scientific journal.

2010

- an article on the low dose effects of receptor binding substances will be presented to an international scientific journal.
- a contribution will be made to at least one article on biomonitoring results that will be presented for publication to an international scientific journal.

2011

- updates will be prepared of the reports on nanoparticles, on non-ionizing radiation,
- a contribution will be made to at least three articles on biomonitoring results that will be presented for publication to an international scientific journal

The authorities will also receive a copy of the personal data base (in File Maker Pro) of the scientist responsible for the information desk.

3.6 Consultation with and participation of the authorities

This will rest essentially on e-mail and telephonic contacts with the civil servants that are involved. If necessary, small ad hoc meetings will be organized. The choice of the subjects of in depth studies will be discussed in a meeting of the steering group.

3.7 Quality Assurance

This will rest on interaction between the different specialists involved in the consortium (see 3.4 Methodology)

4. Research projects on environment and health

4.1 Fine particulate air pollution and nanoparticles

Additional financing from BELSPO will allow to study in the current framework the specific chemical and physical properties of particulates in association to acute effects (4.1.1.1). It will further allow to measure specific markers of lung permeability. The two proposals are complementary.

4.1.1 Studies on the health effects of fine particulate air pollution

Solid and liquid phase material suspended in the atmosphere is referred to as ‘particulate matter’ (PM). Our region has the highest annual mean mass PM concentrations of Europe (figure 1). The proposal deals with four topics in the epidemiology of air pollution and includes: 1/ a longitudinal approach with measurements in the same subject over time focussing on cardiovascular end-points in susceptible segments of the population, 2/ a cross-sectional study on the association between coagulation and air pollution in adolescents, 3/ time-series on the association between preterm delivery and PM and 4/ genotoxic effects of traffic related air pollution. The proposed studies are designed in such a way that we are able to study the effects of air pollution independently of those from outdoor temperature and other climatologic factors.

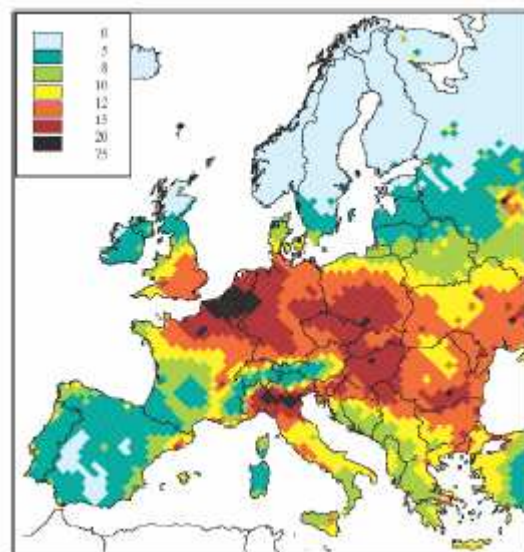


Figure 1: Grid-averaged PM_{2.5} (annual mean, µg/m³), for the emissions of 2002. From the International Institute for Applied Systems Analysis (http://www.iiasa.ac.at/rains/CAFE_files/CAFE-MFR3.pdf)

4.1.1.1. Small particulate air pollution and markers of inflammation and hemostasis in a panel study of elderly, patients with COPD and persons at higher cardiovascular risk

Epidemiological studies reported that exposure to fine particulates (PM) increases susceptibility to ischemia and the occurrence of myocardial infarction.¹⁻³ The research unit of lung toxicology collected unique data for Flanders on the association of fine particulate air pollution, and total, cardiovascular and respiratory mortality.⁴ The novelty of our findings is that we show, without having to resort to complex statistical modelling, that the effects of air pollution are much stronger in the summer months than in the winter months, even in our temperate climate. Moreover, the relation between mortality and pollution is linear in the summer, whereas there seems to be a threshold in winter (figure 2).

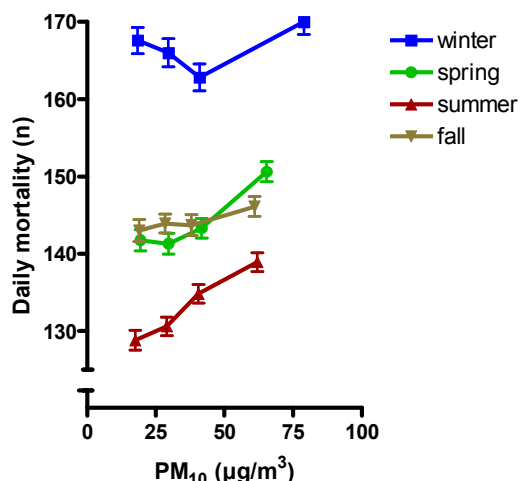


Figure 2: Total daily non-traumatic mortality (means±SE) in Flanders (1997-2003) plotted against quartiles of small particulate air pollution (PM₁₀: particulate matter with a diameter of less than 10 µm), stratified according to season. (n=354 357)

Until now, we can only speculate about the mechanisms underlying the much stronger association between mortality and PM₁₀ during warmer periods, even though the small particulate levels reach higher values in the winter. The

component-specific toxicity of small particulates may differ across the temperature range. Higher relative effects during the summer might be also a consequence of more time spent outdoors or because of lower background mortality in the summer, thus resulting in a larger pool of susceptible subjects. In sensitivity-analysis we showed significant effects for the elderly and that the population attributable risk of fine particulate air pollution on cardiovascular disease is considerably greater than for respiratory disease. In animal experiments our unit also found that pre-treatment with dexamethasone and other substances with anti-inflammatory properties, were capable of reducing thrombotic events caused by diesel exhaust particulates in hamsters.⁵⁻⁸

In line with these epidemiological⁴ and experimental data⁵⁻⁸ we will test the relevance of these associations in a longitudinal panel-study, to control for different possible confounding variables. To this end, we will measure in a cohort of elderly, patients with COPD, diabetes and previous cardiovascular complication, cardiovascular and respiratory parameters in the same person across seasons in association with fine particulate air pollution. In line with our experimental studies,⁵⁻⁸ we will study the effects of air pollution and their possible mitigation by drugs with anti-inflammatory properties. The rationale for testing anti-inflammatory drugs to prevent air pollution-induced cardiovascular effects was recently also addressed by a scientific statement of the American Heart Association.⁹ A cohort of elderly in whom cardiovascular and respiratory parameters will be repeatedly measured in the same subjects but under different conditions (fine particulate air concentrations) should increase the evidence for a possible causal relation. The *a priori* introduced stratification for the use of medication with anti-inflammatory properties allows the study of possible underlying mechanisms in an epidemiological context. The proposed study will further allow for additional analyses on the role of the ecogenetic context on the studied associations.¹²

OBJECTIVES

1. To investigate the short-term effects of air pollution on pulmonary and cardiovascular parameters (endothelial and platelet function) in a group of healthy elderly in which the parameters will be measured in the same person across seasons on days with relatively high and low concentrations of air pollution (fine particulates) in the ambient air.

2. To study whether elderly on medication with anti-inflammatory properties (e.g. statins) are less susceptible of air pollution-induced effects on respiratory and cardiovascular parameters.

DESIGN AND METHODOLOGY

Our target group will include elderly, patients with COPD, diabetes and previous cardiovascular complications. Patients will be recruited via different outpatients clinics of the university hospital of the KULeuven, elderly will be recruited from nursing homes. Sample size calculations reveal that repeated measurements (cold versus warm period of the year) in 64 persons will give enough statistical power (in each group). During a three year period the cardiovascular and respiratory parameters will be repeatedly measured (4 to 8 times) in the same person. Using a portable device (*GT-521, Met One Instruments, Inc.*) we will measure fine particulates in the ambient air 48-h before the start of the examinations (with 30 minute intervals), both PM₁₀, PM_{2.5}-fraction will be measured. Indoor particulate matter will also be measured.

A questionnaire will be administered to update recent medical history, life-style habits including the use of alcohol. Endpoints of interest include standard pulmonary function (spirometry), exhaled NO, standard cardiovascular function (arterial blood pressure)¹⁰, endothelial function (relaxation of brachial artery),¹⁰ blood parameters of inflammation (leukocytes), endothelial activation (ICAM, VCAM), and platelet activation (Platelet Function Analyzer, PFA100®).

4.1.1.2. A cross-sectional analysis of markers of hemostasis and inflammation in association with fine particulate air pollution in adolescents

Air pollution research has indicated that the increase in overall mortality and morbidity that occurs during peaks of air pollution is mainly driven by increases in the number of people who die or are hospitalized from cardiac causes.^{2,4} The same appears to be true for the increase in mortality that is associated with long-term exposure to higher levels of urban pollution.³ The inflammation that occurs in the lungs in response to the deposition of particles may be responsible for alterations in the autonomic nervous control of heart rhythm and/or for the release of proinflammatory mediators in the systemic circulation, thus affecting hemostasis or even the atherogenic process itself. The mechanisms for these acute and chronic cardiovascular effects of inhaled pollutants in the elderly and patients at risk for cardiovascular complications will be studied in a panel study (see point 1). Given that chronic inflammation is an intrinsic part of the ageing process, it is reasonable to assume that the chronic effects of air pollution on cardiovascular parameters may start early in life, in a period that these subtle or pre-clinical effects are well tolerated but over time these chronic effects of air pollution may track and lead to excess morbidity and mortality from cardiovascular causes from middle-life on.

OBJECTIVE

The human biomonitoring campaign in adolescents gives the opportunity to study the cross-sectional nature of the association between coagulation/inflammation and PM taking the other relevant measurements (e.g. immunological parameters) of the biomonitoring project into account.

DESIGN AND METHODOLOGY

In a subgroup of 250 adolescents, the cross-sectional association between platelet function, inflammation and PM will be studied. Using a portable device (*GT-521, Met One Instruments, Inc.*) we will measure fine particulates in the ambient air 48-h before the start of the examinations (with 30 minute intervals). Indoor particulate matter will also be measured. Platelet activation will be measured using a Platelet Function Analyzer (PFA100®), immediately after the blood is drawn. The measurements will be performed both in the warmer and colder period of the year to take the effects of outdoor temperature into account. The statistical analysis will be stratified by sex and we will control for the classical cardiovascular risk factors and in girls additionally for the use of oral contraceptives.

4.1.1.3. Time series on the association between preterm delivery and fine particulate air pollution

Preterm delivery remains the leading cause of perinatal mortality and occurs in approximately 4 to 10% of the pregnancies.¹² Associations between ambient air pollutants and adverse pregnancy outcomes have been reported but the effects of season and temperature have not been characterized in detail.¹³ Weather-related differences over the seasons may modify the association between preterm-delivery and air pollution. Simple statistical adjustments for temperature may be inadequate because some of the effects of pollutants may be associated with outdoor temperature or outdoor temperature might behave as an effect modifier in the association between preterm delivery and PM₁₀.

OBJECTIVE

We will study in relatively highly polluted region of Europe (figure 1) the short-term association between preterm-delivery and PM₁₀ over a recent 9 year period (1997-2006) by season and by quintiles of temperature. We will use the same straightforward statistical approach which we recently applied to study the mortality pattern in Flanders in associations with PM₁₀.⁴

DESIGN AND METHODOLOGY

We have access to the database of the study centre of Perinatal Epidemiology. This birth cohort consists of ~540 000 births in 1997-2006, and data include gestational age, sex, birth date and order, parental age, birth weight and place of residence. Database management and statistical analyses will be done with SAS software (version 8.1). The association with PM₁₀ will be estimated examining the delayed relation up to five days (lag 10), previously and additionally long-term exposure terms will be tested by averaging the PM₁₀ levels over longer periods (monthly). First, we will test the interaction between PM₁₀ of the days before delivery itself and period of the year (warm/cold period defined as April-September/October-March). If the interaction term (period of year * PM₁₀) in a model studying the temporal variation in preterm delivery in association with temporal variation in PM₁₀ would reach the level of significance, we will run the analysis stratified according season or strata of temperature by plotting preterm delivery for quartiles of PM₁₀ in each season, or each quintile of outdoor temperature. Additionally to investigate whether categorization of the data does not bias the pattern, a smooth loess function as implemented in the SAS statistical package will be used to regress preterm delivery against PM₁₀ stratified according to season. If the association is linear, we will calculate dose-response relations using a continuous regression model with adjustments for the day of the week, for outdoor temperature of

the same day (linear and squared term) and the difference in outdoor temperature between the day of the event and that of the previous day.

4.1.1.4. Association between markers of genotoxicity and indicators of traffic-related air pollution

Until now, six prospective studies¹⁴⁻²⁰ show an association between lung cancer and air pollution. It has also been shown that chemical species present in polluted air or extracted from particulate matter sampled from urban centres exhibit mutagenic properties. Cytogenetic findings in human biomonitoring programs must be interpreted carefully given that only a few subjects may have abnormally raised numbers of cultured lymphocytes with chromatid breaks or chromosome abnormalities, these markers might objectivate epidemiological associations. Nevertheless, evidence suggests that within the normal range some of the genotoxic markers including chromosome abnormalities predict the cancer risk in the population. In a pooled analysis of 3541 Nordic and Italian people, chromosome aberrations (within the normal variability) in peripheral lymphocytes were a biomarker of the cancer risk, reflecting either early biological effects of genotoxic carcinogens or individual cancer susceptibility.²⁰

OBJECTIVE

To further objectivate the epidemiological evidence on the mutagenic and/or carcinogenic potential of air pollution we will study acute and (sub)-chronic genotoxic effects in association with living to major roads.

DESIGN AND METHODOLOGY

Markers of genotoxic effects include the comet assay (acute) and micronuclei (chronic) in lymphocytes. These markers are currently available in 1679 adolescents and 1780 women of the previous environmental health studies. Residential addresses and school addresses from questionnaire data will be geocoded using GIS software. Participants living within 100 m of a freeway or within 50 m of a major urban road will be judged as exposed.¹⁸ This definition is internationally accepted and on the basis of data from the Netherlands it has been shown that this results in additional exposure up to the normal background values.¹⁸ By use of a portable device (*GT-521, Met One Instruments, Inc.*) we will check whether this definition applies also to higher PM10 values in the Flemish situation. We will further implement a rural and urban component in the analysis. The interaction term traffic exposure and season will be tested.

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4.1.2 Validation and development of biomarkers for individual exposure to particulate matter

Epidemiologic studies showed that the inhalation of particulate matter is associated with both acute and subacute effects.¹ Most of the studies on the effects of fine particulate matter used external monitoring stations as a reference. Using ambient air pollution from monitoring stations as a surrogate for personal exposure, will result inevitable in a measurement error. Inaccuracies in exposure measurements increase random errors and normally reduce the statistical significance of the health effect air pollution association. Precise biomarkers of internal particulate exposure are not much studied. Recently, the use of the carbon content (mean carbon area) of airway macrophages as a marker of individual exposure to particulate matter has been suggested.^{2,3} However, this method is not fully validated and it is very time consuming what makes it not suitable for large scale epidemiological studies (working load: approximately 1.5 days for 1 subject).

- We will further validate the use of carbon area in macrophages by exposing cell cultures to relevant concentrations of particles. Carbon in macrophages will be microscopically visualized and count to study the dose-effect relations.
- We will look for alternative methods that are less time consuming, e.g. measuring the granulocytosis (morphological changes) in macrophages exposed to particles with FACS-analysis.
- We will study in humans whether carbon in macrophages (collected by induced sputum) is associated with the degree of granulocytosis in macrophages (as an alternative biomarker).
- We will investigate whether we can estimate and differentiate the exposure to nanoparticles (such as TiO₂, and silica particles) and we will investigate whether the dose-response is material specific.

For human studies persons will be recruited from the university hospital (Gasthuisberg). Dependent on the experimental and patient studies the biomarker will further validated in participants of the biomonitoring project (in 2008-2009). The latter is dependent on results both from our studies in cell experiments and in patients. The combination of experimental and the more clinical or epidemiological oriented part may lead to the development of an applicable biomarker of internal exposure to particles in general.

That would be of direct advantage with the biomonitoring program in which we could use this biomarker in different settings. Indeed lung macrophages could be collected non-invasively by induced sputum. Scientific interest lies in the possibility to study subchronic adverse health effects of particulate matter at an individual level. The study will start after approval by the ethical committee of the KULeuven. Lung function will strictly followed-up.

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4.2. Studies on the health effects of endocrine disruptors

In 1985, Hull et al.(Hull, Glazener et al. 1985) published the results of a study in which they assessed sub fertility in 708 couples in a health district in England and concluded that at least one in six couples need specialist help at some point in their lives because of sub fertility. These findings were confirmed in two prospective studies in the Netherlands, estimating the cumulative incidence of sub fertility to be 10.4%(Beurskens, Maas et al. 1995) and 9.9% (Snick, Snick et al. 1997) for women aged between 15 and 45 years.

It is generally assumed that the low fertility rates in the industrialized countries are the result of social and economic changes, such as women's careers, postponed child wish, declining ideal family size, instability of partnership, etc. However, there is growing evidence to suspect that changing lifestyle and increasing environmental exposure to endocrine disruptors, are behind the trends in occurrence of reproductive health problems (Skakkebaek, Jorgensen et al. 2006). Modern life includes many uses and misuses of a number of consumer items, which may be contaminated with a mixture of chemical and natural products with adverse effects.

The use of biomarkers can help to identify possible links between sub fertility and exposure to endocrine disruptors at the individual level.

In two case-control studies - one in males and one in females - sub fertility will be related to exposure to environmental contaminants from historical sources in the environment and to exposure to 'newer' contaminants in our daily life. The historical contaminants such as PCBs, dioxins, pesticides and heavy metals have accumulated in the environment since the seventies and are still relevant problems in Flanders. The 'newer' contaminants such as phthalates, bisphenol A and perfluor compounds are getting increasing attention in scientific research as they are present in an growing number of personal care products and daily consumption products such as clothing, packaging, toys, carpeting, electronic equipment, etc. These chemicals are all known to have hormone disrupting properties, although the relevance of these findings (mostly from in vitro and animal studies) at current environmental exposure levels is still largely unknown. Dioxins are well known anti – estrogens, PCBs have both estrogenic and anti- estrogenic effects depending on the congener (Connor, 1979), phtalates may act as anti-androgens (Latini et al, 2004), bisphenol A has been shown to exhibit estrogenic activity (Maffini et al, 2006) , reproductive and developmental effects from perfluorinated alkyl compounds have been observed in experimental animals as well as changed hormone levels (Lau et al,2003; Austin et al, 2003), cadmium (Schoeters et al, 2006) and lead (Pant et al, 2003) have been shown in a number of studies to affect sperm quality. All these chemicals may adversely affect fertility.

The two studies will be performed in three Flemish fertility centers: Leuvens Universitair Fertilitieitscentrum, K.U. Leuven (Prof. dr. Thomas D'Hooghe), Endocrinologie, UGent (Prof. dr. Jean-Marc Kaufman), Centrum voor Reproductieve Geneeskunde, VUB (Prof. dr. Herman Tournaye).VITO, PIH and KULeuven (dept. of Prof. B. Nemery) will be involved in the coordination of the field work, the toxicological analyses, the database management, statistical analysis and communication of the results.

4.2.1. Case- control study in patients with male sub fertility

Objective

To estimate the possible correlation between exposure to endocrine disruptors and male sub fertility.

Patients

Both cases and controls will be recruited through the fertility centers. For each case, 2 controls will be selected.

- Cases:

1. Men with less than 5 mil. spermatozoa/ml without congenital, genetic or known acquired cause (chromosomal abnormality, Y chromosome micro deletions, cryptorchidism, infection, post-vasectomy,...) with exception of azoospermia.
2. Men with milder forms of idiopathic oligospermia (sperm concentrations between 10-20 mil. spermatozoa/ml) will also be included, to potentially show dose-response effects. Also, environmental effects might rather cause mild to moderate forms of sperm abnormalities rather than severe forms of sub fertility.

- **Controls:** age-matched male patients with normal fertility confirmed by normal sperm parameters, a complete physical and urogenital examination, and hormone analysis. In first instance, controls will be selected from men at the fertility clinic or at the prenatal clinic whose wives are pregnant more than 14 weeks (proven recent fertility). If it is difficult to reach the postulated number of controls, sperm donors and/or vasectomy patients with children are the alternative sampling group.

Materials and methods

After informed consent, patients fill out a questionnaire with questions regarding life style (smoking, drinking, nutrition, etc.), profession, medical history, and history of domicile. Urine, blood and semen samples are collected on the same day as the interview. A single spot urine sample is collected in a sterile specimen cup (no first-morning void) and urine and blood samples are stored at -20°C for future analysis. On a second day, at least one week apart from the first consultation, a second semen sample and blood sample for bisphenol A is collected.

Blood and urine will be analyzed for a number of endocrine disruptors. (see also 4.2) The final selection will depend on the available budget and will be selected from the following list:

- marker PCBs (congeners 118, 138, 153, 156, 170, 180 in serum);
- chlorinated pesticides (p,p'-DDE and hexachlorobenzene in serum);
- perfluoro compounds (PFOS and PFOA in serum);
- phthalates (urinary DEHP and MEHP);
- bisphenol A (because of the low half-life, serum samples of 2 separate days will be pooled);
- heavy metals (urinary cadmium and blood lead).

To assess total estrogenic activity of the blood yeast-based E2-bioassay will be performed.

The following fertility parameters will be measured:

- semen analysis (ideally semen analysis should be performed twice on separate samples; this would greatly improve reliability of classification of the men, which is important taken the rather low number of men planned for inclusion);
- endocrine profile: FSH, LH, inhibine-B, testosterone, SHBG, 17beta-estradiol; (Remark: due to diurnal changes, it is necessary to measure testosterone in the morning);

- testicular volume;
- karyotyping (before inclusion);
- screening for Y micro deletions (before inclusion).

Statistical analysis

The levels of exposure markers in cases will be compared with the levels in control after correction for possible confounding factors (information from questionnaires). Based on previous studies in adolescents and in adults, between 62 and 165 subjects per group are needed to demonstrate a 20% difference in mean level of exposure for marker PCBs or hexachlorobenzene. For the ‘newer’ markers of exposure, no sample size calculations could be performed, as there is no information available about means and variances in the population. It is suggested to include 50 patients and 100 controls in the study.

In order to estimate the risk for sub fertility associated with varying levels of exposure, conditional logistic regression will be performed. This technique will also allow to estimate the impact of combined exposure to several toxic compounds.

4.2.2. Case- control study in patients with female sub fertility

Objective

To estimate the possible correlation between exposure to endocrine disruptors and female sub fertility.

Patients

Both cases and controls will be recruited through the fertility centers. For each case, 2 controls will be selected.

- **Cases:** females with unexplained fertility disorders, i.e. female patients with a husband with normal sperm parameters, with a regular menstrual cycle, with open fallopian tubes as assessed by laparoscopy, and without pelvic pathology (excluding endometriosis) and suffering from infertility for at least 2 years (with the exception of iatrogenic causes and infections). Cases can only be included after a full fertility investigation including laparoscopy.
- **Controls:** age-matched female patients with normal fertility, e.g. patients undergoing tubal sterilization and spouses from men with pure male infertility (sperm density less than 5 mil. /ml).

Materials and methods

After informed consent, patients fill out a questionnaire with questions regarding life style (smoking, drinking, nutrition, etc.), profession, medical history, and history of domicile. Urine and blood samples are collected on the same day as the interview. A single spot urine sample is collected in a sterile specimen cup (no first-morning void) and samples are stored at -20°C for future analysis.

Blood and urine will be analysed for the following endocrine disruptors. The final selection will depend on the available budget and will be selected from the following list:

- Calux assay on serum (total dioxin-like compounds);
- marker PCBs (congeners 118, 138, 153, 156, 170, 180 in serum);
- chlorinated pesticides (p,p'-DDE and hexachlorobenzene in serum);
- perfluoro compounds (PFOS and PFOA in serum);
- phthalates (urinary DEHP and MEHP);

- bisphenol A (because of the low half-life, serum samples of 2 separate days will be pooled);

The following clinical parameters will be measured:

- day 2-4 hormonal assay for FSH, LH, estradiol, Antimullerian Factor, Inhibin A, Inhibin B.

Statistical analysis

The levels of exposure markers in cases will be compared with the levels in control, after correction for possible confounding factors (information from questionnaires). Based on previous studies in adolescents and in adults, between 62 and 165 subjects per group are needed to demonstrate a 20% difference in mean level of exposure for marker PCBs or hexachlorobenzene. For the ‘newer’ markers of exposure, no sample size calculations could be performed, as there is no information available about means and variances in the population. It is suggested to include 50 patients and 100 controls in the study.

In order to estimate the risk for sub fertility associated with varying levels of exposure, conditional logistic regression will be performed. This technique will also allow to estimate the impact of combined exposure to several toxic compounds..

4.2.3 Study of the relation between exposure to endocrine disruptors and biological effects

Next to biomarkers of exposure determination of biomarkers of effect add information to the general picture of environmental hazards. Only a fraction of environmental chemicals can be measured –because of analytical and financial limits-, and synergetic effects may occur. Measuring effects gives an idée on a total impact of environmental factors. The propose case studies can be linked to the surveillance program collecting extra information on biomarkers of effect in well defined subgroups.

4.2.3.1 Study of the relation between exposure to endocrine disruptors and biological effects with attention for effects on fertility in mothers of newborns

Target group: Mothers of newborns participating in the surveillance part of the biomonitoring program

Measurement of modern pesticides, classical pollutants, modern pollutants. Proposed biomarkers of effect: fertility problems

Reporting en communication: “Surveillance” aspects: internal dose, regional differences, if possible effect parameters can be communicated a short time after termination of measurements. “Research” aspects of effect parameters, exposure-effect relationships and more complex relations between measured and questioned parameters requires more in depth analysis and discussion and therefore more time. Communication can be given with different time intervals for the different aspects of biomonitoring

4.2.3.2 Study of the relation between exposure to endocrine disruptors and biological effects with attention for effects on puberty development and ADHD in adolescents

Next to biomarkers of exposure determination of biomarkers of effect add information to the general picture of environmental hazards. Only a fraction of environmental chemicals can be measured –because of analytical and financial limits-, and synergetic effects may occur. Measuring effects gives an idée on a total impact of environmental factors. The propose case studies can be linked to the surveillance program collecting extra information on biomarkers of effect in well defined subgroups.

Target group: adolescents participating in the surveillance part of the biomonitoring program

Measurement of modern pesticides, classical pollutants, modern pollutants. Proposed biomarkers of effect: computer tests for psychomotor development and ADHD. Special attention for sexual development and hormone levels in adolescents.

Analyses:

Biomarkers of exposure: heavy metals, Calux, PCBs, chlorinated pesticides, DDE's, PFOS, other analyses (e.g. Galaxolide, Bisphenol A), Pesticides

Biomarkers of effect: Hormones, Neuropsychic tests,

Reporting en communication: “Surveillance” aspects: internal dose, regional differences, if possible effect parameters can be communicated a short time after termination of measurements. “Research” aspects of effect parameters, exposure-effect relationships and more complex relations between measured and questioned parameters requires more in depth analysis and discussion and therefore more time. Communication can be given with different time intervals for the different aspects of biomonitoring.

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4.3 Social scientific research in support of environmental health surveillance and research

4.3.1 Social inequality and environmental health risks

4.3.1.1. Relevance of the topic and position in this application

‘Social inequality and environmental health’ is a broad research area in itself. Social scientists pay attention to as well empirical studies at the national and local level as to theoretical aspects (OECD, 2004). Empirical studies demonstrate the coincidence or accumulation of socio-economic deprivation and poor environmental quality (air quality, distance to IPC sites, waste sites, flood risk, ...) for instance in the UK (SDRN Sustainable Development Research Network, 2004, Mitchell, 2003), in older urbanized neighborhoods in the Netherlands (RIVM, 2000), in industrialized regions as the Rijnmond area (Kruise/RIVM, 2004 except for aircraft noise; Woudenberg 1998) and in deprived British communities (SDRN) or more specific in areas around specific polluters and along line infrastructure (Miedema, 2001, RIVM, 2000). Basic concepts, used in a more theoretical perspective are environmental (in)justice and equity, ecological racism, procedural fairness, distribution of goods (wealth, environmental quality) and bads (burdens, poor environmental quality, risks), ... (Weintrauw, 1994, Roberts, 2000). These concepts also reveal the attention for political processes behind social inequality in the environmental context and underline the intervention of justice-driven policy. Explanation is to be found in (housing) market efficiency, income inequalities, historical planning processes, deprivation from decision making processes, NIMBY protest in middle class areas, and even distributional effects of policy itself, as well environmental policy as policy in general. Besides sociological and economic research, also political and policy sciences became involved (sub) disciplines in the topic. Several literature studies underline the actual variety and complexity of the topic, as shows the following text fragment of the synthesis OECD-report OECD “Environment and distributional issues: analysis, evidence and policy implications” (2004):

“With respect to environmental quality, some conceptions of "fairness" generally discussed in the literature to assess the distribution of environmental impacts include:

Equality of Environmental Exposure – e.g. all households have the same level of exposure to pollution (concentration);

Equality of Risk – e.g. all households face the same level of risk, taking into physiological and other differences;

Progressive Inequality – e.g. systematically using environmental policy as a redistributive mechanism to favour poorer households;

Procedural Fairness – e.g. ensuring that all households have the opportunity to express their environmental preferences effectively; and,

Situational Fairness – e.g. ensuring that households continue to enjoy the level of environmental quality to which they have become accustomed (such as when a house was purchased).

“Preference-based” notion of equity – e.g. in this approach that reflects personal preferences, a fair distribution may be one in which levels of environmental quality differ according to differences in demand for environmental quality.

Some of these notions are just elaborations upon one another (i.e. equality of exposure and risk). In other cases they are potentially complementary (i.e. procedural fairness and equality of risk). They may also represent different fundamental conceptions of fairness (i.e. preference-based notions of equity vs. equality of environmental exposure). Moreover, it is important to recognise these differences when trying to identify a government's objective with respect to a particular measure which seeks to redress some distributional imbalance.

Source: OECD, Programme on the "Social and Environment Interface" (2004).

Seen from this inclusive perspective, the attention paid to social inequalities, is in line with Sustainable Development (and its pillars) and inspiring policy documents or other institutional 'policy upstream' initiatives in decision-making (e.g. Strategic Impact Assessment taking distributional impacts into account in the US, Canada, UK, EU). Some countries (USA, UK) do indeed have an 'environmental justice agenda' (Walker, s.d., Coenen, 2000, SDRN-briefing, s.d.). All this makes the debate and research on environmental inequalities policy relevant and actual, but also a methodological and interdisciplinary challenge.

In this application, we consider the accumulation of poor environmental quality (exposure) and social deprivation or lower socio-economic status as empirical evidence, although studies are scarcer in Europe (UK, the Netherlands) than in the USA (OECD, 2004, p. 24) and the evidence base remains weak on causation. Reviews for neighbouring countries demonstrate that environmental injustice is "real and a substantive problem; (...) that problems of environmental injustice afflict many of our most deprived communities and socially excluded groups (...) and that in some cases excluded communities are disproportionately vulnerable to its effects (...) and that environmental ills may not only self-perpetuate, but also lead to other environmental, economic and social problems" (www.geog.lancs.ac.uk, SDRN, 2006). So, a demonstration of unequal distribution in Flanders is not our objective. Moreover, the most covering geographical study for Flanders, realized by Kesteloot in 1996 and not focusing on environmental quality, already clearly illustrated the spatial distribution of several socio-economic (as income) and demographic characteristics (as education) of inhabitants at the ward level and the coincidence of lower income with lower housing quality. Actualization of spatial distribution patterns or segregation studies is not easily done, as socio-economic data on households in Flanders is not available in a large scale GIS-context. An updating of this 'Atlas' is expected in June 2007. For detailed areas, exploratory studies do exist (Van Hove, 1987, on the presence of gardens and public areas, on the pressure of nuisance and safety risks on housing conditions (of non-local horeca, industries, waste sites, ...); MIRA, on the availability of green areas at the local level of several cities). This application will restrict to specific aspects, prior to the biomonitoring programme, as many other social scientific research objectives are prior as well (planning for communication, modelling for participation, questionnaires risk perception, ...). One should also notice that the social dimension has to be treated as well at Flemish level (reference values) as at the area specific level (biomonitoring for hot spots). So, also non-responder information on social class is highly recommended for both settings. The key research question here is on the **most optimal proxy** for social class or wealth in the context of the human biomonitoring and specific geographical units and how to **implement them in the questionnaires**. The additional collected information will allow researchers (of this consortium and others later on) to assess the impact of social class for exposure, health, and health concern ("racial

minorities and poor communities it is argued are more likely to be exposed to, and suffer from the effects of environmental risks than their white or more wealthy counterparts”, Walker). Depending on the results, suggestions for additional funding on the social dimension can be strived for (see also research project on environmental equity of the RIVM and the University of Utrecht; UK private research programme of the Sustainable Development Research Network – Rowntree Trust and Friends of the Earth).

4.3.1.2. Objectives 2007-2011

In the biomonitoring study an effort will be made **to assess with greater precision the social class of the participants**. Social class will not be strictly defined in the stage of this application: as well economic status as social deprivation can be of relevance. A screening of the recent literature, in combination with availability of Flemish data and other institutional conditions should make clear which variables are most relevant. It should also be stressed that the opportunity to integrate the social aspect within the biomonitoring campaigns is that there is ample exposure information at the individual level and that this exposure information is gathered with biomarkers which can complement information on ‘perceived’ environmental quality (noise, air pollution, availability of green areas, ...), as frequently used in the questionnaires or inequality studies abroad. As we know, the association between ‘objective’ environmental indicators and ‘perceived’ environmental quality is not strong.

The main research objective is to identify information relevant for explaining individual variances in the measured values within regions and for non-responders research. As we know from results of former biomonitoring campaigns, individual variances are more (statistically) significant than regional variance. These regions, relevant to different types of pollution are very large. Especially in an urbanized environment, wards with a different socio-economic and demographic composition occur. Today, land covering social class information on the level of districts is hard to find. An opportunity is to be found in the questionnaires, accompanying the biomonitoring. Knowing the restrictions of the official data to compare with results of the biomonitoring, also local knowledge of MMK and of other organizations can be solicited. This means that the ‘social mapping’-information and guidelines are important complementary instruments on behalf of these local organizational structures.

The former may seem an easy step, but several complications have to be taken in mind:

- social class information within our surveys will have to be (theoretically) comparable with overall data on social class in Flanders and specific regions;
- social class information should anticipate EU-recommendations (e.g. Eurostat prerequisites): not only on the categories, but even the type of variables (education ?, yearly income at the individual or household level, additional income sources, ...);
- how to cope the interactions of social class and health in general (inequality for disease and death as described in medical sociology);
- social class questions should remain feasible for the respondents to fill out;
- last but not least, study design on social aspects always has to cope with a lot of uncertainties, as well as the analysis of gathered data. Social data and especially data from questionnaires are not easy to interpret.

This implies that a check of literature and research findings is recommended before developing additional questions on social class.

4.3.1.3 Tasks and task division

In the context of Flemish reference values

- further **exploration of the results of former biomonitoring campaigns in the context of social class** (in collaboration with statistical experts of LUC). Hypotheses will be formulated within the Field Work Committee and tested with the support of the Statistical research group.

Specific examples of questions are:

- can differences in the respondent groups of Ghent and Antwerp be explained (f.i. also due to the use of mean income values/income categories (Kruize/RIVM, 2004; PinderHughes, 1996)).
- is comparison to the socio-economic or socio-demographic profile of the districts, selected for the study, feasible? As comparison with 1991 census data at the ward level is not optimal, research results of 30.6.2007 will have to be attended (actual research project Kesteloot, KUL).
- which variables should be added in a non-responders screening?
- a **quick scan** of foreign studies and **usual social indicators** or variables for social class within them, in this specific context of environmental exposure, health and death (desk research);
- if necessary organization of an **expert advice** on the desk research synthesis, in order to detect and explicit uncertainties and make decisions on the ‘best’ options for additional questions for the questionnaire and biomonitoring research (e.g.. exposure is linked up to exposure time and feeding in different households in case of new united families; who’s income or highest education level should be taken into account?).
- the **cleaning and analysis of the new gathered data on social class** is to be integrated in the other biomonitoring activities of the Field Work Committee.

In the context of cases (hot spots)

- **tailoring of the recommendations** of further statistical and desk research to the research conditions of restricted areas or target groups
- recommendations (in Guidelines Social Mapping) and stand-by for the Network of Medisch Milieukundigen (MMK) considering **the local socio-economic profile** of their region and professionals, **working on community building, social deprivation and participation of deprived groups.**

4.3.2 *Interdisciplinary and transdisciplinary research: coordination, action research and reflection*

The social scientific expertise in this application is integrated in different integrated operational research parts of the consortium. First of all, we have to introduce here some concepts from social scientific literature on risk communication; they are of inspiration for several ideas in the application and the elaboration of work packages of the social scientific team. The policy relevance and efficiency of risk surveillance and environment and health research will be significantly higher when contemporary social scientific insights on risk assessment, knowledge production, interdisciplinary and transdisciplinary interaction, and risk communication are taken into account. Apart from this, the role of social science in such settings also is a valuable research topic in itself.

The text below also reveals scientific valorisation outside the daily interaction of disciplines within the consortium. The opportunity to step forward in policy science and interaction research is valuable, as the call underlines scientific academic valorisation and capacity building.

4.3.2.1. Significance and role of social science

The appreciation of and openness towards other views, other disciplines, and transdisciplinary knowledge seems to have increased. At least in the field of environmental problems and environmental policy, and technology assessment issues, as they cope with growing complexity. Examples are to be found in global warming, environment and health (f.i. endocrine disruptors), BSE, GGO, nanotechnology, ... This complexity is partly due to the scale and time frame of environmental problems, to interaction effects within the ecosystem and the human body and other technical characteristics. Controversy and uncertainty reveal the limits of the purely scientific approach. Experts often experience the obligation to decide on issues that they feel not capable of because of societal and political complexities. Social institutions on the other side are not suited to cope the necessary dialogue or risk debate in a risk society (Beck). There also appear to be substantial differences in the way experts, citizens and policymakers perceive risks. Within these groups, too, there are differences in risk awareness. Risk perception is a multidimensional concept, influenced by various factors. It has recently emerged that risk perception is, first and foremost, a process of social construction: groups and individuals conceptualise risks through interaction with others. The specific historical, regional, cultural and social context in which the individuals interact is therefore a determining factor in risk construction. In this context, the notion of ‘trust’ in institutions, experts, authorities and industry is crucially important.

Experts, professionals, policy makers and actors in civic society are all “at stake”. More or less this runs parallel with the development of the work of social scientists. Fisher (2000) uses the concept of coordination when describing the role of social scientists. He speaks of the necessity of developing innovative methods for coordinating between different discursive processes and institutions. This role of the social scientists within the framework of the Centre for Health and Environment can be characterized as ‘emancipating’, just as, about thirty years ago, interdisciplinarity was ‘new’ and emancipating, giving birth to environmental studies. Within the Centre of Expertise on Environment and Health appreciation for ‘other’ capabilities and forms of knowledge gradually grew: from complicated knowledge from ‘another planet’, to the contribution of social scientific insights and methods. Today it is perceived as a necessary asset for the complex scientific and policy endeavour.

4.3.2.2. Methodology for applied and practice oriented research

This kind of social scientific research may be qualified as a form of action research (Boog and Tromp (eds) 2003, Boog et al. (eds.) 1998, Coenen 1987, Leroy 2005): direct intervention into practice is part of the process, the research is action-oriented. This ensures, to some extent, practice-relevance. This also means that complexities that are present in practice will have an effect on the development of the research procedure. Moreover, researcher and research subjects work together, neither separately, nor in any hierarchical relationship and interaction and participation are central concepts. From the perspective of the social scientist, in the case of the Flemish Centre for Health and

Environment it concerns two-layered interactive research. Firstly, the cooperation of the social scientists with other actors in the Centre: different scientific disciplines and policy representatives. Secondly, one of the goals is to involve actors external to the Centre. The social scientists support this process. Depending on the issues at stake at specific stages different social scientific methodologies may be of relevance: surveys, observations, methods for assessment, deliberation and decision making, qualitative analysis of decision making and politics, evaluation methodology, ...

An interesting concept for the dynamic relationship between science and policy is ‘boundary work’ (Gieryn 1983, Jasanoff 1990, Hoppe 2002). Hoppe (2002), specialised in policy science, describes several models of boundary traffic between science and policy. Two dimensions are central. The first entails influence and authority between science and policy. Two extremes are the primacy of science (technocracy) and the primacy of politics. Hoppe distinguishes a third, middle ground typology: more dialogical, pragmatic. The second central dimension concerns the divergence or convergence in the way of working between science and politics. The division between both domains has grown bigger and bigger over time: ‘science and policy are social activities that have different aims and therefore are incompatible ways of life’, according to Hoppe. Also Luhmann emphasised the development in society of almost completely independent social systems and subsystems, each focussing on a specific societal function or social area, science and politics/policy being just two particular examples. Each of these social systems tends to develop its own internal rules, language or jargon, expectations and rationality; and its own way of observing and structuring reality. This evolution makes these systems grow even more apart, making it more and more difficult for them to conscientiously interact. (Luhmann, 1982, 1993, 1995; Brans, M. and Rossbach, S., 1997)

In Hoppe’s (2002) words, a dialogical, pragmatic model interaction between experts and policy representatives dominated during the first period of the Centre for Health and Environment although the application mentioned new boundary-work concepts. Most of the policy representatives and policy experts involved from the start were medical, technical or environmental specialists by training. In that sense no big divergence in ways of approaching the issues under discussion was present. The bridge towards political interpretation nevertheless showed to be problematic: an obvious discrepancy in issue framing between experts and policymakers emerged. In order to bridge this gap the contribution of the social scientists proved to be helpful within the Centre of Expertise itself. A reflective contribution paved the way for the involvement of a diversity of actors, enriching the science assessment with other than technical medical and environmental criteria, and procedures for cooperation, deliberation and decision making were introduced.

4.3.2.3. The scientific valorisation of the applied ‘boundary work’

Boundary work is not an easy but rather labour intensive exercise. The time available for reflection on the work in progress usually is rather limited. Moreover most actors involved in the process have overloaded agendas. Discussing complex issues takes time and energy, and often goes hand in hand with a lot of ‘paperwork’. Part of the work also goes to unforeseen complexities.

Quite some time is spent on actors getting used to working together. Trust building takes time and effort and is an important part of the work. Actors also have to find new

roles for themselves to some extent. In the case of the Centre for Health and Environment scientists suddenly have to discuss work with (sometimes totally) different disciplines. They also have to talk (to) politics. Government representatives suddenly have to discuss science and different fields of policy expertise (the Ministries of Health and Environment) also have to come to terms. Apart from role seeking, this also demands (new) procedures. Furthermore common vocabularies need to be developed: different scientific disciplines, policy makers and other actors use different (technical) language, have different cultural backgrounds and a different knowledge base.

The above mentioned bottle necks and challenges allow us to learn from the applications in daily practice (transparency on biomonitoring, Action Plan, Selection procedure for research topics, input of risk perceptions in the data interpretation, ...). Many publications are a plea for new concepts and models, but remain more or less theoretical concepts ('ivory tower') or a 'ten commandments' level: without actual application in daily practice. The advantage of this application is that we can learn from a real practical application and not remain at the level an artificial 'laboratory' experiment. These new insights will be as much as possible valorised in publications.

4.3.2.4. Interdisciplinary and transdisciplinary action on environment and health risks - leading principles

Environmental and health risks can no longer be considered as purely scientific or technical issues, as they clearly also manifest themselves as social problems. This was already one of the main conclusions drawn in the communication-oriented research line within the concluded pilot project on the 'Environment and Health' (1999-2000) which preceded the former Centre of Expertise on Environment and Health (2001-2006). The most important observations in support of this thesis are:

- Experts, citizens, authorities and producers perceive risks in very different ways. This is due to the varying definitions of the environmental and health issues that present themselves and the different solutions that are put forward. Moreover, these definitions and risk perceptions are dynamic: they evolve.
- The scientific assessment of environmental and health risks involves many uncertainties. It is a science in the making, and therefore inevitably tentative and controversial. Consequently, the 'right' answer to such complex issues cannot possibly come from scientists alone. Furthermore science is the result of social construction and the subject of societal debate as well.
- The persistence of certain scientific and social controversies suggests that traditional models of communication and decision-making about such risks are no longer adequate. New forms of interaction between experts, policy and the actors involved are required which may take shape within the framework of new decision-making models.

This leads us to the following leading research principles. Specific initiatives will commit to these general principles:

- Researchers and governmental representatives involved in the Steunpunt Milieu en Gezondheid act according to their independent and specific professional deontology codes and guidelines. The collaboration of both parties is the

outcome of negotiation and internal and external transparency on the roles and task division within this collaboration (for instance for external communication; an update of the document **Spelregels** will be agreed)? This transparency enhances neutrality and the building of trust.

- Researchers (and government) should provide external **transparency on the surveillance and research activities**; the social scientific team will assist the consortium within cases in line with the successful steps within the former Centre of Expertise. As scientific controversies and uncertainties are normal in this science and policy field, initiatives on transparency include the efforts to detect and to make available information on uncertainties, controversies and assumptions in data gathering and data interpretation. Openness for questions of the outside world is a condition.
- As potentially any perspective is valuable in risk assessment and management (different problem definitions, different knowledge, different solutions to be taken into account) ideas and concepts for a **multi-actor knowledge construction/development will find application within strategic cases** of the consortium. In these cases stakeholder participation is included in the process of data interpretation. There will be feed back on the results of the external consultation. The social scientific team co-ordinates work packages containing initiatives in this domain; other consortium groups will be invited to collaborate in the initiative and vice versa consortium members will be solicited to reflect and comment the design of the initiatives.
- Within the consortium initiatives the **interdisciplinarity of the consortium is solicited**. In Working Groups, representatives of the relevant disciplines are invited. The consortium acts and communicates as a group, not excluding however individual communications and individual expert positions, for instance with minority arguments. Minority positions will first be discussed within the consortium team. The group work also should be reflected in the academic valorisation policy of the consortium.
- In contacts with authorities and the outside world, the **interdisciplinarity should also be reflected**. In formal and informal Steering Committees representatives of the relevant disciplines will be invited
- **Co-production of knowledge and innovative interaction initiatives** between scientists and policy makers are to be encouraged as they broaden and deepen the knowledge basis on issues (*functional argument*), try to involve and enhance support of concerned stakeholders (*instrumenteel argument*) and enhance the democratic character of decision making on risk assessment and management (*normative argument*). These arguments deserve attention in the composition and/or of accompanying groups within and around the Steunpunt Milieu en Gezondheid.
- Consortium member are invited to **evaluation stages** on multi-actor initiatives and external communication.

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(for all the social scientific contributions in the proposal)

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4.4 Neuro-motor development, asthma and allergy prevalence and neuropsychic development in children in relation to their internal levels of persistent chlorinated pollutants and heavy metals (a follow up of the children enrolled in the previous biomonitoring campaign as babies- 2002)

4.4.1. Follow-up study on newborns participating in the biomonitoring program 2001-2006.

The study is a questionnaire study addressed to the parents of the 1200 newborns participating in the biomonitoring program 2001-2006. The aim of the study is to collect follow-up data on health in general and more specifically on asthma and allergy and on neuro-motor development (height, weight, school results and ADHD). These follow-up data can be linked to data on exposure at the start of life collected in 2002-2003.

The fieldwork for this questionnaire follow-up study will be integrated in the fieldwork budget of the PIH.

Reporting and communication: the results of this research study will be available after analysis in depth.

4.4.2 Follow-up study in newborns participating in the biomonitoring program 2001-2006 and the follow-up studies on neuropsychic development, asthma and allergy.

If this program or part of this program can be financed by external sources, the program will not be carried out within this steunpunt. In this case, the results of this research topic carried out (totally) and financed external to the steunpunt, need to be introduced in a proper way into the steunpunt.

About 300 children participated in the follow-up study on neuropsychic development, asthma and allergy in the first human biomonitoring program 2001-2006. This study examined the relation between exposure to environmental chemicals and the impact on the intestinal flora and on neuropsychic development and the development of asthma and allergy until the age of 3 years. Further follow-up of these children concerning neuropsychic development, development of asthma and allergy is proposed at the age of 8 years.

This follow-up includes:

- questionnaires on respiratory complaints
- allergy tests
- pulmonary function (FEV1)
- neuropsychic tests (computer based and paper-based)
- observation of sexual development
- parameters of inflammation: exhaled breath condensate, NO
- parameters of exposure can be explored to a limited extent (capillary blood or urinary sample)

Budgetary consequences

- lung function, allergy tests, parameters of inflammation, 20.000 Euro.
- fieldwork will be integrated in the fieldwork budget of the PIH
- neuropsychic tests, 20.000 Euro.

If available the data on PM10 and PM2.5 from VMM can be included in the analysis

Reporting and communication: the results of this research study will be available after analysis in depth.

4.5 Collection of data on morbidity and mortality for adult participants to previous biomonitoring campaigns

4.5.1. Pilot program for collection of follow-up data on morbidity and mortality in the adults participating in the first Flemish biomonitoring program and pilot study on biomonitoring

Over time 1800 adults participated in Flemish biomonitoring programs. Biomarkers of exposure and of early effect (cancer markers) were measured at ages 50-65. The link between exposure, early markers and disease is not yet completely established and needs to be further explored.

Aim of the current study proposal is to elaborate on further follow-up of these adults and try to complete the pathway from exposure over early markers to morbidity and mortality.

Data on morbidity and mortality will be collected

-through existing data sources: the cancer registry and the registration of death certificates of the Flemish community.

-through questionnaires addressed to the participants

There will be no collection of new samples for biomarker analysis. The aim of the study is to gather a maximum of information from existing databases from earlier participants to our programs.

The program will be carried out after approval of a medical ethical committee and informed consent of the participants.

This study will be considered as a pilot study to explore the possibilities of long term follow-up in these study groups.

Reporting and communication: the results of this research study will be available after analysis in depth.

III. TIME SCHEDULES

Schedule 1: Biomonitoring: a program for environmental health surveillance and research

Biomonitoring: a program for environmental health surveillance and research						
Year	Activities	Target population	Estimated number of participants	Milestone	Deliverable	Partners
2007	Preparation biomonitoring protocol- reference values and ranges			Approval of scenario by ethics and privacy commission	-List of selected biomarkers -Scenario for surveillance	VITO, PIH, VUB, UG, UA
	Development of decision making traject for prioritization of studies on high risk populations (hot spots)			Composition of steering group with relevant stakeholders	-Scenario for practice cycle “green paper” -List of relevant stakeholders -List with assessment criteria for monitoring high risk populations	UA, UG
	Adjustment of the perception survey to the context of Flemish reference value monitoring.				Perception questionnaire biomonitoring	UA
	Social inequality and environmental health risks				analysis of data on social class will be integrated in the biomonitoring activities	UA
2008	Field work biomonitoring: reference values and	Mother newborn pairs	150	Recruitment of participants		VITO, PIH, VUB, UG, UA

Biomonitoring: a program for environmental health surveillance and research						
Year	Activities	Target population	Estimated number of participants	Milestone	Deliverable	Partners
	ranges Cd, Pb, PCBs, CALUX, DDE, HCB and emerging pollutants	Children/ adolescents	150	Recruitment of participants		VITO, PIH, VUB, UG, UA
		adults ¹¹	300	Recruitment of participants		VITO, PIH, VUB, UG, UA
	Prioritization/selection of high risk groups for inclusion in biomonitoring (hot spots)			Approval of protocol -Selection of the first 2 “high risk groups“ to monitor	-Protocol for prioritization - Description of selected high risk groups and rationale for choice	VUB, UG, UA, VITO, PIH
	Study design for monitoring high risk groups (hot spots)			Approval of scenario by ethics and privacy commission	Scenario for biomonitoring“ high risk groups”	VITO, PIH, VUB, UG
	Social inequality and health environmental health risks				- tailoring of the recommendations of further statistical and desk research to the research conditions of restricted areas or target groups - recommendations (in Guidelines Social Mapping) and stand-by for the Network of Medisch Milieukundigen (MMK) considering the local socio-economic profile of their region	UA

¹¹ Selection of participants (age group) in function of the selection of biomarkers and in agreement with the selection of the EU wide biomonitoring program

Biomonitoring: a program for environmental health surveillance and research						
Year	Activities	Target population	Estimated number of participants	Milestone	Deliverable	Partners
					and professionals, working on community building, social deprivation and participation of deprived groups.	
	Adjustment of the perception survey to the context of hot spot surveillance (aimed to compare with Flemish references)				Perception questionnaire hot spot surveillance	UA
2009	Biomonitoring of 2 high risk populations “hot spots” or “specific cases”	Adolescents if indicated as population of choice ¹²	400	Recruitment of participants		VITO, PIH
	Prioritization/selection of other high risk groups for inclusion in biomonitoring (hot spots)			-Approval of protocol -Selection of the 2 “high risk groups” to monitor	-Protocol for prioritization - Description of selected high risk groups and rationale for choice	VUB, UG, UA, VITO, PIH
	Reporting of biomonitoring			Approval of results by management team and	Report on internet and publication (Dutch and English)	VUB, UG, UA, VITO, PIH

¹² Final selection will depend on the monitoring question that has to be addressed, and may change in function of the pollutants to monitor. Preferentially adolescents will be recruited

Biomonitoring: a program for environmental health surveillance and research						
Year	Activities	Target population	Estimated number of participants	Milestone	Deliverable	Partners
	reference ranges for all age groups			steering group		
	Perception research results				Reporting on the results , in line with the time schedule of the biomonitoring campaigns and the internal and external communication of the results;	UA
	Evaluation and modification of action plan			Approved protocol after modification based on current experience	-Review of current action plan -Protocol for modified action plan	VITO, PIH, UA, UG
2010	Biomonitoring of high risk populations “hot spots“ or “specific cases”	adolescents if indicated as population of choice ¹³	400	Recruitment of participants		VITO, PIH
	Start action plan			-Desk research -Stake holder consultation	Synthesis from experts Communication of results	VITO, UA
2011	Reporting of biomonitoring results –			Approval of results by management team and	Report on internet and publication (Dutch and English)	VUB, VITO, UA, PIH, UG

¹³ Final selection will depend on the monitoring question that has to be addressed, and may change in function of the pollutants to monitor. Preferentially adolescents will be recruited

Biomonitoring: a program for environmental health surveillance and research						
Year	Activities	Target population	Estimated number of participants	Milestone	Deliverable	Partners
	results from “ high risk groups ” monitoring			steering group		
	Continuation action plan			Desk research Stake holder consultation	Synthesis from experts Communication of results	VITO, UA

Schedule 2: Research Projects on environment and health

Research Projects on environment and health					
year	topic		Target group	N	Partners
2007	Fine dust	Relation fine dust and inflammation/cardiovascular effects in vulnerable groups (2x/y)	Older adults	65	KUL
	Hormone disruption	Case-control study male/female sub fertility: study design and approval ethical committee			EEC + VITO + PIH + UG + VUB
	Social inequality and environmental health risks	Screening of specific literature on social class in environmental health studies context			UA
	Social scientific research	Research on: interdisciplinary and transdisciplinary research: coordination, action research and reflection			UA
2008	Hormone disruption	Relation chlorinated compounds on fertility disorders	Mothers Newborns	105	PIH + EEC + VITO + VUB + UG
	Hormone disruption	Case control study on hormone disruptors and fertility treatment	men	75	PIH + EEC + VITO + VUB + UG
	Hormone disruption	Case control study on hormone disruptors and fertility treatment	women	75	PIH + EEC + VITO + VUB + UG
	Fine dust	Relation fine dust and inflammation/cardiovascular effects in vulnerable groups (2x/y)	Older adults	65	KUL
	Fine dust and nanoparticles	Validation and development of biomarkers for individual exposure to particulate matter			KUL
	Social scientific research	Research on: interdisciplinary and transdisciplinary research: coordination, action research and reflection			UA

2009	Hormone disruption	Relation hormone disruptors and ADHD and puberty development	adolescents	150	PIH + UG + OPZ + VITO
	Hormone disruption	Case-control study male sub fertility	men	75	EEC + VITO, PIH + VUB + UG
	Hormone disruption	Case-control study female sub fertility	women	75	ECC + VITO + PIH + UG
	Fine dust	Relation fine dust and coagulation/inflammation	adolescents	250	PIH + KUL
	Fine dust	Relation fine dust and inflammation/cardiovascular effects in vulnerable groups (2x/y)	Older adults	65	KUL
	Fine dust and nanoparticles	Validation and development of biomarkers for individual exposure to particulate matter			KUL
	Social scientific research	Research on: interdisciplinary and transdisciplinary research: coordination, action research and reflection			UA
2010	Fine dust	Relation fine dust and prematurity	SPE/VMM data	540 000	KUL
	Fine dust	Relation genotox markers and exposure to traffic in previous studies on adults and adolescents / GIS analysis	adolescents/adults	3 459	KUL
	Fine dust and nanoparticles	Validation and development of biomarkers for individual exposure to particulate matter			KUL
	Hormone disruption	Case-control study male/female sub fertility: analysis of results and reports			EEC + VITO + PIH + UG + VUB
	asthma allergy	Further follow-up on asthma/allergy of newborns participation in the previous asthma and allergy follow-up study (examinations)	children	50	PIH + UA + OPZ + UG
	Social scientific research	Research on: interdisciplinary and transdisciplinary research: coordination, action research and reflection			UA

2011	Fine dust and nanoparticles	Validation and development of biomarkers for individual exposure to particulate matter			KUL
	Follow-up of morbidity and mortality	Pilot program for follow-up of morbidity and mortality data of adults participating in previous biomonitoring programs 2001-2006 and Hoboken, Wilrijk, Peer	Older adults	1800	PIH + UG + VITO
	asthma allergy ADHD	Follow-up on asthma/allergy, ADHD, school results of newborns participation in the previous biomonitoring program 2001-2006, (questionnaires)	children	1200	PIH + UG, UA + OPZ + VITO
	asthma allergy	Further follow-up on asthma/allergy of newborns participation in the previous asthma and allergy follow-up study (examinations)	children	100	PIH + UA + VITO + UG
	Fine dust and nanoparticles	Validation and development of biomarkers for individual exposure to particulate matter			KUL
	Social scientific research	Report on: interdisciplinary and transdisciplinary research: coordination, action research and reflection			UA

III. TABLE OF BUDGETS

	2007	2008	2009	2010	2011
Betoelaging van de Vlaamse Overheid (Indicatief)	925.000	925.000	925.000	925.000	925.000
Totale kost van het steunpunt	925.000	925.000	925.000	925.000	925.000
Overhead “centrale beheerskosten en algemene exploitatiekosten”	54.500*	54.500*	54.500*	54.500*	54.500*
Werkingskosten	205.500*	205.500*	205.500*	205.500*	205.500*
Total					
-Documentatiekosten	5.000	5.000	5.000	5.000	5.000
-Kosten mbt soft- en hardware	5.000	5.000	5.000	5.000	5.000
-Algemene werkingskosten	15.500	15.500	15.500	15.500	15.500
-Analyses die zelf worden uitgevoerd**	180.000	180.000	180.000	180.000	180.000
Kosten van uitbesteding (totaal)	380.000***	380.000***	380.000***	380.000***	380.000***
<i>Uitbesteding taken aan VITO</i>	220.000	220.000	220.000	220.000	220.000
<i>Uitbesteding taken aan PIH</i>	85.000	85.000	85.000	85.000	85.000
<i>Uitbesteding taken aan Endocrine Expert Committee</i>	30.000	30.000	30.000	30.000	30.000
<i>Uitbesteding aan Prof. Dehenauw (UGent)</i>	35.000	35.000	35.000	35.000	35.000
<i>Uitbesteding aan Prof. Molenberghs (UH)</i>	10.000	10.000	10.000	10.000	10.000
Kosten personeel (totaal)	285.000	285.000	285.000	285.000	285.000
- beheersassistente coördinatie (VUB)	55.000	55.000	55.000	55.000	55.000
- assistent vraagbaak (UG)	55.000	55.000	55.000	55.000	55.000
- assistent biomonitoring (VUB + UG)	35.000	35.000	35.000	35.000	35.000
- vorser communicatie (UA)	70.000	70.000	70.000	70.000	70.000
- vorser fijn stof	70.000	70.000	70.000	70.000	70.000

(KUL)					
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* maximaal, tenzij de analyses worden uitbesteed

** er zullen offertes worden gevraagd aan laboratoria die zowel intern als extern aan het steunpunt zijn.

*** minimaal, wordt verhoogd met analyses die worden uitbesteed

Once-only funding for the realization of the complete action plan 2007-2008 regarding the human biomonitoring results gathered in the scope of the first generation Flemish Centre of Expertise for Environment and Health (2002-2006) (*Onderzoek naar de invloed van het voorkomen van milieugevaarlijke stoffen in het milieu op de mens en naar de oorzaken daarvan in opvolging van de groepsresultaten van de biomonitoringcampagne (fasenplan)*)

Year	2007-2008
VITO, PIH and UA	220.000 €