

**MINUTES: Third Meeting**  
**Research Co-ordination Committee**  
**Ettore Majorana Centre, Erice, Italy**  
**26 November, 1999**

**1. OPENING**

Dr Repacholi opened the meeting at 0910 h.. He said that the objectives were to address ongoing research, identify research with relevance to WHO's research agenda and to ensure that any remaining or newly apparent gaps were identified. It was suggested that the previously followed formality of electing a Chair and Rapporteur be dispensed with. There being no objections from the attendees the meeting proceeded under the guidance of Dr Repacholi.

**2. PREVIOUS MINUTES**

The previous minutes had been circulated, commented upon, accepted and finalized by email and copies on the EMF Project web site or were available from WHO for anyone who had not yet received a final approved copy.

One of the actions arising from the previous meeting was the establishment of a database detailing ongoing research. This had been completed and can be accessed on the EMF Project web site. It was essential for updates to be provided in a timely fashion in order for the database to be optimally useful in tracking ongoing research and identifying areas that still required attention. Dr Repacholi specifically asked attendees to check the content of the database and send any ongoing work not included there using the format appearing on the web site. A copy of the research agenda has also been published and circulated but it is also available on the web site. It was essential to identify KEY areas that remain unaddressed or that had been newly identified and needed to be addressed to complete the database of information for cancer and health risk assessments. Dr Swicord agreed to provide an update on remaining gaps at high frequencies and Dr Repacholi would do the same for static and low frequencies. Supplementary information from any of the attendees would be welcome.

***Static magnetic fields***

Dr Repacholi noted out that static magnetic fields, while outside that areas of interest of many attendees at the pulsed RF meeting, it was import in the context of the research agenda because of emerging technologies coming closer to widespread application. Almost no research results were available - little useful epidemiological data and minimal animal or cellular data. Several countries including Japan, Germany and the USA were spending large amounts of money on the development of magnetic levitation transportation systems. It was urgent to undertake research on static magnetic fields so that the same concerns and difficulties experienced with the rapid and widespread introduction of cellular telephones would not be repeated.

In the near future WHO would be establishing an agenda for static magnetic field research that would be the minimum needed to complete basic health risk assessments. This would be circulated for comment and funding sources established to have this research completed as a matter of urgency.

***ELF Fields***

The suggestion that exposure to ELF magnetic fields is associated with an increased incidence of childhood leukemia remains of concern. The long awaited study from the UK is due to be published in December and may shed additional light on the question. Unfortunately it will have the drawback of not having a "transients" component in the exposure assessment. The new study being started in Japan will do so.

Breast cancer, neurodegenerative disorders and hypersensitivities remain unaddressed. There is still a requirement for:

- better exposure assessments including accounting for transients,
- additional animal studies better simulating realistic human exposures,
- additional human studies focussing on memory loss and hypersensitivity, and

- laboratory studies with direct significance to in vivo effects that could lead to adverse health outcomes with emphasis on replication of reported memory loss.

The current reliance on time weighted averages in exposure assessment MUST be supplemented with assessment of transients and harmonics.

### ***RF Fields***

There are still inconsistencies regarding effects on DNA. While there may not be direct effects, it is still unclear whether or not there may be epigenetic effects. Cancer initiation studies also need clarification but would be addressed later by Dr Swicord. Similarly cancer promotion needs further attention. These appear to have been funded by the EC. Epidemiological evidence associating cancer with RF exposure remains far short of the required strength and consistency to reach any conclusions. However the large multinational study being co-ordinated by IARC and funded by the EC has good prospects of filling that gap in the WHO research agenda. Each participating countries will be allowed to publish its own results before the meta analysis is carried out and published by IARC. Finally, additional information is required about workers using high power induction devices and post market surveillance of cellular telephone users should be initiated.

### **3. REVIEW OF THE PRESENT RESEARCH AGENDA FOR RFs**

Dr Repacholi asked Dr Swicord review RF research in progress to assist in identifying gaps. A condensed version of the overheads used by Dr Swicord during his presentation is given in Appendix A.

Dr Swicord stated he would set the stage by addressing what research is currently under way and then deal with each of the seven items in the current WHO research agenda. Studies were summarized from the WHO database but there exists a number of possible ways of counting results which could give different interpretations. For example, the list of completed studies can be expected to be conservative because not necessarily all completed studies have been incorporated in the database. By contrast, any list of ongoing studies may provide an optimistic view of the situation because some of the studies may not be completed. Similarly the list of EU studies is conservative because the exact number is not yet known. Attention focused on what frequencies and modulations were being addressed. There was a clear concentration of current research on cellular telephone frequencies but there was still a good deal of research in other RF areas.

Standard animal tumour bioassays completed to date have shown no increase in tumour formation due to RF exposure. Seven out of eight promotion or progression bioassays have shown no positive effects. A study using a transgenic animals exposed to a GSM simulated signal reported positive findings. Two replication of this study are currently funded or underway. An acute study reported observing DNA damage in rat brain cells. Three attempts at replication or conformation have failed to confirm these findings. This raises the question of when can an issue be considered closed? The same question applies to the calcium efflux and ODC results. In the non-cancer area there were BBB and chicken embryo viability results reported but having questionable validity and subject of serious debate as to whether or not to pursue further.

In the area of human studies, three melatonin studies had both positive and negative results, blood pressure and headache increases might need to be replicated. Studies on sleep disorders have also given both positive and negative results with the overall picture being confusing and therefore needing further consideration.

In vitro calcium efflux results have been both positive and negative but not consistent and probably do not need to be pursued further. DNA damage results have also been both positive and negative, but again no ability to replicate the original findings. Evoked potential changes also give a mixed message but probably should be addressed further. While noting cell transformation, DNA synthesis and cell proliferation results were mixed there was no particular comment on pursuing the areas with additional studies. However ODC changes need to be addressed.

Dr Swicord then turned his attention to the specific WHO research agenda items (see Appendix A).

Agenda item (i) has been fully addressed. There were two rat and two mouse projects, six studies in all at four laboratories. There were two EC studies (Germany and Finland) where animals were either induced with carcinogenic chemicals or were transgenic.

Agenda item (ii) was fully addressed by the pim-1 replication in Australia plus a pim-1 study being supported by the EC in Italy.

Item (iii) is not being fully addressed although a study in France addresses the behavioural elements of the item.

Item (iv) seems to be well addressed by the large scale IARC mobile telephone study which is currently due to cover nine countries in Europe plus Israel (four additional countries have intentions of participating but finding has not been put in place to date). In addition there is a large occupational study in progress in the UK (currently in a pilot study phase).

Items (v) and (vi) are not currently being addressed.

Item (vii) is addressed to large degree. The possible exceptions are replications of ODC results and DNA aberration results.

Dr Repacholi thanked Dr Swicord for his summary and noted that there were additional studies in Australia and Finland. He requested that Prof. Franz Adlkofer (Verum Foundation, Munich) and Prof. Jukka Juutilainen (U of Kuopio, Finland) provide additional specific information to allow for updating the research database.

#### **4. DISCUSSION OF THE RESEARCH AGENDA FOR RFs**

Regarding item (i) Dr Repacholi asked whether there were any other studies besides those already mentioned by Dr Swicord. Dr Ohkubo said there was a long-term study under way in Japan. It was investigating brain effects from RF fields at high levels (0.67 to 2 W/kg average brain SAR). The pilot phase has been completed and the full study is to proceed. He agreed to provide details for inclusion in the database.

Dr Vecchia described a proposed program in Italy that will have some impact on item (i) but it is currently awaiting funding approval. As soon as the situation is final, he will provide details. Dr Murphy noted that there was also relevant activity regarding ultra wide band effects for which he would provide details. Dr Repacholi re-iterated his earlier request that details of funded studies addressing any of the agenda items be provided at the earliest possible dates.

Dr Repacholi posed the question of what might be anticipated after the pim-1 studies were completed. Should some other transgenic model be tried as well? Would, for example, the P53 knockout model give additional information? Dr Juutilainen noted there was another study using both non-transgenic and ODC transgenic mice with UV already in the database but the results were not expected before next summer. Dr Swicord reported that at a workshop prior to the BEMS meeting in Florida the general view was that transgenic models were appropriate if you knew what you were looking for. However, if investigators were looking at general risk of cancer it was far better to use the standard general two-year bioassay. Transgenic models were only suited to specific tumour types. Dr Repacholi pointed out that the standard six month duration for a pim-1 assay was found to be too short in the EMF case where results were found only after 10 months exposure.

Dr Swicord noted that people at the workshop who routinely used the pim-1 model were horrified at running any study using them beyond six months because the model was not designed for such use. Dr Repacholi replied that the pim-1 RF results may still be interpreted as indicating there is some as yet unknown effect of RF. Dr Swicord insisted that independent of what physical or chemical agent might be used, the pim-1 model should be investigated for two years to establish its performance adequately under such circumstances before it is applied for times longer than the standard six months.

Dr Veyret summarized the COMBIO research program being carried out in France. It includes a human study using epileptic patients, animal studies involving the blood brain barrier (BBB) and

a headache model in rats, neurotransmitters in rats, brain metabolism in rats, memory loss in rats, cochlear effects in guinea pigs all using GSM 900 and 1800 signals. The research is funded at 2M Euro over two years. Dr Murphy noted that the US Air Force was replicating and extending the Salford BBB studies with results to be expected in about two years. Dr Schuller reported that two studies in Germany during 2000 will be extending completed agenda items. He would send details through FGF. There has also been an Australian study under way at Swinberg University over the past 8 months looking at human memory loss. Publication was anticipated sometime next year.

Mr Matthes reported on a study on otoacoustic emissions that had been carried out in Germany and he would send details. Dr Murphy noted extensions of studies to mm wave frequencies and an extensive program on neurotransmitters were in progress with details to be supplied. Dr Ohkubo said work was in progress in Japan on auditory brain stem response and a slightly different approach to evaluating RF effects on rat performance in a radial arm maze. Dr Thuroczy offered to send details on human volunteer studies being carried out in Hungary. Regarding item (iv), Dr Repacholi enquired whether there were any more details available on the UK study. Dr McKinlay reported that the complexity of the exposure situation was being explored during the pilot phase. Particular attention was being given to establishing an exposure metric for broadcast fields but that availability of data for establishing work histories in support of exposure assessment was also being investigated. It is anticipated that the pilot phase will take at least 18 months and only then will consideration be given on whether to proceed further. It is still too soon to tell what numbers of subjects will be available. Considerable difficulties associated with fragmentation arising from privatization are complicating matters.

The IARC study has funding in place for the European participants but other countries outside Europe such as Australia, Canada, New Zealand and the US have not approved funding to date. At least a pilot version is expected in Australia but to date its funding has been delayed. A commitment has been made to participate in the full-scale study but possible funding is yet to be found. Dr Israel noted that Bulgaria has three studies in the area of agenda item (iv). Two are complete and one is in progress - broadcasting, power frequencies and railway operators. Details will be sent.

Dr Ohkubo and Prof Taki noted Japan is intending to join the IARC study and will be sending pilot results by year-end. Dr Rubtsova noted that a study on workers in RF broadcasting had started in Russia this year and would be completed next year. She would send information on the protocol for the study. It is based on 2,000 to 3,000 subjects and is receiving funding from special services outside the military. They will also be investigating nervous system parameters in a retrospective cohort study, carrying out a carcinogenic study and looking at the state of the cardiovascular system in 200 to 300 subjects. Dr Repacholi offered to assist in arranging for advice on establishing protocols for the studies.

Upon re-convening the meeting after a brief coffee break, Dr Repacholi invited Dr Adlkofer to outline the proposals funded by the EC. Eleven groups in seven EC countries will carry out a number of projects. They are grouped into six work packages.

- Direct and Indirect Genotoxic Effects.
- Embryonic and Human Stem Cells - Differentiation and Proliferation.
- Gene and Protein Expression.
- Effects on the Immune System.
- Cell Transformation.
- Exposure Equipment and Dosimetry in Support of All Work Packages.

It is recognized that there is a need for in vitro work in support of the search for basic mechanisms. Dr Repacholi enquired whether extra information would be forthcoming on immune system and DNA effects. They will be using a cell bank and comet assay in both the RF and ELF frequency ranges as part of a comprehensive work package. Work package 3 will also be looking into signal transduction and ELF and RF effects on kinases. When queried about the

time scale and equipment for the studies, Dr Adlkofer stated that each project had its own schedule but the program overall will run from 2000 and end in 2002. Where possible the projects will be using existing equipment but where necessary new equipment will be added. Work on differentiation in RF exposed embryonic stem cells has shown no effects to date. The work package includes examination of cell surface receptors and many other end points. They feel that the overall program is so thorough that if it finds no effects there is little likelihood that any effects will ever be found. Dr Adlkofer offered to provide detailed information for inclusion in the WHO research database.

Dr Juutilainen pointed out that there were supplementary studies being carried out by Dr Maria Rosaria Scarfi in Italy in support of in vivo work looking at interactions between carcinogenic chemicals and RF. The study will use a pesticide as well as a carcinogenic chemical that appears in water passed through chlorination systems. Dr Juutilainen will supply information for the database. Dr Swicord noted that some in vitro replication studies put forward to the EC failed to get funded but some were still of interest and would likely be funded from other sources. Examples were replication studies on ODC and DNA aberrations at the University of Bordeaux, and in Italy and Finland costing 1.4 M Euro. Jo Anne Basile (CTIA) said some collaborative work would be running in the US dealing with the replication of micronucleus studies. Prof. Taki said that extensive ELF studies were carried out in Japan had been published and these would all be carried out for the RF as well. Details would be sent.

Dr Hocking raised the issue of epidemiological studies connected with post market surveillance for products like cellular telephones (see Appendix B). Overall he has found that feedback on the effectiveness of programs needs to be strengthened. This can only be done by a health surveillance system based on cases encountered by clinicians. Most countries do not collect such data although in France Dr Miro has set up such a database to report cases. Dr Hocking provided an outline which is presented in Appendix B. Dr Repacholi pointed out that there are no resources at WHO whereby to coordinate such a database. Dr Kheifets commented that there would seem to be a lot of problems since information is being collected but without any information on the population from which it is being drawn. Without developing the process in a refined manner as a part of a well-defined system the prospects for utilizing the information would be highly questionable. Dr Hocking noted that in occupational health, tracking of chest diseases in such a manner shows the occurrence of occupational asthma problems that might otherwise be missed. Dr Ahlbom said that while such a database might not be useful from a strict epidemiological viewpoint it is recognized as useful in situations like surveillance of drug side effects.

Dr Swicord pointed out that it has been very useful in the USA for bringing attention to problems with medical devices and drugs. In the US, the Radiation Control for Health and Safety Act of 1968 requires such reporting of radiation exposures but it has been no public value for non-ionizing radiation safety. Dr Repacholi noted that the US requirement was accident and over exposure related. Dr Miro reported that, for the database set up in France, reporting is carried out at industrial sites to follow the health of workers. At present it contains nine accidents and more than 2,000 health problems. It has been easy to follow the evolution of the workers' health since the inception of the database. It also gives better information about exposures at workplaces and underscores the importance of having good resources for exposure assessment at each workplace. The database nonetheless is still too small and he is hoping to extend it to other countries to include more people. Dr Gronau asked how would problems that come up be dealt with? There is also the beneficial effect that the workers feel they are being "cared for" when information about their health status is being kept and monitored.

Attention then turned to WHO research agenda item (v) on emerging technologies. Dr Murphy referred to ultra wide band effects that are mostly of military interest. A great deal of work has been done on the subject and it is currently being published. Work will be continuing with other studies planned. No epidemiology studies are planned since population exposure is very small

and only of short time duration. Another area is that of extremely high peak power pulses. Dr Pakhomov volunteered to collect information on the subject and provide it to WHO for review. Dr Schuller enquired as to the definition of an "emerging" technology. A cell phone base station and a TV broadcast tower were similar in terms of the carriers and similar in that both have AM and FM modulations although the latter differ in some respects. UMDS is again similar but with differing modulations. Is it reasonable to characterize it as an "emerging" technology? Dr Repacholi stated that it was essential to maintain a rational research agenda and to allow for some reasonable extrapolations from existing knowledge. However, cellular telephones did represent a radical departure from normal RF exposure situations and UWB radars have distinct pulsing with very high intensities. Thus they need to be properly investigated.

Human studies are definitely in need of more work. This type of study is particularly important since it can provide direct evidence for human health assessment with regard to sleep disorders, headaches, non-specific symptoms, memory effects, etc. Dr Repacholi enquired whether there were any other effects of interest in this area. Dr Swicord presented some additional information regarding work proposed by the MMF and GSM Association on cognitive disorders and behaviour. Other human studies included provocation in regard to sleep or EEG disturbances, headaches, blood pressure, hearing, skin irritation and working memory effects. These studies as well as animal behavioural studies that are not currently funded are being actively pursued at Karolinska Institute, University of Strasbourg, NRPB and MRC and are seeking similar government involvement. Prof. D'Inzeo noted that effects on the cochlea, in vitro, in vivo and EEG studies are being proposed for support under the national program (Elettra2000) in Italy. They are looking for partners on neuron studies in other countries. Dr Schuller stated that sleep disorder and EEG studies were under way at the University of Kiel and details would be provided to WHO.

With the discussion of the existing research agenda for RFs completed, Dr Repacholi opened the floor to each of the countries to raise items that they considered might still be needed but none was put forward.

## **5. ADDITIONAL ITEM**

Since some time was still available before the break for lunch, Dr Repacholi invited Dr Nesrin Seyhan Atalay, the delegate from Turkey, to provide an introductory summary of work being carried out there.

Dr Seyhan reported that work was under way looking at guinea pigs exposed to 1.9 kV/m electric fields - changes in Hp (hydroxyproline) in lung, liver, kidney, hematocrit and blood protein and albumin. All were found to be elevated for vertical fields. Similar studies were to be carried out using horizontal fields and for reduced field intensities of 0.9 kV/m and would be extended to include effects of 50 Hz 20 G magnetic fields on blood and brain ions. Work had also been carried out with the same magnetic field exposures applied to an epileptic mouse model with no significant effects observed. It was anticipated that similar work on ELF would continue in Turkey.

In response to a query about objective versus subjective aspects of agenda items (iii) and (v) it was noted that one relates to animal and the other to human studies.

## **6. REVIEW OF THE PRESENT RESEARCH AGENDA FOR ELFs**

When the meeting reconvened after the lunch break attention turned to a review of ELF studies. Dr Repacholi noted that the ELF database was to be improved over the next few months. In the epidemiological area there was a childhood leukaemia study under way which was to include an evaluation of transients. Dr Ohkubo reported that the study was being carried out in Japan with Dr Kabuto as the principal investigator. It had started this year and would continue through 2001 and conclude in March 2002 with a report due that summer. It was to include 1,000 leukaemia cases and 500 brain tumour cases. Prof Leitgeb enquired what was the age limit for the children. It was replied that they were under 15 years of age.

Dr Repacholi enquired whether there were any other cancer studies under way. Dr Rubtsova reported that Russia was starting a childhood leukaemia study to be completed by the end of 2000 that would include 600 cases and a similar number of controls taken from children presenting as trauma cases. A copy of the protocol would be provided. Dr Vecchia reported on a study to start in Italy in February 2000. A pilot study had been carried out over the past two years. What was envisaged was a broad study covering many different cancers. The protocol would cover 16 of the 20 Italian regions. It was expected to run at least three years and cover most cases of childhood cancer amounting to about 1,200 per year. Exposure assessment was to be based on dosimeters, spot measurements and long term area measurements in houses and be supported with extensive questionnaires. Dr Repacholi suggested that it might be possible to collaborate with the Japanese study in the exposure assessment protocol to hopefully improve the possibility of intercomparisons. Perhaps it would be useful to convene a workshop. He also suggested a determination of the frequency of exposure to short-term transients should be included in the exposure assessment.

Dr Rubtsova said that the Russian study would be using an exposure load calculation that she presented to the attendees with a series of overheads. The calculations were developed for application in occupational situations but could easily be extended to childhood cases. She emphasized the need to take into account the highest expected values rather than the average values since effects are dependent on the induced currents. Mr Matthes reported that a German study was close to completion. It took into account appliances, power lines and included 16 2/3 Hz fields from railways. A report was expected within about 6 months. Dr Kheifets noted there were 3 studies under way in the USA - one in the San Francisco area involving about 600 cases, another focussing on childhood leukaemia plus there were also a couple due from the UK with results due in a couple of years.

Dr Repacholi asked about studies investigating other diseases such as breast cancer, other cancers in adults, and neurodegenerative diseases. Dr Kheifets noted there were three breast cancer (residential) studies under way - Long Island, Southern California and Seattle.

Consideration is being given to an occupational breast cancer study with other dosimetry parameters. Blood pressure is also being studied but nothing else in the area of neurodegenerative diseases to her knowledge. Dr Ahlbom stated that there was a breast cancer study in Sweden using a retrospective database combined with a job exposure matrix that will be conducted over the next couple of years. While the study is funded, it is looking for extra funding to improve the job exposure matrix to better address women's issues. It was also reported that a study on pregnancy outcome from EMF exposure was being carried out in Sweden. It will investigate time to pregnancy and birth weight. However, difficulties were experienced in finding "exposed" subjects. Details to be sent to WHO. Dr Kheifets noted that there was another pregnancy outcome study in progress in the San Francisco area that was due to conclude in about two years.

The epidemiology database should be well satisfied once the studies currently in progress are reported.

Dr Repacholi noted that animal studies have been conducted using almost entirely "clean" sinusoidal fields and enquired whether any more "realistic" field conditions had been explored. Dr Ohkubo responded that in Japan a study looking at mammary tumour promotion in rats using circularly polarized magnetic fields had just been completed. They are also starting a skin cancer promotion study and a brain tumour promotion study and a leukaemia promotion study is being planned. All are due to be completed over the next couple of years. In the rat cancer promotion study no effects were observed up to field strengths of 350  $\mu$ T. A mammary tumour study is being carried through with a similar protocol. Results to date have been interpreted as showing no significant differences between exposed, sham exposed and control groups.

Dr Repacholi enquired whether there were any human studies investigating memory and hypersensitivity or changes in blood pressure. Dr Kheifets said some work had been completed

on heart rate variability but the data was itself variable and a search was being made for more data from occupational or field studies among highly exposed individuals. Dr Israel noted there was data from two studies that had been carried out in Bulgaria and he offered to provide data from those studies. In response to a query about what was "hypersensitivity," Dr Repacholi responded that the term referred to people who report symptoms such as headaches, dizziness, skin rashes etc that they attribute to EMF fields. However, when challenged blind these people cannot identify whether fields are present or not.

Dr Ohkubo noted that in Japan effects have been seen at 100  $\mu$ T in a study replicating the Liburdy melatonin results. Details are soon to be published.

Dr Kheifets reported that work was being funded on cell differentiation and cellular communication at Battelle and elsewhere. Dr Veyret noted that a group at the Pasteur Institute in Paris had observed effects at 600  $\mu$ T and publication of the results was due soon. Dr He reported that studies in China have shown induction of gene expression by ELF supporting the hypothesis that 50 Hz fields can promote leukaemia. The previous work will be extended in similar directions. Details will be sent. Dr Juutilainen noted that experiments were being carried out on yeast cells following up on effects observed in animals. Further information will be sent.

## **7. GENERAL RESEARCH**

Dr Repacholi reminded attendees that a summary of ongoing studies was needed for researchers to limit unnecessary research and provide opportunities for collaboration. Interest has been expressed in establishing a general research database that can be interrogated externally. However, the database that WHO is developing and maintaining is only intended to focus on studies of particular relevance to the research agenda. Dr Repacholi then opened the floor to discussion of general research topics.

Dr Kheifets acknowledged that there was a focus on studies needed for the research agenda but there was no reference to timing. Dr Repacholi stated that the IARC/WHO reviews would occur in 2001 and 2002 for ELF and in 2003 and 2004 for RF. In particular, the IARC ELF carcinogenicity meeting is due to be held in June 2001. It would provide an updated classification of ELF carcinogenicity similar to that carried out by the NIEHS. Then WHO would use the IARC results on cancer and conduct a full health risk assessment for cancer and non-cancer effects in 2002. Thus ELF research results are needed by mid 2001. He also noted that peer review publication acceptance prior to the completion of the health risk assessments would be considered.

The "fate" of studies published after the project review was questioned. Dr Repacholi noted that this deadline reflects is the date targeted for the WHO Project to terminate since it cannot continue indefinitely. It is not envisaged that subsequent reports would have an effect on the health risk assessment unless very significant new results were discovered. Furthermore, IARC and ICNIRP would carry on ongoing reviews. The prospects for a sufficiently complete database appear excellent on the basis of the research currently in progress.

Prof Taki, Japan stated that there appeared to be too much focus on low level effects. Reports showing effects at high levels need to be dealt with because of the possibility of extrapolation to low levels. In the low frequency region there has been less limitation on levels suggested but in the RF region the temperature elevation is taken as a basis for limiting research.

Dr Juutilainen noted that there was data lacking, both CW and pulsed, for the frequency range from 1 to 100 kHz. Dr Repacholi agreed but pointed out that the IF working group report stemming from the meeting in Maastricht earlier this year could be expected soon and it would help clarify the situation for those frequencies.

Prof Leitgeb asked about research on risk assessment itself since it would appear most likely that a definite risk will not be identified. Therefore it is important to ask about the implications for limits and for public health and what would be acceptable risk levels. Dr Repacholi stated that two efforts are addressing such matters. First, WHO is working with NIEHS to develop a protocol on criteria for acceptance of literature and second, WHO will advise national authorities

regarding public health impact through standards and standards harmonization and by comparisons with known risks (e.g. ionizing) to put them all in perspective. All these results will come out in the WHO EHC document on risk perception and communication.

Dr Santomaa stressed that the target should be to aim for standardization and harmonization.

There should be a special research effort to address averaging issues - 1 g versus 10 g - and an expansion of harmonization to cover Russia and China. Dr Repacholi suggested the topic of averaging might best be addressed by a working group between IEEE and ICNIRP.

Prof Taki requested clarification about what is meant by transient fields and, in particular, what differences might be expected in RF effects when field levels are changing rapidly. It was apparent that the term is very loosely used and does not have a clearly defined meaning. Dr Veyret pointed out that the subject is of sufficient concern that the COST bis244 has organized a meeting for 6-7 May, 2000 that will be dealing specifically with the subject of transients.

Dr Veyret continued with a question as to how long citations are intended to be in the database and how is accuracy of the information maintained. Dr Repacholi stated that citations extend from approximately 1995 onwards. Errors are corrected as they are noted but there is no specific active checking process in place. It is essential that principal investigators and others who have an interest in the database review the contents and provide feedback. Corrections will be made according to information received. Dr Veyret suggested that the citations be expanded to include the address of the principal investigator, a full list of authors and a full abstract. Dr Murphy made reference to the IEEE database that currently has 1,200 references. It will also be cross-referenced. Dr Schuller made reference to a similar database being maintained in Germany. It is a multi-step database with published papers. At the second level it has protocol details and biological models. He suggested consideration might be given to merging all the databases under the WHO. Then the only separate database would be for ongoing research. Dr Repacholi stated the possibility of collaborating with the IEEE to set up a combined database would be explored and WHO would look into the ongoing maintenance of it.

## **8. NEXT MEETING**

The EMF Project collaborating centre at Brooks Air Force Base, Texas, USA has graciously offered to host the next meeting at their facilities in November 2000. The final date would be circulated as soon as it is decided.

## **9. CLOSING**

Dr Repacholi thanked all attendees for their contributions to the meeting. The results of this meeting have been very helpful, both to WHO and to researchers in the field who need to know what further research is needed to better health risk assessments from EMF exposure. There is still much work to be done. The list of attendees is shown in Appendix C. He also thanked Dr Tony Muc for taking the minutes of the meeting.

## **APPENDIX A**

### **Condensed version of overheads used by Dr Swicord**

WHO agenda item (i)

Several animal experiments, using various RF exposure regimens, are currently under way, and their results should add to the required database for health risk assessment. However, at least two more, large-scale standard 2-year animal bioassays, such as those typically conducted by the US National Toxicology Program, are needed to test for cancer initiation, promotion, co-promotion and progression. These experiments should expose normal animals and *animals initiated with chemical carcinogens* to RF fields in the mobile telephone frequency range, using one of the common mobile telephone system pulsing patterns, for 2-6 hours daily. Each study should use a range of intensities (normally 4 different SARs), with the highest being just below the level that may induce temperature changes.

PERFORM A . (1) GSM 1800 Bioassay (Mouse study & Rat study). (2) GSM 900 Bioassay (Mouse study & Rat study). Approved for support by EC

*PERFORM A. DMBA Replication study. Approved for support by EC. "Combined effects of EMF with environmental carcinogens". Univ. of Kuopio. Approved for support by EC.*

This agenda item is fully addressed by the above listed studies

WHO agenda item (ii)

A large study has suggested that exposure to RF fields increases the incidence of lymphomas in genetically manipulated (transgenic) mice. There is need for at least a further two large studies, using designs similar to (i) above, to clarify the issues raised by this study. Follow-up research is also needed that provides information on the health implications of effects found in transgenic animals.

PIM-1 replication conducted in Australia

PIM-1 replication conducted under PERFORM A. Approved for support by EC.

This agenda item is fully addressed by the above listed studies

WHO agenda item (iii)

Additional studies are needed to test the reproducibility of reported changes in hormone levels, effects on the eye, inner ear and cochlea, memory loss, *neurodegenerative* diseases and neurophysiological effects. These studies can be performed on animals, but where possible, they should be conducted on human volunteers.

COMOBIO project on behavior

*France Telecom project on MS using EAE in rats.*

PERFORM C, a proposal to the EC that was not funded would address inner ear and cochlea, memory loss through human studies, and address memory loss by an animal behavioral study that would also attempt to replicate the work of Lai et al.

No funded studies addressing most of these issues. Please note: human studies are preferred (see item vi).

WHO agenda item (iv)

There needs to be conducted at least two large-scale epidemiological studies with well characterized, higher-level RF exposures to investigate cancers, particularly in the head and neck, and any disorders associated with the eye or inner ear. These studies should preferably be on mobile telephone users or on workers in industries giving high RF exposures provided valid exposure assessments can be developed.

*Multi-country case control study of mobile telephone users coordinated by IARC - Approved for support by EC. UK National study to investigate occupational exposure to RF.*

The extremely large IARC study and the UK occupational study appear to address this agenda item with the exception of disorders associated with the eye.

WHO agenda item (v)

Both epidemiological and laboratory studies are needed to provide basic information that allows better assessments of any health risks from exposure to radar technology, particularly emerging systems such as ultra-wide band radars.

Current proposed work does not address this agenda item.

WHO agenda item (vi)

Well controlled studies are needed to test people reporting specific symptoms, such as headache, sleep disorders or auditory effects, and who attribute these symptoms to RF exposure. Past human volunteer studies of this type have not successfully linked the symptoms and exposure. Several more controlled investigations should be performed to investigate neurological, neuroendocrine, and immunological effects.

Currently funded programs do not address this item

WHO agenda item (vii)

In vitro studies normally have a lower priority than in vivo or human studies in health risk assessment. However, such studies can be of great assistance if they are directly relevant to possible in vivo effects, and address the issues of RF exposure thresholds and reproducibility for reported positive effects on cell cycle kinetics, proliferation, gene expression, signal transduction

pathways and membrane changes. Theoretical modeling investigations can be useful if they support in vivo studies by proposing testable basic mechanisms of RF field exposure. In vitro studies supported by the EC. "Risk evaluation of potential environmental hazards from low-energy EMF exposure using sensitive in vitro methods". VerUm Foundation. Approved for support by EC.

It appears that currently sponsored research addresses this issue with the exception of some replication issues on ODC and DNA aberrations.

Summary of studies related to related to cellular telephony and health

	Completed	Ongoing	EU Approved	Total
Epidemiology studies	8	3	(IARC, 14 inst.)	12+
Human Studies	25	20	-	45
In vivo studies (acute) Cancer relevant	5	4	-	9
Cancer related	13	11	-	24
Non-cancer	5	5	-	10
In vivo( bioassays) Standard	7	3	4	14
Sensitized	8	6	3	17
In vitro studies	45	18	12	75
Grand Totals	116	70	20+	206

Studies are listed on the WHO web site: <http://www.who.int/peh-emf/database.htm>

Animal Tumor Bioassays (standard):

Completed studies - 7

Ongoing studies - 3

EC Approved - 4

(-) No increase in tumor formation reported in animals exposed in completed studies.

Animal Tumor Bioassays (promotion & progression models):

Completed studies - 8

Ongoing studies - 6

EC Approved - 3

(+) One study reported increased lymphoma mortality in transgenic mice:

Repacholi 1997, Rad Res 147:631-640). Ongoing replication study by Kuchel et al., funded by the Australian Government. Replication to be conducted in Austria -EC Approved project, PERFORM A.

Acute Animal studies (cancer relevant):

Completed studies - 5

Ongoing studies - 4

EC Approved - 0

(+) DNA damage in rat brains (with 2450 MHz exposure was reported by Lai & Singh (1996 Int J Rad Biol 69:513-21, Bioelectromag 16:207-210, Bioelectromag 18:446-454). (-) Attempts to confirm and replicate involving three additional laboratories have failed:

(1)Malyapa (2450 MHz CW replication) Radiation Research 148:608-617, (2) (ongoing)

LaGroye (2450 MHz PW replication) (manuscript in preparation), (3) (ongoing) Lai & Singh and Tice joint replication.

Acute Animal studies (Cancer related):

Completed studies - 13

Ongoing studies -11

EC Approved - 0

Ca<sup>++</sup> efflux

(+) Alterations in Ca<sup>++</sup> levels were reported in the rat temporal cortex (Thuroczy 1997 World Congress). (-) Findings of Meyer et al. 1998 BEMS meeting (in vitro study using neuroblastoma cells) do not confirm this result.

ODC activity

(+) Decreased ODC activity and increased polyamines in fetal rat brain were reported by Cain et al. (1999 BEMS meeting). A replication of this work is to be conducted at Battelle PNL.

Acute Animal studies (Non-cancer):

Completed studies - 5

Ongoing studies -5

EC Approved - 0

Blood Brain Barrier

(+) Increased blood brain barrier permeability was reported by Salford et al. 1994 (Microsc Res Tech 27(6):535-542). (-) Two additional studies failed to confirm these findings. (Fritz & Hossman 1997, Acta Neuropathol 94(5): 465-470 & Nagawa & Uneo (manuscript in preparation).

Body weight changes

(+) Increased body weight and sperm cell ratio was reported by Lerchl et al. (1998 BEMS meeting). (-) No similar reports have been made by the investigators conducting animal bioassay or other animal experiments.

Chick egg viability

(+) Yobicier-Simo et al. reported effects on chick embryos (1998 BEMS meeting). Experimental procedures are questionable.

Human studies:

Completed studies - 25

Ongoing studies -20

EC Approved - 0

Melatonin decreases

(+) Burch, 1997 Ann Rev Res Biol Effects of Electric & Mag. Fields. (-) de Seze et al 1999, Journal of Pineal Research (in press)

Blood pressure increases

(+) Braune 1998 Lancet 351:1857-8

Headaches

(+) Mild 1998 BEMS meeting. Hocking 1998, OccupMed 40:357-360

Sleep disorders

(+) Mann & Roschke 1996 Neuropsychobiol. 33:41-47

EEG & brain potential changes

(+) Eulitz & Freude (Bioelectromag 1998, 19:384-87 & Neuroreport 1998, 9:3229-32; Reiser, Dimpfel & Shober (European J of Medical Res (1995) 1:27-32); Mann & Roschke 1996 Neuropsychobiol. 33:41-47; von Klitzing 1995 Phys Med April/June:77-80; Dec et al 1997 World Congress; Thuroczy 1997 World Congress; Kim et al 1998 BEMS meeting. (-) Hietanen 1997 World Congress; Calabrese & Gehlen 1997 World Congress; Spittler & Gehlen 1997 World Congress; (ongoing) 4 studies.

In Vitro studies:

Completed studies - 45

Ongoing studies -18

EC Approved - 12

Ca<sup>++</sup> efflux

(+)  $\text{Ca}^{++}$  efflux in neuroblastoma cells was reported by Dutta et al. (1984 Bioelectromagnetics 5:71-78). (-) Meyer et al (1998 BEMS meeting) was unable to find effects on  $\text{Ca}^{++}$ .

#### DNA damage

(+) DNA damage in Molt-4 cells was reported by Phillips et al. (1998, Bioelectrochem Bioenerg 45:103-110). (-) Others have reported negative findings on other cell lines and other procedures. These include - Malyapa et al (Rad Res 148:618-627, 149:396-400, 149:637-646), Maes and Verschaeve (1997 Mut Res 393:151-156), Ruger (Submitted for publication), Gos (Submitted for publication), Tice et al. (Submitted for publication). An exact replication is under way LaGroye et al., Molt-4 replication study.

#### Evoked potential changes

(+) Wood & Tattersal have reported Spontaneous & evoked potential changes in hippocampal brain slices with 700 & 900 MHz exposure (1998 BEMS meeting). (-) Health implications of this effect are unclear but should lead to behavior changes that would be observed by studies proposed in PERFORM C.

#### Chromosome aberrations & micronuclei formation

(+) Maes et al., (1993 Bioelectromag 11:495-501, 1995 ElectroMagnetobiol 14:91-98 & 1997 Mut Res 393:151-156), Garaj Vhrovak et al. (1992 Mut Res 282:265-271), Sarkar (1994 Mut Res 320:141-147) and Tice et al (manuscript in preparation) have reported various observations of chromosomal aberrations. The dosimetry in these studies is in question. (-) Antonopoulos & Obe (FGF report, manuscript in preparation), Eberle & Diener (FGF report, manuscript in preparation), d'Ambrosio et al. (ongoing) have not replicated these findings. These studies would be addressed by the proposed work of PERFORM B and proposed follow on studies to the micronuclei observations of Tyce in the US.

#### Increased transformation (with 2450 MHz exposure)

(+) Balcer Kubiczek 1985 Carcinogenesis 6:859-864, 1989 Rad Res 117:531-537, 1991 Rad Res 126:65-72. (-) Cain 1997 Bioelectromagnetics 18:237-243; Malyapa (manuscript in preparation); (ongoing) Malyapa et al., 2450 MHz replication study in C3H 10T1/2 cells.

#### Increased DNA synthesis and/or proliferation

(+) Kwee and Rasmark 1998 Bioelectrochem Bioenerg 44:251-255; French & Donnellan 1997 Cell Biology Int'l (1997) 21:427-39 & 1998 Bioelectrochem.Bioenerg. 43:13-18. (-) Stagg 1997 Bioelectromagnetics 18:230-236; Higashikubo (manuscript in preparation); Antonopoulos & Obe (FGF report, manuscript in preparation); Eberle & Diener (FGF report, manuscript in preparation); (ongoing) studies by Veyret et al. & German Institute for Radiohygiene.

#### Modulation of conductivity in artificial membranes by pulsed RF

(+) Meyer 1998 BEMS meeting.

#### ODC activity increases and decreases

(+) Litovitz et al 1997 Bioelectromagnetics 18:422-30; Cain (manuscript in preparation).

## **APPENDIX B**

### **Health Surveillance**

#### **B. Hocking**

Good public and occupational health systems include a surveillance system to monitor their effectiveness. There is at present a paucity of such databases regarding ill health arising from EMF (0-300 GHz) exposures in workplaces or the community. It is desirable that a health surveillance database for EMF be developed and that data be collected in a standardized manner to permit statistical comparisons and sharing of data.

Dr Miro (France) has developed a database for monitoring workplace exposures. It is proposed that usefulness of this model elsewhere be considered. Should the model be found helpful in workplace exposures, its extension to community health events should be considered.

Issues that should be considered include:

Privacy: - de-identification and security of data.

Technical: - exposure details(equipment, job, industry), measurements(where available)

- medical details: symptoms/diagnosis (classify EMF injuries) - coding system to be used.  
Database issues: - comparability - structure  
Publicity: - inform medical profession, industry and unions.  
It is proposed that the above concept be refined by a working party of health practitioners.

### **APPENDIX C**

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