SEVENTH FRAMEWORK PROGRAMME
THE PEOPLE PROGRAMME

Grant agreement for: **Initial Training Networks**

Annex I - "Description of Work"

Project acronym: INFLAME
Project full title: Indoor Contamination with Flame Retardant Chemicals: Causes and Impacts
Grant agreement no.: 264600
Date of approval of Annex I by Research Executive Agency :

PART A:
A 1 List of beneficiaries and project summary

A.1.1 List of Beneficiaries

Beneficiary Number *	Beneficiary name	Beneficiary short name	Country	Date enter project**	Date exit project**
1a (Coordinator)	School of Geography, Earth & Environmental Sciences, University of Birmingham	UB1	UK	Month 1	Month 48
1b	School of Biosciences, University of Birmingham	UB2	UK	Month 1	Month 48
2a	Department of Pharmaceutical Sciences, Toxicological Center, University of Antwerp	UA1	Belgium	Month 1	Month 48
2a	Ecophysiology, Biochemistry and Toxicology, University of Antwerp	UA2	Belgium	Month 1	Month 48
3a	Institute for Environmental Studies, Free University of Amsterdam	VU1	Netherlands	Month 1	Month 48
3b	Institute for Health Studies, Free University of Amsterdam	VU2	Netherlands	Month 1	Month 48
4	Environmental analysis and Technology, Flemish Institute for Technological Research	VITO	Belgium	Month 1	Month 48
5	Swedish Environmental Research Institute Limited	IVL	Sweden	Month 1	Month 48
6	Department of Applied Environmental Science,	SU	Sweden	Month 1	Month 48

	Stockholm University				
7	Department of Analytical Chemistry, Norwegian Institute of Public Health	NIPH	Norway	Month 1	Month 48
8	Amsterdam Medical Centre, University of Amsterdam	UvA	Netherlands	Month 1	Month 48
9	Department of Soil Science, Reading University	UoR	UK	Month 1	Month 48

List of Associated Partners

List of Associated partners including the level of participation and organisation status

Associated partner Number	Associated Partner name	Associated Partner short name	Country	Role in the project (*)	Organisation Status (**)
1	Maverick Television	MAV	UK	Complementary skills training	Private
2	Phosphorus, Inorganic and Nitrogen Flame Retardants Association	PINFA	BE	Complementary skills training	Private

A.1.2 Project Summary

Free Keywords: Environmental science, Environmental protection, Exposure assessment, Health and environment (Environmental protection), Control of chemicals

Abstract:
The main research goal is to further understanding of how and to what extent flame retardant (FR) chemicals used in every-day consumer goods and construction materials enter humans and of the risk to health that such exposure presents. Our vision is that this enhanced understanding will inform assessment of risk associated both with recent and current-use flame retardant chemicals, and of those under development, and ultimately lead to more sustainable approaches to meeting fire safety regulations. Our principal objectives are to discover:
(1) the mechanisms via which FRs migrate from products within which they are incorporated;
(2) how and to what extent such migration leads to human exposure; and
(3) the effects of such exposure.
To achieve our goal and objectives we will use a range of state-of-the-art techniques associated with analytical chemistry, electron microscopy, mathematical modelling, in vitro toxicology, and "omics". The network is an interdisciplinary cooperative of chemists, biologists, physicists and toxicologists. Intersectoral aspects unite basic and applied scientists working in universities, two SMEs, a large (nonuniversity) public sector research organisation and a government research institute. The project's S&T objectives will be delivered through research in 3 Work Packages (WPs): viz. WP1- Migration pathways, WP2- Human exposure (pathways and monitoring), and WP3-Understanding effects of human exposure. The aim of the Training Programme is to increase the knowledge base and experience of trainees in the different research areas and to develop their transferable skills for future careers in the private sector, public sector, or the regulatory community. Six training objectives will be

delivered through a suite of 6 Core Skills Areas (Research Project, Advanced Training Courses, Project Meetings, Career Development Plan, Generic Research Skills, Transferable Research Skills).

PART B:

Table 1: List of acronyms used in Appendix 1

Acronym	Definition
FR	Flame retardant
RO	Research objective
TO	Training objective
ATC	Advanced training course

B.1 Description of the joint Research Training Project

B.1.1 Project Overview

The main research goal is to further understanding of how and to what extent flame retardant (FR) chemicals used in every-day consumer goods and construction materials enter humans and of the risk to health that such exposure presents. Our vision is that this enhanced understanding will inform assessment of risk associated both with recent and current-use flame retardant chemicals, and of those under development, and ultimately lead to more sustainable approaches to meeting fire safety regulations. Our principal objectives are to discover:
(1) the mechanisms via which FRs migrate from products within which they are incorporated;
(2) how and to what extent such migration leads to human exposure; and
(3) the effects of such exposure.
To achieve our goal and objectives we will use a range of state-of-the-art techniques associated with analytical chemistry, electron microscopy, human biomonitoring, *in vitro* toxicology mathematical modelling, and "omics". The network is an interdisciplinary cooperative of chemists, biologists, physicists and toxicologists. Intersectoral aspects unite basic and applied scientists working in universities, two SMEs, a large (non-university) public sector research organisation and a government research institute. The project's S&T objectives will be delivered through research in 3 Work Packages (WPs): viz. WP1- *Migration pathways*, WP2- *Human exposure (pathways and monitoring)*, and WP3- Understanding effects of human exposure.
The aim of the Training Programme is to increase the knowledge base and experience of a cohort of trainees (12 ESRs and 2 ERs) in the different research areas and to develop their transferable skills for future careers in the private sector, public sector, or the regulatory community. To date, while the environmental impacts of FRs are the subject of intense global interest, the majority of research is conducted by research groups isolated within their own narrow disciplines. This approach whereby groups pursue their own research in *e.g.* analytical chemistry, exposure assessment, and toxicology *etc.* in isolation is a major obstacle to developing sustainable approaches to achieving flame retardancy given the supradisciplinary nature of the issues that require to be addressed. Furthermore, exchange of knowledge between policy-makers and the research base in academia, government institutes, and the private sector is restricted by their differing perspectives and drivers. Our **training vision** is thus to develop a cohort of young scientists with the necessary depth and breadth of experience combined with the research and transferable skills required to communicate and work effectively across disciplinary and sectoral boundaries. Moreover, we envisage that INFLAME will lead to collaborations beyond the network's lifetime that will facilitate the further development and

optimisation of programmes for training future cohorts of researchers capable of supradisciplinary work. In particular, we will harness complementary public and private sector expertise in research, training, e-learning technology, market identification and exploitation to develop a lasting legacy of research training materials. Within INFLAME, six training objectives will be delivered through a suite of 6 Core Skills Areas (Research Project, Advanced Training Courses, Project Meetings, Career Development Plan, Generic Research Skills, Transferable Research Skills).

B.1.2 Concept and Project Objective(s)

Background to the Research Topic

There is mounting evidence that FRs have migrated into the environment. Therefore, the **overriding hypothesis** that INFLAME will test, is that the FRs present in everyday consumer goods, toys, and building materials, are contaminating the environment at levels that constitute an important pathway of human exposure to these chemicals, at levels detrimental to human health. There is already substantial evidence that concentrations of brominated FRs like polybrominated diphenyl ethers (PBDEs) and hexabromocyclododecane (HBCD) in indoor environments are of a magnitude that represents a potential *direct* exposure hazard via inhalation and ingestion of dust. INFLAME will explore further emerging evidence that indoor contamination by FRs constitutes a significant source of these chemicals to the outdoor environment. For FRs capable of bioaccumulation, such indoor contamination contributes potentially to future human exposure (*indirectly*) via the diet. Furthermore, continuing emissions of FRs even after restrictions on their manufacture are introduced, will lead to on-going future exposure both *directly* and *indirectly*. INFLAME will investigate continuing emissions from flame-retarded goods both while in use and post-disposal (e.g. electronic waste).

Against this backdrop, the **overall aim** of the INFLAME project is to **improve understanding of the processes** via which chemicalsincorporated as FRs within consumer goods and building materials migrate into indoor air and dust; the extent of this contamination and its influence on human exposure and the impacts of such exposure on human health. Ultimately, **our vision** is that such enhanced understanding of the underpinning science will lead to **more environmentally sustainable approaches to compliance with fire safety regulations within Europe**, while facilitating development of strategies to mitigate the impacts of both currently and recently-used FRs. To achieve this, INFLAME has 3 complementary research objectives (ROs):

RO1: *to comprehend better the mechanisms via which FRs in consumer goods and construction materials migrate into and behave in the indoor environment, the extent of such migration, and to horizon-scan such goods and materials (while in-use and after end-of-life) for FRs likely to constitute future monitoring and risk assessment targets (achieved through WP1).* Achievement of this RO will: (a) facilitate the development of strategies (e.g. new FRs and/or methods of incorporation into goods) to minimise migration of FRs from consumer products to the environment and (b) enable potential problems associated with "emerging" FRs and disposal of flame-retarded items to be addressed earlier and more rapidly thereby reducing the legacy of contamination.

RO2: *to develop understanding of the extent to which indoor contamination with FRs impacts on human exposure. An important component will be an effort to develop methods via which exposure of infants and toddlers can be monitored. Exposure via both direct ingestion of dust and inhalation of indoor air will be considered, as well as indirect dietary exposure arising via migration of indoor contamination to outdoors and subsequent incorporation within the food chain (achieved through WP2).* By identifying the relative role exerted by different exposure pathways on overall human exposure, INFLAME will help regulators develop effective approaches to minimising body burdens. Moreover, INFLAME's novel consideration of prospective dietary exposure arising from indoor application of FRs, will help develop strategies to minimise such exposure. INFLAME will also help develop non-invasive approaches to biomonitoring infants and toddlers;

RO3: *to advance our knowledge of the effects of exposure to FRs arising from their indoor use using human and animal in vitro toxicological tests and a mouse model (achieved through WP3).* Achieving this will help identify the mechanisms of action of FRs at multiple levels of hierarchy including gene

expression, protein levels and metabolite concentrations, in both cellular and mammalian models. The 'omics approaches used will be capable of detecting the anticipated alterations within molecular pathways as well as potentially novel modes of toxicity. The potency of the FRs will be established in relation to cellular toxicity endpoints and the disturbance of critical adverse effects pathways informed by 'omic analyses and associated bioinformatics. Ultimately this will help guide understanding of the mechanisms of FR effects in biological systems and the dose-response relationships and facilitate the development of scientifically robust health based limits to protect public health.

B.1.3 Scientific and technological objectives of the research and training Programme

Research

Delivery of the research objectives will be achieved through work in 3 complementary Work Packages (WPs), each involving multiple teams (Table 2). Table 3 describes the different trainee projects.

Table 2: Outline of Work Packages

WP1- Migration Pathways (Lead – UA1; Principal partners UA1, UB1, VITO, IVL, VU1, & SU)
The **objective of WP1 is to further understanding of how FRs employed in indoor applications migrate into the environment (both indoor and outdoor).** WP1 consists of 6 linked projects involving 5 ESRs and 1 ER. The overall approach is to enhance the currently limited knowledge about how FRs incorporated within consumer goods and building materials migrate into the indoor environment. Moreover, while to date most research in this area has addressed issues pertaining to indoor contamination with brominated FRs (BFRs), like PBDEs and HBCDs; recent and impending restrictions on the use of such BFRs with no concomitant changes in fire safety legislation, means that use of alternative FRs is likely to be increasing. Hence, WP1 includes a "horizon-scanning" characterisation of such "emerging" FRs in contemporary indoor environments, in currently-used flame-retarded materials and also in discarded materials (ESR1 and ER1). The outputs of this "horizon-scan" will feed dynamically on an on-going basis into INFLAME as a whole, and where feasible, an "emerging" FR identified within WP1 will be included in other trainee projects. For example, either monitoring exposure to such FRs (WP2) or evaluating the effects of such exposure (WP3). ESR2 and ESR3 use state-of-the-art technology (environmental scanning electron microscopy and the VITO emission test chamber) in a novel fashion to address the lack of understanding about how and at what rate FRs migrate into indoor air and dust. Similarly, ER1 will use sophisticated instrumentation (hyphenated chromatography-mass spectrometry, XRF and laser ablation ICP-MS) to further understanding of the pathways of FR migration from discarded materials into the outdoor environment. Data provided by ESR2 and ESR3 will contribute valuable input data for ESR4 who will construct mathematical models of the fate of FRs within the indoor environment. The project of ESR5 takes a mixed experimental and modelling approach to evaluating the influence that indoor contamination can exert on outdoor contamination.
WP2- Human Exposure (Pathways and Monitoring) (Lead –SU; Principal partners NIPH, UoR, VU2, VITO & SU)
The **objective of WP2 is to develop knowledge of the extent to which indoor contamination with FRs contributes to human body burdens**. It comprises 5 related projects offering training to 4 ESRs and 1 ER. The project of ESR6 takes an experimental approach to elucidate the extent to which body burdens of adult volunteers and their children are correlated with external exposures via indoor air, dust, and diet. Complementary to ESR6, ER2 uses data generated by ESR6 (and also ESR4 and ESR5) as source term data for a mathematical model linking human body burdens with external exposure via dietary intake, indoor air and dust. A crucial knowledge gap is the extent to which FRs present in indoor dust are absorbed across the gastro-intestinal tract, and ESR7 uses a state-of-the-art physiologically based extraction test method to examine the extent of such absorption and the factors that affect it. This issue is particularly pertinent in scenarios where concentrations of FRs could lead

to exposure at levels thought detrimental to health, where bioaccessibilities well below 100% would diminish the risk substantially. Likewise, current assessments of human exposure to FRs via ingestion of contaminated indoor dust use estimates of the quantity of indoor dust ingested by humans that are based on a very small number of primary studies designed to derive estimates of soil ingestion. This crucial research gap will be addressed by ESR8. Finally, while ingestion of dust has been suggested as a particularly important exposure pathway for young children, evidence for this remains inconclusive. This is largely because efforts to identify the principal exposure pathways to FRs for young children on an individual basis have foundered due to the conflict between analytical requirements for large blood sample volumes and ethical and practical constraints of procuring such samples from individual children. Hence, ESR9 will evaluate the utility of non-invasive matrices such as hair, nails, urine, and saliva for providing accurate measures of internal exposure to FRs.
WP3-Understanding Effects of Human Exposure (Lead – VU1; Principal partners UA2, UB2, UvA & VU1)
The **objective of WP3 is to further understanding of the effects of human exposure to FRs.** To do so, a co-ordinated combined genomics, metabolomics, and proteomics approach will be taken involving three partners with significant expertise in these areas. Reciprocal secondments and visits of the three ESRs in this WP (as well as with other trainee projects) will provide a particularly rich training environment. At UA, ESR10 will evaluate the toxicological mode of action of FRs in relation to general stress responses and endocrine disruption. For this goal, a battery of engineered and targeted eukaryotic and prokaryotic *in vitro* systems will be exposed to indoor air and dust samples as well as to relevant pure compounds. Besides more general reporter gene assays, work will be performed on mammalian *in vitro* systems (i.e. MCF-7, HepG2, H295R) using a combination of proteomic and flow cytometric techniques which will provide a comprehensive mechanistic and cell physiologic profiling of the samples and FRs, that complements the powerful and novel combination of transcriptomic and metabolomic approaches to developing biomarkers of human exposure and effect used by ESR11 at UB2. There will also be specific 'omic analyses completed at UB2, e.g. use of complementary mammalian microarrays. These studies will focus on mammalian (including human) cellular systems. ESR12 at UvA/VU1 will investigate the potential immunomodulatory role of FRs to facilitate or aggravate the immune response to inhaled allergens in a murine asthma model. A set of FRs representing different chemical classes (e.g. BFRs, organophosphorus FRs (OPFRs)) will be selected based on their relevance for human exposure (including those determined by ESR1). An important benefit of INFLAME's holistic approach is that WP1 and WP2 provide information within the same closely integrated training programme on the levels of human exposure against which WP3's enhanced understanding of the effects of such exposure may be placed. The training opportunities afforded by this will be exploited by the fact that ESRs 10, 11, and 12 will learn techniques for environmental monitoring (either via a training visit - ESR12 – or from other centres of expertise within their host institutions – ESRs 10 & 11). These will be applied to the acquisition of air and dust samples necessary for their projects.

Table 3: Description of trainee research projects

Trainee & Lead beneficiary	Title and Description of Project
	Early Stage Researchers
ESR1 UA1	*Migration Pathways to the environment – "Horizon Scanning" for FRs present in consumer goods and construction materials* – see also ER1. At UA1 and complementary to the work of ER1 at VU1, a broad range of commonly-used consumer goods (electronics, furniture, carpets, curtains, plastic toys etc.) and building construction materials will be investigated using screening tools such as GC-MS and LC-TOFMS. The principal focus will be on identifying and quantifying FRs hitherto

	either un- or rarely-detected. Any such "emerging" FRs detected in products will be screened for their presence in indoor air and dust. The work of ESR1 contributes to WPs 2 and 3, by highlighting and providing analytical methods for "emerging" FRs that where feasible will be investigated by other trainees. Moreover, during a secondment to VU1, ESR1 will conduct studies to estimate leaching of FRs present in hard plastic toys as a result of "mouthing" by infants and toddlers. ESR1 thus contributes to WP2 by enhancing estimates of such exposure.
ESR2 UB1	*Using forensic microscopy to elucidate pathways of halogenated FR migration into indoor dust*. At UB1 and complementary to the work of ESRs 3, 4, 5, & 7, forensic microscopic techniques (e.g. environmental scanning electron microscopy (ESEM) and energy dispersive X-ray microanalysis (EDX)) will be utilised to elucidate the mechanisms via which halogenated FRs enter indoor dust. ESR2 will test the hypothesis that more volatile FRs evaporate from treated goods before partitioning to dust, thus leaving a fingerprint of homogeneous distribution of halogen throughout the dust (detectable via XRF). In contrast, non-volatile FRs are hypothesised to enter dust via abrasion of particles or fibres from treated goods, thus leaving a highly heterogeneous halogen distribution within dust. Initial experiments will be conducted using dust acquired from UB1's extensive sample bank. During the secondment to VITO (involving collaboration with ESR3), ESR2 will utilise their emission test chamber to acquire additional dust samples associated with the presence of known sources of halogenated FRs of different volatility. These samples will be examined using ESEM/EDX at UB1. Visits will also be made to IVL and SU to exploit synergies with ESR4 and ESR5 – specifically by provision of emission factors, and also to benefit from synergies with the on-going Swedish ChEmiTecs project "Emissions of organic substances from Technosphere articles", co-ordinated by IVL (see also ESRs 3 & 4). ESR2 will also visit UoR and provide dust samples for bioaccessibility testing (ESR7), and visit VU1 for exposure to techniques for measurement of "emerging" FRs. Contribution to WP3 will be made by the provision of chemically-characterised dust samples for *in vitro* testing by ESR10 and ESR12.
ESR3 VITO	*Determining FR emission factors from treated goods*. At VITO, ESR3 will use their state-of-the-art emission test chamber ($1m^3$) to determine emission factors of FRs from a range of potential source items (e.g. PCs, consumer electronics, fabrics, building materials, etc.). Experiments will be conducted under a range of environmentally relevant conditions (e.g. air exchange rate, relative humidity, room temperature) selected to reflect plausible indoor conditions in different microenvironments (homes, offices) and different climates. Air and dust samples generated during these experiments will be analysed for FR content. Additionally, feasibility of the methodology downscaling will be assessed using a micro emission test chamber. Determination of HBCDs in samples will be conducted during a secondment to UB1 to provide experience of a different research culture with specific expertise in this task and to facilitate networking with ESR2. Visits will also be made to IVL and SU to exploit synergies with ESR4 and ESR5 via provision of emission factors and also to benefit from synergies with on-going work at IVL on product emissions (ChemiTecs project) – see also ESRs 2 & 4. A further visit will be made to UA1 for exposure to techniques for measurement of "emerging" FRs.
ESR4 IVL	*Modelling indoor emissions and fate of FRs*. At IVL, ESR4 will exploit outputs of ESRs 1, 2, 3, and 5 as a basis for the development of fate models assessing the indoor fate of both "established" and "emerging" FRs. While the models developed will focus largely on pure indoor models, taking a detailed approach to indoor processes, consideration will be given to the impact of the indoor environment in larger context, e.g. the urban or even the regional scale. In this respect, there will be significant complementarity with the modelling work of ESR5 at SU. The models developed will build on previous work e.g.[1, 2], but will also take into account new information derived

[1] Zhang, X. et al. *Environ. Sci. Technol.* **2009**, *43*, 2845–2850.

	from e.g. the currently on-going Swedish research programme ChEmiTecs, co-ordinated by IVL (ChEmiTecs aims to identify and quantify emissions of organic chemicals from products in use, thus complementing activities of ESR2 and ESR3) and from ESRs 5 & 6. Models will be developed in a suitable programming environment, e.g. Visual Basic for Excel, Matlab for pure indoor models or in a GIS environment for urban/regional scale models. The work at IVL will be performed in close collaboration with the modelling group at SU, and ESR4 will be seconded to SU to exploit training synergies with ESR5 and ER2. ESR4 will also undertake visits to both VITO and UB1 to interact with ESRs 2 and 3 to develop understanding of the processes via which FRs migrate from products into the indoor environment, and to benefit from emission factors derived by these ESRs.
ESR5 SU	*Determining the contribution of indoor air ventilation to outdoor contamination*. At SU, ESR5 will quantify FRs in outgoing air from building ventilation systems, as well as outdoor air, and topsoils from an urban site near the city and a rural site (background air monitoring station 90 km SW of Stockholm). Data generated will provide source terms to enable optimisation of an existing multimedia fate model of Stockholm to quantify the contribution of indoor environments to outdoor concentrations, and permit comparison of predicted *vs* observed outdoor air concentrations. During a secondment to UB1, ESR5 will exploit in a source apportionment context, the forensic utility of chiral signatures of FRs like HBCDs to evaluate relationships between indoor and outdoor air. Contribution to WP2 is provided by links to ER2. Visits will be made to VU1 and UA1 for exposure to techniques for measurement of "emerging" FRs, and to IVL for exposure to alternative modelling approaches.
ESR6 NIPH	*An experimental approach to examining correlation between external exposure and human body burdens* – see also ER2. At NIPH, ESR6 will collect matched samples of indoor air, dust, hair, saliva, and urine from 40 households each comprising mother and 1 child aged 6-12 years. Blood serum will be collected from mothers and if possible from the child, with dietary intake for mothers and children estimated via food frequency questionnaire. Training in collection of air and dust samples will be provided by an initial short secondment to SU. This secondment will also provide opportunity to benefit from synergies with the work of ER2, with similar benefits provided by a visit to VITO (ESR9). ESR6 will determine concentrations of "persistent" FRs (PBDEs and HBCDs) and of emerging "metabolisable" FRs (brominated phthalates and organophosphorus FRs - OPFRs) in air and dust during a 2nd secondment to SU. PBDEs and HBCDs will be determined in serum samples and "metabolisable" FRs in urine at NIPH. Hair, nail, and saliva samples will be analysed by ESR9 (see below). Total external exposure will be estimated for children and adults separately from data on the indoor environment and food frequency questionnaires. These exposure estimates will be compared to information on internal exposures obtained from urinary excretion ("metabolisable" FRs) and blood concentrations ("persistent" FRs). Approval for the study will be sought from the local Committee for Medical and Research Ethics and Data Inspectorate. *Exposure to complementary state-of-the-art analytical techniques will be provided by visits to VU1 & UA1.*
ESR7 UoR	*Determining the bioaccessibility of FRs in indoor dust*. At UOR, ESR7 will use a colon enhanced physiologically based extraction test (CEPBET) configuration to examine the extent to which BFRs present in dust are available in the human gastrointestinal tract for uptake across biological membranes (bioaccessible). The influence on bioaccessibility of a variety of factors will be investigated including: BFR concentration and physicochemical properties; properties of dust like particle size and organic carbon content; the quantity of dust ingested; and physiological

[2] Bennett, D. H.; Furtaw, E. J. *Environ. Sci. Technol.* **2004**, *38*, 2142-2152.

	factors such as fed and fasted state. A further factor linked strongly with ESR2, is the influence on bioaccessibility of the mode of FR incorporation within the dust. The hypothesis to be tested is that bioaccessibility is reduced in highly contaminated dusts where FR contamination is highly heterogeneous arising from the presence of a small number of abraded particles/fibres of high FR content (see ESR2). ESR7 will examine dust samples provided by ESR2 for which information is available on the mode of FR migration to the dust. ESR7 will undertake secondments to UB1 to receive training in indoor dust sampling and experience of forensic microscopy and to VITO to conduct determination of FRs in samples. Exposure to complementary state-of-the-art analytical techniques will be provided by visits to VU1 and UA1.
ESR8 VU2	*The relevance of indoor dust for human exposure*. At VU2, ESR8 will develop an integrated approach to assess the relevance of indoor dust for human exposure to FRs by means of observational studies (e.g. of hand/mouth-to-object and hand-to-mouth contact), personal sampling (inhalation and handwipes), saliva analyses, markers of dust and behavioural questionnaires. A method to quantify the observational data will be developed as well as specific questionnaires with regard to the indoor environment. The observational and questionnaire data used to assess exposure to indoor dust will be compared with concentrations of markers of dust in samples obtained via personal body sampling (e.g. via handwipes) and in saliva. A secondment to VITO (ESR9) will provide additional training in analysis of saliva. This will be augmented by further visits to SU for training in personal inhalation sampling, and to UB1 and UoR to exploit synergies with ESRs 2 and 7.
ESR9 VITO	*Developing non-invasive methods for monitoring human body burdens*. At VITO, ESR9 will explore the utility of non-invasive matrices like hair, saliva, and urine as biomarkers of internal exposure to FRs. A secondment to UA1 will provide additional training in sampling and preparation for analysis of such matrices. Concentrations of FRs in such samples will be examined for correlation with those present in matched samples of validated biomarkers such as blood serum. Samples will be collected during a secondment to NIPH exploiting training synergy with ESR6. *Exposure to complementary state-of-the-art analytical techniques will be provided by visits to VU1 and UA1.*
ESR10 UA2	*Mechanistic profiling of flame FRs in general systemic stress and endocrine disruption*. At UA2, ESR10 will evaluate the stress-related and endocrine disruptive mechanisms of toxicity of FRs present in indoor air and dust. For this purpose, a battery of targeted prokaryotic and human *in vitro* systems is implemented (E. coli, MCF-7, HepG2, H295R). Both indoor air and dust samples acquired in collaboration with UA1, as well as relevant pure compounds will be tested. In this way, not only a fast screening of the stress-inducing and endocrine disruptive activity of the samples, but also a more in depth evaluation of the mode of action of relevant FRs is provided. A combination of proteomic and flow cytometric techniques will allow a comprehensive mechanistic and cell physiologic profiling of FRs that complements the genomics and metabolomics approach of ESR11. Based on the mechanistic profiles obtained from air/dust samples as well as from pure compounds, interesting new biomarkers can be derived. Secondment to UB2 and a visit to UvA will exploit the synergies with ESRs 11 and 12. Target FRs will be selected based on their relevance for human exposure as determined by ESR1 and ER1 (WP1). UA2 and UB2 have complementary bioinformatic expertise and therefore both will contribute to the interrogation of the 'omic datasets and the derivation of predictive biomarkers.
ESR11 UB2	*A transcriptomic and metabolomic approach to biomarkers of exposure and effect*. At UB2, ESR11 will apply two state-of-the-art complementary approaches for metabolomic measurements: direct infusion Fourier transform ion cyclotron resonance mass spectrometry (FT-ICR MS) and ^{1}H nuclear magnetic resonance (NMR) spectroscopy. These will be used to study the metabolic consequences of air and dust exposures to several engineered eukaryotic and prokaryotic cell lines (in collaboration with UA and ESR10). ESR11 will also study samples from a murine asthma model

	(ESR12) The transcriptomic analyses conducted by ESR11 will focus on human and mouse Agilent microarrays. Raw data will be captured by Axon GenePix 4000B. Experiments will comply with MIAME/MGED. Data will be deposited in ArrayExpress using Maxdload2. Functional significance of gene expression changes will be assessed by hierarchical clustering and Gene Ontology using the Blast2GO. We will use qRT-PCR to quantify gene transcript levels of selected candidate genes. Bioinformatic analyses will identify combinations of molecular markers associated with specific treatments and phenotypic responses. Data analysis will be based primarily on multivariate methods, designed to select "optimal" subsets of features predictive of an outcome variable. Initially data will be analyzed by univariate hypothesis-testing techniques identifying differentially-expressed genes and metabolites across different exposure groups. This initial analysis will - combined with pathway analysis software tools - identify the pathways potentially involved in response to FRs. Modelling will be performed at the gene level as well as on indices of pathway activity in order to facilitate mechanistic interpretation. Secondment to UA2, and a visit to UvA will exploit the synergies with ESRs 10 and 12 including the associated transcriptomic analyses. Moreover, during the secondment to UA2, ESR11 will benefit from UA2's expertise and facilities in hyphenated chromatographic-mass spectrometric techniques to help establish a complementary analytical platform for metabolomics studies. The work of ESR11 will be informed by the FRs identified by ESR1 and ER1 (WP1). Air & dust samples for study will be procured in collaboration with UB1.
ESR12 UvA	*The role of FRs in indoor dust in potentiating/facilitating allergic responses to inhaled allergens*. In collaboration between UvA and VU (where a series of secondments will take place), ESR12 will test the hypothesis that FRs present in indoor air and/or dust can act as an adjuvant for the induction of immune responses against indoor allergens. This hypothesis is based on the observation that both indoor exposure to FRs and the prevalence of asthma have increased tremendously over the last decades. In atopic asthma, allergens, like house dust mite, provoke an aberrant immune response. ESR12 will investigate the potential immunomodulatory role of flame retardants to facilitate or aggravate the immune response to inhaled allergens in a murine asthma model. A set of FRs representing different chemical classes (e.g. BFRs, OPFRs) will be selected based on their relevance for human exposure as determined by ESR1 and ER1 (WP1). Underlying mechanisms of FR-related immuneresponses will be elucidated using transgenic and knockout mice, flow cytometry, ELISA, histology and in vitro co-cultures of immune cells. Mechanistic research is further supported by proteomics and metabolomics analyses to be performed in close collaboration with UA2 (where a secondment will be made to work with ESR10 on proteomics) and a visit to UB2 (to discuss the results of metabolomics analyses conducted on murine asthma model samples by ESR11), respectively. Allergenic markers for exposure to FR will be identified and their prognostic value for allergenic potencies of individual compounds will be studied in *in vitro* models such as lung epithelial cells. Finally, the potency to induce an allergic response will not only be determined for pure compounds, but also for allergen-free extracts from house-dust samples collected by ESR 8 and/or reconstituted mixtures reflecting FR-profiles in real-life house-dust samples. A visit will be made to SU where experience will be gained of air and dust sampling methods.
	Experienced Researchers
ER1 VU1	*Migration Pathways to the environment –"Horizon Scanning" for FRs present in e-waste* – see also ESR1. At VU1, complementary to the work of ESR1 at UA1 (to whom ER1 will provide additional supervision and training), ER1 will exploit the potential of state-of-the-art GCxGC-TOF-MS techniques coupled with sophisticated multivariate data analyses to identify and quantify concentrations of both "established" and "emerging" FRs in a range of electronic waste. The same techniques

	will be applied to field and laboratory studies of weathering of flame-retarded polymers and FR migration to water and soil. Conditions studied will mimic those encountered during outdoor storage of waste materials and post-disposal in landfill. Methods will be developed to follow the biodegradation of BFRs in waste from landfills using rapid in vitro assays (e.g. microsomes). Further, XRF and laser ablation ICP-MS detection techniques will provide information on weathering. ER1 will undertake a secondment to UA where complementary analytical techniques like LC-Q-TOF-MS will provide additional information.
ER2 SU	*Examining correlation between external exposure and human body burdens – a modelling approach* – see also ESR6. At SU, ER2 will mathematically model the relationships between a range of FRs in indoor air, dust, diet, and human tissues. Data generated by ESR6 on air, dust, and human tissue contamination with FRs will provide source term and output data for the model. Additional data will be obtained via collaboration with ESRs 2 and 3. Target FRs will be informed by those determined by ESR1 and ER1 (WP1), but will include PBDEs, HBCDs, brominated phthalates, and OPFRs. ER2 will provide important additional technical training to ESR4 and ESR6 on the complex scientific processes relating external and internal exposure and how these may be represented via mathematical modelling. ER2 will undergo secondments to NIPH and IVL, and a visit to UB1; to gain experience of human biomonitoring (NIPH), exposure to alternative modelling approaches (IVL), and experience of alternative air and dust sampling methods (UB1).

Risk and contingency plan

Each of the individual research projects (ESR1-12 and ER1 and 2) that constitute the INFLAME programme is embedded into the research programme of the main host group. In every instance, the host group is internationally leading in that area of research, has proposed the topic of the project they will host and thus have "ownership" of the project in a very real sense. As a result, the specialist research equipment and expertise required to conduct each project successfully is inherently available to each fellow. Moreover, where human volunteers require to be recruited, the host organisations have substantial experience with such issues. Progress with all research projects will be monitored at the network level via 6-monthly reports, and any signs of significant difficulties can be addressed by the supervisory board. Possible contingencies for projects experiencing unforeseen difficulties will be discussed and if necessary alternative research objectives and strategies for that project agreed with all parties. This is in addition to the progress monitoring procedures in place within individual partner organisations. Overall then, no insurmountable problems are anticipated with the completion of any of the individual projects. Timely recruitment of high-quality fellows is a related concern. However, each host organisation is well-versed in recruitment of early stage researchers, and will make full use of all appropriate recruitment portals. The generous stipends available to appointed fellows will ensure that recruitment can be made from a large pool of highly-qualified applicants, and problems with recruiting fellows of the required standard are not anticipated. The planned programme of secondments and visits by fellows between partners is also not thought to present significant risks. This is partly because the programme will be monitored and reviewed regularly to ensure that secondments and visits will take place at the times that are of maximum benefit to the fellows and their projects. Moreover, these secondments and visits are considered highly likely to succeed as there is already significant collaboration and exchange of personnel between the partners involved in INFLAME. With respect to the ATCs, the organisation of each will be the responsibility of a specific individual within the consortium. They will be responsible for preparing a draft

programme for the ATC, which will be discussed and if necessary amended prior to being approved by the supervisory board at the earliest possible opportunity. This will allow tutors to be booked as far as possible in advance and a suitable venue booked. The partners chosen to head each ATC will have significant previous experience of organising such events, and will also have the assistance where needed of the network administrator based at the co-ordinating organisation (e.g. in publicising ATCs and registering external participants). Finally, all of the partner organisations have substantial previous experience with participation in large collaborative European projects, and the administration and financial management issues associated with INFLAME are therefore not anticipated to present any difficulties.

Training

The network as a whole undertakes to provide a minimum of 480 person-months of Early Stage and Experienced Researchers plus 2 person-months of Visiting Researchers whose appointment will be financed by the contract. Quantitative progress on this, with reference to the table contained in Part C and in conformance with relevant contractual provisions, will be regularly monitored at the consortium level.

The network has the following Training Objectives (TOs):

TO1: To meet the expectations of potential employers in the academic, commercial, regulatory, and public sector research sectors by providing trainees with the range of research and analytical skills necessary to tackle specific research projects. This specialist knowledge will be coupled with a broad supradisciplinary understanding of the research challenges to be overcome and the approaches required to achieve sustainable flame retardancy.

TO2: To enhance the achievements of trainees by providing an optimum learning environment and by developing their capabilities for transforming the knowledge base into efficient research practices.

TO3: To promote transnational, interdisciplinary and intersectoral research whereby each trainee interacts with several teams and has access to all the joint research infrastructures.

TO4: To provide each trainee with transferable lifetime skills that will be valuable to trainees throughout their subsequent careers.

TO5: To require each trainee to formulate a Personal Career Development Plan including detailed planning of the research project and which graduate courses to follow.

TO6: To prepare all trainees for effective interaction and communication with stakeholders from all relevant sectors (e.g. public, research base, policy-makers, and flame retardant industry).

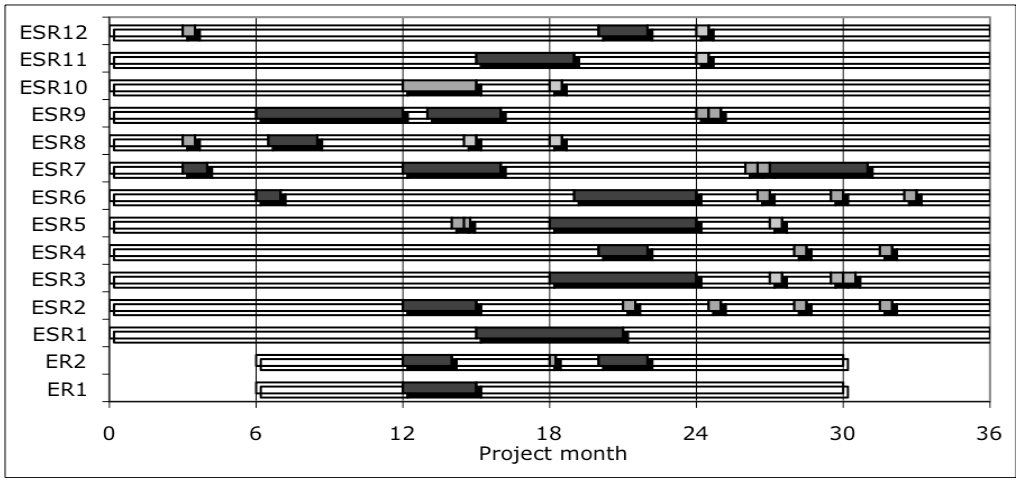
All ESRs and ERs will undergo at least one secondment to another partner as part of their training. The planned schedule for these is outlined in Table 4.

Table 4: Secondment Plan for Fellows (based on a start date of Project Month 1 for all ESRs and Project Month 6 for both ERs. Actual dates may be changed to accommodate fellows starting later than these dates. For example, if ESR1 starts month 6, then end month is 42, and secondment at VU1 will take place month 21-27)

Fellow code	Fellow type	Lead Beneficiary	Start month	End month	Secondment Host	Start month	End month
ESR1	ESR	UA1	1	36	VU1	15	21
ESR2	ESR	UB1	1	36	VITO	12	15
ESR2	ESR	UB1	1	36	IVL	21	21.5
ESR2	ESR	UB1	1	36	SU	25	25.5
ESR2	ESR	UB1	1	36	UoR	28	28.5
ESR2	ESR	UB1	1	36	VU1	31.5	32
ESR3	ESR	VITO	1	36	UB1	18	24
ESR3	ESR	VITO	1	36	UA1	27	27.5
ESR3	ESR	VITO	1	36	IVL	29.5	30
ESR3	ESR	VITO	1	36	SU	30	30.5
ESR4	ESR	IVL	1	36	SU	20	22
ESR4	ESR	IVL	1	36	VITO	28	28.5
ESR4	ESR	IVL	1	36	UB1	31.5	32
ESR5	ESR	SU	1	36	VU1	14	14.5
ESR5	ESR	SU	1	36	UA1	14.5	14.75
ESR5	ESR	SU	1	36	UB1	18	24
ESR5	ESR	SU	1	36	IVL	27	27.5
ESR6	ESR	NIPH	1	36	SU	6	7
ESR6	ESR	NIPH	1	36	SU	19	24
ESR6	ESR	NIPH	1	36	VITO	26.5	27
ESR6	ESR	NIPH	1	36	VU1	29.5	30
ESR6	ESR	NIPH	1	36	UA1	32.5	33
ESR7	ESR	UoR	1	36	UB1	3	4
ESR7	ESR	UoR	1	36	VITO	12	16
ESR7	ESR	UoR	1	36	VU1	26	26.5
ESR7	ESR	UoR	1	36	UA1	26.5	27
ESR7	ESR	UoR	1	36	VITO	27	31
ESR8	ESR	VU2	1	36	SU	3	3.5
ESR8	ESR	VU2	1	36	VITO	6.5	8.5
ESR8	ESR	VU2	1	36	UoR	14.5	15
ESR8	ESR	VU1	1	36	UB1	18	18.5
ESR9	ESR	VITO	1	36	UA1	6	12
ESR9	ESR	VITO	1	36	NIPH	13	16
ESR9	ESR	VITO	1	36	VU1	24	24.5
ESR9	ESR	VITO	1	36	UA1	24.5	25
ESR10	ESR	UA2	1	36	UB2	12	15
ESR10	ESR	UA2	1	36	UvA	18	18.5
ESR11	ESR	UB2	1	36	UA2	15	19
ESR11	ESR	UB2	1	36	UvA	24	24.5
ESR12*	ESR	UvA	1	36	SU	3	3.5
ESR12	ESR	UvA	1	36	UA2	20	22
ESR12	ESR	UvA	1	36	UB2	24	24.5
ER1	ER	VU	6	30	UA1	12	15
ER2	ER	SU	6	30	IVL	12	14
ER2	ER	SU	6	30	UB1	18	18.25
ER2	ER	SU	6	30	NIPH	20	22

** Fellow #12 (ESR12) will spend frequent periods at VU1, but these will not exceed 6 months overall*

Figure 1: Gantt Chart showing schedule of secondments and visits (secondments shaded dark, visits shaded light). For beneficiaries refer to Table 3.



Tailoring and complementarity of local training with network-wide training

Tailoring of the training: ESRs and ERs will work on research projects involving specific combinations of techniques and skills sets (Table 2). By definition, therefore, skills training must be tailored to individual trainees and Table 4 identifies the task-specific training that each will receive. Each trainee will have a clearly identified supervisor to whom they can refer for performance of their research. Trainees and supervisors will carry out an initial analysis of training needs (ITNA) based on the trainees' existing skills. The ITNA will be used to develop a Personal Career Development Plan (CDP), approved by the Supervisory Board, which will form the basis of the trainee's training programme and individualised learning outcomes. The training programme developed from the CDP will include a balance of training achieved through combinations of structured delivery methods tailored to the individual trainee. Progress on the CDP timetable will be checked every 6 months through a meeting between the trainee and supervisors. Trainees will submit 6-monthly written progress reports to be evaluated by the Director of Training and Director of Research. Trainees' presentations will be evaluated at 6-monthly Network Meetings, with feedback. Towards the end of the traineeship, trainees will update their CDP with input from the supervisors for implementation after the traineeship. ERs will contribute to the training programme by supporting ESRs via their own recent experiences as ESRs. ERs will be given more independence in managing their own research and shaping the nature of their collaborations within the network.

Combination of local- vs. network-wide- activities. *INFLAME* will extract maximum value from existing resources within the network, and create dedicated training opportunities beyond the capacities of individual institutions. Training in research skills is achieved via both local training and network-wide activities. Existing structured training courses will be exploited for local training; however, the list of training courses to be collated and made available by the Director of Training will allow trainees and supervisors to access training resources from elsewhere in the network. Where a training gap is identified for a specific trainee that is not addressed adequately at the host, then a training visit may be made to where the training is available. In addition, e-learning facilities (WebCT) at UB will be employed using management funds to allow training materials developed at one partner to be accessed on a network-wide basis. On-the-job research training will be delivered both locally and through secondments (Tables 2, 3, and 4). The five ATCs will exploit local expertise as well as pooling network-wide resources.

Advanced Training Courses (ATCs) – See B.2.2 Planning of conference

In addition to the public events described in session B.2.2, there will be an introductory orientation and training event to be held at UB in month 9. This is restricted to INFLAME researchers only as its aim is to encourage and foster supradisciplinary methods of working with specific reference to INFLAME.

Private sector involvement and commitment

Public-private sector collaboration in the field of environmental chemicals risk assessment is unusual and INFLAME involves a significant degree of such collaboration in the context of training the next generation of researchers contributing towards the development of sustainable solutions to achieving flame retardancy. IVL benefits from the expertise within the network and the possibility for future collaborations. Their commitment is demonstrated by the fact that IVL is a 'full' Participant, hosting a research project (ESR4), plus a secondment (ER2), visits from ESRs 2, 3, and 5, as well as hosting a Visiting Researcher, and guaranteeing network-wide access to their expertise and facilities. IVL will play also a significant role in the organisation, content and delivery of ATCs 4 and 5. With respect to ATC 5 and the Network Conference, the organisational role played by the IVL educational unit "IVL Kunskap" (IVL Knowledge) enables full access to large customer and stakeholder registers, and a well-established infrastructure in organisation of workshops and larger seminars, thus providing the opportunity to reach a wider audience for expert training in e.g. science communication, but also to disseminate the scientific outcomes of INFLAME. Moreover, a representative from IVL will act as the Equal Opportunities Champion within INFLAME. The independent private sector media SME Maverick will contribute to the network advice on e-communication and design and deliver a unique complementary skills course on communicating science to non-scientists via broadcast media as part of ATC 5. Additionally, representatives from a major international trade association representing flame retardant producers (PINFA), will contribute training in ATC5 by providing an industry perspective on the need for FRs, their mode of action, and current strategies towards sustainable FRs. A representative of IVL, Maverick, and PINFA will sit on the Supervisory Board.

Exploitation of synergies and complementarities

Trainees will be seconded to exploit complementary methods and generate new research synergies. In addition we will take the following steps to ensure effective team-working:

- Participation of all team members in a orientation and training event designed to facilitate supradisciplinary working methods
- The research objectives contained in each trainees' CDP will provide a framework to define goals and expectations for exchanges and collaborative working
- Electronic communication and the network's website will provide an important focus for information exchange, including the sharing of training materials, data, analysis tools and software.
- Regular meetings between Participants at international conferences, network workshops and training courses will facilitate collaborative working and plans for exchange visits.
- Presentations by trainees and supervisors at network meetings will disseminate techniques and methods through the network, fostering new collaborations and synergies.
- Specific tasks executed by the network (e.g. ATCs) will have devolved structures with clearly defined responsibilities.

Table 6: Overview of Task-Specific Research Skills received by Individual Trainees

Trainee, Training Labs	**Skills acquired at home (H) and in Seconded (S) or Visited (V) Lab. Links to other trainees**
ESR1 UA1 (H), VU1 (S)	General principles of trace chemical analysis, GC-MS, LC-Q-TOFMS (UA1); GCxGC-TOFMS, laboratory leaching studies (VU1) **Links to ER1**.
ESR2 UB1 (H), VITO (S), IVL (V),	Forensic microscopy, focusing on ESEM with EDX, general principles of trace analysis, GC-MS and LC-MS/MS, indoor dust sampling techniques

SU (V), UoR (V), UA1 (V)	(UB); emissions chamber testing operation (VITO), general approaches to mathematical modelling (IVL & SU); in vitro bioaccessibility testing (UoR); LC-Q-TOFMS (UA1). **Links to ESRs 3, 4, 5, & 7.**
ESR3 VITO (H), UB1 (S), IVL (V), SU (V), VU1 (V)	Emissions chamber testing operation, general principles of trace analysis, GC-MS, LC-MS (VITO); techniques for indoor air sampling, LC-MS/MS and HBCD analysis (UB1); general approaches to mathematical modelling (IVL & SU); GCxGC-TOFMS (VU1). **Links to ESRs 2, 4, & 5.**
ESR4 IVL (H), SU (S), VITO (V), UB1 (V)	General approaches to mathematical modelling, programming in *inter alia*: Visual Basic for Excel, Matlab, or in a GIS environment (IVL); complementary mathematical modelling and programming skills (SU); emissions chamber testing operation (VITO), forensic microscopy (UB1). **Links to ESRs 1, 2, 3, & 5, plus ER2.**
ESR5 SU (H), UB1 (S), VU1 (V), UA1 (V), IVL (V)	Techniques for sampling indoor and outdoor air and soils, GC-MS, LC-MS, general approaches to mathematical modelling (SU) enantioselective analysis (UB1), complementary mathematical modelling and programming skills (IVL), LC-Q-TOFMS (UA1); GCxGC-TOFMS (VU1). **Links to ESR4 & ER2.**
ESR6 NIPH (H), SU (S), VITO (V), VU1 (V), UA1 (V)	Human biomonitoring (e.g. study design, ethics, sample acquisition, questionnaire design), general principles of trace chemical analysis, GC-MS & LC-MS applied to serum (NIPH); indoor air and dust sampling techniques, GC-MS and LC-MS applied to air and dust (SU); general principles of trace chemical analysis applied to non-invasive tissues/excretions (VITO), LC-Q-TOFMS (UA11); GCxGC-TOFMS (VU). **Links to ESR9 & ER2.**
ESR7 UoR (H), VITO (S), UB1 (S), VU1 (V), UA1 (V)	*In vitro* bioaccessibility testing (UoR); indoor dust sampling techniques, forensic microscopy (UB1); general principles of trace analysis, GC-MS & LC-MS (VITO) LC-Q-TOFMS (UA1); GCxGC-TOFMS (VU1). **Links to ESRs 2 & 8, plus ER2.**
ESR8 VU2 (H), VITO (S), SU (V), UB1 (V), UoR (V)	General principles of trace chemical analysis, GC-MS & LC-MS applied to dust and handwipe samples. observational studies, and behavioural questionnaires (VU2). GC-MS and LC-MS applied to analysis of saliva (VITO). Personal inhalation sampling (SU); forensic microscopy (UB1); in vitro bioaccessibility testing applied to indoor dust (UoR). **Links to ESRs 2 & 7, plus ER2**.
ESR9 VITO (H), UA1 (S), NIPH (S), VU1 (V)	General principles of trace chemical analysis, GC-MS & LC-MS applied to non-invasive tissues/excretions; (VITO); general principles of using non-invasive indicators of body burden and their analysis, LC-Q-TOFMS (UA1); general principles of human biomonitoring (NIPH); GCxGC-TOFMS (VU1). **Links to ESR6 and ER2.**
ESR10 UA2 (H), UB2 (S), UvA/VU (S)	General principles of *in vitro* testing, proteomics, use of engineered cell-lines, flow cytometry, indoor air and dust sampling, bioinformatics, transcriptomics anlsyses using prokaryotic microarrays (UA2); transcriptomic analyses using human and mouse Agilent microarrays, general principles of metabolomics (UB2); *in vivo* testing approaches (UvA/VU). **Links to ESRs 11 & 12.**
ESR11 UB2 (H), UA2 (S) UvA/VU (S)	General principles of metabolomics and transcriptomics approaches, FT-ICR-MS, NMR, indoor air and dust sampling, bioinformatics, transcriptomic analyses using human and mouse Agilent microarrays (UB2); transcriptomics anlsyses using prokaryotic microarrays, GC-MS, LC-MS, LC-Q-TOFMS approaches to metabolomics (UA2); *in vivo* testing approaches (UvA, VU). **Links to ESRs 10 & 12.**
ESR12 UvA/VU (H), UB2 (S), UA2 (S)	General principles and practice of *in vivo* testing, flow cytometry, ELISA, histology, indoor air and dust sampling (UvA/VU); *in vitro* testing approaches (UA2); general principles of metabolomics (UB2). **Links to**

	ESRs 10 & 11.
ER1 VU1 (H), UA1 (S)	GCxGC-TOFMS, laboratory leaching studies applied to e-waste (VU1); LC-Q-TOFMS (UA1). **Links to ESR1.**
ER2 SU (H), IVL (S), NIPH (V)	General mathematical modelling approaches, programming including Visual Basic for Excel and Matlab, overview of biological relationships between external and internal exposure (SU); complementary mathematical modelling and programming skills (IVL); General human biomonitoring principles (NIPH). **Links to ESRs 4,5,6 & 9.**

Career Development Plan*:* All trainees will complete a self-assessed Initial Training Needs Analysis (ITNA) at the start of their training. The ITNA will then be used to develop a Personal Career Development Plan (CDP), in discussion with the trainees' supervisors, which will address identified training needs and how they will be acquired from the portfolio of generic and transferable skills training courses provided by the Network or external organisations. The CDP will also encompass career planning and trainees will be encouraged to use career planning resources such as the UK Research Councils' 'Career Mapping Tool' and those available on the UK graduate student website (www.grad.ac.uk). The CDP will be prepared annually and be subject to approval and 6-monthly progress checks by the Directors of Training and Research.

Generic Research Skills The network will cover a range of research-related skills:

- *Empirical techniques* (defining a scientific question, formulating hypotheses, designing efficient experiments to test hypotheses, quantitative data analysis and statistics)
- *Health & Safety in the Workplace*
- *Ethics in Scientific Research* (what constitutes an "ethical issue"? logistics of obtaining ethical approval). This training need will be addressed primarily at the outset of each trainee project, but will be updated annually where identified as part of a trainee's CDP – e.g. where significant changes in regulations and practices have occurred since initial training.
- *Managing Scientific Research* (project planning, time-management and record keeping, deliverables and milestones, information retrieval and bibliographic skills)
- *Scientific Communication* (presentation skills, writing reports and publications, peer review, cross-disciplinary communication)
- *Commercialisation of Research* (IPR, patenting, industrial collaboration, start-ups)

Transferable Skills The network will address the following:

- *Public engagement and dissemination* (communicating science to the wider public)
- *Communicating science across sectors* (e.g. to policy-makers)
- *Communicating ideas and insights* (structuring knowledge for written and oral communication; teaching others; ability to summarise, document and reflect on progress)
- *Personal effectiveness and career development* (presenting yourself, interview techniques, preparing a cv)
- *Team working and leadership* (appreciating learning and working styles, mentoring, cooperation with supervisors, colleagues and peers)
- *Work-life balance* (women in research, career breaks for child rearing)

Generic Research Skills and Transferable Skills will be delivered principally locally by Graduate Schools and Staff Development Units in the Participant institutions. At project outset, the Director of Training will review and collate information from participants on the locally-available provision for such training courses. This exercise will ensure the most effective use of network resources and avoid duplication of effort. If any gaps in training provision at specific institutions are identified, then the trainees involved will be required to participate in appropriate courses provide elsewhere in the network. Wherever possible, this will be in person (during a scheduled training secondment or visit), but if necessary and feasible, it will be conducted on-line via the INFLAME e-learning web portal. Public engagement and intersectoral communication (with a focus on working with broadcast media) will be addressed at network level by ATC5. In addition, cross-disciplinary communication will be addressed at network level by a workshop hosted by Birmingham as early as possible in the project.

This orientation and training event will be attended by all PIs and researchers. It will concentrate on establishing a baseline understanding of the key opportunities, challenges and debates within each of the discipline areas involved, and develop key interdisciplinary skills within the project team.

B.1.4 Management structure and procedures

Strategy for Management of Training and Research

The Supervisory Board will be the executive body with overall responsibility for the network. It will be chaired by the Coordinator and will include 1 representative from each Participant, the Director of Training, Director of Research, and 2 representatives of the trainees. There will be 2 meetings per year coinciding with the 6-monthly Network Meetings and the Visiting Researchers will each attend one supervisory board meeting *per annum*. The Supervisory Board will:

- Facilitate the technical and managerial operation of the network based on fair principles of Participant inclusion and even distribution of workload and responsibilities
- Approve reports prepared by the Network Coordinator for delivery to the REA
- Monitor the progress of individual trainees and research tasks via reports from the Director of Training and recommend specific actions where required
- Monitor and evaluate progress towards the research objectives
- Promote additional collaborations and interactions between teams
- Obtain, and respond to advice from the Visiting Researchers on programme direction and international competitiveness.
- Approve the finances and agendas for network ATCs, conference and workshop.
- Facilitate communication between Participants in skills training, sharing of techniques and expanding projects in new directions.

Individual Management Responsibilities within the Network

The Network Coordinator (NC): will be the principal point of contact between INFLAME and the REA. The NC will lead the network, prepare summary reports, assess the overall performance of the project in relation to its objectives and deliverables, monitor the performance of specified tasks by each participant, ensure the correct financial management of the network, promote information exchange between participants, facilitate dispute resolution and coordinate the preparation of documents for the REA. The NC will provide advice to participants on matters concerning intellectual property and publications in the context of the Consortium Agreement. The NC will organise implementation of the network webpage and portal, assemble agendas, publish minutes, circulate reports, field queries from trainees and supervisors and disseminate information to participants. They will coordinate the progress reviews of trainees, maintain progress records and provide a common point of contact for trainees and supervisors. A further important task will be to ensure that researcher agreements for all trainees are in place and implemented at all partner organisations. The NC will be supported by a dedicated network assistant from the Management Funds. They will also be supported by a network website/e-learning coordinator.

Director of Research (DR): Given the interdisciplinary nature of the project, and the extensive interchanges between participants, it is essential that there should be some expert management oversight of the research programme to provide direction, coordination and advice. Critical inputs will include advice to trainees on issues connected with research (e.g. formulating appropriate hypotheses, correct experimental design including the most appropriate controls, avoidance of toxicity issues), and providing a point of contact in the event of difficulties with trainee secondments. Any such problems will be discussed in confidence by the NC, DR, and DT, who will devise, agree, and suggest a solution to the parties involved. If this does not resolve the problem, then the dispute resolution process will be invoked.

Director of Training (DT): For each trainee the DT will assess CPDs, monitor the training aspect of progress reports, evaluate outcomes and action remedial interventions as required. The DT's broad knowledge of the training resources within the network will enable the DT to make suggestions to trainees and supervisors, to ensure that the network achieves its maximum training potential. The DT will also ensure excellence in recruitment, targeting trainees from diverse disciplinary, sectoral and nationality backgrounds. The DT will encourage trainees in the management of their career development.

Equal Opportunities Champion (EOC): will promote equal opportunity in all aspects of the network's activity. The EOC will work with the Director of Training to ensure that the network's equal opportunity policies are rigorously applied, notifying the Network Coordinator of problems. The EOC will act as a point of contact for trainees if they feel subject to any form of discrimination.
Ethical Lead (EL): While responsibility for seeking and securing the necessary ethical approval from the relevant local and national committees for any studies within INFLAME rests with local supervisory teams, the EL will act as a central consultation point for network participants on ethical matters. He will report any concerns direct to the network coordinator, who will then consult the Supervisory Board as to the necessary action. Section B4 outlines the ethical issues associated with INFLAME and how these will be addressed.
Supervisors: will coordinate the appointment of trainees and assist them in drawing up CDPs based on their research projects and career aspirations. They will have monthly structured meetings with trainees to ensure progression in research and training, and assist trainees in the development of their careers and provide constructive feedback, training and direct intervention as necessary. They will organise agreed exchange visits and will inform the DT in cases of problems with a trainee's progression.

Communication within INFLAME

Good communication between teams will be facilitated by:

- Project Meetings and Training Courses will bring team members together – in particular, the orientation and training event.
- Well defined individual roles within the network, associated with specific tasks, and a simple, direct management structure.
- Regular exchanges between trainees in person during secondments, visits, and Project meetings, as well as electronically, fostering information exchange.
- The use of email lists and the network's webpage as a portal for information exchange.

Recruitment Procedures

Recruitment: Local supervisors will oversee recruitment following the principles of the EC Recommendation (11 March 2005) on the European Charter for Researchers and the Code of Conduct for the Recruitment of Researchers, in particular concerning working conditions, transparency of recruitment, and career development. Vacancies will be advertised as widely as possible. Publicity will highlight the equal opportunities policy of the network: we will seek and encourage female candidates and candidates returning to a research career. We will emphasize the interdisciplinary potential for candidates with non-traditional backgrounds in subjects other than physical and life sciences (e.g. Engineering), as well as highlighting the intersectoral opportunities (e.g. temporary movement from private sector for purposes of training). Vacancies will be advertised on relevant internet sites (e.g. the EU's Euraxess gateway), through YEAR (Young European Associated Researchers www.year-network.eu/index.html), Eurodoc, national chemical societies, the network's own website and the web sites of Participants. We will use contacts established through international societies, academic and industrial collaborations and previous European projects. This will be especially useful in seeking applications from under-represented states. Members of INFLAME will use attendance at international meetings (e.g. SETAC-Europe, BFR International Workshops, and Dioxin Symposia) to publicise vacancies.
Selection and appointment of trainees: Due to the interdisciplinary nature of the research, the network will be open to candidates with undergraduate backgrounds in chemistry (including relevant engineering disciplines), environmental sciences, physics, and the life sciences depending on the precise balance of activities in their research project. The network will ***target recruits from accession states*** by using existing international contacts (e.g. provided by previous collaborations). The network will ***seek a gender balance in recruitment***, and will ***harness the experience of female researchers within the network*** to promote equal opportunity in career development. Trainees will be selected locally by Supervisors adhering to network-wide guidelines to ensure transparency and equality in selection (see above). Initially, applications will be screened using eligibility criteria based on Marie-Curie rules for nationality, mobility and previous research experience. Thereafter, applicants will be informed about the recruitment process, selection criteria and invited for interview (in person or by phone). The interview will assess candidates according to their existing skills, knowledge and relevant

research/industrial experience; their capacity and enthusiasm to undertake the training activities; the expected impact on their future career whether in the public or private sector, in academia, consultancy, science communication, or as a regulator. Our primary selection criterion will be ability and potential; however, we will seek to ensure the representation of females and minorities in the network. As such, a female or minority candidate will be selected when two candidates are of equal calibre.

Timetable: The project will commence January 2011. Recruitment will commence either at project start or in advance. All ESRs will start as early as possible, but as far as is possible no later than at month 6 in order to take full advantage of the Advanced Training Courses. The 48 month grant allows some flexibility for later appointments should problems be encountered in filling vacancies.

Gender issues and equal opportunities: All Participant institutions have formalised equal opportunities policies. We will take all necessary and reasonable measures to recruit 50% female fellows to the network, including:

- Selection committees, where possible, will have equal numbers of men and women
- Career breaks will be seen as a potentially valuable contribution to professional development.
- Flexible working will be offered to trainees with changing family circumstances
- Training events will include female keynote speakers and other minorities where possible
- A dedicated Equal Opportunities champion will be appointed to ensure that gender balance issues are raised at all levels of the network.

Network-wide coherence of recruitment and employment conditions: Participants will honour EU and national employment law in relation to the recruitment of researchers and to ensure that trainees enjoy the same rights and health and safety standards as local researchers. We aim to train young scientists to become professional researchers able to work between sectors and disciplines. As such, Participants will ensure that trainees are treated as professionals by their co-workers and as an integral part of their institution. The Supervisory Board would take a very strong line should complaints of discrimination be made. All institutions recognise researchers' rights for parental leave and hosts will provide working conditions that enable researchers to combine work and career development with family life and responsibilities. Supervisors will ensure trainees' work does not contravene scientific, budgetary or ethical constraints. The fair principles of intellectual property and joint ownership of collaborative work will be recognised by both supervisors and trainees in line with the Consortium Agreement and Code of Conduct for Researchers.

Financial Management

Financial management will be overseen by the NC; day-to-day management, the prompt transfer of payments to Participants and preparation of financial statements will be handled by the European Finance Office Team of UB. Individual Participant institutions will be responsible for the management of funds allocated to them in line with their own rules and regulations.

Monitoring and quality assurance for training and research

Quality in research and training will be monitored and assured as follows:

At a network level - the Network Coordinator and the Supervisory Board will monitor performance by the following indicators: (i) delivering on a timely basis of the Deliverables and achievement of the Milestones, (ii) the generation of new knowledge that is of high quality as shown by the publication in high impact peer reviewed journals and/or generation of quality IP, (iii) annual feedback from the Visiting Researchers to the Supervisory Board on progress and international competitiveness, and (iv) interest that is shown in the research and training achievements of INFLAME by other EU and international organizations (e.g. invited contributions of INFLAME researchers to environmental risk assessment of FRs).

At an individual trainee level – (i) Trainees will have individualised CDPs with identified research and training objectives. These will be reviewed regularly in partnership between the trainee and supervisor and stem from an annual training needs analysis, (ii) performance of each trainee will be monitored formally via 6-monthly reports submitted by trainees to the Directors of Training and Research (who will feedback the outcome to the trainees) and through the trainees' presentations at each Network Meeting.

Consortium Agreement and Dispute Resolution

The Consortium Agreement will be finalised and signed before the signature of the grant agreement with the EC following INFLAME funding. Issues that will be specified in the Consortium Agreement will include (but not be limited to) (i) handling of confidential information, (ii) procedures and remedies for dealing with defaulting partners, (iii) usage rights for IP generated in *INFLAME* by partners who withdraw from the project before its completion, (iv) settlement of disputes that cannot be resolved by the Supervisory Board, (v) duties of the Supervisory Board, (vi) role of the Project Coordinator and advisors, (vii) schedule for report and meetings, (viii) IP protection and licensing and (ix) financial management of the EU contribution.

Where required, disputes will be resolved in accordance with a clearly defined process. Firstly a solution congruent with the aims and objectives of all parties should be found. Secondly the dispute should be resolved at the appropriate level, with all discussions conducted in an open and honest manner. In the case of a dispute the NC shall be informed immediately. The Network Coordinator will assess the potential effect of the dispute on the entire project, and following consultation with appropriate experts of the EU project team at UB, will decide on the appropriate approach for resolving the dispute. This can be achieved by either local intervention or in extreme cases calling an emergency meeting of the Supervisory Board where possible courses of action can be discussed and voted upon. The Supervisory Board will seek consensus when making decisions. In cases where consensus is not possible, then decisions will be made by a simple (two-thirds quorate majority), with facility for secret ballots if necessary. The Network coordinator will hold the deciding vote in the event of a tie.

B.2 Implementation

B.2. 1 Planning of work packages, milestones and deliverables

Table 7: List and schedule of Milestones (assuming that all ESRs start month 1 and ERs month 6. Dates will be delayed pro-rata should actual start dates be later)

Milestone no.	Milestone name	WP involved	Lead beneficiary	Delivery date	Comments
1	Establishment of Project website	1,2,3	UB	6	Website fully operational
2	Evaluation of range of FRs present in consumer goods	1,2,3	UA1 (ESR1)	30	Data obtained
3	Forensic microscopic evidence of modes of FR incorporation in indoor dust	1,2	UB1 (ESR2)	30	Data obtained
4	Initial database on FR emission factors from consumer goods	1	VITO (ESR3)	24	Data available for modelling
5	Indoor fate models	1	IVL (ESR4)	30	Model optimized and validated
6	Analysis of ventilation air, outdoor air, topsoils	1, 2	SU (ESR 5)	27	Data obtained
7	Model of indoor air contamination contribution to outdoors	1, 2	SU (ESR 5)	30	Model optimized and validated
8	Relationship between external exposure and biomarkers	2	NIPH (ESR6)	30	Data available for modelling
9	Database on bioaccessibility of FRs in indoor dust	1,2	UoR (ESR7)	30	Data obtained
10	Database on rates of human dust ingestion	2	VU (ESR8)	30	Data obtained

11	Evaluation of relationship between FRs in blood and in non-invasive matrices	2	VITO (ESR9)	30	Data obtained
12	Database on responses to FR exposures of engineered eukaryotic and prokaryotic cell lines	3	UA2 (ESR10)	30	Data obtained
13	Database on metabolic responses of cell line and murine asthma model samples to FR exposures	3	UB2 (ESR11)	30	Data obtained
14	Evaluation of the potential of FRs to induce allergic responses in murine asthma and in vitro models	3	UvA (ESR12)	30	Data obtained
15	Database on FR migration to water and soil from e-waste	1	VU1 (ER1)	24	Data obtained
16	Exposure vs body burden model	1, 2	SU (ER2)	27	Model optimized and validated

Table 8: Tentative schedule of project reviews

Review no.	Tentative timing, i.e. after month X = end of a reporting period	*planned venue of review*	*Comments , if any*
1	After project month: 12	IVL	
2	After project month: 22	UoR	
3	After project month: 36	VU1	
4	After project month: 45	VITO	

Table 9: Work package list

Work package No	Work package title	Type of activity	Lead beneficiary No	Lead beneficiary short name	Person months	Start month	End month
1	Migration Pathways	Research	2	UA1	179.8	0	48
2	Human Exposure (Pathways & Monitoring)	Research	7	SU	187.7	0	48
3	Understanding Effects of Human Exposure	Research	3	VU1	114.5	0	48
				TOTAL	482		

Table 10: List of Deliverables (DL)

Del. no.	Deliverable name	WP no.	Lead beneficiary	*Estimated indicative person-months*	Nature	Dissemination level	Delivery date *(project. month)*

				(only recruited fellows)			
1	Delivery of kick-off project meeting	1,2,3	UB1	-	O	CO	1
2	Delivery of Project Website	1,2,3	UB1	-	O	PU (although some aspects CO)	6
3	Delivery of ATC1	1,2	UA1	-	O	PU	6
4	Delivery of ATC2	1,2	VU1	-	O	PU	7
5	Delivery of ATC3	3	UB2	-	O	PU	9
6	Delivery of orientation and training event	1,2,3	UB1	-	O	CO	9
7	Delivery of ATC4	2,3	IVL	-	O	PU	12
8	Delivery of ATC5	1,2,3	IVL	-	O	PU	15
9	Progress Reports from ESRs	1,2,3	All	18 ESR	R	CO	6,12,18,24,30,36 (some later if actual start dates delayed)
10	Progress Reports from ERs	1,2	VU1, SU	1.5 ER	R	CO	12,18,24 (some later if actual start dates delayed)
11	Delivery of project meeting 2	1,2,3	UA1	-	O	CO	6
12	Delivery of project meeting 3	1,2,3	IVL	-	O	CO	12
13	Progress Report to the REA	1,2,3	UB1	-	R	CO	12
14	Delivery of project meeting 4	1,2,3	NIPH	-	O	CO	18
15	Mid Term Report to REA	1,2,3	UB1	-	R	CO	21
16	Delivery of mid-term review meeting	1,2,3	UoR	-	O	CO	22
17	Periodic Report to the REA	1,2,3	UB1	-	R	CO	24
18	Delivery of	1,2,3	IVL	-	O	CO	30

	project meeting 5						
19	Delivery of project meeting 6	1,2,3	VU1	-	O	CO	36
20	Progress Report to the REA	1,2,3	UB1	-	R	CO	36
21	Delivery of final project meeting	1,2,3	VITO	-	O	CO	45
22	Delivery of Network Conference	1,2,3	IVL	(12 ESR, 2 ER)	O	PU	30
23	Presentations at scientific conferences	1,2,3	UB1	(6 ESR, 1 ER)	O	PU	Various but collated for REA at 36, 48
24	Final Report to REA	1,2,3	UB1	-	R	CO	48
25	Publications in peer-reviewed journals	1,2,3	UB1	(36 ESR, 6 ER)	O	PU	Various but collated for REA at 36,48
26	Annual financial reports	1,2,3	UB1	-	R	CO	12,24,36,48
			TOTAL	72 ESR, 10.5 ER			

Work package descriptions

Work package number	1				**Start date or starting event:**		1					
Work package title	Migration Pathways											
Activity Type	RTD											
Participant id	UB1	UB2	UA1	UA2	VU1	VU2	VITO	IVL	SU	NIPH	UvA	UoR
Person-months per beneficiary:	31.25		25.65		21.8		31.5	30.3	33.1			6.2

Objectives To comprehend better the mechanisms via which FRs in consumer goods and construction materials migrate into and behave in the indoor environment, the extent of such migration, and to horizon-scan such goods and materials (while in-use and after end-of-life) for FRs likely to constitute future monitoring and risk assessment targets.

Description of work WP1 consists of 6 linked projects involving 5 ESRs and 1 ER. The overall approach is to enhance the currently limited knowledge about how FRs incorporated within consumer goods and building materials migrate into the indoor environment. Moreover, while to date most research in this area has addressed issues pertaining to indoor contamination with brominated FRs (BFRs), like PBDEs and HBCDs; recent and impending restrictions on the use of such BFRs with no concomitant changes in fire safety legislation, means that use of alternative FRs is likely to be increasing. Hence, WP1 includes a "horizon-scanning" characterisation of such "emerging" FRs in contemporary indoor environments, in currently-used flame-retarded materials and also in discarded materials (ESR1 and ER1). The outputs of this "horizon-scan" will feed dynamically on an on-going basis into INFLAME as a whole, and where feasible, an "emerging" FR identified within WP1 will be included in other trainee projects. For example, either monitoring exposure to such FRs (WP2) or evaluating the effects of such exposure (WP3). ESR2 and ESR3 use state-of-the-art technology (environmental scanning electron microscopy and the VITO emission test chamber) in a novel fashion to address the lack of understanding about how and at what rate FRs migrate into indoor air and dust. Similarly, ER1 will use sophisticated instrumentation (hyphenated chromatography-mass spectrometry, XRF and laser ablation ICP-MS) to further understanding of the pathways of FR migration from discarded materials into the outdoor environment. Data provided by ESR2 and ESR3 will contribute valuable input data for ESR4 who will construct mathematical models of the fate of FRs within the indoor environment. The project of ESR5 takes a mixed experimental and modelling approach to evaluating the influence that indoor contamination can exert on outdoor contamination.

Deliverables
Project website (DL2)
ATC1 (DL3)
ATC2 (DL4)
Orientation and training event (DL6)
ATC5 (DL8)
Progress reports from ESRs 1,2,3,4 & 5, plus ER1 (DLs 9, 10)
Project Meetings (DLs 1, 11, 12, 14, 16, 18, 19, and 21)
Periodic Reports to the REA (DLs 13, 17, & 20)
Network Conference (DL22)
Presentations at scientific conferences (DL23)
Mid Term Report to REA (DL15)
Final Report to REA (DL24)
Publications in peer-reviewed journals (DL25)
Annual financial reports (DL26)

Recruited researchers to be involved:
ESR1, ESR2, ESR3, ESR4, ESR5, ER1

Work package number	2				**Start date or starting event:**					1		
Work package title	Human Exposure (Pathways and Monitoring)											
Activity Type	RTD											
Participant id	UB1	UB2	UA1	UA2	VU1	VU2	VITO	IVL	SU	NIPH	UvA	UoR

Person-months per beneficiary:	13.2		13.8		4.8	32.5	37	7.2	24.9	33.5		20.8

Objectives To develop understanding of the extent to which indoor contamination with FRs impacts on human exposure. An important component will be an effort to develop methods via which exposure of infants and toddlers can be monitored. Exposure via both direct ingestion of dust and inhalation of indoor air will be considered, as well as indirect dietary exposure arising via migration of indoor contamination to outdoors and subsequent incorporation within the food chain.

Description of work WP2 comprises 5 related projects offering training to 4 ESRs and 1 ER. The project of ESR6 takes an experimental approach to elucidate the extent to which body burdens of adult volunteers and their children are correlated with external exposures via indoor air, dust, and diet. Complementary to ESR6, ER2 uses data generated by ESR6 (and also ESR4 and ESR5) as source term data for a mathematical model linking human body burdens with external exposure via dietary intake, indoor air and dust. A crucial knowledge gap is the extent to which FRs present in indoor dust are absorbed across the gastro-intestinal tract, and ESR7 uses a state-of-the-art physiologically based extraction test method to examine the extent of such absorption and the factors that affect it. This issue is particularly pertinent in scenarios where concentrations of FRs could lead to exposure at levels thought detrimental to health, where bioaccessibilities well below 100% would diminish the risk substantially. Likewise, current assessments of human exposure to FRs via ingestion of contaminated indoor dust use estimates of the quantity of indoor dust ingested by humans that are based on a very small number of primary studies designed to derive estimates of soil ingestion. This crucial research gap will be addressed by ESR8. Finally, while ingestion of dust has been suggested as a particularly important exposure pathway for young children, evidence for this remains inconclusive. This is largely because efforts to identify the principal exposure pathways to FRs for young children on an individual basis have foundered due to the conflict between analytical requirements for large blood sample volumes and ethical and practical constraints of procuring such samples from individual children. Hence, ESR9 will evaluate the utility of non-invasive matrices such as hair, nails, urine, and saliva for providing accurate measures of internal exposure to FRs.

Deliverables
Project website (DL2)
ATC1 (DL3)
ATC2 (DL4)
Orientation and training event (DL6)
ATC4 (DL7)
ATC5 (DL8)
Progress reports from ESRs 6,7,8 & 9, plus ER2 (DLs 9,10)
Project Meetings (DLs 1, 11, 12, 14, 16, 18, 19, and 21)
Periodic Reports to the REA (DLs 13, 17, & 20)
Network Conference (DL22)
Presentations at scientific conferences (DL23)
Mid Term Report to REA (DL15)
Final Report to REA (DL24)
Publications in peer-reviewed journals (DL25)
Annual financial reports (DL26)

Recruited researchers to be involved:
ESR6, ESR7, ESR8, ESR9, ER2

Work package number	3						**Start date or starting event:**		1			
Work package title	Understanding Effects of Human Exposure											
Activity Type	RTD											
Participant id	UB1	UB2	UA1	UA2	VU1	VU2	VITO	IVL	SU	NIPH	UvA	UoR
Person-months per beneficiary:	1.8	35	1.8	38.5	2.4				0.5		34	

Objectives To advance knowledge of the effects of exposure to FRs arising from their indoor use using human and animal in vitro toxicological tests and a mouse model.

Description of work WP3 involves a co-ordinated combined genomics, metabolomics, and proteomics approach involving three partners with significant expertise in these areas. Reciprocal secondments and visits of the three ESRs in this WP (as well as with other trainee projects) will provide a particularly rich training environment. At UA2, ESR10 will evaluate the toxicological mode of action of FRs in relation to general stress responses and endocrine disruption. For this goal, a battery of engineered and targeted eukaryotic and prokaryotic *in vitro* systems will be exposed to indoor air and dust samples as well as to relevant pure compounds. Besides more general reporter gene assays, work will be performed on mammalian *in vitro* systems (i.e. MCF-7, HepG2, H295R) using a combination of proteomic and flow cytometric techniques which will provide a comprehensive mechanistic and cell physiologic profiling of the samples and FRs, that complements the powerful and novel combination of transcriptomic and metabolomic approaches to developing biomarkers of human exposure and effect used by ESR11 at UB2. There will also be specific 'omic analyses completed at UB2, e.g. use of complementary mammalian microarrays. These studies will focus on mammalian (including human) cellular systems. ESR12 at UvA/VU1 will investigate the potential immunomodulatory role of FRs to facilitate or aggravate the immune response to inhaled allergens in a murine asthma model. A set of FRs representing different chemical classes (e.g. BFRs, organophosphorus FRs (OPFRs)) will be selected based on their relevance for human exposure (including those determined by ESR1). An important benefit of INFLAME's holistic approach is that WP1 and WP2 provide information within the same closely integrated training programme on the levels of human exposure against which WP3's enhanced understanding of the effects of such exposure may be placed. The training opportunities afforded by this will be exploited by the fact that ESRs 10, 11, and 12 will learn techniques for environmental monitoring (either via a training visit - ESR12 – or from other centres of expertise within their host institutions – ESRs 10 & 11). These will be applied to the acquisition of air and dust samples necessary for their projects.

Deliverables
Project website (DL2)
ATC3 (DL5)
Orientation and training event (DL6)
ATC5 (DL8)
Progress reports from ESRs 10,11 & 12 (DL9)
Project Meetings (DLs 1, 11, 12, 14, 16, 18, 19, and 21)
Periodic Reports to the REA (DLs 13, 17, & 20)
Network Conference (DL22)
Presentations at scientific conferences (DL23)
Mid Term Report to REA (DL15)

Final Report to REA (DL24) Publications in peer-reviewed journals (DL25) Annual financial reports (DL26)

Recruited researchers to be involved: ESR10, ESR11, ESR12

Table 11: Composition of the Network

ESRs, ERs, and Visiting Researchers (VRs) funded by the grant agreement (person months)					
Team		**ESR**	**ER**	**VSs**	**Total (A+B+C)**
1	UB	72	0	1	73
2	UA	72	0	0	72
3	VU	36	24	0	60
4	VITO	72	0	0	72
5	IVL	36	0	1	37
6	SU	36	24	0	60
7	NIPH	36	0	0	36
8	UvA	36	0	0	36
9	UOR	36	0	0	36
	Totals	**432**	**48**	**2**	**482**

B.*2.2 Planning of conference and Visiting Researchers contribution*

Advanced Training Courses (ATCs)

Five ATCs will be provided to cover the theory and application of research techniques relevant to meeting the Research Objectives, and an insight into techniques of communication with the public, policy-makers, the media, alongside exposure to the perspectives of regulators and researchers from both private and public sectors. The topics are selected on the basis that they cover the key skills in which trainees require training to achieve the ROs (ATCs 1-4), and a crucial suite of skills required to meet TO6 (ATC5). Training will be provided by experts within INFLAME and the Visiting Scientists, augmented where appropriate by invited speakers. Five courses will be run. **All ATCs and the network conference are compulsory for all INFLAME trainees.** These are:

ATC1: Techniques for Monitoring Exposure to FRs. **Of particular relevance to RO2 (ESRs 1, 6, 7, 8, 9) along with TO1 and TO2.**

ATC2:Techniques for Monitoring FRs in the Environment. **Particularly relevant to RO1 and RO2 (ESRs 1, 2, 3, 5, 6, 7, 8, 9, plus ER1), as well as TO1 and TO2.**

ATC3**: *Techniques for Evaluating Effects of Human Exposure to FRs*****. Especially relevant to RO3 (ESRs 10, 11, 12), TO1, and TO2.**

ATC4: Mathematical Modelling Approaches to Understanding Environmental Fate and Behaviour of FRs: **Particularly relevant to RO1 and RO2 (ESRs 4, 5, and ER2), TO1 and TO2.**

ATC5: The Role of Science outside Academia: Communication with other Stakeholders: **This ATC is of specific relevance to TO6 and to all trainees.**

All ATCs will be open to external early stage researchers and other professionals to maximise the benefits provided by these courses within the research community, and to help gauge potential demand for such courses beyond the lifetime of INFLAME. Table 5 summarises the events of the network that are all open to external researchers.

Table 5: Public Events of INFLAME

Event No.	Event name	Organiser	Tentative timing (project month)	Expected No. of external researchers	Outline of the programme
1	ATC1	UA1	6	<20	Tuition in the approaches available to monitor human exposure to FRs. Ethical considerations of human biomonitoring will be addressed.
2	ATC2	VU1	7	<20	A comprehensive introduction to the principles (e.g. isotope dilution) and techniques required for sampling and analysis of FRs in the environment.
3	ATC3	UB2	9	<20	An overview of the approaches available to study the effects of human exposure, and how combined information on exposure and effects is incorporated into assessment of risk.
4	ATC4	IVL	12	<20	The theory, application, and benefits of mathematical models in understanding environmental fate and behaviour of FRs.
5	ATC5	IVL	15	<20	Training in communicating their science to the public, regulators, industry and the media. This will involve a combination of practical and theoretical media training by a private sector media SME (Maverick TV), and exposure to the perspectives of other stakeholders (regulators, FR industry, and environmental NGOs) in the FR field.
6	Network Conference	IVL	30	<50	Presentations of research results from INFLAME and related researchers.

Relevance of the role of Visiting Researchers in the training programme

Two Visiting Researchers will play an important role in the project through study visits to specific Network Participants and through contributions to ATCs 1 and 4. They will also advise the Supervisory Board on international competitiveness. They are excellent role models for young researchers and we expect the network to benefit significantly:

- Trainees will interact with them and receive feedback on their research work at network meetings. Specific study visits to UB and IVL will benefit local and visiting trainees.
- Presentations at ATCs 1 and 4 as well as at network meetings will provide trainees with state-of-the-art training in specific research skills and techniques, as well as general training in research methods, scientific communication and dissemination
- They will attend at least one Project Meeting per year and will be encouraged to provide constructive, critical evaluation of the research and training activities, thus exposing the network to alternative views from a non-European perspective.
- The Visiting Researchers will act as a bridge to North American research in environmental exposure and risk assessment of FRs, helping to advance trainees' careers by publicising their work and facilitating further international collaborations.

Visiting Researchers ID	Expertise areas	Contribution to the project	Years of experience (<10 or >10 years)	Host Institution	Person-months
VR1	Chemicals exposure assessment	ATC1, membership of supervisory board, study visit(s) to UB1	>10 years	UB1	1
VR2	Mathematical modelling of environmental fate of chemicals	ATC4, membership of supervisory board, study visit(s) to IVL	>10 years	IVL	1
				Total:	2

B.3 Impact

B. 3.1Research Indicators of Progress

The network will provide the following indicators of progress in its periodic, mid-term review and final reports.

B. 3.1.1 Research Activities

- General progress with research activities programmed at individual, participant team and network level. Possible problems encountered and nature/justification for adjustments, if any, to the original research work plan and/or timetable.
- Highlights of scientific achievements and recognitions (innovative developments, scientific/technological breakthrough, publications, patents, awards and prizes etc...).
- Progress on cross interaction among disciplines and between academic and industrial partners other stakeholder or relevant users groups.
- Specialist exchange among network teams and visit of Senior Researchers from inside and/or outside the network.
- Individual and joint publications, directly related to the work undertaken within the project (including citation index).

B. 3.1.2 Training Activities

- General progress with training programmed at individual, participant team and network level (Career development Plan, supervision, coaching or mentoring in place at each host institution).
- The rate of recruitment of ESR/ER for each participant and for the network as a whole (ratio person-months filled/offered) and time and duration of each individual appointment [Please note that these must be from 3 up to 36 months for ESR and between 3 and 24 months for ER. Short visits and secondments although part of the training are not counted as appointments, but as part of the networking activities.].
- The nature and justification for any deviation from the original plan (as refereed to table A3.1 of part C) or adjustments, if any, to the original research work plan and/or timetable.
- The number and place of the short visits/secondments undertaken or organised by each ESR and ER within the network (full participant and associated members including number of visits of the ESR and ER to their home scientific community).
- Participation in training events and network meetings (workshops, seminars, summer schools...) and to international conferences (number, names, place date).
- Achievements regarding the acquisition of complementary skills.

- Level of satisfaction of the trainees (e.g. as expressed in response to questionnaire and their expectation to present their PhD thesis and when.).
- Highlights on more particularly innovative developments (novel concepts, approaches, methods and / or products) and on wider societal and/or ethical components of the project, such as public outreach activities.
- Participation of fellows in international conferences / dissemination of their own results.

B. 3.1.3 Management and impact

- Effectiveness of networking, communication and decision-making between partners (at all levels: co-ordinator, team leaders, supervisor, ESRs and ERs), between the network and the REA, and with the Industrial and/or other relevant stakeholders.
- Effectiveness of the recruitment strategy in terms of equal opportunities (including gender balance) and open competition at international level.
- Effectiveness of the "training events and conferences" open to external participants and integration in the training programme.
- Effective contribution of Visiting Researchers to the research training programme.
- Development of any specific planning and management tool(s) and databases management of intellectual property and commercialisation of network research output. (if applicable)
- Nature and justification for adjustments, if any, to the original training plan and/or timetable (e.g. opportunities for new collaborations regarding training activities).

B.3.2 Dissemination and Impact

DISSEMINATION

***Disseminating results*:** The main route for specialist dissemination of the results of the network will be through presentations at international conferences, and publication in prestigious peer-reviewed journals. Wider dissemination of results to the general public will involve the use of lay summaries of research aims and results on the network's website, plus where appropriate press releases and general articles in web-based or printed media. The network conference will be open to external participants, widely advertised and used to showcase work conducted by the network. It is held in month 30 to ensure the participation of all network trainees, including ERs 1 and 2 who are involved between months 6 and 30. High impact publications and presentations to specialists and lay people will ensure impact beyond INFLAME's lifetime. Trainees will be encouraged to disseminate their research in popular science journals and broadcast media, with ATC5 delivering high quality training in this skills area. It is stressed also that where possible INFLAME will aim to make scientific publications generated from its activities openly accessible. In doing so and depending on the most appropriate publishing route both open access publishing and/or self-archiving in an appropriate repository will be considered as well as any necessary embargo periods. The latter is foreseen to range between 6 and 12 months after initial publication.

Spreading best practice:

- The Supervisory Board's evaluations will highlight the significant developments of individual Participants and areas where techniques and methods could be used more widely. The Director of Training will collate and make available a list of training courses available at different partner organisations.
- Personal meetings between supervisors at network meetings will enhance strategies for effective supervision of students. Researchers working on common themes will get together at network meetings to discuss method development and newly acquired data.
- Trainees' personal meetings and on-line exchanges (e.g. via the network portal), as well as trainee experiences during secondments and visits will help disseminate best practice
- Experimental protocols will be shared between Participants avoiding the duplication of effort and providing constructive feedback.
- Each ATC will be available to up to 20 external participants to spread best practice beyond the network.

IMPACT

Improvement of trainees' career prospects

The significant involvement of IVL and Maverick in the network will provide trainees with an invaluable insight into the perspective of the private sector and its skills requirements. *INFLAME foresees that the skills sets acquired by its trainees will not only enable them to achieve the ROs of INFLAME, but will equip them with knowledge that they will be able to exploit throughout their careers.*

Enhancing general capacities for conducting and managing research. Realising the potential of ESRs and ERs requires integration of training in personal and professional skills with training in specific research skills. We will use each trainee's CDP to ensure that all key aspects of skills training are embedded in their day-to-day training experience, rather than included as an add-on. The network exposes researchers to the benefits of working with Participants in other labs, countries and different sectors. The personal mobility and flexibility of perspective provides potential to improve problem solving skills by synthesising interdisciplinary tools and evaluating issues from different research perspectives (academic, commercial). Further, training is tailored to the career stage of the researchers providing ESRs with the key methodological and research skills needed for career progression, whilst enabling ERs to expand their competencies and develop skills enabling them to become independent researchers in the near future (e.g. managing research, working with ESRs, showing leadership, taking organisational roles (e.g. assisting with meeting and conference organisation), formulating research targets and securing funding for future projects). *Moreover, INFLAME's intersectoral ethos will encourage and equip trainees for work in both the private sector (e.g. as consultants, analytical chemists, toxicologists) and outside the research base – e.g. as regulators and science communicators* – as well as within the public sector research base.

Enhancing specific capacities for research on indoor contamination by flame retardants. This research area is increasingly interdisciplinary and to make significant progress researchers require a portfolio of multidisciplinary techniques. INFLAME brings together diverse, but complementary techniques and approaches (e.g as in ESR2 where an unusual combination of forensic microscopy and chromatography-mass spectrometry is used), to provide training that crosses traditional boundaries.

Enhancing capacities for intersectoral careers. INFLAME will provide trainees with the necessary skills base to carry out research, development and innovation within a variety of research environments (including the commercial sector), and in addition, ATC5 will provide an understanding of the varied and often contrasting perspectives of the different stakeholder sectors with interests in flame retardant chemicals. By so doing, it will enhance greatly the capacity of trainees to both communicate and work across sectors and disciplines.

Longer-term benefits. The following impacts on the longer term career prospects for trainees are anticipated:

- Presentations at the network conference and other workshops/symposia will raise trainee profiles by showcasing achievements.
- INFLAME participants have a strong track record of high-impact publications and presentations, thus trainees' work in the network will likely be disseminated widely, with beneficial impacts on future job/fellowship applications.
- Mentoring support provided by senior researchers and the visiting scientists will provide trainees with role models, helping them identify a career structure leading to independence.
- Trainees' broad yet deep expertise and experience gained from working within such a supradisciplinary project will provide an excellent springboard from which they may become the research leaders of the future.
- Trainees' experience of geographical and sectoral mobility will give them a competitive edge and confidence to start an independent career.

Strengthening longer term collaborations and structured training at European level

We anticipate that collaborations fostered by INFLAME will have significant impact on training practices that will be advantageous in the future beyond the ITN. INFLAME will facilitate pan-European training in research into the environmental and human health risk assessment of industrial chemicals providing early career researchers with durable broad interdisciplinary

experience. The techniques and approaches exploited in INFLAME to study FRs, have broad application to similar issues with other such chemicals. Each of INFLAME's ATCs will be available to up to 20 external participants. Feedback from these and from INFLAME trainees will be used to enhance the training value of future iterations of these ATCs, as it is our intention to make these ATCs (as well as others that may be identified as of potential value during the course of INFLAME) available across Europe as Continuing Professional Development (CPD) courses beyond the end of INFLAME. This will represent a significant enhancement of research training capacity within the European Research Area (ERA) for researchers involved in environmental chemicals risk assessment. Interactions with more experienced colleagues will be particularly useful for younger supervisors as they can seek advice when establishing the highest professional standards for supervision. Longer term benefits are expected as trainees advance through their careers and become supervisors in their own right. The structured training offered by INFLAME will provide a model for trainees who will implement similar practices for ESRs trained under them.

Enhancing public-private sector collaborations in terms of research training.
INFLAME intends to leave a legacy of ATCs that will be available as CPD courses to all interested European researchers. The private sector expertise and input from IVL's Knowledge Division, Maverick, and PINFA will prove invaluable in identifying research training needs, designing CPD courses that fulfil them in a commercially viable fashion. Moreover, the techniques and methodologies disseminated to INFLAME trainees are of general relevance to a much wider cohort of researchers working in the area of source identification, exposure and risk assessment of industrial chemicals. Hence, the potential value of INFLAME's CPD courses and e-learning material is likely substantial, and we will explore actively the potential for making such research training materials available to an expanded training network post-INFLAME.

B4. Ethical issues

Ethical Overview
INFLAME employs established methods in research involving human subjects and laboratory animals, and will be conducted under the supervision of research ethics committees in each relevant institution, with the utmost care taken to adhere to the ethical regulations and guidelines of international and institutional authorities. In the projects involving human participation (primarily ESR6, ESR8, and ESR9) the work will be conducted with the fully informed consent of each participant. The host institutions for such work are all highly experienced in the conduct of such studies and are fully conversant with the ethical issues involved. All work will have full ethical approval prior to commencement. Personal data relating to participants will be protected, with only essential data collected. INFLAME recognises fully the importance of such issues and hence provides training in how these are recognised and addressed. INFLAME also has an ethical lead.

We address below how INFLAME participants will address the ethical issues associated with specific trainee projects hosted by their organisation. All trainee projects within INFLAME will be required to provide to the Ethical Lead evidence of approval by the appropriate local and national ethics committees at their outset.

NIPH – ESR6 (also VITO – ESR9)
Ethical issues; Human studies

WP 2 "An experimental approach to examining relationships between external exposure and human body burdens" performed by ESR6 involves collection of matched samples of indoor air, dust, hair, saliva, urine and blood serum from 40 households each comprising mother and a child aged 6-12 years.

We assure that the research will abide to international ethics standards such as the Helsinki declaration, to national legislation by approval of the study through the Regional Committee for

Medical Research Ethics and the Data Inspectorate, as well as the Norwegian Institute of Public Health's policy on information security and privacy, which is based on NS-ISO 27001.

We aim at recruiting volunteers at one or two primary schools. The process will start by contacting headmasters and informing them about the study in an information letter. In case of positive response, the pupils and their families will receive a detailed information letter.
In particular, we will here inform that:

- all samples will be treated anonymously,
- the participants can withdraw from the study at any time without giving a reason,
- the participants at any time can require their samples destroyed,
- the study has been approved by the Regional Committee for Medical Research Ethics and the Data Inspectorate,
- all data will be collected, stored and destroyed according to national legislation.

The letter will also contain background information of the study and information on how the study will proceed (time-frame for sampling, how the samples will be taken, volume needed etc.).

Informed consent will be obtained from all mothers and parent or guardian before sampling. We will sample about 50 mL urine and two vacutainer tubes of blood resulting in 5-10 mL serum. The blood samples will be taken **at home** in the presence of one parent by an experienced nurse specially trained to take blood from children to minimize pain and stress.

If possible, we will also sample air/dust in some class rooms, and plan to involve the pupils in this.

VU1 – ESR8

The project of ESR8 involves saliva analyses for determining dust ingestion rates for infants who are hypothesised to be a highly-exposed group. The samples will be analysed at VU1. Ethical issues associated with this study are addressed below.

Ethical approval

Approval from the accredited Ethical Committee will be ensured before commencement of human studies. Written consent will be requested and a copy of the consent will be provided to the Commission.

Recruitment and consent

Women will be requested to participate at the first antenatal visit to the midwifery clinic. It will be ensured that sufficient information is provided in order for women to make a well-informed decision regarding participation. It will be stressed that participants may leave the project at any time if they should desire to do so and that neither withdrawal nor the decision not to participate will affect the care provided to them by midwives. No financial compensation will be offered and written consent will be required for registration as participant.

Inclusion criteria

Women eligible for participation should be less than twelve weeks pregnant at their first visit to the midwifery clinic. They should be able to fill out Dutch questionnaires. Incapacitated subjects will not be asked to participate.

Exclusion criteria

Women with pre-eclampsia or twin pregnancies are excluded from further participation. Pre-eclampsia is defined as pregnancy-induced hypertension (1x > diastolic pressure > 90 mmHg) in association with proteinuria (>0.3 g/day). Furthermore major congenital anomalies at birth will be reason for exclusion.

Objection by minors or incapacitated subjects

The target group of this research is infants aged 0-12 months. Consent for the infant is given by the mother, who is specifically requested to give consent for both herself as well as her child. Participants have the right to discontinue the project at any time if they desire to do so. Incapacitated mothers are excluded from participation, as well as infants born with mental handicaps.

Risk assessment

Data collection for INFLAME will be non-invasive. The majority of the data will be collected through regular health care provided by midwives. Furthermore questionnaires will be administered and saliva samples will be collected. Collection of saliva is non-invasive and no sensitive information will be covered in questionnaires. Privacy and anonymity will be guaranteed through coding of participant information. The key to this code will only be known to an independent third party unrelated to any other aspects of the research.
As privacy and anonymity are guaranteed and all measures are non-invasive, no risks or injuries are expected for participants.

UA2 – ESR10 and UB2 ESR11

All the *in vitro* tests conducted by ESR10 will be performed in a laboratory with biohazard safety strict regulations at restriction level L2 (file number: AMV/14042005/SBB219.2004/0879). However, the various tests with cell lines described in the proposal need only restriction level L1, for which there is no need to submit an application to the local Ethical committee. The same situation applies with the transcriptomic studies conducted at UB2 by ESR 11. The needed measures (including laminar air flow) are available in both laboratories with a long tradition in cell culture, on the one hand, and with the analysis and handling of different chemicals.

UvA - ESR12

This project raises ethical issues concerning its conduct of experimental animal studies using mice. These are addressed here.
The role of exposure to flame retardants via the airways and the facilitation of sensitisation to inhaled allergens will be studied in different animal studies by ESR 12.

In vitro screening for immunomodulatory effects on dendritic cells: Dendritic cells will be cultured from bone marrow of untreated Balb/c mice. Bone marrow of only one animal will be sufficient to test one PBDE congener. The dendritic cells will be pulsed with the model allergen ovalbumin in the presence or absence of flame retardant and the immunomodulatory effects of exposure to flame retardants will be analysed by a coculture with transgenic T cells expressing an ovalbumin specific T cell receptor. The polarisation of these T cells towards a pro-allergic Th2 phenotype will be determined. We expect that we will need 50 Balb/c mice and 50 transgenic DO11.10 mice.
In vivo asthma model to test the immunomodulatory effects of flame retardants: The dendritic cells that have been exposed to the flame retardant will be tested in an established asthma model in mice to investigate their potential to induce an asthma phenotype in mice. From extensive experience with this model, it is known that 8 mice per group will be sufficient to obtain a power of 0.80 and a significance level of 0.05. We will need 24 mice per experiment including control groups; we estimate that we will need 240 Balb/c mice for these series of experiments.
A second series of experiments will be aimed at the immunomodulating effect of flame retardants directly at the airways. Inhalation of an antigen normally leads to tolerance to the antigen in mice, only when adjuvants are added an inflammatory immune response can be induced. Flame retardants will be administered directly into the airways to investigate whether tolerance to inhaled antigens can be broken and will facilitate sensitisation to the antigen. For these experiments we will need 240 Balb/c mice.
Dendritic cells are essential for sensitisation of T cells, however there is recent evidence that many cell types are involved in sensitisation. To test whether dendritic cells are necessary and sufficient for flame retardant mediated sensitisation we will make use of dendritic cell conditional knockout mice (CD11cDTR transgenic mice). We estimate that we will need 240 transgenic mice for these experiments.

In total, approximately 800 mice will be used of which 290 will be transgenic. These models have been classified by local ethical animal committees as a procedure that will not exceed moderate levels of discomfort. Mice will be monitored daily for discomfort level.

B5. Gender aspects

Gender issues and equal opportunities: All Participant institutions have formalised equal opportunities policies. We will take all necessary and reasonable measures to recruit 50% female fellows to the network, including:

- Selection committees, where possible, will have equal numbers of men and women
- Career breaks will be seen as a potentially valuable contribution to professional development.
- Flexible working will be offered to trainees with changing family circumstances
- Training events will include female keynote speakers and other minorities where possible
- A dedicated Equal Opportunities champion will be appointed to ensure that gender balance issues are raised at all levels of the network.