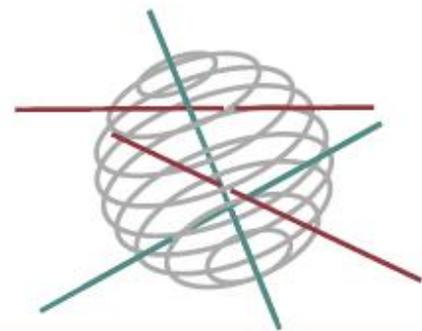


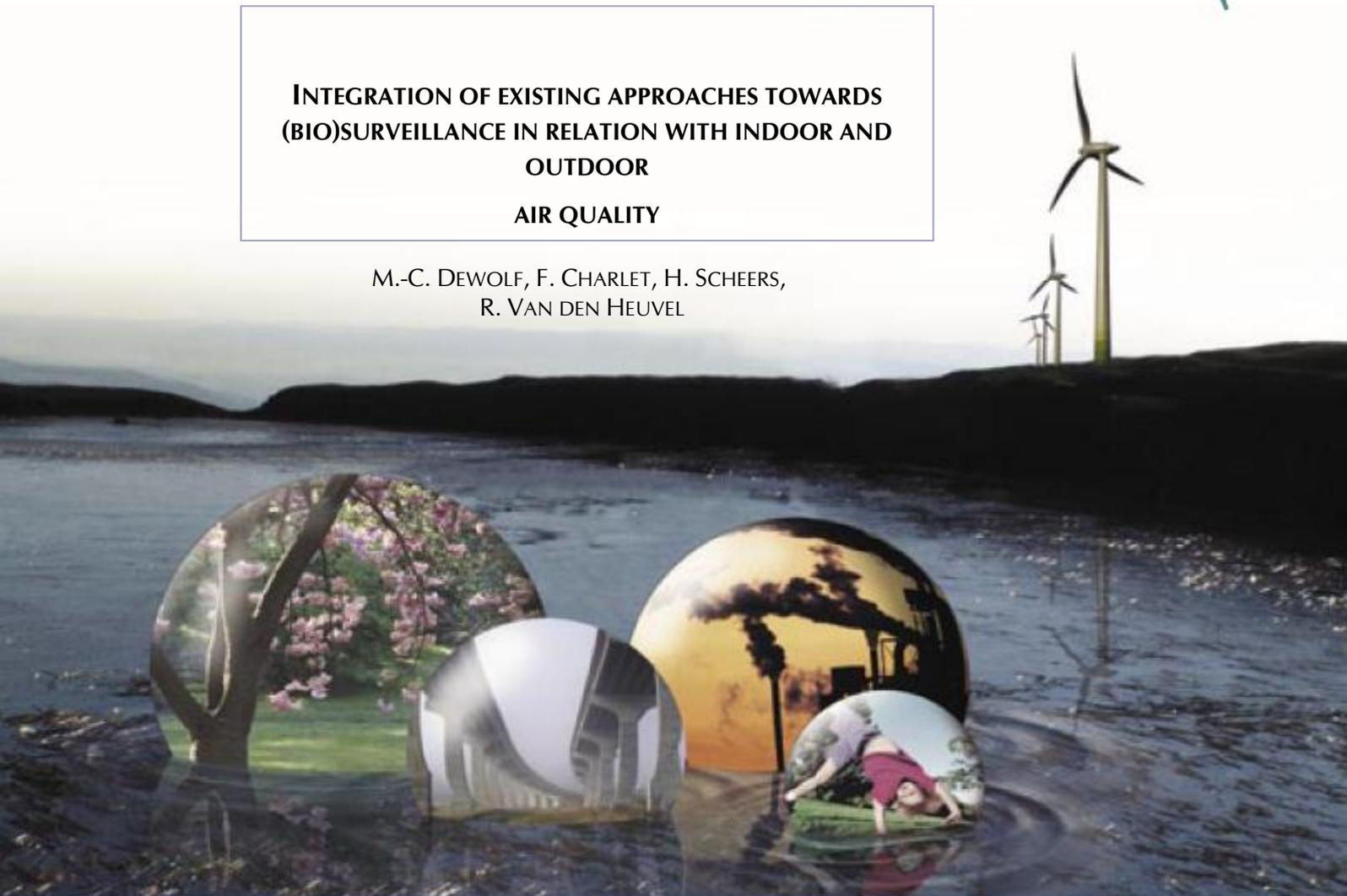
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**INTEGRATION OF EXISTING APPROACHES TOWARDS
(BIO)SURVEILLANCE IN RELATION WITH INDOOR AND
OUTDOOR
AIR QUALITY**

M.-C. DEWOLF, F. CHARLET, H. SCHEERS,
R. VAN DEN HEUVEL



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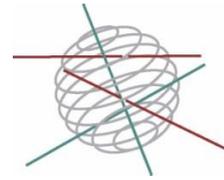
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Health and Environment

FINAL REPORT

INTEGRATION OF EXISTING APPROACHES TOWARDS
(BIO)SURVEILLANCE IN RELATION
WITH INDOOR AND OUTDOOR AIR QUALITY

"AIR QUALITY"

SD/CL/04



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SUMMARY

Context:

The population health is affected by both indoor and outdoor air quality, with probably cumulated exposure and effects. In order to develop appropriate strategies to manage public health effects of indoor and outdoor air quality, different aspects should be considered in an integrated way and with a multidisciplinary approach. Therefore “time activity patterns” and “human biomonitoring” represent effective tools to assess personal exposure, link it to health effects, better understand potential risk factors and therefore integrate health and environment

Indeed human biomonitoring integrates the contribution of different sources of exposure, different routes of exposure or exposure during the whole lifespan. It also takes into consideration the differences between individuals with regards to exposure and uptake. In order to interpret results properly, these should be looked at while considering aspects such as emissions, immission, time activity patterns, exposure and health effects.

Objectives:

The overall aim of the Cluster Air Quality was to integrate existing approaches towards health surveillance in relation with indoor and outdoor air quality, which was strongly supported by national and international strategies. This has been achieved through a multidisciplinary dialogue between scientists and authorities at different levels to on one hand identify existing methods, data, information and (bio)surveillance programs in relation with indoor and outdoor air, time activity patterns, health effects (particularly (cardio)respiratory diseases) and human biomonitoring; highlight strengths, weaknesses, gaps and further perspectives in terms of research needs or actions; and test data comparability for potential further integration; on the other hand initiate an active multidisciplinary network and support transfer of knowledge between disciplines.

Results

Integration of existing projects and study of cohorts

In this cluster the relation between indoor exposure and respiratory health outcome has been investigated in both study cohorts from the ANIMO and the MIC-ATR project. Both projects assessed population exposure and health effects partly by means of a questionnaire. On one hand MIC-ATR focused on the environmental exposure of the patients, on the other hand ANIMO focused on the use of non-invasive biomarkers (exhaled NO (eNO)) for respiratory diseases in healthy children. The use of the same questions related to indoor exposure and health outcome in the framework of the cluster have allowed performing a statistical analysis to identify potential environmental risk factors and highlight the interest of such non analytical tool in a surveillance program. Exhaled NO measurements were also done while visiting MIC-ATR/LPI patients.

Correlation analyses were performed to study the effect of the indoor risk factors on the health outcome biomarkers

In the ANIMO cohort, significant positive correlations were found between rattling and the TCB (total chemical burden) ($r=0.179$, $p=0.03$), the sum score for using sprays ($r=0.161$, $p=0.05$) and the score for frequency of using sprays ($r=0.21$, $p=0.01$). The presence of mould was associated with eczema ($r=0.165$, $p=0.04$). For the MIC-ATR cohort ($N = 77$), cough was significantly associated with the presence of mould ($n=72$, $r=0.237$, $p=0.04$). Heating using a stove (coal/wood/open fire) was associated with wheezing ($n=68$; $r=0.244$, $p=0.05$) and rattling ($n=65$, $r=0.333$, $p=0.01$). Current asthma was associated with indoor burning ($r=0.288$; $p=0.01$). Indoor VOC exposure was identified as a risk factor for having allergy ($r=0.246$, $p=0.03$).

The relation between health outcome parameters and indoor risk factors were further analysed in multiple regression models. Fixed confounders (age, gender, parental asthma/allergy and ETS) were included in all models. For the ANIMO cohort, significant positive associations could be demonstrated between rattling and TCB (sum score indoor use of household cleaning products) (Odds ratio 1.17, (95% confidence interval (CI) 1.02-1.35), $p=0.02$). For the MIC-ATR cohort, after correction for confounding variables no significant associations were found between eNO, bronchitis, cough, wheezing, shortness of breath, asthma ever, doctor diagnosed asthma and indoor parameters with exposure. Significant positive associations could be demonstrated between airway infections and the sum score of flame retardants (Odds ratio 1.43, (95% confidence interval (CI) 1.05-1.95), $p=0.02$), between rattling and the presence of a stove (Odds ratio 13.4 (95% CI 1.4-128.9), $p=0.02$), any allergy and VOC (Odds ratio 1.4 (95% CI 1.0-2.04), $p=0.05$), eczema and the use of pesticides (Odds ratio 1.15 (95% CI 1.0-1.3), $p=0.04$). Current asthma was negatively associated with moisture (Odds ratio 0.07 (95% CI 0.01-0.34), $p=0.001$).

Cohort studies to identify risk factors need to be large enough to draw reliable conclusions. Compared to other studies found in the literature investigating the relation of indoor exposure (chemical, biological) on respiratory health outcome the study populations in this cluster project were small. This restricted further potential assessment foreseen in the cluster. Nevertheless, significant associations were found between health outcome and indoor risk factors in both the healthy child cohort and the patient cohort. These results confirmed that children are a vulnerable group. Current findings emphasize the need to monitor health effect related to indoor air quality with regard to vulnerable groups (children, elderly) in changing housing technologies.

SWOT analysis

Information concerning Environment as well as Environment and Health is relatively segmented. Such fragmentation is part of the complexity of the Belgian institutional levels (federal, community, and regional, provincial and local levels) but also of the thematic itself. In order to tackle environmental and health issues in a sustainable way, decision makers have to ensure that policies and actions don't move one issue from one scientific network to the next one. Therefore a holistic view is necessary and efficient communication between scientific networks and all stakeholders needs to be supported. A good understanding of the complex picture is also a good way to

achieve a sustainable development and induce long term behavioural change at all levels. The Cluster air quality has contributed to identify the concerned actors but also studies, programs, methods, data and information managed at the different levels. The SWOT analysis of the identified studies and programs has allowed highlighting gaps and opportunities for further researches and policy making.

Transfer of knowledge between scientific networks

The project implementation by the setting of an interdisciplinary dialogue has encouraged communication and collaboration between the scientific networks and identified working teams. Considering how the different “scientific networks” (indoor air quality, outdoor air quality, biomonitoring, time activity pattern and health) could benefit from each other’s experience, two ways of integration have been highlighted: through *transfer of knowledge* from one field of expertise to another or through the implementation of a *global approach* which seeks for horizontal or integrative tools allowing further transfer of data and information.

Within those 2 potential processes of cooperation, a few priority themes of work have been identified. For the *transfer of knowledge*, the definition of “reference” values (threshold, guideline or target values) and their role, the development of sampling and recruitment strategies and the elaboration of communication processes addressing different target publics (participants, policy makers, large public,...) and precisising which communication channels and tools have been efficient have been highlighted. With regards to the implementation of a *global approach*, integrative tools such questionnaires (content, format, process ...), Geographic Information Systems (GIS), Time Activity Patterns and health analyses have been pinpointed.

As an example, the cluster focused on the different strategies developed to define “reference” values. Setting “reference” values aims to protect the population from adverse health effects resulting from environmental exposure through the suppression or at least the reduction of the level of pollution brought by the different potential sources of exposure and different pathways. It supports the decision making process in terms of policy making and risk management. It also has as objectives to assess population exposure or exposure of individuals and facilitate the communication addressing different targeted stakeholders.

Among the strategies developed to define “reference” values, the cluster identified: health based, statistically based, health observed based and mixed strategies. If the aim is to protect the population, the vulnerable ones are not necessarily protected by those “reference” values and adverse effects may appear at levels below or equal to defined, even health based, values. Besides, guidelines usually define values for substances considered individually (sometimes in a specific setting). Therefore they don’t take into account potential effects resulting from exposure to multiple chemicals (cocktail effect).

Conclusions

Top-down and bottom-up communication between stakeholders is a good way to translate findings into efficient strategies and actions aiming to reduce environmental exposure and improve public health and the related health costs. However information

concerning Environment as well as Environment and Health is relatively segmented. Therefore a holistic view and a good understanding of the complex picture guaranteeing sustainable measures are necessary and efficient communication between all stakeholders needs to be supported. In order to better identify strategies and actions towards sustainable development for the next generations, the SWOT analysis of the existing data sets could eventually be completed by a PESTLE analysis assessing Political, Economical, Social (which includes public health), Technological, Legal and Environmental analysis of existing and emerging issues.

Contribution of the project in a context of scientific support to a sustainable development policy

The SWOT analysis conducted in the framework of the Cluster Air Quality and identifying Strengths, Weaknesses, Opportunities and Threats of the existing data sets and tools developed in environment and health, as well as the integration exercise between projects contributed to a better understanding of whether collected data in the framework of different programs could be integrated in a more global approach. It also allowed highlighting needs for research or policy making and actions (for example, in terms of harmonisation between the monitoring programmes, etc.). By identifying concerned actors and supporting communication between the scientific networks, the cluster has contributed to build bridges between these networks which is a first important step to manage unavoidably interconnected issues that need to be tackled together to ensure a sustainable development.

Keywords

Air quality, outdoor air, indoor air, human biomonitoring, environment and health, children's health, reference values

1. Introduction

1.1 Context

Exposure to air pollution (both outdoor and indoor) has many potential adverse effects on human health (Bernstein and al. 2004). Recent studies have observed positive associations between outdoor air pollution and emergency department visits (Villeneuve, 2007) and between improved outdoor air quality and increased life expectancy (Pope and al. 2009).

Historically health effects of air pollution have mostly been derived from effects in large populations and based on a statistical association with outdoor air quality. The emerging possibility to either model or measure exposure with a high spatial and temporal resolution with activity based models or sensor networks may lead to new insights and new policies (Beckx and al, 2009). Recent progress in personal exposure and health effects assessment has therefore led to a focus on specific target groups and specific risk factors. Also, about 90% of our time is spent indoors (homes, workplaces, schools, public spaces, vehicles) where we are exposed for example to chemicals, particulate matters and biological contaminants. Indoor environments are on the other side influenced by outdoor air pollution (e.g. Van Roosbroek et al. 2007 for schools) depending on their location (urban, rural, ...), architecture or close environment. Exposure to indoor air pollutants is now recognized as contributing significantly to a wide range of environmentally related health impacts (Parma declaration, 2010).

The population's health is therefore affected by both indoor and outdoor air quality, with probably cumulated exposure and effects. In order to develop appropriate strategies to manage the public health effects of indoor and outdoor air quality, both aspects, "indoor" and "outdoor" air should be considered in an integrated approach. Therefore surveillance protocols, collected results and processing of data should be appropriate and managed with harmonised methodologies in order to ensure comparability and enable potential integration.

Human biomonitoring (HBM) has long been applied in occupational health in the medical surveillance of workers. Currently it is increasingly used as a tool in environment and health to assess exposure (biomarkers of exposure) and health effects (biomarkers of effects) as well as raise awareness related to potential risk factors and develop efficient environmental and health policies. HBM is therefore considered as an essential tool in a strategy aiming to integrate health and environment. It integrates the contribution of different sources of exposure, different routes of exposure or exposure during the whole lifespan. It also takes into consideration the differences between individuals with regards to exposure and uptake. In order to interpret HBM results properly, these should be looked at with a multidisciplinary approach considering emissions, immission, time activity patterns, exposure and health effects.

The aims of the project are supported by national and international strategies: the Parma declaration (2010) setting clear targets to reduce health effects from environmental threats in the next decade (including indoor and outdoor air quality), the EU CAFÉ strategy (Clean Air for Europe), the EU Environmental and Health action plan

2004-2010, the Belgian NEHAP and CEHAP (National Environmental and Health Action Plan and Children Environmental and Health Action Plan), the conclusions of the Belgian EU Presidency (2010), the drafting of a Green Book on indoor air quality and the strategic objectives of the program to strengthen the integration of outdoor and indoor air quality related to human health in the context of sustainable development.

1.2 Objectives

The overall aim of the cluster Air Quality is to integrate existing approaches towards health surveillance in relation with indoor and outdoor air quality. This has been achieved through:

- a multidisciplinary dialogue to identify:
 - existing methods, data, information and (bio)surveillance programs in relation with indoor air, outdoor air, time activity pattern, health effects and particularly (cardio)respiratory diseases and human biomonitoring;
 - strengths, weaknesses and gaps and further perspectives in terms of research needs or actions;
 - data comparability for potential further integration;

- an activation of the dialogue between scientists and policy makers in order to initiate an active multidisciplinary network and support transfer of knowledge between disciplines.

2. Methodology and Results

2.1 Methodology

2.1.1. 1st step: Identification of actors and programs

The objective of the first step was to identify, with the support of the concerned stakeholders, partners and existing programs related to the 5 themes of activities we aimed to consider in an integrated approach: indoor air quality, outdoor air quality, human biomonitoring, time activity patterns and health effects (focusing on respiratory diseases).

To do this, the actors from different institutional levels (local, regional or federal levels) have been listed in a database in the form of an Excel file entitled “actors” (Annex 1). This document has been divided into different sheets, each one referring to the 5 studied themes. For each identified actor, the type of activity he performs has been registered: research, data management, fieldwork.

A second Excel file entitled “parameters” (Annex 2) has been created to list projects and programs related to the 5 studied themes and to collect information concerning the monitoring protocols: parameter(s) tested, sampling and measurement protocols, influence of the sampling conditions, detection limits, quantification limits, results variability over time and aspects regarding standardisation. The aim was to allow possible subsequent comparison. To obtain as much accuracy as possible, this process has been completed in collaboration with the different actors and supported by the concerned stakeholders.

The “parameters file” includes data from projects composing the cluster (MIC-ATR, ANIMO, SHAPES, PM²TEN and PARHEALTH) but also from local, regional or national initiatives such as:

* projects and programs linked to the theme ‘Indoor air quality’:

- Protocole of the so-called “green ambulances” (cf. SAMI (Luxembourg, Walloon Brabant, Namur and Liege provinces), LPI (Hainaut Province), CRIPI (Brussels-Capital region))
- National and provincial “Crèches” projects (cf. HPH, SAMI, LPI, CRIPI)
- MIC-ATR (cf. HPH, UMH, UCL, ISP, ULB)
- SHAPES (cf. VITO, UCL, VUB)
- PM²₁₀ (cf. VITO, KUL)
- BIBA (cf. Flemish Region, VITO)
- “School” project (cf. SAMI-Lux)

* projects and programs linked to the theme ‘Outdoor air quality’:

- Outdoor air quality monitoring network (cf. ISSeP, IBGE, VMM and IRCELINE (a body that centralises all data collected by third parties))
- “Cities and Pollution” project (cf. IBGE, ISSEP, KU Leuven)
- APHEIS and APHECOM EU projects (cf. IBGE, EU partners)

* Projects and programs linked to the theme 'Human Biomonitoring' and considering air quality aspects:

- "Children – Hainaut" project (cf. HVS, UMONS, ULB)
- ANIMO (cf. Flemish and Walloon region, VITO, UCL)
- Flemish biomonitoring (Steunpunt) (cf. Flemish region, VITO)
- Biomonitoring in Charleroi and Ath (cf. ISP)
- COPHES & DEMOCOPHES (cf. SPF)

Projects and programs linked to the theme 'Health' and considering air quality aspects:

- ANIMO project (cf. Flemish and Walloon region, VITO, UCL)
- The SHAPES project (cf. VITO, UCL, VUB)
- The PM₁₀² project > VITO, KUL
- The PARHEALTH project (cf. KUL, UA, UCL and UGent)
- Flemish biomonitoring (cf. Flemish region, VITO)

Project linked to the theme 'Time activity pattern':

- The SHAPES project (cf. VITO, UCL, VUB)

Among the tools used in the framework of the different studies and programs to identify environmental risk factors and potential health effects, questionnaires covering different aspects (revenue, physical activity, swimming, food, smoking, hygiene, hobbies,...) are quite important. These represent a good mean to make the link between the different fields of expertise and develop a global approach in environment and health.

Results interpretation and communication are 2 others crucial steps in studies implementation. Therefore threshold or reference values are often used. They allow better highlighting of the pollution and exposure level but also, depending on the strategy elaborated to define these values, a better understanding of the potential health effects. These values related to indoor and outdoor air quality have been included in the "parameters" file as well.

2.1.2. 2nd step: Assessment process: SWOT analysis

The objective of this second step was to undertake a SWOT analysis of the protocols and methods used in projects related to indoor and outdoor air quality, human biomonitoring and health effects. Strengths, weaknesses, opportunities and threats have been looked at. The aim of this SWOT analysis was to better understand whether collected data in the framework of different programs could be integrated in a more global approach but also to highlight needs for research or policy making and actions (for example, in terms of harmonisation between the monitoring programmes, etc.).

This process has been supported by a consultation of stakeholders during a workshop organised in the framework of the cluster itself. Complementary observations have been included in the results.

2.1.3. 3rd step: Integration process

In order to further assess the possibilities of integration, new datasets resulting from joined methodologies issued from the different projects of the cluster have been

developed. Statistical analysis have been undertaken in order to better highlight potential risk factors and health effects as well as opportunities and difficulties with regards to integration.

The ANIMO and MIC-ATR projects studied population exposure in indoor environment and health effects. They partly assessed potential sources of exposure via a questionnaire. Furthermore MIC-ATR looked at the environmental exposure of patients through physical, chemical and biological analyses of their housing environment. ANIMO studied non-invasive bio-markers to diagnose respiratory diseases in children.

The questionnaire used for the ANIMO project is similar to the ones used within the scope of epidemiological or biomonitoring studies. It was developed with reference to on going studies and the most recent literature. It investigated the respiratory health conditions during the last 12 months, exposure to environmental factors, confounding factors for asthma/allergies (ex. environmental tobacco smoke, family history) and time activity pattern elements.

MIC-ATR based its investigations on a site (house) visit document used in the framework of indoor housing diagnosis on medical request by the Belgian services of indoor environment also called "green ambulances". This document helps characterising the building itself, the environment and some behavioural habits of the house inhabitants (for example with regards to smoking, cleaning, ventilation ...).

In order to integrate approaches like a biomonitoring approach (as the one applied by the ANIMO project) and an analytical and medical approach (as the one used within MIC-ATR), we translated and reviewed the ANIMO questionnaire. In order to address the population concerned by MIC-ATR visits, some categories of questions therefore less relevant in the scope of the cluster (such as food, vaccination and nursery conditions) were not included anymore and a reviewed version has been edited (cf. Annex 3).

The dosage of NO in exhaled air (eNO) has also been proposed to MIC-ATR (LPI) patients. The exhaled NO is a well-known indicator of lower respiratory tract inflammation. Higher levels of exhaled NO have been observed while exposed to allergens (pollens, dust mites ...) or to environmental pollutions. A good correlation has been highlighted with others inflammatory biomarkers. It has been used in the scope of different projects, including in some projects of the cluster such as the ANIMO projects. In order to ensure comparability, the measures that have been done in the framework of the cluster used the same equipment as the one used in the previously mentioned studies (a portable version of the NIOX MINO Airway Inflammation Monitor, made by Aerocrine in Sweden). It is an easy, non-invasive, standardised method. A task force of the American Thoracic Society and the European Respiratory Society (ATS/ERS) (Kharitonov, 1997) established consensus guidelines (revised in 2001) for the measure of eNO in adults and children. The single-breath online technique is the "gold standard" technique: the children inhale NO-free gas to total lung capacity and exhale at a constant flow of 50 ml/sec until an NO plateau of more than 2 seconds can be identified during an exhalation of more than 4 seconds. Mobile instruments to measure eNO (such as NIOX MINO using an electrochemical method) are now available. Results have been compared to static device (EcoMedics). Procedures for use of CLD 88 SP

analyser (EcoMedics, Switzerland), NIOX (Aerocrine, Sweden) and mobile NIOX MINO Airway Inflammation Monitor (Aerocrine, Sweden) have been described and tested.

The up-dated questionnaire as well as information with regards to exhaled NO measurement have been sent to the “Ordre des médecins” (medical board) for approval. Indeed the protocol applied by the Belgian service of indoor environment of the Hainaut Province (the Laboratory for prevention of indoor pollution (LPI)) has been approved in 2000 by their local section. Adding health measurement (exhaled NO) and an extended questionnaire of health aspects to the protocol requested a new approval. The approval has been received on September 2010.

As soon as we received the approval for the protocol, the Institute Hainaut Vigilance Sanitaire sent to all patients whose doctor was requesting an assessment of their indoor environment the questionnaire to fill in and turn back to the LPI during their visit.

According to the diagnosed health problem, the service for analysis of indoor environment adapts its home investigation to the problem encountered. The list of parameters he can choose to analyse and the related methodologies applied are standard and harmonized methodologies among equivalent services.

The temperature and relative humidity are measured by means of a CTN device and CO and CO₂, respectively by means of an electrochemical device and a PID device (all TESTO 400).

VOCs are analysed by GCMS according to the NBN EN ISO 16017-1 standard after 4 hours of sampling (300 ml/min) with a Gilair 5 programmable personal sampling pump (Gillian) having a capacity of 20 ml to 6 l/min. on carbotrap cartridges. Formaldehyde and acetaldehyde are analysed by HPLC (ISO 16000-3) after 48 hours of passive sampling on a DNPH cartridge. An alpha counter (RADIM 3A) allows to identified the level of radon. Mould in air is sampled by means of a RCS + Biotest and on surfaces by means of the RCS method and RODAC boxes. Legionella, for which the lab is certified ISO 17025 is identified through a PCR research method and culture undertaken when PCR is positive (standard NF T90-431). Dust mites are tested with an Acarex test.

For this service, the participating lab is regularly participating to Ring test for the following parameters: VOCs, formaldehyde and acetaldehyde, lead in painting, lead in water (also certified ISO 17025).

All data from the up-dated ANIMO questionnaire (Annex 3), MIC-ATR house visit document (Annex 4), exhaled NO and environmental analysis from patients visited from October 2010 to May 2011 have been gathered in a unique database.

2.2. Results

2.2.1. Identification of actors and programs

One of the objectives of the cluster was to identify existing actors, methods, data, information and biomonitoring programmes related to indoor and outdoor air quality, human bio-monitoring and health effects, especially with regard to cardio-respiratory

disease, taking into account the time activity pattern and socio-economic aspects. In order to do this, 2 Excel files were created (Annexes 1 and 2).

Excel file “actors”

This file lists the various key actors in their domains of activities. The document is subdivided according to the different themes of the cluster and the institutional levels (Flemish region, Brussels-Capital region, Walloon region and national level). Depending of their field activities, some actors could be listed more than once. A distinction has been made regarding the type of activities managed by the identified actors (research, data management, in-the-field activity). This list is obviously not exhaustive.

Table 1: Breakdown of the selected actors selected

	Indoor pollution	Outdoor pollution	Human Biomonitoring	Diseases surveillance	Time Activity Patterns	Occupational medicine	Socio-economic aspects
Flemish region	8	8	17	5	4	2	3
Brussels region	4	2	4	5	/	1	1
Walloon region	11	6	7	12	1	1	2
National level	3	6	4	9	1	2	2
Total	26	22	32	31	6	6	8

Excel file “parameters”

This file was created in order to list a certain number of key projects, studies and databases focusing on one of the studied themes of the cluster. The aim was to collect information in order to further assess potential of comparability and integration. It includes the projects of the cluster as well as other initiatives at the regional, national or international level.

2.2.2. « SWOT » analysis

Once the inventory work was well underway, a SWOT analysis (identification of strengths, weaknesses, opportunities and threats) has been undertaken.

Strengths: highlights the advantages and strong points of the listed projects and studies, elements bringing “a plus” (for example in terms of sampling or analytical methods, etc.) but also the similarities between the databases, enabling greater comparability of results.

Outdoor air quality

- To check the air quality, every Region developed its own monitoring network:
 - Walloon Region ⇒ Institut scientifique de service public (ISSeP)
 - Brussels-Capital Region ⇒ Bruxelles Environnement - IBGE
 - Flemish Region ⇒ Vlaamse Milieumaatschappij (VMM)
- Central organization ⇒ Measurements registered by the telemetry network (permanent surveillance) of the 3 Regions are collected at the Belgian level by the Belgian Interregional Environment Agency (IRCEL-CELINE)
- IRCEL-CELINE provides information on air quality for the three Belgian Regions to the public: measurements and air quality index, near real time maps, forecast and alert information
- Alert and information procedures exists for ozone and NO₂ (EU legislation) and for PM₁₀ and NO₂ (thresholds defined by the Coordination protocol of the 3 Regions)
- Action plans have to be implemented in case of alert and exceeding of threshold values
- Use of the results of the monitoring network (IRCELINE, ISSeP, IBGE, VMM) for studies like:
 - « La pollution de l'air par les particules en suspension: Impact sur la santé de la population de la ville et l'arrondissement de Charleroi » realized by the ISP in 2007.
 - Project APHEIS « Air Pollution and Health: a European Information System » (modélisation of the health impact of exposure to particulate matters)
 - Project « Ville et pollutions »: 3 Belgian cities (Brussels-Capital Region, Antwerp and Liège)
- Database already existing for several years allowing comparison between data and observation of time trends (positive or negative)

Indoor air quality

- The results of different studies led to series of recommendations for environmental and health policies.
- Both approaches to assess indoor air quality (the studies approach tacking a specific pollutant and/or a specific setting and the holistic approach of the services for analysis of indoor environment (“green ambulances” (SAMI-LPI-CRIP)) increased the level of awareness of different publics (population, health care professionals, policy makers, ...) of potential health effects of indoor air pollution
- Use of 10 years of expertise of the “green ambulances” ⇒ Database which can serve in national and/or regional projects.
- “Green ambulances”: similarity in sampling conditions and analytical methods for the different services (Walloon and Brussels-Capital Regions) ⇒ potential comparison of datasets in many cases
- Studies have been focusing on settings where children (as part of the vulnerable population) live
- Studies generally tested the same parameters (VOC's, formaldehyde, radon, mould, PM_{2,5} and PM₁₀, ...).
- *Holistic approach* of the “green ambulances” responds to a medical request. It responds to a diagnosed pathology and allows to:
 - highlight signals
 - lead to effective behavioural changes
 - tackle the most vulnerable populations including people from different socio-economical levels
- *Systematic approach* implemented in studies focusing either on a specific parameters or settings allow to:
 - highlight trends
 - identify “normal” values and potentially threshold values
- Both approaches the *Holistic approach* and the *Systematic approach* are complementary and support each other

Human biomonitoring

- HBM is an excellent tool to provide an overview of exposure to chemicals (from different sources of exposure and during the whole lifespan), taking into account inter-individual variability in life-style, time-activity patterns and toxicokinetic parameters
- HBM represents a direct measurement of pollutant load in humans : internal dose of short/long life pollutants (closer to health effects than environmental monitoring)
- HBM accounts for all sources and routes of uptake (integrative measure) ... so it can reveal unknown exposure processes
- HBM is a summary measure: it incorporates bioaccumulation, excretion, metabolism
- It is a strong risk assessment tool allowing to highlight trends in exposure, populations with highest exposure levels, potential sources/routes of exposure, chemicals with highest prevalence/frequency
- "pollution gets personal": stronger "message" triggering for actions at personal and societal level and ensure behavioural changes
- HBM allows the establishment of reference values for the general population and population subgroups
- Extensive HBM programme exists in Flanders with continuity since 1999
- Flemish approach is unique in Europe: it includes an assessment of different age groups (newborns, adolescents, adults) and a prospective birth cohort since 2002-2003
- The Flemish Prevention Decree foresees the possibility of using HBM as a tool for the prevention of health effects from physical and chemical agents
- By using biomarkers of exposure and biomarkers of effect in the same individual, exposure-response relationships can be assessed

Health

- Individual assessment of health as a result from the aggregate exposure to chemicals
- Extensive program in Flanders, continuity since 1999,
- Flemish approach includes: assessment of different age groups (newborns, adolescents, adults) and a prospective birth cohort since 2002-2003 for asthma and allergy as well as for neurodevelopment.
- Appropriate questionnaires can provide a lot of information without physical examination of the study population.

Weaknesses (or limitations): list the disparities between the programs, the factors that do not encourage consolidation of information and the gaps in precision of the information.

Concerning weaknesses, the partners also identified the efforts to be made to enable better harmonisation between collected data. This aspect also includes the possible improvements to be brought to studies, action plans and programs in terms of communication, awareness raising and strategies to define reference values, etc.

Outdoor air quality

- Parameters are rather similar with some differences (according to Regions) as the number of compounds (VOC's) analyzed or the number of heavy metals (cf. excel file)
- Cost of analyses and programs is an information quite difficult to collect (cf. excel file)
- Storage conditions have not been specified by the concerned actors for the samples which are periodically removed and analyzed in laboratory (VOC, PAH, heavy metals) (cf. excel file)
- Detection and quantification limits have not been specified by the concerned actors (cf. excel file)
- Number of measurement stations (telemetry network) is very different according to regions

Indoor air quality
<ul style="list-style-type: none">• Cost of analyses and programs is an information quite difficult to collect (cf. excel file)• Individual sensitivity to exposure and multiplicity of sources and situations increase the difficulty to give the “good” diagnosis.• Threshold values don't take into account the complexity of the situations, the individual susceptibility or the mixture of pollutants (cocktail effect)
Human biomonitoring
<ul style="list-style-type: none">• Differences in sensitivity of analytical methods (detection limit) exist between labs (cf. Excel file)• Differences in sample collection methods (e.g. morning urine, 24h urine), storage and handling conditions appear between studies and programs (cf. Excel file)• For some biomarkers invasive techniques are required (e.g. blood).• Information from Brussels-Capital region and Walloon region is scarce compared to Flanders.• Scope and focus of studies can vary much (respiratory health, endocrine disruption, etc.)• Most appropriate biomarkers are not always available (e.g. exposure to PAH)• Some biomarkers measure only recent exposure• Biomarker of effect do not provide information about the source of an exposure and how long a substance has been in the body• Biomonitoring data do not provide per se information on health effects• Need for agreed calculation process to define thresholds/limit values and reference values/background level of the population in order to, if necessary, take corrective actions• Fragmented activities, various purposes, different populations groups using different protocols reduce results comparability and health impact assessment
Health
<ul style="list-style-type: none">• Differences in formulation of questions to assess a health effect• Invasive sampling methods (e.g. blood).• Information from Brussels-Capital region and Walloon region is scarce compared to Flanders.• Self-reporting can be misleading (e.g. smoking behaviour).

Opportunities: try to show the possibilities in terms of future developments.

Outdoor air quality
<ul style="list-style-type: none">• Full harmonisation of sampling and analytical methods• Air quality assessment using in vitro biological tests• Interpolation model for PM_{2.5} (similar to PM₁₀ and ozone) once the number of monitoring stations measuring PM_{2.5} concentrations is sufficient
Indoor air quality
<ul style="list-style-type: none">• Investigate other specific settings (ex. home taking care of old people ...)• Develop coherent reference values and threshold values protecting the most vulnerable populations• Inform and raise awareness of all actors at all levels :<ul style="list-style-type: none">• individual level: consumer and inhabitant level ;• professional level: architects, building industry, chemical industry, health care professionals, teachers, maintenance professionals...• policy makers level• Support further research and actions taking into account multiple exposures, cocktail effect, critical windows of exposure/sensibility, vulnerable populations, IAQ and energy performance of buildings• Consider health as a priority objective and real case scenarios for product certification policies

- Consider health as a priority objective in housing policies and architectural developments
- Develop long-life learning programs on environment and health for professionals (including tools such as “green ambulances”)

Human biomonitoring

- Develop long term programs in order to follow time trends with regards to environmental exposure
- Develop biobanks for potential future assessment of emerging issues, for further assessment of present and future situations with new analytical techniques (lower detection limit, ...) or for later assessment when specific diseases are diagnosed
- Develop new non-invasive biomarkers, easier to apply
- Develop non invasive and inexpensive biomarkers, easier to apply to a wider population
- Develop new biomarkers of exposure and effects (for ex. more specific) and assess dose-effect relationship at the individual level
- Develop new molecular biomarkers
- Develop a coherent (consistent and rational) approach to HBM in Europe.
- Evaluate the opportunities of including HBM as a complementary section of the Health Examination Interview Survey and the Environmental and Health Information System (ENHIS)
- Develop a strategy to define HBM reference values and health-based guidance values protecting the most vulnerable ones (including children) taking into account the experience of existing programmes and of occupational health
- Transfer data between projects and between relevant agencies (ECHA (European Chemicals Agency), EEA (European Environment Agency), EFSA (European Food safety Authority) as proposed in the framework Directives INSPIRE
- Complementary tool for epidemiological studies
- Develop cohorts and longitudinal studies (integration of neonatal period and early childhood, assessment of long term effects)
- Strong risk assessment and management tool: good support to identify priorities for further actions, assess impact of policies, control interventions...
- Choice of chemical:
 - persistent pollutants (long term effects) versus non PP but pollutants with high population impact (such as mycotoxins)
 - health relevance (known or suspected)
 - potential for policy making or action plan
 - pollutant metabolism information

Health

- Continuous monitoring in order to follow time trends
- Development of new non-invasive biomarkers
- Development of new molecular/genetic biomarkers
- Development of a coherent (consistent and rational) approach to health effect assessment in Europe.
- Development of standardized questionnaires

Threats: describes, for example, the elements to which attention must be given, to avoid making errors in interpretation.

Indoor air quality

- Avoid preconceived ideas (Industrial environment = most polluted environment)
- Ensure that policies (product certification) and guidelines (ventilation, architectural recommendations,...) protect the most vulnerable ones and all socio-economic levels

Human biomonitoring
<ul style="list-style-type: none">• Secure funding of HBM programs• Develop specific biomarkers of exposure and effects in order to ensure reliable results interpretation• Ensure reliable statistical analyses: transformation and handling of data below detection limit still representative of the situation within the population• Develop efficient strategies to assess life-style factors and cofounders (correct questioning)• Ensure adequate treatment and storage of samples.• Address ethical issues (including privacy policies)• Lack of markers of effect sensitive enough at the concentrations found in HBM• Magnitude of imprecision (including preanalytical imprecision) can cause underestimation of dose-related biomarker (Ph. Grandjean)• Interpretation outside the scope of the objectives and study design• All exposure assessment tools have uncertainties• The timing and duration of exposure might lead to different conclusions in terms of health effects• Exposure to a mixture of pollutants, which might lead to different conclusions in terms of health effects• Choice of biomarkers: non sensitive biomarker might lead to wrong conclusions• Communication aspects to participants related to some specific biomarkers: ex. cytogenic analyses
Health
<ul style="list-style-type: none">• Approach to assess life-style factors (correct questioning)• Ethical issues• Difficulties related to privacy policy and data management

2.2.3. Integration process

Relation between ANIMO en MIC-ATR

1. Relation of health outcome with indoor air quality

Studies of the respiratory health effects of air pollution to date have focused primarily on outdoor sources, and the effects of indoor pollutants are less clearly understood. However, several epidemiological studies have indicated that indoor exposure affects the respiratory health of children and adults.

Indoor air pollutants, such as environmental tobacco smoke (ETS), nitrogen dioxide and formaldehyde, have been associated with adverse respiratory health outcomes in children. For young children, the most important indoor environment is the home. There have been concerns about domestic exposure to volatile organic compounds (VOCs) and other air toxics emitted from a broad range of sources, including cleaning agents, furnishings, paints, cosmetics, aerosol sprays and pesticides. These products also contain chlorine, ammonia, surfactants, acids, bases and oxidants, and reactions between compounds can create highly irritative secondary pollutants. The health effects of this chemical mix, at concentrations normally encountered in homes, is not yet known but there is some evidence that these exposures may be associated with wheeze, airway inflammation e.g. respiratory tract infections, asthma, asthmatic symptoms such as nocturnal breathlessness, increased bronchial responsiveness, decreased lung

function and allergy in young children (Herbarth et al. 2006; Roda et al. 2011; Rumchev et al. 2004; Sherriff et al. 2005; Venn et al. 2003).

In the population based Avon Longitudinal Study of Parents and Children (ALSPAC), the frequency of use of 11 chemical based domestic products was determined from questionnaires completed by women during pregnancy and a total chemical burden (TCB) score was derived (Henderson et al. 2008). Increased use of domestic chemical based products in the prenatal period was associated with persistent wheezing during early childhood

Epidemiological studies have identified specific professional cleaning products associated with asthma, including bleach (Medina-Ramon et al. 2003) and sprays (Zock et al. 2007). Frequent use of common household cleaning sprays may be an important risk factor for adult asthma in the European Community Respiratory Health Survey (ECRHS II, 4267 participants) The use of cleaning sprays at least weekly (42% of participants) was associated with the incidence of asthma symptoms or medication and wheeze. The incidence of physician-diagnosed asthma was higher among those using sprays at least 4 days per week. Dose–response relationships were apparent for the frequency of use and the number of different sprays. Risks were predominantly found for the commonly used glass-cleaning, furniture, and air-refreshing sprays. Cleaning products not applied in spray form were not associated with asthma.

Several epidemiological studies have also indicated that mould and building dampness affects the respiratory health of the inhabitants (Fisk et al. 2007; Hagmolen of Ten Have et al. 2007).

In this cluster project the relation between indoor exposure and respiratory health outcome has been investigated in both the study cohort from the ANIMO project and study cohort from the MIC-ATR project.

Both projects assessed population exposure and health effects partly by means of a questionnaire. On one hand MIC-ATR focused on the environmental exposure of the patients, on the other hand ANIMO focused on the use of non-invasive biomarkers for respiratory diseases in healthy children. The use of the same questions related to indoor exposure and health outcome in both projects have allowed us to perform a statistical analysis to identify potential environmental risk factors and to highlight the interest of such non analytical tool in a surveillance program. Exhaled NO measurements were done while visiting MIC-ATR/LPI patients.

2. Statistical analysis

Linear/non-linear regression models were used to study relations between health outcome with confounders (gender, age, parental history of asthma/allergy, environmental tobacco smoke, smoking during pregnancy, breastfeeding, day-care attendance) and explanatory parameters. The level of significance was set at $p=0.05$). In a first phase of the analysis, only one explanatory parameter was tested in correlation analyses (Spearman Rang correlation). Respiratory health outcome parameters and indoor explanatory variables are listed and described in table 2. Data from eNO are not normally distributed and a natural logarithmic transformation was used.

Statistical significant results were further analyzed using multiple regression models. For the continuous endpoint log N, linear regression models were used, for all other (binary) endpoints logistic regression models were used. Confounders were included in all models. If the p-value of the environmental exposure in the model with the confounders was <0.20, this exposure was included in the multiple model. Some indoor environmental exposures are correlated with each other and should not sit together in one model (multicollinearity). The environmental exposure which correlated best with the health endpoint was included in the multiple model.

Table 2: Description of health outcome variables and explanatory parameters.

Health outcome variables	
eNO	Nitric oxide (NO) from exhaled breath is a marker for airway inflammation.
Airway infection (0/1)	Positive, when answered positive to one of the following question <ul style="list-style-type: none"> • Last 12 months lung/airway infection • Before age of 1 yr lung/airway infection • Period between lung/airway infection
Cough (0/1)	Positive, when answered positive to the following question <ul style="list-style-type: none"> • Last 12 months cough at night
Wheezing (0/1)	Positive, when answered positive to the following question <ul style="list-style-type: none"> • Last 12 months wheezing
Rattling (0/1)	Positive, when answered positive to the following question <ul style="list-style-type: none"> • Last 12 months rattling
Shortness of breath (0/1)	Positive, when answered positive to the following question <ul style="list-style-type: none"> • Last 12 months shortness of breath
Doctor diagnosed asthma (0/1)	Positive, when answered positive to the following question: <ul style="list-style-type: none"> • Ever had asthma, confirmed by a doctor.
Current asthma (0/1)	Positive, when answered positive to one of the following questions: <ul style="list-style-type: none"> • Last 12 months asthma attack • Last 12 months medication for asthma
Asthma ever(0/1)	Positive, when answered positive to one of the following questions: <ul style="list-style-type: none"> • Last 12 months asthma attack • Last 12 months medication for asthma • Ever had asthma, confirmed by a doctor • Last 12 months wheezing • Last 12 months shortness of breath
Any allergy (0/1)	Positive, when answered positive to one of the following questions: <ul style="list-style-type: none"> • Allergy symptoms after insect bite • Allergy symptoms after contact with food • Allergy symptoms after contact with pets • Allergy symptoms after contact with metal • Allergy symptoms after contact with medication • Allergy symptoms after contact with cleaning products, soap,... • Allergy symptoms after contact other items

Insect allergy (0/1)	Positive, when answered positive to the following question: <ul style="list-style-type: none"> Allergy symptoms after insect bite
Food allergy (0/1)	Positive, when answered positive to the following question: <ul style="list-style-type: none"> Allergy symptoms after contact with food
Pet allergy (0/1)	Positive, when answered positive to the following question: <ul style="list-style-type: none"> Allergy symptoms after contact with pets
Skin allergy (0/1)	Positive, when answered positive to the following question: <ul style="list-style-type: none"> Allergy symptoms after contact with metal
Eczema (0/1)	Positive, when answered positive to one of the following questions: <ul style="list-style-type: none"> Last 12 months eczema Last 12 months eczema confirmed by doctor Last 12 months medication for eczema or itchy rash
Explanatory variables	
Environmental tobacco smoke (0/1)	Positive, when answered positive to the question: <ul style="list-style-type: none"> Last 12 months smoking in room
House cleaning with bleach (0/1)	Positive, when answered positive to the question: <ul style="list-style-type: none"> Use of chlorinated products
Air-refreshing spray (0/1)	Positive, when answered positive to the question: <ul style="list-style-type: none"> Use of air-refreshing spray
Air fresheners (0/1)	Positive, when answered positive to the question: <ul style="list-style-type: none"> Use of air fresheners
TCB= total chemical burden (sum score)	Total sum for indoor use of the following products: bug exterminator, antifungal product, anti flea means, mothballs, waterproof spray, air refreshing spray, air freshener, scented spray, scented candles, cleaning spray, liquid multi-use cleaning products, furniture spray, chlorinated products, ammonia, decalcifier, solvents, stains spray, other sprays, washing powders. (score per item: 0= never, 1= now and then, 2= almost every day, 3=every day; max score=57)
Stove (0/1)	Heating with wood stove or open fire or coal stove.
Indoor burning (0/1)	Indoor use of open fire.
Moulds (0/1)	Any sign of mould in the house/bedroom
Moisture (0/1)	Any sign of moisture in the house/bedroom
VOC= volatile organic compounds (sum score)	Total sum for indoor home improvement activities: constructions, painting, wall paper, flooring, new furniture, installation kitchen, new curtains, use of wood-pressed products, other. (score per item: 0=no, 1= yes; max score= 10)
VOC (0/1)	Any of the above mentioned activities.
Pesticides (sum score)	Total sum for indoor use of the following products: anti-mosquitoes means, bug exterminator, antifungal product, anti flea means, mothballs, waterproof spray, air freshener spray, air freshener, scented candles, cleaning spray. (score per item: 0= never, 1= now and then, 2= almost every day, 3=every day; max score=30)

Flame retardants (sum score)	Total sum for indoor flame-retardants containing products in living room and bedroom: fitted carpet, wallpaper, draperies, seats, computers, TV, alarm clock, stereo. (max score=16)
Any spray (sum score)	Total sum for indoor use of sprays: waterproof spray, air freshener spray, scented spray, cleaning spray, stains spray, other spray.(score per item: 0=no, 1= yes; max score=6)
Any spray (frequency score)	Total sum for indoor use of sprays: waterproof spray, air freshener spray, scented spray, cleaning spray, stains spray, other spray.(score per item: 0= never, 1= now and then, 2= almost every day, 3=every day; max score=18)

3. ANIMO cohort

Description: recruitment

This study included a further follow-up of an existing Flemish child cohort¹ at the age of 7 years.

In a separate subgroup of this Flemish cohort, non-invasive measurements were performed at the age of 7 years. 547 children were contacted, however the response was very low: only 65 children and their parents agreed to participate to this follow-up study. During the examination, their body weight and height were determined, exhaled NO was measured, urine samples and EBC (during 5 minutes) were collected, and spirometry with free-running test were performed. These last tests, however, were unsuccessful in a lot of children, and as a consequence these data will not be used for analysis. Additionally, an extensive questionnaire was completed.

An additional subgroup of this Flemish cohort was asked to complete the same questionnaire (n=86).

Characteristics

Tables 3 describes the characteristics, respiratory health and indoor exposure of the children from the Flemish cohort followed-up at the age of 7 years. In total, 151 children participated from which 65 children were examined. The mean age of the population was 7.33 years old (range 6.64-9.15).

Confounding factors

A number of variables were considered as potential confounders of the association between respiratory/allergy health outcome and indoor environmental exposure.

Confounding factors (gender, parental history of asthma/allergy, day-care attendance, breastfeeding, environmental tobacco smoke, smoking during pregnancy) for health outcome were tested (table 4). Doctor-diagnosed asthma, pet allergy were significantly associated with parental asthma/allergy (respectively $r=0.168$, $p=0.04$; $r=0.192$, $p=0.02$). Daycare attendance was protective for shortness of breath ($r=-0.188$, $p=0.02$)

¹ Flemish Environment and Health study (2002 - 2006) – www.milieu-en-gezondheid.be.

but associated with increased prevalence of wheezing ($r= 0.165$, $p=0.05$), and having allergy ($r=0.194$, $p=0.02$). The presence of environmental tobacco smoke was related with increase reporting of airway infections ($r=0.292$, $p=0.0004$).

The eNO concentrations were significantly associated with the health outcomes doctor-diagnosed asthma ($r=0.318$; $p=0.01$) and current asthma ($r=0.339$; $p=0.004$).

Table 3: Characteristics of 7 years old children (Flemish cohort, ANIMO project).

	N	Prevalence (%)
Gender – Male	151	47,0
Infancy characteristics		
Maternal smoking during pregnancy	121	5,0
Breastfeeding	143	78,3
Day-care attendance	150	60,7
Family characteristics		
Parental history of asthma or allergy	149	55,7
Respiratory health		
eNO	62 (65)	13.77±2.24*
Airway infection	146	6,8
Cough	151	57,0
Wheezing	149	14,1
Rattling	149	9,4
Shortness of breath	148	4,1
Doctor diagnosed asthma	150	6,0
Current asthma	151	7,9
Asthma ever	151	17,9
Any allergy	151	27,8
Insect allergy	142	16,2
Food allergy	144	3,5
Pet allergy	146	4,1
Skin allergy	147	10,9
Eczema	151	21,2
Indoor characteristics		
Environmental tobacco smoke	150	24,0
House cleaning with bleach	151	72,2
Air-fresheners sprays	151	37,1
Air fresheners	151	59,6
Stove	150	28,0
Indoor burning	151	32,5
Moulds	150	7,3
Moisture	150	14,7

*Average ±95 % CL

Indoor risk factors for respiratory health

Correlation analyses were performed to study the effect of the indoor risk factors on the health outcome biomarkers. Results are summarized in table 5. Significant positive correlations were found between rattling and the TCB (total chemical burden) ($r=0.179$, $p=0.03$), the sum score for using sprays ($r=0.161$, $p=0.05$) and the score for frequency of using sprays ($r=0.21$, $p=0.01$). The presence of mould was associated with eczema ($r=0.165$, $p=0.04$).

The significant relations between health outcome parameters and indoor risk factors were further analysed in multiple regression models. Fixed confounders gender, parental asthma/allergy and ETS were included in all models. Significant positive associations could be demonstrated between rattling and TCB (sum score indoor use of household cleaning products) (Odds ratio 1.17, (95% confidence interval (CI) 1.02-1.35), $p=0.02$), between rattling and the frequency of using sprays (Odds ratio 1.35 (95% CI 1.05-1.74), $p=0.02$). After correction for confounding variables significance between eczema with mould and rattling with use of sprays disappeared.

Table 4: Statistical analyses of confounders (Spearman rank correlation)

Variables	*	eNO	Airway infection	Cough	Wheezing	Rattling	Shortness of breath	Asthma doctor diagnosed	Asthma current	Asthma ever	Allergy	Food allergy	Pet allergy	Skin allergy	Insect allergy	Eczema
Sex (1 = boy; 2 = girl)	r	0,109	-0,127	-0,122	-0,121	0,091	-0,080	-0,045	-0,018	-0,045	0,052	0,030	-0,014	0,149	0,001	0,002
	p	0,398	0,126	0,135	0,141	0,267	0,335	0,584	0,831	0,582	0,528	0,721	0,865	0,072	0,995	0,985
	n	62	146	151	149	149	148	150	151	151	151	144	146	147	142	151
Asthma/allergy parents (0/1)	r	0,044	-0,034	0,142	0,089	0,027	0,116	0,168	0,065	0,104	0,138	0,017	0,192	-0,037	0,130	0,157
	p	0,736	0,682	0,084	0,281	0,749	0,163	0,041	0,429	0,208	0,093	0,843	0,021	0,662	0,126	0,055
	n	62	144	149	147	148	146	148	149	149	149	142	144	145	140	149
Daycare attendance (0/1)	r	-0,016	0,054	0,158	0,165	0,116	-0,188	-0,085	-0,017	0,090	0,194	-0,074	0,027	0,153	0,201	0,049
	p	0,906	0,524	0,054	0,045	0,164	0,023	0,303	0,840	0,277	0,018	0,379	0,751	0,067	0,017	0,554
	n	61	144	149	147	147	146	148	149	149	149	142	144	145	141	149
Breastfeeding (0/1)	r	0,073	0,056	-0,022	0,047	-0,066	-0,071	-0,098	-0,122	-0,115	0,086	0,093	-0,090	-0,057	0,039	0,046
	p	0,591	0,517	0,790	0,583	0,439	0,408	0,246	0,147	0,170	0,307	0,284	0,292	0,506	0,653	0,587
	n	56	138	143	141	141	140	142	143	143	143	136	138	139	134	143
ETS** (0/1)	r	-0,216	0,292	0,082	0,094	0,024	-0,035	-0,008	0,007	0,021	-0,107	-0,017	-0,039	-0,146	-0,063	0,012
	p	0,094	0,0004	0,319	0,254	0,774	0,677	0,927	0,933	0,798	0,192	0,841	0,639	0,079	0,460	0,882
	n	61	145	150	149	148	147	149	150	150	150	143	145	146	141	150

* r= correlation coefficient, p= p-value, n=number of cases

*ETS: environmental tobacco smoke

Table 5: Correlation analyses between health outcome variables and indoor risk factors (Spearman rank correlation)

Variables	*	Wheezing	Rattling	Shortness of breath	Asthma doctor diagnosed	Allergy	Eczema
Bleach (0/1)	r	0,039	0,156	-0,026	0,033	-0,010	0,033
	p	0,633	0,057	0,755	0,693	0,898	0,691
	n	149	149	148	150	151	151
TCB	r	0,026	0,179	-0,139	-0,062	-0,011	0,076
	p	0,750	0,029	0,092	0,448	0,890	0,352
	n	149	149	148	150	151	151
Moulds (0/1)	r	0,039	0,076	-0,059	-0,067	0,052	0,166
	p	0,641	0,361	0,480	0,415	0,524	0,043
	n	148	148	147	149	150	150
Moisture (0/1)	r	-0,047	0,056	-0,082	-0,011	0,035	0,106
	p	0,567	0,500	0,324	0,895	0,668	0,196
	n	148	148	147	149	150	150
Any spray (sum score)	r	0,028	0,161	-0,099	-0,112	-0,102	0,012
	p	0,736	0,050	0,232	0,173	0,216	0,882
	n	148	148	147	149	150	150
Any spray (frequency)	r	0,070	0,211	-0,073	-0,038	0,008	0,026
	p	0,400	0,010	0,379	0,648	0,919	0,751
	n	148	148	147	149	150	150

* r= correlation coefficient, p= p-value, n=number of cases

4. MIC-ATR cohort

Description: recruitment

The patients followed are patients diagnosed with health problems potentially related to their indoor environment. On medical request the Laboratory for studies and Prevention of indoor pollution of the Hainaut Province (LPI) is visiting those patients and assesses the indoor environment of their habitation. The choice of the environmental parameters tested depends on the diagnosed pathology but the approach developed is always a global approach looking for different potential sources of exposure and pathways.

The updated questionnaire of the ANIMO project has been sent to all patients visited in the framework of the MIC-ATR project and LPI.

From October 2010 to May 2011, 150 questionnaires have been sent to patients or their parents. Of these 150 questionnaires, only 50 % of the patients (75) completed their questionnaire and turned it in to the services for indoor environment analysis (LPI) during their home visit.

All data and results have been treated anonymously.

Characteristics

The study population consisted of 77 patients. The age of the cohort varied between 6 months and 83 years with an average of 35 years (Figure 1).

Patients were asked to fill out almost the same questionnaire as in the ANIMO study. Exhaled NO was tested in 34 patients. Indeed LPI visits are organised during weekdays and in some cases patients are not at home during their visit and assessment. No significant correlation was found between eNO and asthma. Characteristics of the population can be found in table 6.

Confounders

Confounding factors (age, gender, parental history of asthma/allergy, environmental tobacco smoke, smoking during pregnancy) for health outcome parameters were tested (table 7).

Rattling decrease with age ($r=-0.323$; $p=0.01$). ETS was associated with shortness of breath ($n=63$; $r=0.254$; $p=0.04$). Smoking during pregnancy was a risk factor for bronchitis ($n=27$; $r=0.5$; $p=0.01$). Parental allergy is a risk factor for allergy development ($n=30$; $r=0.619$, $p<0.001$).

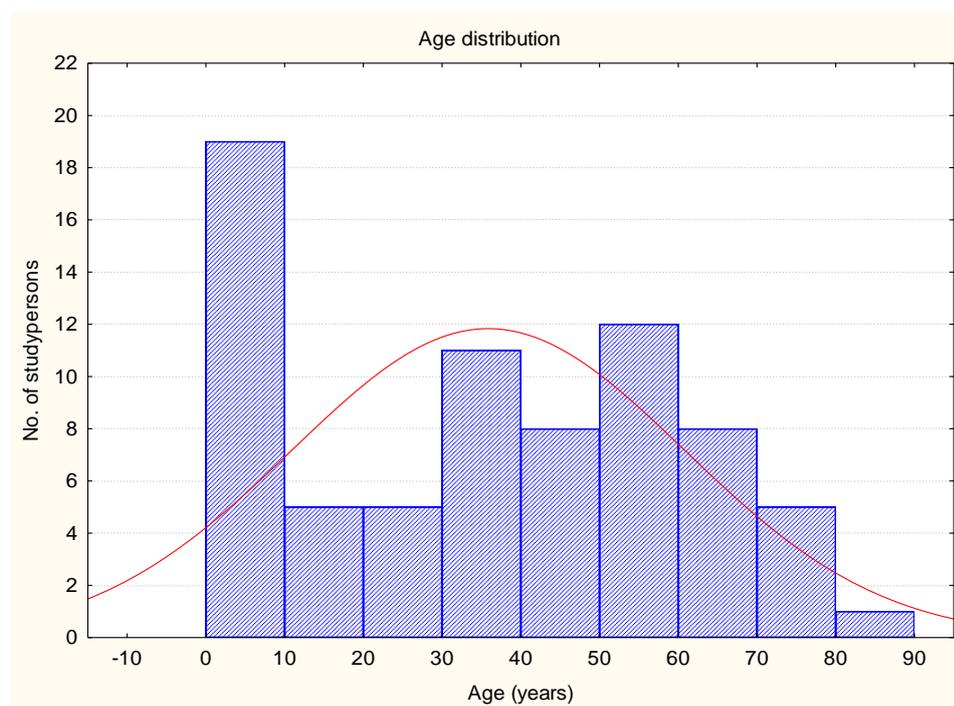


Figure 1: Age distribution of the study population.

Table 6: Characteristics of patient's cohort

	N	Prevalence (%)
Gender – Male	33 (76)	43.4
Infancy characteristics		
Maternal smoking during pregnancy	10 (30)	33.3
Family characteristics		
Parental history of asthma or allergy	17 (32)	53.1
Respiratory health		
eNO	34 (77)	15.6±3.4*
Airway infection	34 (69)	49.3
Bronchitis	43 (71)	60.6
Cough	64 (76)	84.2
Wheezing	53 (71)	74.6
Rattling	27 (67)	40.3
Shortness of breath	49 (71)	69.0
Doctor diagnosed asthma	12 (69)	17.4
Current asthma	38 (75)	50.7
Asthma ever	64 (74)	86.5
Any allergy	50 (77)	64.9
Insect allergy	16 (56)	28.6
Food allergy	11 (61)	18.0
Pet allergy	34 (75)	45.3
Skin allergy	24 (66)	36.4
Eczema	27 (72)	37.5

Indoor characteristics		
Environmental tobacco smoke	24 (69)	34.8
House cleaning with bleach	63 (76)	82.9
Air-fresheners sprays	48 (74)	64.9
Air fresheners	43 (76)	56.6
Stove	12 (74)	16.2
Indoor burning	20 (75)	26.7
Moulds	51 (72)	70.8
Moisture	53 (74)	71.6

**Average \pm 95 % CL

Indoor risk factors for respiratory health

Correlation analyses were performed to study the effect of the indoor risk factors on the health outcome biomarkers (table 8). It has to be kept in mind that the number of participants in this cohort is relatively small (N = 77).

Cough was significantly associated with the presence of mould (n=72, r=0.237, p=0.04). Heating using a stove (coal/wood/open fire) is associated with wheezing (n=68; r=0.244, p=0.05) and rattling (n=65, r=0.333, p=0.01). Current asthma is associated with indoor burning (r=0.288; p=0.01). Indoor VOC exposure is a risk factor for having allergy (r=0.246, p=0.03).

The relation between health outcome parameters and indoor risk factors were further analysed in multiple regression models. Fixed confounders age, gender and ETS were included in all models. If the p-value of the environmental exposure in the model with the confounders was <0.20, this exposure was included in the multiple model. The level of significance was set at p=0.05.

After correction for confounding variables no significant associations were found between eNO, bronchitis, cough, wheezing, shortness of breath, asthma ever, doctor diagnosed asthma and indoor parameters with exposure. Significant positive associations could be demonstrated between airway infections and the sum score of flame retardants (Odds ratio 1.43, (95% confidence interval (CI) 1.05-1.95), p=0.02), between rattling and the presence of a stove (Odds ratio 13.4 (95% CI 1.4-128.9), p=0.02), any allergy and VOC (Odds ratio 1.4 (95% CI 1.0-2.04), p=0.05), eczema and the use of pesticides (Odds ratio 1.15 (95% CI 1.0-1.3), p=0.04). Current asthma was negatively associated with moisture (Odds ratio 0.07 (95% CI 0.01-0.34), p=0.001).

5. Conclusion

Cohort studies to identify risk factors need to be large enough to draw reliable conclusions. Compared to other studies found in the literature investigating the relation of indoor exposure (chemical, biological) on respiratory health outcome the study populations in this cluster project are small. Nevertheless, significant associations were found between health outcome and indoor risk factors in both the healthy child cohort and the patient cohort. These results confirm that children are a

vulnerable group. Current findings emphasize the need to monitor health effects related to indoor air quality with regard to vulnerable groups (children, elderly) in changing housing technologies.

Table 7: Statistical analyses for confounders in patient cohort (Spearman Rank correlation)

Variables	eNO	Bronchitis	Airway infection	Cough	Wheezing	Rattling	Shortness of breath	Asthma ever	Asthma doctor diagnosed	Asthma current	Allergy (any)	Eczema
Age (in years)	0.1288 p = 0.47 N = 34	-0.1600 p = 0.19 N = 69	-0.0479 p = 0.70 N = 67	-0.2180 p = 0.06 N = 74	-0.1326 p = 0.28 N = 69	-0.3231 p = 0.01 N = 65	0.2103 p = 0.08 N = 69	-0.0039 p = 0.97 N = 72	0.2005 p = 0.10 N = 68	-0.0429 p = 0.72 N = 73	-0.1307 p = 0.26 N = 75	-0.0661 p = 0.59 N = 70
Sex (1 = boy; 2 = girl)	-0.3796 p = 0.03 N = 34	-0.1639 p = 0.18 N = 70	-0.0277 p = 0.82 N = 68	-0.0938 p = 0.42 N = 75	-0.1297 p = 0.28 N = 70	-0.0360 p = 0.77 N = 66	0.1200 p = 0.32 N = 70	0.0495 p = 0.68 N = 73	0.0433 p = 0.72 N = 69	-0.0272 p = 0.82 N = 74	0.0153 p = 0.90 N = 76	0.1631 p = 0.17 N = 71
Asthma/allergy parents (0/1)	-0.1667 p = 0.69 N = 8	-0.1321 p = 0.49 N = 30	-0.5483 p = 0.001 N = 30	-0.1657 p = 0.37 N = 31	-0.2892 p = 0.13 N = 29	-0.1348 p = 0.50 N = 27	0.0773 p = 0.68 N = 31	-0.0778 p = 0.68 N = 31	0.0301 p = 0.87 N = 30	0.0882 p = 0.64 N = 31	0.6659 p < 0.0001 N = 32	0.0958 p = 0.61 N = 31
ETS* (0/1)	0.1934 p = 0.30 N = 31	0.0420 p = 0.74 N = 64	-0.0466 p = 0.72 N = 61	-0.0934 p = 0.45 N = 68	0.0186 p = 0.88 N = 63	-0.0538 p = 0.69 N = 59	0.2541 p = 0.04 N = 63	0.0250 p = 0.84 N = 66	0.0726 p = 0.58 N = 61	0.1134 p = 0.36 N = 67	-0.0417 p = 0.73 N = 69	-0.0420 p = 0.74 N = 64
Smoking during pregnancy (0/1)	-0.5132 p = 0.19 N = 8	0.5000 p = 0.01 N = 27	0.3162 p = 0.11 N = 27	-0.2605 p = 0.17 N = 29	0.1915 p = 0.32 N = 29	0.2958 p = 0.14 N = 26	-0.2028 p = 0.30 N = 28	0.0082 p = 0.97 N = 29	-0.0271 p = 0.89 N = 27	-0.2213 p = 0.25 N = 29	0.0500 p = 0.79 N = 30	-0.1550 p = 0.42 N = 29

*ETS: environmental tobacco smoke

Table 8: Correlation between indoor risk factors and health outcome parameters (patient's cohort).

Variables	eNO	Bronchitis	Airway infection	Cough	Wheezing	Rattling	Shortness of breath	Asthma ever	Asthma doctor diagnosed	Asthma current	Allergy (any)	Eczema
Bleach (0/1)	0.0782 p = 0.66 N = 34	0.2120 p = 0.08 N = 71	0.1125 p = 0.36 N = 69	0.1845 p = 0.11 N = 75	0.1691 p = 0.16 N = 71	0.1177 p = 0.34 N = 67	0.0229 p = 0.85 N = 71	0.1291 p = 0.27 N = 74	0.0088 p = 0.94 N = 69	0.0480 p = 0.68 N = 74	0.0279 p = 0.81 N = 76	0.2144 p = 0.07 N = 72
Air fresheners (0/1)	-0.2700 p = 0.12 N = 34	0.0450 p = 0.71 N = 71	0.1028 p = 0.40 N = 69	-0.0205 p = 0.86 N = 75	-0.1866 p = 0.12 N = 71	-0.0557 p = 0.65 N = 67	-0.0748 p = 0.54 N = 71	-0.1956 p = 0.09 N = 74	-0.0741 p = 0.55 N = 69	-0.1661 p = 0.16 N = 74	-0.0401 p = 0.73 N = 76	0.1155 p = 0.33 N = 72
TCB	0.0115 p = 0.95 N = 34	0.1176 p = 0.33 N = 71	-0.2122 p = 0.08 N = 69	0.0058 p = 0.96 N = 76	-0.0285 p = 0.81 N = 71	0.2025 p = 0.10 N = 67	0.0067 p = 0.96 N = 71	-0.0454 p = 0.70 N = 74	-0.0115 p = 0.93 N = 69	0.0827 p = 0.48 N = 75	0.1350 p = 0.24 N = 77	0.1549 p = 0.19 N = 72
Stove (0/1)	-0.1155 p = 0.52 N = 34	0.1693 p = 0.17 N = 68	0.0900 p = 0.47 N = 67	0.1868 p = 0.11 N = 73	0.2437 p = 0.05 N = 68	0.3328 p = 0.01 N = 65	0.1498 p = 0.22 N = 69	0.1718 p = 0.15 N = 71	0.1054 p = 0.40 N = 66	0.1491 p = 0.21 N = 72	0.1050 p = 0.37 N = 74	0.1314 p = 0.28 N = 69
Indoor burning (0/1)	-0.0970 p = 0.59 N = 33	0.1705 p = 0.16 N = 70	0.0177 p = 0.89 N = 68	0.0201 p = 0.87 N = 74	0.1386 p = 0.25 N = 70	0.0737 p = 0.56 N = 66	0.0876 p = 0.47 N = 70	0.0661 p = 0.58 N = 73	0.1245 p = 0.31 N = 68	0.2880 p = 0.01 N = 74	0.1858 p = 0.11 N = 75	0.1349 p = 0.26 N = 71
Moulds (0/1)	-0.0680 p = 0.71 N = 32	-0.0871 p = 0.48 N = 68	0.0118 p = 0.92 N = 66	0.2371 p = 0.04 N = 72	-0.0919 p = 0.46 N = 68	0.1197 p = 0.35 N = 64	-0.1712 p = 0.16 N = 68	-0.1542 p = 0.20 N = 71	-0.1341 p = 0.28 N = 66	-0.2506 p = 0.04 N = 71	-0.0648 p = 0.59 N = 72	0.1329 p = 0.28 N = 68
Moisture (0/1)	-0.1929 p = 0.29 N = 32	-0.1345 p = 0.27 N = 70	-0.1592 p = 0.19 N = 68	0.1553 p = 0.19 N = 73	-0.0800 p = 0.51 N = 70	0.0793 p = 0.53 N = 66	-0.2245 p = 0.06 N = 70	-0.2383 p = 0.04 N = 73	-0.1416 p = 0.25 N = 68	-0.4282 p = 0.0002 N = 73	-0.0060 p = 0.96 N = 74	0.1083 p = 0.37 N = 71
Any spray (sum score)	0.0461 p = 0.80 N = 34	-0.0932 p = 0.44 N = 71	-0.3005 p = 0.01 N = 69	0.0206 p = 0.86 N = 75	-0.1957 p = 0.10 N = 71	-0.0265 p = 0.83 N = 67	-0.0417 p = 0.73 N = 71	-0.1604 p = 0.17 N = 74	-0.1705 p = 0.16 N = 69	0.0600 p = 0.61 N = 74	0.1067 p = 0.36 N = 76	0.2213 p = 0.06 N = 72
Any spray (frequency)	-0.0182 p = 0.92 N = 34	0.0290 p = 0.81 N = 71	-0.2357 p = 0.05 N = 69	0.0422 p = 0.72 N = 75	-0.0445 p = 0.71 N = 71	0.0965 p = 0.44 N = 67	-0.0277 p = 0.82 N = 71	-0.1126 p = 0.34 N = 74	-0.1091 p = 0.37 N = 69	0.0134 p = 0.91 N = 74	0.0895 p = 0.44 N = 76	0.1291 p = 0.28 N = 72

Relation between SHAPES, PM²TEN and MIC-ATR

NO is a common gas and air pollutant (e.g. emitted by vehicles using internal combustion engines). In outside air it is quickly converted into NO₂ which is therefore commonly used as a proxy for traffic related air pollution. The epidemiological associations that are found between NO/NO₂ and health effects may in reality be caused by other components such as PM.

NO is also found in exhaled air (that was previously filtered from ambient NO). In medical studies, exhaled nitric oxide (eNO) is often measured as a breath test for asthma or airway inflammation. Nitric oxide (NO) is produced by several cell types during a non-specific inflammatory response but the release of exhaled NO is usually assumed to be from production in the lower airways.

Nitric oxide is produced in the body from L-arginine by three different forms of the enzyme nitric oxide synthase (NOS): inducible (iNOS), endothelial (eNOS), and neuronal (nNOS). eNOS is active in endothelial cells of blood vessels and nNOS in neurons. iNOS activity can be triggered by exposure (triggering the release of large quantities of NO several hours after exposure) and inflammation (mediated by proinflammatory cytokines). During inflammation, iNOS produces NO in several cell types (e.g. white blood cells such as eosinophils and possibly neutrophils as well as mast cells and macrophages).

It is well known that asthmatics have higher eNO levels and that eNO is a more specific diagnostic test than lung function results.

Previous studies have found positive associations between exhaled NO and exposure to air pollution both in healthy people and asthmatics (see Jacobs et al., 2010 for a review). Briefly, smokers tend to have lower levels of exhaled NO, compared to non-smokers and ETS exposure is also associated with decreases in exhaled NO although the mechanisms are unclear (Jacobs et al., 2010).

The role of eNO in reaction of the body to air pollution exposure or in medical conditions other than asthma is poorly known. Exposure to air pollution has been associated with decreased or increased eNO levels without the reasons being understood.

Studies investigating real-life exposure of traffic participation have also found significant associations with adverse health effects. "Participation in traffic" is e.g. associated with the risk of developing a myocardial infarction in the hour afterwards. Exposure to traffic-related air pollution in a group of asthmatic subjects was also found to produce a greater reduction in lung function, when subjects walked for two hours along a busy street compared to walking in a park in the UK. On the other hand, in The Netherlands researchers found only weak evidence for an association between exposure of cyclists during rush hour and changes in lung function and airway inflammation.

In this study we have measured Fractional exhaled NO (FeNO) with an electrochemistry-based NIOX MINO device (Aerocrine, Sweden). This instrument

complies with ATS/ERS recommendations. The device contains a scrubber which makes the inhaled air NO-free (because NO is also found in ambient air especially close to sources of traffic related air pollution). The procedure consists of maximal inhalation. Subjects were instructed to monitor a flow rate as visualized on a display to maintain a flow rate of 50 ml/second (similar to the procedure use in an earlier experiment and described in Jacobs et al., 2010).

After careful analysis of all the e-NO data available from the MIC-ATR project for this cluster, we could not find any correlation with any of the other parameters (see all correlation graphs in annex 5).

Surprisingly, we did not find a correlation with diagnosed asthma (for which it is a well-known marker, see above). It was therefore decided that it makes no sense to attempt any further analysis based on the Time-Activity patterns (TAP) as previously planned. If asthma cannot be detected by our eNO measurements then any other correlation is likely to be spurious. Information on TAP was questioned specifically for this study with respect to the time spent in transport. It was expected to find a correlation in this study based on the results of the earlier studies mentioned above under the assumption that eNO would reflect inflammation induced by exposure to traffic related air pollution.

We can only suppose here why no relationship could be detected in this cluster project. Maybe the number of people from our cohort that actually took the e-NO test (and answered the TAP related questions) was just too low. On the other hand we have previously found statistically significant results in at least two other experiments on even smaller test-groups. Because of these uncertainties it was decided not to discuss the eNO and TAP relationship in further detail in this report.

Relation between PARHEALTH and MIC-ATR

1. Description of PARHEALTH project

The main objective of the PARHEALTH project (2007-2010) was to investigate the short-term effects of particulates (both mass and physical-chemical characteristics) and ozone using sensitive endpoints of cardiovascular and respiratory responses in two susceptible segments of the population: children and elderly.

Five different studies were executed within the frame of the PARHEALTH projects:

- Acute mortality and modelled chemical composition of PM
- Acute health effects of particulate air pollution in elderly
- Acute health effects of particulate air pollution and ozone in children
- Associations between infant mortality and air pollution in an affluent society
- Subclinical responses in healthy cyclists briefly exposed to traffic-related air pollution.

One of the important discoveries of these epidemiological studies was that the increased mortality and morbidity associated with increases in PM was not due only to pulmonary disease, but mainly to cardiovascular diseases.

2. Integration of PARHEALTH approach in MIC-ATR dataset

The MIC-ATR dataset consists of a questionnaire, completed with descriptions and measurements of the interviewee's indoor environment. Personal and environmental data were collected for 77 persons in the province of Hainaut.

The approach of the PARHEALTH project is not appropriate for the MIC-ATR dataset, for several reasons.

First, PARHEALTH focuses on short-term effects of air pollution (trigger effects), whereas the information on personal health, obtained by the MIC-ATR questionnaire, typically concerns long-term or permanent data (exposure to smoke or traffic, allergies,...).

Second, analyses would suffer from a massive lack of accuracy and statistical power. It is true that in the MIC-ATR questionnaire, exhaled NO was measured in the study subjects, and in theory, these data can be linked to daily PM (or ozone) levels in order to estimate instant respiratory inflammation in association to short-term changes in PM. However, the number of subjects (77) is much too small for such an ecological approach. Personal exposure to PM was not measured in the MIC-ATR study and would have to be estimated by interpolation of PM measurements by IRCEL monitor stations, which is of course much less accurate than direct personal exposure. Furthermore, within the scope of PARHEALTH, only children (-12y) and elderly (+80y) (two susceptible subgroups of the population) have been included. Applied to the MIC-ATR dataset, this would result in only 20 subjects left to analyze.

Therefore, we conclude that PARHEALTH and MIC-ATR, although both projects on the exposure to air pollution, are not compatible for joint analyses, neither in focus of interest (short-term variation in outdoor PM vs. long-term pollution of the indoor environment), nor in the actual data at hand (dataset is too small for adequate analyses).

2.2.4. Focus on the SWOT analysis

At the follow-up committee meeting of February 2011, the results of the SWOT analysis have been fully discussed in order to better identify how the different "scientific networks" (indoor air quality, outdoor air quality, biomonitoring, time activity pattern and health) could benefit from each other's experience and different levels of maturity. Two ways of integration have been identified, through *transfer of knowledge* from one field of expertise to another or through the implementation of a *global approach* which seeks for horizontal or integrative tools allowing further transfer of data and information between the different "scientific networks".

Within those 2 potential processes of cooperation, a few priority themes of work have been highlighted.

For the *transfer of knowledge*:

- the definition of "reference" values (threshold, guideline or target values) defining which "reference" value for which use);

- the development of sampling and recruitment strategies;
- the elaboration of communication processes addressing different publics (participants, policy makers, large public,...) precisising which communication channels and tools have been efficient.

With regards to integrative tools allowing the implementation of potential global approach:

- the use of the different type of questionnaires (content, format, process, ...);
- the use of Geographic Information Systems (GIS) and Time Activity Patterns;
- the use of the health aspects.

It has been decided (by electronic vote) that the cluster would in the second year of implementation focus on one specific aspect: **the definition of “reference” values.**

WHO definition of a guideline value (WHO, 2000)

«A guideline value is a particular form of guideline. It has a numerical value expressed either as e.g. a concentration in ambient air, which is linked to an averaging time. In the case of human health, the guideline value provides a concentration below which no adverse effect or (in the case of odorous compounds), no nuisance or indirect health significance are expected, although it does not guarantee the absolute exclusion of effects at concentrations below the given value».

Setting “reference” values aims to protect the population from adverse health effects resulting from environmental exposure through the suppression or at least the reduction of the level of pollution brought by the different potential sources of exposure and different pathways. It supports the decision making process in terms of policy making (whatever the scope of the regulation (legally or non legally binding)) and risk management. Protective for the population, they although cannot be seen as “authorization for pollution”.

If the aim is to protect the population, the vulnerable ones are not necessarily protected by “reference” values and adverse effects may appear at levels below or equal to defined (even health based) values. Besides, guidelines usually define values for substances considered individually (sometimes in a specific setting). Therefore they don't take into account potential effects resulting from exposure to multiple chemicals (cocktail effect).

Setting “reference” has also as objectives to:

- assess population exposure or exposure of individuals and potential diverse effects;
- facilitate the communication addressing different targeted stakeholders.

Practically different strategies exist within the different scientific networks to elaborate “reference’ values.

“Reference” values in human biomonitoring

Two strategies are used in human biomonitoring to define “reference” values: the so-called “reference” values which are statistically based and health based values.

1. Statistically based values in human biomonitoring

A reference value in this case is a concentration of a substance in human biological material which is *statistically derived* from a defined group (representative) of the general population (e.g. 95th percentile) at a certain time.

This allows establishing “background or baseline exposure” levels of environmental chemicals measured in the population. These values serve as a starting point for further comparisons and trend analysis in order to assess the efficiency of policies and actions aiming to reduce population exposure.

2. Health based values in human biomonitoring

A second strategy consists of defining *health based human biomonitoring values* for the population, eventually linked to an action plan or alerts. These values can be defined for the whole population (and therefore don't take into account the most vulnerable ones) or for specific target groups such as children, pregnant women, adolescents or others.

In order to be able to define health based human biomonitoring values scientific studies are necessary to understand the health risks associated with the blood, urine or hair levels. German health based human biomonitoring values (HBM I) have for example been derived from tolerable daily intakes data. However for many chemicals more researches are needed to better understand health effects. Even more in other cases new findings imply to review and lower the previously defined health based biomonitoring values. Recent researches have indeed highlighted for some chemicals potential health effects at low doses. Indeed over the past century, as knowledge of lead toxicity evolved, blood lead levels previously considered as safe could be seen as such any more (Needleman, 2004).

Therefore, depending on the literature referred to and the uncertainty factor chosen to define those health based biomonitoring values, differences can appear in the proposed targets from one country to another.

Note that in some cases cost-benefit analyses and policy issues are peripheral to the decision making process.

Table 9: Reference values and HBM values in Germany – example of the metals

Metal	matrix	reference value	Remarks reference values	HBM I	HBM II	Remarks HBM
Arsenic	Urine	X	adults - no fish consumption 48 h			
Cadmium	Urine	X	children, adults (non-smokers)	X	X	children, adolescents, adults nephrotoxicity
	Blood	X		-	-	
Lead	Blood	X	children, women, men	-	-	children, women, men - neurotoxicity
Mercury	Blood	X	children, adults - fish consumption < 3/month	X	X	women < 45 years
	Urine	X	total population – no amalgam fillings	X	X	prenatal neurotoxicity
Nickel	Urine	X	total population			

Platinum	Urine	X	total population – no dental gold			
Thallium	Urine	X				
Uranium	Urine	X				

“Reference” values in indoor air quality

To define “reference” values for indoor air quality, 3 different strategies have been highlighted: health based, statistically based and health observed based values.

1. Health based “reference” values for indoor air quality

WHO guidelines related to air quality are based on the existing scientific literature and data related to air pollution and its potential health effects. Although knowledge gaps and uncertainties still exist, it offers strong baselines to the proposed recommendations.

Health Canada published in 1987 its “Exposure guidelines for Residential Indoor Air Quality”. These directives have been updated in 1989 to add radon to the concerned chemicals and in 2006 to lower values for formaldehyde. They aim to support individuals and public bodies in the assessment of the indoor environment in a coherent way, and the need for the implementation of corrective actions. These target exclusively private dwellings. For Health Canada these guidelines constitute the first step to improve indoor air quality: from these values, rates for air renewal can be defined, emission values can be calculated for building products or furniture’s or other management measure can be proposed. For Canadians they have increased awareness of the population concerning indoor air quality while giving a better perspective and understanding of analytical results [Santé Canada 1987,1989 et 2006].

Germany has published in 1977 guidelines for formaldehyde in indoor air. This proposal has been motivated by the observation of adverse health effects (nausea, headache and sleeping disorders) associated with higher concentrations in formaldehyde measured in German schools. These guidelines have set the framework to further develop regulations and standard for the emission of formaldehyde from panels and foams. The objective has been achieved. Standards have been published in 1980 and 1985 and certified materials (non emitting formaldehyde) exist now in Germany. Since then the initiative has been extended to more chemicals. Two guide value categories have been established and published by the IRK/AOLG Ad hoc working group. Guide value II (RW II – legally binding) is an effect-related value based on current toxicological and epidemiological knowledge of a substance’s effect threshold that takes uncertainty factors into account. It represents the concentration of a substance which, if reached or exceeded, requires immediate action as this concentration could pose a health hazard, especially for sensitive people who reside in these rooms over long periods of time. Guide value I (RW I – precautionary value) represents the concentration of a substance in indoor air for which, when considered individually, there is currently no evidence that even life-long exposure is expected to cause any adverse health impacts. Concentrations

higher than RW I are deemed to constitute an exposure that is higher than normal and therefore undesirable. RW I can also be considered as a target value during rehabilitation efforts. Like in many proposed recommendations, the guide values apply to individual substances and provide no indication of any possible combined effects with different substances. For some substances or group of substances, hygiene-based assessment values have been proposed when systematic practical experience indicates that the likelihood of complaints or adverse health effects increases with increasing concentration but current knowledge is insufficient to derive a toxicology-based guide value. To date, such values have been established for carbon dioxide, total volatile organic compounds (TVOC) and fine particulate matter (PM_{2.5}).

In France, guideline values have been established for different priority chemicals. Those values have been set according to the level of priority of the substance considered, the potential health effects and the data available. In case of effect with threshold value, the proposed exposure levels have been built from a critical observed dose (cf. epidemiological and toxicological studies, elaboration of reference toxicological values, values with non adverse effects) adjusted if necessary by factors of uncertainties (cf. toxicological studies applied to animals,) in order to obtain an acceptable exposure level for the man. They have been expressed as a concentration in the air for a specific time of exposure which corresponds to the maximal exposure time without expected effect. In case of effect without threshold value (such as the carcinogenic effects), the proposed values have been elaborated according to calculated "equivalent of dose" for the man, a modelling of experimental data and the extrapolation towards low dose exposures associated with potential low risks. These have been expressed as concentrations corresponding to various probability of occurrence of effect (for example 10^{-4} , 10^{-5} , 10^{-6}).

In the United Kingdom, the principles for the elaboration of not binding guidelines values have been proposed in 2001 (Institute for Environment and Health (IEH on 2001)). First series of values for five chemicals have been published in December, 2004 (COMEAP on 2004). It has been clearly mentioned that the proposed guidelines were addressing manufacturers of materials and products susceptible to emit volatile compounds indoors in order to support the decision-making process in products testing and market development, architects and engineers to set appropriate ventilation rates and inhabitants in order to allow them to better understand their own exposure in their own dwelling.

For the European Commission the INDEX project coordinated par the Joint Research Centre (JRC) has elaborated guideline values for 14 chemicals recognized to be found in indoor environments and to have known health effects [European Commission 2005].

In the Scandinavian countries, indoor air quality guideline values have been proposed for a large number of compounds (mainly VOC's) within the Nordic Committee (Nielsen on 1996). In Finland, these values are part, among other elements, of the criteria defining the quality of indoor environments within the framework of the label "Finnish Classification of Indoor Climate" (2000). In the same way, guideline values in Hong-Kong have been proposed for offices and public

places in the framework of a voluntary certification process for buildings (Hong-Kong 2003a and 2003b).

In Japan, in the 1980s, further to complaints for eyes irritation and eczema associated with some resins (urea-formol resins), the government set up regulations related to emissions from plywood (standards JAS, on 1980) and from particles and fibers panels (standards JIS, on 1983). In the 1990s, noticing that the syndrome of unhealthy buildings was still regularly reported, the Ministry of Health proposed in 1997 legally binding guidelines values for the formaldehyde in order to assess the impact of the regulation and the possible needs for further strengthening. This led to a significant decrease of the percentage of housing exceeding the set guideline value (from 25 % to 5.6 %) (Azuma, 2005).

As we can see health based “reference” values for indoor air quality have been proposed for different priority chemicals in quite a few countries. Depending on the factors stressing the need for “reference” values, the priority list of regulated compounds count different chemicals or the definition of the compound itself may also vary. Formaldehyde appears to be the most regulated chemical. This example (table 10) illustrates quite well the variety of values proposed, the difficulty to make possible comparisons and therefore to interpret results. Another illustrative example concerns guidelines set for total VOC’s where guidelines don’t necessarily refer to the same list of VOC’s.

Different factors may be explaining these differences: lifestyles and behavioural factors, the targeted populations (characterised by different socio-economical levels), building habits, type of building materials but also the methodology used to elaborate the guidelines, the decision making process, the factors stressing the need for “reference” values and the state of the art at the time of their elaboration.

Table 10: Guidelines values for formaldehyde

Regulation	Recommended value
WHO	The thresholds values recommended in 1995 are 10 µg/m ³ for the sensitive persons and of 100 µg/m ³ for non sensitive persons during 30 minutes. The value of 10 µg/m ³ included within the recommendations published in 2000. The guide value proposed by WHO in 2000 is 100 µg/m ³ for 30 minutes exposure (threshold beyond which irritations of the superior respiratory tracts of the general population can appear).
Flanders	10 µg/m ³ for good indoor air quality; 100 µg/m ³ as intervention value
Health Canada (2006)	123 µg/m ³ for 1 hour exposure and 50 µg/m ³ for 8 hours
European project INDEX	30 µg/m ³ with the objective to obtain the lowest concentration as possible (ALARA principle)
Norway	100 µg/m ³ during 30 minutes
Australia	120 µg/m ³
California EPA	95 µg/m ³ during 1 hour; 34 µg/m ³ during 8 hours
Finland	Category S1 : 30 µg/m ³ Category S2 : 50 µg/m ³ Category S3 : 100 µg/m ³
France (AFSSET, 2007)	50 µg/m ³ for 2 hours; 10 µg/m ³ for long term exposure
Portugal	100 µg/m ³

The elaboration of recommendations values for indoor air quality has been stressed either as corrective measures in case of health complaints (example of Japan) or as preventive measures to protect population from adverse health effects resulting from exposure to bad indoor air quality and set up certification standards for buildings (Finnish example). Indoor air quality guidelines have in some cases set the framework to further develop other regulations and standards. In Germany for example, they have supported the development of policies related to emission from building materials and consumption products.

2. Statistically based “reference” values for indoor air quality

In Brussels, the service for indoor air quality or the so-called green ambulance” (CRIPI) has developed a “Global Chemical Pollution Index” based on a database of more than 1500 visits of private dwellings. This is a statistically based index. The concerned private dwellings are suspected to have health effects. They are tested on medical request after a health diagnosis. Percentiles of indoor air quality data collected from these private dwellings over 10 years have been calculated. Increasing ranges of values have then been linked to a colourful and visual scale (table 11).

Table 11: Brussels Region Global Chemical Index for indoor air quality (CRIPI – IBGE)

	PERCENTILES (µg/m³)					
	0→P20	P20→P50	P50→P70	P70→P90	P90→P95	> P95
Benzene	0-1,7	1,7-3,6	3,6-6	6-14,6	14,6-22,7	> 22,7
Toluene	0-8,8	8,8-17	17-27	27-62	62-93	>93
Trichlorethylene	0-0,1	0,1-0,6	0,6-1,5	1,5-6	6-13	>13
Tetrachlorethylene	0-0,3	0,3-1,2	1,2-2,7	2,7-7,5	7,5-12	>12
Limonene	0-3,4	3,4-9	9-15	15-34	34-54	>54
pinene	0-3,5	3,5-8,3	8,3-15	15-38	38-58	>58
Formaldehyde	0-14	14-24	24-34	34-54	54-65	> 65
TVOCs	0-44	44-83	83-122	122-239	239-445	> 445
INDEX	Excellent	Good	Normal	Bad	Very Bad	Execrable

3. Health observed based “reference” values for indoor air quality

Between 1987 and 1992, BAUBIOLOGIE MAES developed the Standard of Building Biology Testing Methods and the accompanying Building Biology Evaluation Guidelines on behalf and with the support of the Institut für Baubiologie und Ökologie Neubeuern IBN. The Standard was issued for the first time in May 1992. The most current Standard SBM-2008 is the seventh edition and was published at the beginning of 2008. Since 1999 a 10-member expert commission assists in maintaining and updating the Standard, including the Guidelines and specific testing protocols.

The Standard gives an overview of the physical, chemical and biological risks encountered in sleeping areas, living spaces, workplaces and properties. It offers guidelines on how to perform specific measurements and assess possible health risks.

The guidelines include values ranged into 4 levels of concern (no concern, slight, severe and extreme concern). These values and levels of concern are the results of

about 10000 house inspections comparing the measuring results with the reported health effects (illnesses, sensitivities) of the inhabitants.

This approach allows integrating the combined effect of all indoor sources of exposure, including the ones we cannot measure or even haven't identified. It also allows considering the most vulnerable ones, including sensitive persons. These reference values are meant as a guide, as an orientation and not strict rules. They cannot be interpreted as strict categories.

“Reference” values in outdoor air quality

1. Health based “reference” values for outdoor air quality

In Europe and the United States, the principles for the setting of outdoor air quality aim to protect population's exposure and reduce potential health adverse effects. The methodology to define those health based standards included references to epidemiological, toxicological and clinical studies looking at the potential associations between environmental exposure and health effects or looking at the physiological mechanism responsible for these health effects.

However if proposed standards aim to protect the population, they don't necessarily protect the whole population. As an example, particulate matters can have a wide range of effects although the respiratory and cardiovascular systems are the most affected by higher exposure levels so that standards values often focus more on these effects. The PARHEALTH study also highlighted the importance of the timing of exposure which is not always considered in the setting of health base “reference” values. The late neonatal stage (2-4 weeks) seems to be the most critical period for exposure to PM₁₀ which makes the current EU limit value for PM₁₀ not protective to prevent triggering infant mortality. The absence of a threshold value and the high interindividual variability (variability of exposure and variability of response to a defined exposure) suggest that the risk exists even below 50 µg/m³ and that standard or indicative values are not necessarily likely to completely protect each individual against all possible adverse effects.

Different factors might lead to differences in the setting of air quality standards: the health effects considered, the targeted populations (including the most vulnerable ones or not) but also socio-economic aspects, technical factors and local or regional priorities. Drafting and implementing effective EU policies on air pollution and ensuring compliance with them over time underscores potential health impact but also monetary benefits. Therefore setting standards implies to look for the lowest exposure levels but also in some cases to find the equilibrium between the socio-economic and technical factors. The APHEKOM study, implemented in 22 cities, has shown that a decrease of annual PM₁₀ levels to 20 µg/m³ (table 12: EU and WHO recommendations) could lead to a decrease by more than 2,500 in the annual number of cardiac hospitalisations and by more than 5,300 in the annual number of respiratory hospitalisations !

Table 12: EU and WHO standard air quality guidelines for PM₁₀

<p>EU reference values for PM10 (2005):</p> <ul style="list-style-type: none"> • Annual average < 40 µg/m³ • Daily average > 50 µg/m³ on ≤ 35 days/year <p>WHO recommendations for PM10 (2005):</p> <ul style="list-style-type: none"> • Annual average < 20 µg/m³ • Daily average > 50 µg/m³ on ≤ 3 days/year
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2. Health and statistically based “reference” values for outdoor air quality

The outdoor air quality index provides a number indicating the level of health risk associated with local air quality. The index associates and integrates different pollutants. The indicator is quite visual and easily addresses different populations which makes it a strong tool for awareness raising.

Table 13: Outdoor air quality index

Pollutant		Concentration µg/m ³									
SO ₂	Mean value 24h	0 - 15	16 - 30	31 - 45	46 - 60	61 - 80	81 - 100	101 - 125	126 - 165	166 - 250	> 250
NO ₂	Daily maximum of the hourly average	0 - 25	26 - 45	46 - 60	61 - 80	81 - 110	111 - 150	151 - 200	201 - 270	271 - 400	> 400
O ₃	Daily maximum of the 8 hours average	0 - 30	31 - 45	46 - 60	61 - 80	81 - 100	101 - 120	121 - 150	151 - 200	201 - 270	> 270
PM ₁₀	Mean value 24h	0 - 10	11 - 20	21 - 30	31 - 40	41 - 50	51 - 70	71 - 100	101 - 150	151 - 200	> 200
Index		1	2	3	4	5	6	7	8	9	10
Appreciation		excellent	really good	good	quite good	average	mediocre	very mediocre	bad	Really bad	Execrable

3. Policy Support

Different themes in environment and health (outdoor air quality, indoor air quality and human biomonitoring) have reached at this stage different levels of maturity. One of the aims of the cluster was to break walls and build bridges between these scientific networks.

The identification of the main actors' active in these different fields as well as their role is an important step to develop communication processes between researchers, field experts and workers but also with policy makers and the general public. Top-down and bottom-up communication between stakeholders is a good way to translate findings into efficient strategies and actions aiming to reduce environmental exposure and to improve public health and related health costs. However information concerning Environment as well as Environment and Health is relatively fragmented. This fragmentation is due to the complexity of the institutional levels (federal, community, and regional, provincial and local levels) but also of the thematic itself. In order to tackle environmental and health issues in a sustainable way, decision makers have to ensure that policies and actions don't move one issue from one scientific network to the next one. Therefore a holistic view is necessary and efficient communication between all stakeholders needs to be supported. A good understanding of the complex picture is also a good way to achieve a sustainable development and induce long term behavioural change at all levels. The Cluster air quality has contributed to identify these actors but also studies, programs, methods, data and information managed at the different levels. The project implementation by the setting of an interdisciplinary dialogue in the framework of the organization of the stakeholders and follow-up committee meetings and workshops has encouraged communication and collaboration between the scientific networks and identified working teams. The SWOT analysis of the identified studies and programs has allowed highlighting gaps and opportunities for further researches and policy making. This could eventually be completed by a PESTLE analysis which stands for Political, Economical, Social, Technological, Legal and Environmental analysis.

“For too long environmental, social and economic concerns (but also health aspects) have been handled as separate issues but the rising global environmental challenges, financial crises, food price volatility and commodity price increases show that these issues are unavoidably interconnected and must be tackled together”.
Kate Raworth, A safe and just space for Humanity, February 2012 (in preparation of the Rio+20 Conference)

4. Dissemination and valorisation

The Cluster Air Quality has been active in the dissemination on information relative to the project through the organisation of workshops and stakeholders meetings.

In the framework of EU Belgian Presidency, a conference entitled “Indoor air quality in different living settings: results of investigations and consequences in terms of decision making” has been organised by Hainaut Vigilance Sanitaire - Hygiene Publique in Hainaut. Conference conclusions and recommendations have been transmitted to policy makers at the EU level and a press release has been edited.

During the EU Belgian Presidency different conferences focusing on the themes of work of the cluster have been organised. At the same time Germany also organised in Berlin a conference on Human Biomonitoring (September 2010). Cluster partners attended these different meetings and the results have been reported during the 1st cluster workshop in November 2010.

The ANIMO and EU COPHES projects have organised in December 2010 a common workshop on non invasive sampling techniques for human biomonitoring.

In September 2011, a few cluster partners attended the ISEE conference (International Society for Environmental Epidemiology Conference) in order to further complete the information collected so far and prepare the next cluster workshop.

A second cluster workshop has been organised in the framework of the human biomonitoring week “HBM and indoor/outdoor” air quality where the PARHEALTH project or other identified key projects presented some of their project results: “Role of the EU reference value in the association between PM10 air pollution and infant mortality in Belgium”, PARHEALTH; “APHECOM: WHO limits and health impact”, APHECOM; ESCAPE project.

An abstract proposal has been submitted to the Fifth International Congress on Epidemiology, organised in partnership with the University of Brussels in September 2012 as an oral presentation. Other dissemination activities (oral presentation, posters and scientific articles) will be further developed and proposed beyond the end the Cluster.

Some of the cluster partners have been implementing the DES project aiming to develop an interactive web based database including activities, actors, policy goals related to environment and health (cf. Belspo Agora projects). Workshops organised in the framework of that other complementary project has supported the dissemination and networking activities undertaken in the framework of the cluster.

5. Publications

- Special number (n°11) of the “Cahiers du Fonds Houtman” published in December 2010 and available in French on the Fonds Houtman website
<http://www.fondshoutman.be/cahiers>
- Marie-Christine Dewolf, Dr. E. Noël, Ph. Fierro, W. Fris, P. Bouvriez, M. Hakimi, A. Marijns, C. Passelecq, W.H. Zhang (2010) Biomonitoring study of children exposed to different levels of pollution in the Hainaut Province, Belgium, Poster presented at the 1st European Congress « Preconception Care and Preconception Health » and the conferences « Human Biomonitoring : Political benefits – scientific challenges » and “Environmental health and social vulnerabilities”
- Dewolf MC., Charlet F., Roger M., Kuske M., Bladt S., Chasseur C., Worobiec A., Horemans B., Biot P., Mampaey M., Berhin MP., Vanderheyden N. , Peeters H., Verlaek M. (2010) Development of an auto-assessment tool and analysis of the indoor environment in Belgian nurseries”, Poster presented at the 1st European Congress « Preconception Care and Preconception Health » and the conference “Environmental health and social vulnerabilities”
- Dr. Noel E., Roger M., Dewolf MC. (2010) Lead poisoning and other infantile pathologies associated to housing, Poster presented at the 1st European Congress « Preconception Care and Preconception Health » and the conference “Environmental health and social vulnerabilities”
- Wei-Hong Zhang, Marie-Christine Dewolf, Samia Hammadi, Wendy Fris, Etienne Noël, Rosalie Lorenzo, Sophie Alexander, the PLOMB 6 Group (2011) Lead levels in umbilical cord blood in Belgium: A cross-sectional study in five maternity units, International Journal of Hygiene and Environmental Health
- Marie-Christine Dewolf, François Charlet, Hans Scheers, Luc Int Panis and Rosette Van Den Heuvel, Stratégies pour définir des valeurs "de référence", Abstracts submitted to the Fifth International Congress on Epidemiology (ADELF/EPITER), September 2012

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8. Annexes

ANNEX 1: EXCELL FILE ACTORS

ANNEX 2: EXCELL FILE PARAMETERS

ANNEX 3: STUDY QUESTIONNAIRE (REVIEWED VERSION OF THE ANIMO QUESTIONNAIRE)

ANNEX 4: LPI SITE VISIT DOCUMENT (TABLEAU MÉDICO-SOCIAL)

ANNEX 5: CORRELATION GRAPHS

THE ANNEXES ARE AVAILABLE ON OUR WEBSITE:

[HTTP://WWW.BELSPO.BE/BELSPO/SSD/SCIENCE/PR_CLUSTER_EN.STM](http://www.belspo.be/belspo/ssd/science/pr_cluster_en.stm)