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ENVIRONMENTAL HEALTH TRUST  
WASHINGTON RESEARCH AGENDA

2009

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RESULTING FROM THE WASHINGTON, D.C. EXPERT CONFERENCE ON  
CELL PHONES AND HEALTH  
SEPTEMBER 12<sup>TH</sup>-14<sup>TH</sup>, 2009

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## PREAMBLE - INTRODUCTION

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Convened by the non-profit research organization, Environmental Health Trust, the Washington Conference on Cell Phones and Health (September 2009) evaluated biological and possible health effects of exposure to radiofrequency electromagnetic fields (RF-EMF) emitted from mobile phones. Participants of the Conference have reviewed the current status of scientific knowledge and identified major gaps in knowledge

It is an ongoing controversy whether the users of mobile phones should be concerned about the health safety of the radiation emitted by these devices, and whether the safety guidelines are adequate. Because of the methodological and study design limitations that are intrinsic to different types of studies (epidemiology, human volunteer, animal and in vitro studies) scientific evidence amassed to date is still insufficient to support safety claims regarding current patterns of use of RF-EMF.

In addition to the already available scientific evidence, there is the need to consider the “missing” evidence and to develop a coherent plan for conducting additional interdisciplinary studies. Only when considering both the available and the missing evidence can we determine the reliability of the current safety guidelines.

The Washington conference participants, as scientists directly involved in research on the effects of mobile phone radiation, recognize the difficulties in carrying out research caused by the shortage of funding. They recognize the need for a major, sustained commitment of funding to initiate, conduct and complete the necessary research on biological and health effects of mobile phone radiation.

Considering the large number of exposed citizens worldwide, even a small health effect associated with RF-EMF might pose a serious financial problem for health care providers. Therefore, in the present situation of scientific uncertainty, it is wise to promote research that will help to increase reliability of the current safety guidelines in addition to advocate use of precautionary approaches to mobile phone use. The research proposed in this Environmental Health Trust Washington Research Agenda-2009 is specifically tailored to answer the most urgent questions, as outlined below.

The Environmental Health Trust Washington Research Agenda-2009 acknowledges and largely agrees with the WHO Research Agenda 2006 (Annex-1). However, the new Agenda considers also the new evidence that has become available between 2006 and 2009. Finally, this Agenda also recognizes the critical need to create a well-funded, multi-year, broad, multi-disciplinary program of undergraduate, graduate, post-doctoral and continuing professional education in biomedical sciences, epidemiology, biophysics, toxicology, engineering, translational sciences and other relevant fields.

To ensure the independence of these activities, it will be important to create an independent advisory group that will identify priorities and data gaps and provide overall guidance. Funding appropriation and selection of projects for funding should be based on an impartial peer-review process free of conflict of interest. It is recommended that the research-proposal review guidelines similar to those of the US National Institutes of Health be adopted.

## TABLE OF CONTENTS

1	Exposure assessment.....	4
1.1	human living environment exposure.....	4
1.2	Modeling of child-head exposures .....	4
1.3	Microdosimetry .....	5
2	Sensitive vs Non-sensitive biological matter.....	6
2.1	Laboratory studies (mechanisms of sensitivity).....	6
2.2	Define thresholds (dose and time) .....	7
3	Define active EMF parameters.....	7
3.1	in vitro (Cell culture).....	8
3.2	<i>In vivo</i> Animal Research.....	8
3.3	Behavioural Animal studies .....	8
3.4	Human volunteer studies .....	8
4	Neuro function, cognitive effects .....	9
4.1	Human acute studies.....	9
4.2	Human studies “Long term EXPOSUREexposure effects” .....	9
4.3	Animal “acute” .....	9
4.4	Animal studies (long term effects).....	9
5	Long term effects .....	9
5.1	Animal studies.....	9
5.2	Human Epidemiology.....	10
6	Networking - Conferences .....	11
7	Annex - 1, Graphical Overview .....	12
8	Annex - 2: WHO-Research Agenda 2006.....	13

## 1 EXPOSURE ASSESSMENT

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RF-EMF exposures concern both work and private life. The range and number of RF-EMF-emitting devices is constantly changing and there are gaps in the knowledge about the assessment of such combined exposures from multiple sources of exposure, and with varying between near- and far-field exposures.

As already recognized by the WHO (Research Agenda 2006; see Annex-1), qualified surveys require a collaborative effort between epidemiologists, physicists and engineers. The studies should focus on the general population and should include, for instance, the relative contribution of occupational and residential exposures, and the impact of age, gender and mobility. Regional variations also need to be assessed. These studies will inform the feasibility of future epidemiologic studies and, if appropriate, the proper design of residential epidemiological studies.

### 1.1 HUMAN LIVING ENVIRONMENT EXPOSURE

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The EMF emission of every single commercially available device meets the FCC and ICNIRP safety standards. However, there is no sufficient information about the human EMF exposures in environments with various devices emitting EMF simultaneously.

Research Needs:

- **Assessment** of typical and “worst case” exposure conditions in environments with various EMF-emitting devices.
- **Simulations**, real-time dosimetric monitoring and questionnaires regarding real-time patterns of use and exposure for persons of varying age groups and use conditions, ranging from children to workers whose jobs require frequent use regularly.

The research output will provide life scientists with more realistic EMF exposure scenarios for the examination of effects in cells, animals and humans, which may indicate a biological effect or health risk.

### 1.2 MODELING OF CHILD-HEAD EXPOSURES

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There is general consensus that children’s brain tissues absorb higher level of energy from exposure to mobile phones (held to the ear) compared to adults. More realistic models for device testing are critically needed. Research projects will require an interdisciplinary approach by experienced life scientists (anatomists), physicists, and engineers.

Research needs:

- Develop model-skulls for children of various age, and
- Simulate the absorption of mobile phone radiation in children’s heads.
- Conduct simulations and validations of multiple-RF whole body exposures to
  - validate whole-body modeling of adults and children, man and woman,
  - including all stages of pregnancy, and
  - the male reproductive system.

The research output will provide safety standard setting tools with more realistic exposure scenarios for children. This will indicate whether it is appropriate to develop new safety standards addressing specifically the exposure of children.

### 1.3 MICRODOSIMETRY

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Qualified research consortia will include an interdisciplinary team of life scientists, physicists, and engineers, and will include large scale computation of model simulations. So called ‘hotspots’ can vary by 1000 folds or more within a gram of tissue. Currently the use of larger tissue volumes does systematically underestimate the local radiation intensity. We can detect and measure ‘hotspots’ on the macro-scale but we do not have yet technology to measure whether ‘hotspots’ are created on the micro-scale (sub-cellular scale). Living tissues and cells are not homogenous environments but they are compartmentalized into cells and sub-cellular size volumes (organelles) that are delineated by lipid-containing hydrophobic membranes. Presently, dosimetry and modeling of the distribution and intensity of mobile phone radiation in the brain uses as a model a plastic container molded in the form of half-head and filled with “physiological solution” consisting of water, salt and sugar. Such models of human heads are a great oversimplification of the reality. Strong electromagnetic fields can disrupt the function of selective transport mechanisms of cellular membranes and cause profound physiological changes (e.g. electroporation). The research output will provide evidence for the understanding of cellular reaction patterns and the determination of compliance with exposure limits.

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## 2 SENSITIVE VS NON-SENSITIVE BIOLOGICAL MATTER

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There is evidence that **individual sensitivity** phenomenon might explain differences in reports on the biological response to RF-EMF radiation.

Therefore this research line requires two steps:

1. Define sensitive populations (cells, animal species, humans)
2. Define the exposure thresholds (Intensity and time) in sensitive populations

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### 2.1 LABORATORY STUDIES (MECHANISMS OF SENSITIVITY)

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The majority of research on the biological effects of mobile phone radiation has been done in *in vitro* studies. Some of these studies suggest that mobile phone radiation might alter cell physiology, e.g. by triggering cellular stress response, causing DNA damage, altering gene and protein expression, etc. However, there are also studies that do not reveal such effects.

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#### 2.1.1 CELL CULTURE: ALTERATION OF DNA PROTEIN, ETC.

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One of the more vigorously debated issues is whether RF-EMF exposure is associated with DNA damage. It seems clear that without further research the issue of DNA damage will not be resolved. The same might apply to many other cellular effects.

*In vitro* studies cannot be directly used to determine the probability of health risks; they are indispensable to discover the cellular biological and biochemical mechanisms needed to complement positive outcomes from human and animal studies and to reveal the interaction mechanisms between RF-EMF and living organisms.

Therefore interdisciplinary proposals with the following aims should be given high priority:

- Appropriate measures of
  - genotoxicity,
  - gene and protein expression,
  - protein de novo synthesis, etc
- Intervention studies with anti-oxidants and other free radical scavengers to identify potential chemo-protective measures.
- Intervention studies with known “sensitizing” chemicals.

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#### 2.1.2 ANIMAL STUDIES

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The following issues (awaiting the outcome of *in vitro* research) should be pursued with various animal species/strains:

- *in vivo* laboratory studies with sensitive species/strains
- fertility and developmental studies
- experimental studies with flatworm *C. Elegans* and other lower species to determine impacts of RF on growth and development
- compare responses of young-developing vs. adult animals.

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### 2.1.3 HUMAN VOLUNTEER STUDIES

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So far human volunteer studies have focused on mobile phone radiation effects on cognition, brain electrophysiology, blood pressure, headaches, allergy-like symptoms, sleep disorders, and direct exposure-recognition by the exposed subject.

In addition to such studies we also need to examine whether human bodies (tissues, cells) respond to mobile phone radiation at molecular levels. Such studies with methods of proteomics, transcriptomics and other reliable biochemical analyses, are urgently needed to demonstrate whether or not human tissues, organs, or cells are altered by RF-EMF exposure. Such studies will not only show whether or not humans (or human tissues) respond to RF-EMF, but also will provide information which molecules, proteins and genes react to mobile phone radiation. With this information, it will be possible to confirm existing safety standards or, alternatively, formulate new knowledge-based hypotheses for further health-risk related studies in humans.

By using easily accessible bodily materials and widely accepted methods, the exploration of various materials should be subjected to double blind tests in real and sham exposed cohorts of about 50 to 150 participants to describe thresholds in dose & time.

High priority studies to examine molecular level response in humans should investigate:

- gene expression,
- protein expression,
- protein phosphorylation,
- protein synthesis

Samples for analysis can be

- Buccal smears, hair follicles, skin biopsies, blood samples, saliva, or semen

Low priority studies to investigate cognitive functions

- Cohort and case-cross over design tests of brain function, short- and long-term memories, recall, and other performance measures on standardized cognitive tests, etc.

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## 2.2 DEFINE THRESHOLDS (DOSE AND TIME)

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Following studies with sensitive biological matter, in a series of systematic research we need to establish thresholds in dose and time. For this research different endpoints can be used:

- Cell cultures (DNA, Proteins, etc. )
- Animal studies
- Human volunteers
  - Cognitive tests
  - Investigation of exposed samples

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## 3 DEFINE ACTIVE EMF PARAMETERS

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Knowledge on EMF-Exposure parameters (e.g. frequency, modulation, etc ), which provoke or increase sensitive reactions, will have an important impact on

- the development of safe EMF emitting devices, and

future setting of safety standards. This programme line aims to investigate

- the contribution of different component show each component of RF-EMF signals (frequency, modulation, etc.) contributes to biological responses
- the impact and contribution of the specific field (e.g. various modulations) on molecular alterations in human cells
- the threshold (intensity and time) of exposure with fields of different modulations.

Therefore, in interdisciplinary projects, involving life-scientists and engineers, the following conditions should be systematically investigated in sensitive species.

- Various EMF signal parameters (carrier frequency, modulation, etc. )
- Exposure parameters (intensity and exposure time)
- Exposure patterns (e.g., on/off pattern compared to continuous exposure)

### 3.1 IN VITRO (CELL CULTURE)

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For this programme line, using *in vitro* tests with widely accepted methods (e.g. DNA alterations and “protein expression”) studies of effects of EMF signal parameters on cells with established sensitivity are required.

Proposals with the following endpoints and aims should be given high priority:

- genotoxicity, protein expression and synthesis,
- investigation with free radical scavengers and
- “sensitizing” chemicals to identify potential mechanisms.

### 3.2 IN VIVO ANIMAL RESEARCH

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In this programme line animal experiments have low priority. However, the following issues (awaiting the outcome of *in vitro* research) should be pursued with various animal species/strains:

- *in vivo* laboratory studies with lifetime exposure protocols
- reproductive and developmental studies
- developmental, behavioral and cognitive sensitive model animals (e.g. planaria)

### 3.3 BEHAVIOURAL ANIMAL STUDIES

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Either as part of other animal studies or in projects with lower species such as flatworm the focus on neurofunction and behavior a variety of strains should be tested for their ability to

- Learn
- Memorize
- Orient
- Reaction Time and with experimental mammals decision Quality)

### 3.4 HUMAN VOLUNTEER STUDIES

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In this programme line (impact of specific exposure parameters), by using clearly defined test systems and easily accessible bodily samples and widely accepted methods, the exploration of various field conditions should be subjected to double blind tests in real and sham exposed cohorts. In case of positive findings further systematic research should be carried out to define thresholds (dose and time).

High priority studies to examine in humans should be about:



- gene expression,
- protein expression,
- protein phosphorylation,
- protein synthesis
- cellular signaling pathways

Samples for analysis can be

- Buccal smears, hair follicles, skin biopsies, blood, saliva, or semen.

Low priority: studies to investigate cognitive functions

- Cohort and case-cross over design tests of brain function, short- and long-term memories, recall, and other performance measures on standardized cognitive tests
- post exposure effects
- Cognitive function, in adults and children,
- Interference with sleep.

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## 4 NEURO FUNCTION, COGNITIVE EFFECTS

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### 4.1 HUMAN ACUTE STUDIES

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So far most studies investigated reaction time, little is known about decision quality. We therefore recommend investigating in laboratory settings the quality of decision making under exposure.

### 4.2 HUMAN STUDIES “LONG TERM EXPOSURE EXPOSURE EFFECTS”

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Short term and long term memory

### 4.3 ANIMAL “ACUTE”

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- Decision making
- Decision quality

### 4.4 ANIMAL STUDIES (LONG TERM EFFECTS)

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Memory after long term exposure

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## 5 LONG TERM EFFECTS

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A specific difference to toxicological research is that EMF field intensities cannot be exaggerated to create a Maximum Tolerated Dose (MTD). At high RF-EMF intensities, heat-related damage occurs. Clearly the risk is associated with long term exposure to low-intensity (without measurable heating). Therefore, the investigation of exposure associated toxicology must be studied with an approach, which increases the dose by extending exposure time (sometimes over years).

### 5.1 ANIMAL STUDIES

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In vivo research (on animals) should focus on the following endpoints

- Tumor Initiation / promotion
- Other chronic endpoints evaluated in lifetime studies, such as those currently being carried out by the Ramazzini Foundation (Italy)
- life expectancy
- Teratogenesis and other developmental studies including male-mediated teratogenesis

## 5.2 HUMAN EPIDEMIOLOGY

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In view of the currently ongoing cohort study COSMOS, which recently has started in Europe (5 countries), similar studies should be launched in the USA to have some sort of “replication”.

In agreement with the WHO (Research agenda – 2006, Annex-1) the following epidemiological studies can contribute to describe the exposure associated risk after long term exposure to RF-EMF emitting devices.

- Epidemiology, cohort and cross-sectional evaluations of self-reported long term exposure and validated records of cell phone use with: Alzheimer’s and
- brain
- salivary gland,
- other head and neck tumors, lymphoma,
- other tumors;
- Parkinson’s, Alzheimer’s and other neurodegenerative conditions;
- reproductive impairment in men and women, including measures of sperm count, motility, morphology;
- measure changes in hearing and visual acuity;
- Brain development in children

## 6 NETWORKING - CONFERENCES

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Because the programme is fundamentally international in scope, it is critical that there be created electronic networks to enhance opportunities for exchange of information. To increase the research program's impact and reach the interested public, an extended audience should be given the opportunity to communicate with the research consortia within this programme. Information on worldwide independent research protocols and funded studies should be exchanged among researchers.

The network communication will require and achieve:

- organization of regularly held SKYPE or goto meeting exchanges between experts on selected topics outlined
- to enhance international collaboration and exchange of information
- regular international conferences organized around major areas of expertise that will feature the results of the research agenda proposed in this document.
- involvement of extended audience
- first line information of stakeholders

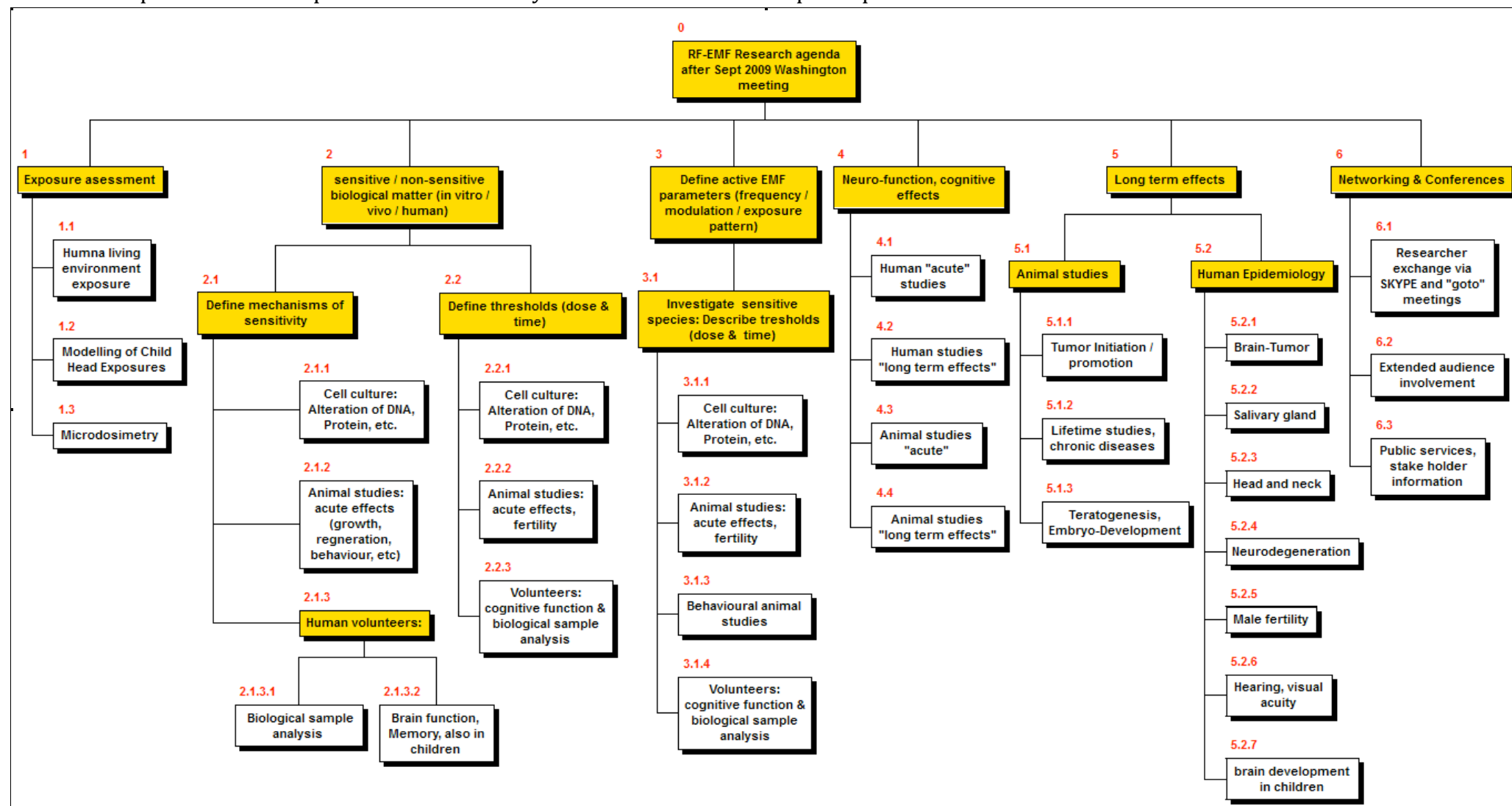
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Washington, Dec. 121, 2009

A list of the conference participants

## 7 ANNEX - 1, GRAPHICAL OVERVIEW

The diagram summarizes major research lines and tasks as detailed in the text.  
 The views expressed in this report do not necessarily reflect the views of each participant..



## 8 ANNEX - 2: WHO-RESEARCH AGENDA 2006

Pos	Priority	Research type	Additional information
	1	<b>EPIDEMIOLOGY</b>	
1a	High	<b>Large scale, longitudinal, cohort, mobile phones, incidence, mortality</b>	A prospective cohort study is being recommended to build on the results of case-control studies, such as the INTERPHONE study, which examines cell phone use for periods of < 10 years, and for which it is not possible to rule out health effects that might appear after a greater latency period or longer exposure. The high priority given to the cohort study on adults reflects the recent findings from case-control studies indicating some risk increases for certain tumours, but where recall bias or selection bias may have affected the results. Non-cancer endpoints (e.g. sleep, headache) for adults are of interest because some studies have suggested these endpoints may be related, and because they can be evaluated concurrently in a cohort study. Note: Though such a study is being established in Europe, it could be significantly strengthened by increasing the size of the cohort through broader international collaboration and additional funding.
1b	High	<b>A large-scale multinational case-control study of brain cancer risk in children in relation to mobile phone use, following a feasibility study</b>	Few relevant epidemiological or laboratory studies have addressed the possible effects of RF exposure on children [INTERPHONE study did not include children as the number of long term users among children at the start of the study was too low for such a study to be informative]. Because of widespread use of mobile phones among children and adolescents and relatively high exposures to the brain, investigation of the potential effects of RF fields on the development of childhood brain tumours is warranted. The uncertainty about the recent findings in adults also applies to children. Because brain cancer in young people is quite rare, a case-control study is recommended as the most appropriate and cost-effective approach.
1c	Other	<b>Large-scale studies of subjects with high occupational RF exposure, including cohort studies as well as the use of the RF occupational exposure data within large scale existing case-control studies</b>	Workers exposed to RF fields in some occupations receive high exposure levels (often to large areas of the body, and sometimes exceeding ICNIRP guidelines). Thus these populations may be well-suited to assess whether a health impact of RF exposure exists. However particular attention needs to be paid to the exposure metric.
1d	Other	<b>Prospective cohort study of children and adolescent mobile phone users and all health outcomes other than brain cancer such as cognitive effects and effects on sleep quality.</b>	Cognitive effects and other general health outcomes have been anecdotally reported in mobile phone users. These endpoints are critical for children because of the importance of cognitive abilities and learning in early development. The outcomes can be assessed in a prospective cohort study of children.
1e	Other	<b>Surveys to characterize population exposures from all RF sources.</b>	Such surveys need to be conducted as collaboration between epidemiologists, physicists and engineers. The studies should focus on the general population and should include for instance, the relative contribution of occupational and residential exposures, and the impact of age, gender and mobility. Regional variations also need to be assessed. These studies will inform the feasibility of future epidemiologic studies and, if appropriate, the proper design of residential epidemiological studies.

2		HUMAN STUDIES	
2a	High:	<b>If ethical approval can be obtained, acute effects on cognition and EEGs should also be investigated in children exposed to RF fields in the laboratory</b>	Possible RF effects on children were specifically raised by the UK's Independent Expert Group on Mobile Telephones (IEGMP, 2000) and the Istanbul WHO workshop (Kheifets et al. Pediatrics. 2005 116: 303-313). Cognitive effects are a priority research area in RF studies. However there are only a few results concerning RF effects on children.
2b	Other	NONE	n/a

3		ANIMAL STUDIES	
3a	High:	<b>Studies investigating effects from exposure of immature animals to RF fields on the development and maturation of the CNS, and on the development of the haemopoietic and immune systems using functional, morphological and molecular endpoints. Genotoxic endpoints should also be included. Experimental protocols should include prenatal and/or early postnatal exposure to RF fields.</b>	In both the UK's Independent Expert Group on Mobile Telephones (IEGMP,2000) and the Istanbul WHO workshop (Kheifets et al. Pediatrics. 2005, 116: 303-313) the central nervous system (CNS), and the haemopoietic and immune systems were considered potentially the most susceptible of the various organs and tissues that continue to develop during childhood.
3b	Other	NONE	n/a

4		CELLULAR STUDIES	
4a	High:	<b>Independent replication studies of recently reported findings on HSP and DNA damage using low level (below 2 W/kg) and/or modulation- or intermittency-specific signals. The dependence of the effects on SAR levels and frequency should be included.</b>	The most useful contribution of in vitro studies is to establish whether there are any reproducible biological effects at low level that are signal and/or cell specific, especially those relevant to cancer (e.g. genotoxicity) or affecting the nervous system. Therefore, in view of some recently published results (e.g. REFLEX), there is a need to ascertain the validity of the findings, possibly via a multicentre study.
4b	Other	<b>Studies of RF effects on cell differentiation, e.g., during haemopoiesis in bone marrow, and on nerve cell growth using brain slices/cultured neurons.</b>	Cancer cells are generally locked into a rapidly dividing and relatively undifferentiated state. The possibility that haemopoietic and/or neuronal tissue might show an abnormal growth response to RF exposure would be important because of lack of investigation in this area.

5		<b>MECHANISMS</b>	
<b>5a</b>	<b>High</b>	<b>NONE</b>	n/a
<b>5b</b>	<b>Other</b>	<b>NONE</b>	n/a

6		<b>DOSIMETRY</b>	
<b>6a</b>	<b>High</b>	<b>Research is needed to document rapidly changing patterns of wireless communication usage and exposure of different parts of the body (especially for children and foetuses), including multiple exposure from several sources.</b>	Experimental exposure conditions need to be based on information gathered from exposure surveys (in contrast to simple source evaluations), especially for children. Little information on individuals' exposure in the general population is available which makes it problematic to estimate the exposure from all radio frequency emitting sources. Due to advancing wireless communication technology, communication devices used in close proximity to the body are getting popular in the general public including children and pregnant women; however dosimetry of different parts of the body in each organ is still limited.
<b>6b</b>		<b>Further work on dosimetric models of children of different ages and of pregnant women. Improvement in dosimetric models of RF energy deposition in animals and humans combined with appropriate models of the human thermoregulatory responses (e.g. inner ear, head, eye, trunk, embryo, and foetus).</b>	The relationship between SAR and temperature elevation should be better modelled to predict potential hazards associated with specific RF exposure conditions and improve the quality of the exposure systems.
<b>6c</b>	<b>Other</b>	<b>Micro-dosimetry research (i.e., at the cellular or subcellular levels) that may yield new insights concerning biologically relevant targets of RF exposure.</b>	Little is known about the field distribution at the micro-scale and consequences of non-uniformity of fields on sub-cellular structures and molecules in terms of mechanisms of bioeffects.

7	<b>SOCIAL ISSUES</b>	
7a	<b>Risk perception of individuals, including studies on the formation of beliefs and perceptions about the relationship between RF exposure and health.</b>	To adequately communicate research results, and to contribute to an informed public debate about RF exposure and health, more knowledge about the prevalence of perception patterns, and the concerns shaping these patterns and their diffusion, is needed.
7b	<b>Studies that analyse, if possible, in an international perspective, conditions of trust and confidence of stakeholders and the general public in technologies, policies, and risk communication and management strategies associated with RF applications.</b>	This would contribute to a general framework of analysis that helps to understand the responses of various stakeholders and experts to public concerns and to increase the effectiveness of communications, and institutional responses to those concerns.
7c	<b>Assess impacts of precautionary measures on public concern and the adoption of voluntary or mandatory policies.</b>	There is scientific evidence that precautionary measures can increase public concern. This evidence is preliminary and needs to be confirmed. In addition, studies should investigate the relevant motives and mechanisms in order to enhance our understanding about impacts of precautionary measures on policy.
7d	<b>Assess the role of health definitions (well-being) and other important concepts in RF risk communication on risk perception and risk management policies.</b>	In order to effectively inform stakeholders, and society at large, there is a need to tune the relevant information to target groups. There is an urgent need to know what role key concepts routinely used in RF risk communication (e.g. "well-being", "significance", etc.) play and their relevance for risk perception and risk framing.
7e	<b>Quantify the health related beneficial effects of wireless communication.</b>	An informed health assessment has to value both possible health risks as well as health opportunities associated with wireless communication (e.g. increased security, decreased feelings of anxiety, etc.).
7f	<b>Evaluate the success of programmes for public and stakeholder participation in various countries.</b>	In order to increase trust in national and international risk management, citizens and stakeholder involvement in risk management has to be secured. In Europe, such programs could be carried out in association with the European program Trustnet.