

Identification of further research needs relating to EMF by the American National Academies

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In spring 2007, the U.S. Food and Drug Administration (FDA) asked the National Academies (www.nationalacademies.org) to „identify research needs and gaps in knowledge of biological effects and adverse health outcomes of exposure to radiofrequency (RF) energy from wireless communications devices“. There upon the National Academies appointed a seven member committee to plan an appropriate scientific workshop. Following the workshop, the committee issued a report of about 80 pages in January 2008 [1]. Divided into areas of research, this report specifies the still unresolved questions according to the invited experts' opinion and gives reasons for it. Broader statements, like e.g. the evaluation of health effects or recommendations about how to meet the identified research needs, are not included.

The committee and the workshop

The "National Academies" are an American consultative body that brings together committees of experts in all areas of scientific and technological endeavour to address „critical national issues“ and give advice to the federal government and the public. The present project was performed by one of the four sub-organizations of the National Academies, the "National Academy of Sciences" (NAS) and was chaired by Frank Barnes (University of Colorado,

Boulder). The workshop of high reputed international experts was held at the NAS in Washington, DC, on August 7-9, 2007. In the workshop also statements of private individuals, external scientists and health officials were considered, which had been submitted in the run-up to the workshop in order to contribute research needs and gaps in knowledge from their perspective.



The workshop was organized into six sessions:

- Exposure and Dosimetry
 - Exposure Systems
 - Dosimetry
 - Exposure Assessment
- Epidemiology
 - Cancer Epidemiology
 - Non-cancer Epidemiology
 - Epidemiology Methods
- Human Laboratory Studies
 - Sleep, Cognition
 - Electrohypersensitivity and Well-being
 - Human Peripheral and Central Auditory and Cardiovascular Systems
- Interaction Mechanisms
 - Biology

- Biophysics
- Models of Interaction
- Animal and Cell Studies
 - In vivo
 - In vitro
- Overarching Issues
 - Short-term vs. Long-term Exposure
 - Local vs. Whole-body Exposure
 - The Question of extrapolating Current Exposure Scenarios to emerging Scenarios
 - are there non-thermal Effects?
 - Differences in Risk to Children
 - Differences in Risk to other Subpopulations such as Elderly and Individuals with underlying Disease States

going research are dealt with in a more comprehensive way. There is a division into „**Research Needs**“ (i.e. 1st priority) and „**Research Gaps**“ (i.e. 2nd priority) for each subject area. This can be only briefly presented in the following.

In brief, the 10 identified Research Needs are:

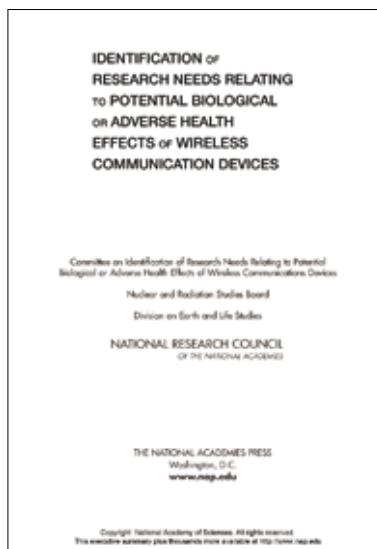
Exposure and Dosimetry

1. Characterization of exposure to juveniles, children, pregnant women and fetuses from personal wireless devices and base station antennas.
2. Characterization of radiated electromagnetic fields for typical multiple element base station antennas and exposures to affected individuals.
3. Characterization of the dosimetry of evolving antenna configurations for mobile telephones (MTE) and text messaging devices.

The report and the results

After the workshop the members of the committee appointed by the „National Academies“ submitted a draft report. Another eleven internationally high reputed and independent scientists or representatives of official bodies were additionally asked to review the report in order to ensure its quality and, where appropriate, to strengthen it by own contributions. In the version now released for publication [1] in summary **ten research needs**, based on the presentations and discussions of the workshop, are

listed. Three items each refer to the first two research areas „Exposure/Dosimetry“ and „Epidemiology“ mentioned above, one refers to the subject area of „Human Laboratory Studies“, two other ones to „Interaction Mechanisms“ and the last one to „Animal and Cell Studies“. In the detailed part of the report the available findings, gaps in knowledge and still on-




It was stressed that the conditions of exposure (environment in which devices are used, different exposure sources from various angles and with multiple frequencies) should be considered, if possible for the worst case (highest radiated power conditions, also at locations close to the antennas). Different body heights have to be considered regarding operational personnel, and for the general population even more emphasis should be placed on the different body statures of adults as well as of

children of various ages when calculating their exposure conditions.

Epidemiology

4. A prospective epidemiologic cohort study of children and pregnant women.
5. An epidemiologic case-control study on child-



hood cancers, including brain cancer.

6. Prospective epidemiologic cohort studies of adults in a general population and retrospective cohorts with medium to high occupational exposures.

Regarding adults it was stressed that the workplaces of occupationally exposed persons with the highest potential exposures should be identified and characterized before the main investigation gets started. In this context, working areas of antenna construction and maintenance as well as the possible exposure of fire-fighters to voice radio signals emitted close to their body were specially mentioned. Moreover, present findings on the following types of cancer would need follow-up studies: uveal melanoma, leukemia, lung, breast, testicular cancers, and (as a non-cancer endpoint) also sperm quality. Regarding children possible behavioural and cognitive effects were emphasized. Studies on brain tumours would be also important, but as these tumours are rare in children, a cohort study would be unlikely to be feasible.

Human Laboratory Studies

7. Laboratory studies including a sufficient number of subjects, with focus on possible adverse effects on the human brain activity identified by means of the electroencephalography (EEG).

Great importance would have to be attached to appropriate exposure arrangements, reliable EEG analysis techniques and multi-center cooperations using identical test protocols. Moreover, little knowledge existed about possible neurophysiological effects under long-term exposure to RF fields. There are still few studies of possible special risks of elderly people, and there is a continuing need to examine a possible disturbance of cognitive performance functions by RF fields, the report states. Of lower priority, but increasingly important would be investigations of the interaction of mobile phones with hearing aids and cochlear implants.

Interaction Mechanisms

8. Investigation of the effects of RF electromagnetic fields on neural networks.
9. Evaluation of doses occurring on the microscopic level.

The aim of this research above all should be to determine more precisely the threshold, i.e. the minimum signal level in the central nervous system that the biological system (e.g. a network of nerve cells) can sense and distinguish from background noise (natural internal signals), i.e. where the „biological perception“ of a radio signal begins. Moreover, it is still unclear whether there is a higher energy absorption at the microscopic scale, e.g. at the boundary between cellular structures with different dielectric properties. The possibility of demodulation of pulse-modulated RF signals by nonlinear biological mechanisms is being studied in ongoing investigations. Lower priority was given to investigations regarding the question whether low-level RF exposure can trigger effects through stimulation of cellular thermoreceptors, as well as the investigation of field effects on ion and molecular transport through the cell membrane. Nevertheless, these questions would also be of interest.

Animal and Cell Studies (in *In vivo* and *In vitro* model systems)

Additional experimental research focused on the identification of potential biophysical and biochemical/molecular interaction mechanisms of RF fields.

This research recommendation is very general; perhaps it reflects the difficulties in agreeing on concrete “Research Needs” under this topic. Accordingly, many topics were listed under “Research Gaps”, subdivided into the sections „Cancer“, „Cancer-related Endpoints (Genetic Toxicology)“, „Cancer-related Endpoints (Other)“, and „Other Health Effects (Non-cancer)“.

Regarding „Cancer“ it is important to note that some studies are still ongoing. If research needs should be left after evaluation of these studies, recommendations on the use of genetically engineered animals (to increase the sensitivity of laboratory studies) would be given, and also on the use of multistage model systems for cancer in tissues that have been hypothesized to be targets of RF action (such as brain tissue). Further genetic toxicology studies may be considered only if evidence of oncogenicity should be identified in any of the ongoing chronic toxicity/ oncogenicity bioassay of RF fields in laboratory animals. According to the report, the following endpoints have still been left relatively unexplored: „Immune System“, „Hormonal System“, „Cell Proliferation/ Apoptosis“, „Gene and Protein Expression“, „Fetal and Neonatal Development“ as well as „Structure and Function of the Central Nervous System“. Here, amongst others, data gaps exist with view to prenatal, neonatal, and juvenile exposures.

Comparison with the WHO research agenda

In January 2006, the World Health Organization (WHO) published the last update of its “RF Research Agenda” [2] within the „WHO International EMF project“. The “RF Research Agenda” gives recommendations for international research activities in the field. The revision was based on a two-day expert meeting in October 2005 at the WHO in Geneva. The Agenda contains a prioritization of research needs, similar to the here described report of the National Academies. „High-priority research needs“ and „Other research needs“ are distinguished in the categories „Epidemiology“, „Human & Animal studies“, „Cellular studies and Mechanisms“, „Dosimetry“ and „Social Issues“. Social issues are

not considered in the assessment of research needs by the National Academies, but the subdivision of the other topics is more or less similar to that of the WHO Research Agenda. On closer examination it turns out that the content of the recommendations is widely identical, too.

Under the topic “**Dosimetry**” the research aims are nearly identical in both documents. Additional key aspects mentioned in the WHO Research Agenda are the exposure dosimetry in different parts of the body and dosimetric models of the energy absorption in tissue combined with appropriate models of the human thermo-regulatory responses. Microdosimetry research at the cellular or subcellular level recommended under „Other research needs“ in the WHO document can be found in “Research Need (9)” under „Interaction Mechanisms“ in the research recommendations of the National Academies (see above).



The recommendations listed in the WHO Research Agenda chapter „**Epidemiology**“ are to be found under (4), (5) and (6) as well as in the accompanying text to the topic „Epidemiology“ in the National Academies Report. This report additionally mentions case-control studies on rare diseases and prospective cohort studies on subjective symptoms as possible study targets in adults and for children case-control studies of childhood cancer diseases taking into account all major fixed point RF exposure sources (mobile radio base stations, AM, FM, TV transmitters, etc.). Here special attention should be directed to the proximity of the residences to base stations.



Regarding „**Human Laboratory Studies**“ both research recommendations emphasize the need for further investigation of acute effects on human brain activity measured by electroencephalography (EEG), but only in the WHO Research Agenda with a clear focus on investigations in children. In contrast to this the American NAS recommendation sets a high value on methodological improvements, special risks or problems of elderly people as well as on suspected long-term effects in the field of neurophysiology.

Both recommendations in parts also match regarding the recommended research endpoints of „**Animal Studies**“. Here the WHO mentions brain development, hematopoietic system, immune system, and genotoxicity as possible endpoints. The National Academies focus on the identification of potential biophysical and biochemical/molecular interaction mechanisms of RF fields whereas the WHO stresses the childhood development (neonatal or prenatal exposure) in its recommendation on „Animal Studies“. This aspect regarding children, however, can be found in the American research recommendation in the accompanying text to this item.

As mentioned above, the microdosimetry studies mentioned in both recommendations are not addressed under „**Interaction Mechanisms**“ in the WHO Research Agenda, but instead under „Dosimetry“. Here the WHO Research Agenda gives no explicit recommendation for „Interaction Mechanisms“ research and refers to ongoing studies. Besides Microdosimetry investigations, the National Academies mention in their recommendations also the study of neural networks under field exposure as well as further points listed under „Research Gaps“ (see above under „Interaction Mechanisms“), in part also here referring to ongoing studies.

Finally, the paragraph on „**Cellular Studies**“ in the WHO Research Agenda describes more concrete research aims than the recommendation of the National Academies, which in part might have been due

to the situation in this research area at that time. So in 2005, when the WHO Research Agenda was drafted, high priority was given for independent replication studies on the expression of heat-shock proteins (HSP) and on DNA damage under field influence. Moreover, with less priority, also studies on cell differentiation, e.g. during sanguification processes in bone marrow, and on the growth of nerve cells were mentioned - both with regard to the fundamental processes during cancer development. The National Academies here - as also in the case of „Animal Studies“ - focus on research needs for the identification of potential biophysical and biochemical/molecular interaction mechanisms of RF fields. Many other topics of lower priority are listed under „Research Gaps“, among them also the topics mentioned in the WHO Research Agenda, with the exception of hematopoiesis (see above under „Animal and Cell Studies“). Thus the comparison of the research agendas of both institutions reveals differences rather in the accentuation of the viewpoints the recommended research shall be based on than in the basic setting of priorities.

Literature

- [1] Identification of Research Needs Relating to Potential Biological or Adverse Health Effects of Wireless Communication. National Academy of Sciences. The National Academies Press, 2008. <http://www.nap.edu/catalog/12036.html>
- [2] 2006 WHO Research Agenda for Radio Frequency Fields. World Health Organization, 2006. http://www.who.int/peh-emf/research/rf_research_agenda_2006.pdf



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