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SECTION 19

Fetal and Neonatal Effects of EMF

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I. INTRODUCTION

The exposure of the developing fetus and of children to electromagnetic fields (EMF) including both radiofrequency radiation (RF) used in new wireless technologies, and to extremely low frequency or power frequency fields (ELF-EMF) has raised public health concerns because of the possible effects (cancer, neurological effects, developmental disability effects, etc) from the long-term exposure to low-intensity, environmental level fields in daily life. This chapter documents some studies on RF and ELF-EMF that report bioeffects and adverse health impacts to the fetus, and young child where exposure levels are still well within the current legal limits of many nations. Several studies report adverse health effects at levels below safety standards [Kheifets and Oksuzyan, 2008; Comba and Fazzo, 2009; World Health Organization. 2007]**;** the evidence to date suggests that special attention should be devoted to the protection of embryos, fetuses and newborns who can be exposed to many diverse frequencies and intensities of EMF throughout their lifetimes, where the health and wellness consequences on these subjects are still scarcely explored.

The studies of fetuses and newborns are an important subset of those made on older children. Infants' exposure to EMF has raised concern recently, and some countries have developed guidelines to limit it, by avoiding the presence of hospitals or schools within a certain range of kilometers around high EMF emission sources [http://www.emfs.info/Related+Issues/limits/]. Nevertheless, children and babies are chronically exposed to many sources of EMF, in particular at home, where they can spend much time playing with computers and other wireless-enabled devices, watching television or near electronic baby monitors that emit RF in their cribs (or sleeping areas). These exposures are relatively new in the last two decades, and may represent a potential new carcinogen and neurotoxin, that, with chronic and indiscriminate exposure, may have health consequences in the long term.

II. EMF AND RISK OF TUMORS

The evidentiary basis for evaluating an association between RF EMF exposure and brain cancer in children is much smaller than for adults [Wiedemann P, et al. 2009]. There is only one study available for mobile phone use. Elliott et al. [2010] found no association between risk of early childhood cancers (leukemia and non-Hodgkin's lymphoma, cancer of brain and central nervous system) and mothers' exposure to mobile phone base stations during pregnancy. Studies investigated brain cancer or leukemia with respect to EMF emitted from TV or radio transmitters

[Hocking et al. 1996; Dolk H, et al.1997; Cooper D, et al. 1997; Michelozzi P, et al. 2002; Park et al. 2004; McKenzie et al. 1998; Cooper et al. 2001; Maskarinec et al. 1994].

Few studies showed a significant increase of brain cancer in children with the use of cellular phones [Söderqvist et al. 2011; Merzenich et al. 2008], while some evidence exists for an association of RF EMF exposure to childhood leukemia. The argument for a causal influence of RF EMF exposure on leukemia in children is based on studies that found a statistically significant association between RF EMF exposure from radio or TV transmission towers and childhood leukemia. For instance, one case-control study [Ha, 2007.] found a significant increase for lymphocytic leukemia, but not for myelocytic leukemia in the highest exposure category.

Some authors suggested that genetic susceptibility to leukemia may amplify the adverse effects of magnetic field exposure, namely that the magnetic fields may have a causal role in the aetiology of leukemia among a genetically susceptible subgroup (i.e., children). For instance, Mejia-Arangure et al. [2007] observed a significant increase of childhood acute leukemia among Down syndrome subjects resident in dwellings with levels of magnetic flux density over 0.6 μT (OR= 3.7; 95% CI: 1.05-13.3). A recent paper [Kheifets and Oksuzyan, 2008] specifically addresses leukemia and it indicates as a priority the study of highly exposed children who live in apartments next to built-in transformers or electrical equipment rooms, emphasizing the investigation of joint effects of ELF environmental exposure and genetic co-factors.

III. EMF AND GENERAL HEALTH

Some studies address the question whether RF EMF exposure might cause general health disturbances in children [Milde-Busch et al. 2010; Heinrich et al. 2008; Divan et al. 2008; Söderqvist, 2008; Thomas, 2010; Vrijheid et al. 2010]. In a cross-sectional study Koivusilta et al. [2007] examined in a representative sample of 12–18-year-olds the association of mobile phone use with self- reported health status. Intensive use of communication technology, especially of mobile phones, was associated with health problems;. Van den Buick [2007] conducted a cohort study to assess the association between phone use by adolescents after lights out and levels of tiredness. Participants were adolescents with an average age of 14 in the youngest group and 17 in the oldest group. The authors found that those who used the mobile phone for calling and sending text messages after lights out were more likely to be very tired. Nevertheless, the results of these two studies were not proven to be due to EMF.

1V. EMF AND COGNITIVE FUNCTIONS

Original papers address the effect of RF EMF on cognitive function and CNS in children [Krause et al. 2006; Thomas et al. 2010; Abramson et al. 2009]. The age of the children investigated in these studies was in the range of 10–17 years. The argument supporting a causal influence of EMF exposure on cognitive function in children is based on the studies by several authors [Krause et al. 2006; Thomas et al. 2010; Abramson et al. 2009]. Lee et al [2001] administered three different tests that measure attention to 72 adolescents, who reported to either use a mobile phone or not. They found a statistically significant effect for one, the *Trail Making Test*. For the other two tests administered in the study, no statistically significant effects were found. The evidence for effects of RF EMF exposure on cognitive performance and CNS of children so far does not provide substantial hints for exposure-related changes. The very limited but provocative studies we do have suggest we cannot rule out that RF EMF exposure might influence cognitive and other CNS functions in children. If it is so, the consequences to public health can be enormous, if ignored.

V. FETUSES, NEWBORNS AND EMF

The early phases of human development have scarcely been studied with regard to their correlation with EMF. Nevertheless, the very young should receive more attention because of greater fragility and susceptibility of the developing embryo, fetus, and young child to environmental toxins of all kinds. Since fetuses and babies have a high number of stem cells and scarce immunity-mediated resources, any threat –in particular those due to physical and chemical agents – can have surprising and detrimental effects, since the environment influences even the DNA epigenetic expression [Davis and Lowell, 2008]. Czyz et al [2004] reported that GSM cell phone exposure affected gene expression levels in embryonic stem cells (p53-deficient); and significantly increased heat shock protein HSP 70 production. Belyaev et al [2010] reported that 915 MHz microwave exposure significantly affects human stem cells and may be important as a cancer risk. “The strongest microwave effects were always observed in stem cells. This result may suggest both significant misbalance in DSB repair, and severe stress response. Our findings that stem cells are the most sensitive to microwave exposure, and react to more frequencies than do differentiated cells may be important for cancer risk assessment and indicate that stem cells are the most relevant cellular model for validating safe mobile communication signals.”

In an animal study of mice, Aldad et al [2012] added support in a to the hypothesis that in-utero, whole-body exposure to RFR from cell phone radiation of the pregnant mother can result in hyperactivity, impaired memory and behavioral changes in the offspring.

Infante-Rivard and Deadman [2003] showed that maternal EMF exposure during pregnancy increased the risk of children 0-9 years of age developing leukemia (OR = 2.5, 95% CI = 1.2-3.0, for children of mothers in the highest 10% of exposure). Divan et al. [2008] reported that even prenatal exposure to cell-phone frequencies was associated with a significant increase in behavioral problems of emotion and hyperactivity around the age of school entry (OR = 1.80, 95% CI = 1.45-2.23). Although the results need replication, they point out an elevated susceptibility of the fetus and suggest a variety of adverse effects of cell-phone frequencies beyond just cancer. A recent study assessed that the exposure to EMF in pregnancy is linked to subsequent babies' asthma [Li et al. 2011].

Some researchers studied the possible effects of the exposure of fetuses to Magnetic Resonance Imaging (MRI) [Pediaditis et al. 2008]. Data seem to show that during abdominal MRI exposure limits of the mother "is not sufficient to protect the fetus if limits of the general populations are applied to it". In that case, fetal whole-body SAR exceeds limits by 7.4-fold. It is up to the physician and/or the ethics commission to decide upon justification for abdominal MRI of pregnant women if public safety limits are exceeded. The results indicate the need for specifically addressing fetal exposure to EMF and refining general recommendations by radiation protection bodies in line with the emerging science. Since the infant and young child are particularly vulnerable in general than adults, more care is needed to screen out unnecessary medical imaging of the pregnant woman and child and limit it to what is clearly medically necessary.

VI. LAPTOP COMPUTERS AND FETUSES

Bellieni et al [2012a] assessed EMF exposure levels of the 26-week fetus in the womb of a pregnant woman using a laptop computer in tight contact with pregnant women's belly. The word "laptop" means "a portable, usually battery-powered microcomputer small enough to rest on the user's lap," and this means that they are often used at close contact with the body in a very delicate area close to skin, bones, blood, genitals, and in the case of a pregnant woman, very close to her fetus. Since LTCs are often used in tight contact with the body even by pregnant women, fetal exposures to extremely low frequency (ELF-EMF) magnetic fields and induced electric currents within the fetus are generated by these units. These fields pass directly through the mother's tissues to the fetus. We measured the ELF-EMF emissions in five models of portable computers of

different brands. Experiments were performed using a NARDA ELF 400 electromagnetic field measuring system (1 Hz to 400 kHz range) after determining the ambient background level was no higher than 0.01 μT. The point of highest emission was measured at the surface of the laptop. The voxel model used to calculate intracorporal electric current density distributions was a whole-body human database of average pregnant woman, jointly developed by the National Institute of Information and Communications Technology and Ciba University, which represents a pregnant woman at the 26th week of gestation. In this model, mother and fetus tissues are defined according to NICT (National Institute of Information and Communications Technology) pregnant female voxel phantom. Dielectric properties of mother tissues are calculated using the parametric model developed by C. Gabriel and colleagues that reproduces the tissue conductivities in a wide range of frequencies. In the five brands of LTC we examined, ELF-EMF levels for their dominant frequency ranges from 1.8 to 6 μT, whereas those produced from the power supply ranges from 0.7 to 29.5 μT.

Induced electric currents were estimated for both the pregnant woman and the fetus. Statistical values of the averaged current density were evaluated for body tissues including the body of the fetus, and the grey and white matter of the brain of the mother; the mother's cerebellum, the mother's cerebrospinal fluid and mother's muscle tissue. In each case, the larger exposure was generated by the power supply rather than the laptop operation. Levels of induced current substantially exceeded ICNIRP public safety limits, assuming close proximity of the laptop to the belly of the pregnant woman (for the fetus, between 182% and 263.7% of the ICNIRP standard); and for the woman (between 346.7% and 483.5% of the ICNIRP standard).

Simple measures to distance the laptop during use (placing it on a table or desk and not on the body of the user) will result in significant reduction of ELF-EMF exposure and induced electric current in both mother and fetus.

VII. NEWBORN (INFANT) INCUBATORS

Fetuses can also be born prematurely, and very often are protected in neonatal incubators for several weeks. Only a few studies of incubators (or isolettes) have assessed ELF-EMF magnetic field exposures to the newborn baby inside an incubator where the source is a motor that generates these emissions. The motors of neonatal incubators produce electromagnetic fields in their vicinity. Although premature babies are often exposed to incubator ELF-EMF for months, little research has been done into the effects of EMFs on newborns, and most has regarded newborn

animals [Luchini and Parazzini, 1992; Watilliaux et al. 2011; Orendáčováet et al. 2011; Miyakoshi et al. 2012] so that the impact of this emission on the developing body's enhanced sensitivity to environmental insult is still largely unknown. In order to determine safe distances, ELF-EMF emissions must be measured and mapped, and these exposures need to be reduced to levels below that reported to cause adverse health effects in children (at or below 0.01 μT). To allow what is an essential medical intervention for the growing premature baby, or the sick infant who needs exceptional care following birth, at least two possible solutions to reduce ELF-EMF levels are:

- Designing incubators with the motor far from the baby (some incubators already have adopted this measure) and
- Using ELF-EMF absorbing panels to shield the baby's body from emissions (like Mu metal).

In Bellieni et al [2003], ELF-EMF levels are characterized in some common neonatal incubators. Levels of magnetic flux density at mattress level well over 10 milliGauss (mG) at mattress level: up to 88.4 mG in common incubators, and up to 357.0 mG in a transport incubator. These values are in line with those of two previous studies on ELF-EMFs in infant incubators[Lie and Kjaerheim, 2003; Babincova et al. 2000; Lie and Kjaerheim, 2003], and higher than the values recorded in two other reports [Aasen et al. 1996; Ramstad et al. 1998]. Another paper showed that nurses are also exposed to high EMF while working near incubators [Bellieni, 2002].

Bellieni et al [2008] reported that the exposure to high electromagnetic fields can interfere with the sympathetic nervous system in altering babies' heart rate variability. Heart rate variability (HRV) of 43 newborns in incubators was studied. HRV is an index of Autonomous Nervous System activity. The study group comprised 27 newborns whose HRV was studied throughout three 5-minute periods: 1) with incubator motor on, 2) with incubator off, and 3) with incubator on again, respectively. Mean HRV values obtained during each period were compared. The control group comprised 16 newborns but exposed to no source of ELF-EMF; they were exposed to changes in background noise similar to those provoked by the incubator motor (to reproduce the conditions of the first cohort). Mean total power and the high-frequency (HF) component of HRV increased significantly and the mean low-frequency (LF)/HF ratio decreased significantly when the incubator motor was turned off. Basal values were restored when incubators were turned on again. Changes in background noise did not provoke any significant change in HRV. We therefore concluded that ELF-EMFs produced by incubators influence newborns' HRV, showing an influence on their

autonomous nervous system. More research is needed to assess possible long-term consequences, since premature newborns may be exposed to these high ELF-EMFs for months.

Even melatonin production – as was signaled in adults [Wilson et al. 1989] – was inhibited in the newborn by exposure to ELF-EMF [Bellieni et al. 2012b]. The study concerned 28 babies (study group), who had spent at least 48-hr in common incubators with the presence of significant ELF-EMF. Measurements of mean 6-hydroxy-melatonin-sulfate (6OHMS) urine excretion were recorded at the end of their stay in the incubators, and compared with their mean 6OHMS excretion after having been put in cribs, where EMF are below the detectable limit (<0.01 μT). Mean 6OHMS/cr values were respectively 5.34±4.6 and 7.68±5.1ng/mg (p=0.026) when babies were exposed to ELF-EMF in incubators, and after having been put in the crib. We have compared these changes with a control group of babies, who were not exposed to EMF either before the first sampling nor before the second. We therefore measured urine 6OHMS twice, with an interval of 48-hr, in a control group of 27 babies who were not exposed to EMF during both samples. In the control group, mean 6OHMS/cr values in the first and in the second sample were respectively 5.91±5.41 vs 6.17±3.94 ng/mg (p=0.679). The transitory increase in melatonin production soon after removing newborns from incubators demonstrates a possible influence of EMF on melatonin production in newborns. We should point out that the two groups were similar in all but their mean corrected age. It was greater in the control group (the time as measured from conception).

VIII. CONCLUSIONS

Some studies [Lowenthal et al. 2007; Infante-Rivard and Deadman, 2003] report that the fetus and young children are at greater risk than are adults from exposure to environmental toxins. This is consistent with a large body of information showing that the fetus and young child are more vulnerable than older persons are to chemicals [Makri A, et al. 2004] and ionizing radiation [Preston, 2004]. These considerations have led the US Environmental Protection Agency (EPA) to propose a 10-fold risk adjustment for the first 2 years of life exposure to carcinogens, and a 3-fold adjustment for years 3 to 5 [http://www.epa.gov/sab/pdf/sab_04003_resp.pdf].

This susceptibility may be why, according to some authors (60)[Carpenter and Sage, 2008], “the evidence for the relation between magnetic field exposure and leukemia in children is stronger than that for adults”.

The World Health Organization Agency International Agency for Research on Cancer (or IARC) classifies both ELF-EMF and RF EMF as Possible Human Carcinogens or Group 2B [http://microwavenews.com/news/backissues/j-a01issue.pdf]. These proposed US EPA adjustments do not deal with fetal risk, and the possibility of extending this protection to the fetus should be examined, because of fetus' rapid organ development. Classification of these related electromagnetic field exposures (ELF-EMF and RF EMF) as having the potential for serious potential health consequences for adults certainly justifies additional protections for the fetus, the newborn and young children who have greater sensitive to such exposures. Further, there is good evidence to suggest that many toxic exposures to the fetus and very young child have especially detrimental consequences depending on when they occur during critical phases of growth and development (time windows of critical development), where such exposures may lay the seeds of health harm that develops even decades later. See Appendix 1 for international statements of concern and delineation of priority research needs published by the WHO and US National Academy of Sciences, National Research Council.

Important bioeffects and some adverse health effects of chronic exposure to low-intensity (non-thermal) non-ionizing radiation have been reported on babies, and important open questions still remain.

Existing FCC and ICNIRP public safety limits seem to be not sufficiently protective of public health, in particular for the young (embryo, fetus, neonate, very young child).

The World Health Organization International Agency for Research on Cancer has classified both ELF-EMF and RF EMF (wireless radiofrequency) as Possible Human Carcinogens (Group 2B).

New, biologically-based public exposure standards are critically needed.

Common sense measures to limit both ELF-EMF and RF EMF in these populations is needed, especially with respect to avoidable exposures like incubators that can be modified; and where education of the pregnant mother with respect to laptop computers, mobile phones and other sources of ELF-EMF and RF EMF are easily instituted.

It is not in the public interest to wait: A precautionary approach may provide the frame for decision making where remediation actions have to be realized to prevent high exposures of children and pregnant woman.

APPENDIX 1

INTERNATIONAL STATEMENTS

World Health Organization Research Agenda for Radiofrequency Fields (2010) Children and EMF: Related Recommendations by World Health Groups

In 2010, the WHO produced a research agenda to address growing scientific questions and public concern about health effects of radiofrequency radiation, particularly with the explosive rise in exposures from new telecommunications technologies. It replaced a 2006 research agenda developed by the International EMF Project.

Priority: Epidemiology

> ***High -*** *Prospective cohort studies of children and adolescents with outcomes including behavioural and neurological disorders and cancer*
>
> *Rationale: As yet, little research has been conducted in children and adolescents and it is still an open question whether children are more susceptible to RF EMF since the brain continues to develop during childhood and adolescence. also, children are starting to use mobile phones at a younger age, given the existence of large-scale cohort studies of mothers and children with follow-up started during or before pregnancy, an RF sources component could be added at a reasonably low cost. Billing records for mobile phones are not valid for children, therefore the prospective collection of exposure data is needed. for neuropsychological studies, one challenge is to distinguish the "training" of motor and neuropsychological skills caused by the use of a mobile phone from the effects of the RF field. any future study should try to address this issue. in any case it should be of longitudinal design, thereby allowing the study of several outcomes and changes in technology and the use of mobile phones as well as other sources of RF EMF exposure, such as wireless laptops.*

Priority: Human studies

> ***High*** *- further RF EMF provocation studies on children of different ages*
>
> *Rationale: current research has focused primarily on adolescents; very little is known about possible effects in younger children. longitudinal testing at different ages, for example by studying children already participating in current cohort studies, is recommended. This would allow consideration of the influence of potentially confounding factors such as lifestyle.*

Priority: Animal studies

> ***High*** *- Effects of early-life and prenatal RF exposure on development and behaviour*
>
> *Rationale: There is still a paucity of information concerning the effects of prenatal and early life exposure to RF EMF on subsequent development and behaviour. Such studies are regarded as important because of the widespread use of mobile phones by children and the*

increasing exposure to other RF sources such as wireless local area networks (Wlans) and the reported effects of RF EMF on the adult EEG. Further study is required which should include partial (head only) exposure to mobile phones at relatively high specific absorption rate (SAR) levels.

National Research Council, National Academy of Sciences (2008)

The U.S. Food and Drug Administration (FDA) of the Department of Health and Human Services asked the National Academies to organize a workshop of national and international experts 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. To accomplish this task, the National Academies appointed a seven-member committee to plan the workshop (Committee on Identification of Research Needs Relating to Potential Biological or Adverse Health Effects of Wireless Communications Devices.). In their report, the Committee recommended these actions with respect to RF exposure for the developing fetus, and for young children:

- Characterization of exposure to juveniles, children, pregnant women, and fetuses from personal wireless devices and RF fields from base station antennas.

- Prospective epidemiologic cohort studies of children and pregnant women.

- Epidemiologic case-control studies and childhood cancers, including brain cancer.

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SECTION 20

Findings in Autism (ASD) Consistent with Electromagnetic Fields (EMF) and Radiofrequency Radiation (RFR)

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I. INTRODUCTION

The premise of this review is that although scant attention has been paid to possible links between electromagnetic fields and radiofrequency exposures (EMF/RFR) and Autism Spectrum Disorders (ASDs), such links probably exist. The rationale for this premise is that the physiological impacts of EMF/RFR and a host of increasingly well-documented pathophysiological phenomena in ASDs have remarkable similarities. Additional support may be found in the parallels between the rise in reported cases of ASDs and the remarkable increases in EMF/RFR exposures over the past few decades. Reviewing these similarities does not prove that these parallels imply causality – that kind of research has not been done. Moreover, the physiological processes affected by EMF/RFR are also impacted by other environmental factors. Yet EMF/RFR does not need to be a unique contributor to ASDs to add significantly to system overload ('allostatic load') and dysfunction. Even so these pathophysiological overlaps do suggest that the potential for an EMF/RFR-ASD connection should be taken seriously, and that their vulnerable biological features may make many with ASDs more likely to experience adverse EMF/RFR impacts. This is a sufficient basis to recommend that precautionary measures should be implemented and respected, that further research should be prioritized, and that policy level interventions based on existing and emerging data should be designed and pursued. Moreover, pursuing this link could help us understand ASDs better and find more ways to improve the lives of people with ASDs and of so many others.

A. How are Biology and Behavior Related?

Considering a potential link between ASDs and EMF/RFR (or indeed of any potential contributor to incidence or pathogenesis) requires taking account of the evolution that has been occurring in our understanding of the relationship between ASD's behavioral and biological features. ASDs were first labeled as 'autism' in 1943 by Leo Kanner, a child psychiatrist who extracted several key behavioral features, related to communication and social interaction challenges and a tendency toward restricted interests and repetitive behaviors, characteristic of all 11 of the children in his first case series (Kanner 1943). Although in the seven decades since this condition was first constructed as a category there has been some modification of the way these behavioral features have been characterized, ASDs are still defined behaviorally, although sensory issues such as hypo- or hyper-reactivity have recently been included in the diagnostic criteria (Diagnostic and Statistical Manual of Mental Disorders or DSM-V) (American Psychiatric Association 2000, 2013, May).

1. Transduction is fundamental but poorly understood

Yet in considering how an environmental factor such as EMF/RFR could lead to autism and/or influence its severity or incidence, we need to think about how underlying biology is transduced into changes in nervous system electrical activity, and how these in turn generate the set of behaviors we have categorized as 'autism.' (Herbert 2005) This means not taking behaviors as given, or as purely determined by genetics, but exploring the full range of biology that generates these features and challenges.

2. More than brain

Although 'autism' has long been considered to be a psychiatric or neurological brain-based disorder (Rapin and Katzman 1998; Polleux and Lauder 2004), it has become undeniable that people diagnosed with ASDs often also have a multitude of biological features – including systemic pathophysiological disturbances (such as oxidative stress, mitochondrial dysfunction and metabolic and immune abnormalities) (Ming et al. 2012; Tsaluchidu et al. 2008; Pieczenik and Neustadt 2007; Gonzalez et al. 2011) as well as symptomatic medical comorbidities (such as gastrointestinal distress, recurrent infections, epilepsy, autonomic dysregulation and sleep disruption) (Nikolov et al. 2009; Kotagal and Broomall 2012; Kaartinen et al. 2012; Daluwatte et al. 2012; Tuchman and Cuccaro 2011; Canitano 2007; Malow 2004; Kang and Barnes 2013; Jyonouchi et al. 2011) – in addition to the core defining behaviors – and many of these occur commonly (Kohane et al. 2012). The problem has been that no one such biological feature has turned out to be present in every single person carrying an ASD diagnosis – and they are not specific to ASDs, either. Moreover there has been much variability in many of the features of autism – not only between individuals but in many cases within individuals at different points in time or under different circumstances. Because of this variability, the relevance of many of these biological features has been dismissed as secondary and not intrinsically related to the 'autism.' Instead, many have considered the behavioral features as fundamental not only to how autism manifests and is definedbut also to the core intrinsic nature of ASDs, even though the biological basis of these behaviors has by no means been established.

3. Heterogeneity: More genetic and environmental than physiological

It is not as if this variability is unique to the 'environmental side.' At the present time over 800 genes have been associated with ASDs, and over 100 different rare genetic syndromes are frequently accompanied by ASD, with no clear specific unifying mechanism uniting this remarkable heterogeneity (Trikalinos et al. 2006; Ring et al. 2008; Pelphrey et al. 2011; Mandell 2011; Hall et al. 2012; Bill and Geschwind 2009). Similarly a large number of potential environmental contributors are under investigation

ranging from toxicants and Vitamin D deficiency or failure to take prenatal vitamins to air pollution and stress or infection in pregnancy (Whitehouse et al. 2012; Kocovska et al. 2012; Schmidt et al. 2011; Landrigan 2010; Roberts et al. 2007; Shelton, Hertz-Picciotto, and Pessah 2012; Becerra et al. 2012; Volk et al. 2011). Yet at the physiological level a smaller set of disturbances are showing up as common across substantial numbers of people with ASDs – and in fact not uniquely to ASDs but also in myriad other chronic conditions whose prevalence also appears to be increasing (Bilbo Jones, and Parker 2012; Knox 2010). Prominent among these are immune disturbances including inflammation, mitochondrial dysfunction, and oxidative stress, as well as toxic body burden. Vulnerability to all of these can be increased mildly or substantially by a variety of often common genetic mutations, but may remain latent without the overlay of environmental triggers. Conversely, with substantial enough environmental input, genetic vulnerability may not be necessary.

4. Mechanism is more than correlation

Just HOW biological features might be related to the behavioral features that have up until now defined ASDs has not been clarified; until recently the main research effort regarding pathophysiology in ASDs has been to establish the presence of these phenomena in the first place. Even so, some correlations between biological and behavioral features have been identified – e.g. a higher level of immune abnormalities correlates with more aberrant behaviors (Wei et al. 2012; Careaga and Ashwood 2012; Jyonouchi et al. 2011; Ashwood et al. 2011; Heuer et al. 2008; Zerrate et al. 2007; Curran et al. 2007). Still, such correlations in themselves do not explain the *mechanisms* by which the *transduction of pathophysiology into behavior* might actually occur. In order to do that, an important component would be to study the relationship between systemic pathophysiology and nervous system electrophysiology.

5. EMF/RFR research may help us understand how ASDs 'work'

Assessing the potential contribution of EMF/RFR to ASDs puts this question of the nature of the pathophysiology-behavior transduction into an interesting and provocative light since the brain is simultaneously a tissue-based physical organ that can be compromised by cellular pathophysiology as well as altered developmental processes, and an information processing system that operates through networks of synchronized electrical oscillations (brain waves) – and EMF/RFR impacts may occur directly at both of these levels. To date the emphasis in ASD research has largely been on 'structure-function' relationships that have been anatomy-centered. This research has generated correlations between brain structures and behaviors, and has found some genetic correlates as well, but it has made assumptions that these phenomena are rooted in genetics and genetically perturbed molecular structures and substances. This leads to targeting the molecular level with pharmaceuticals, but not to the broader agenda of

understanding environmental or physiological contributions or dynamic features of brain and behavior. Thus, exploring how EMF/RFR impacts ASDs may help to force the question of how these pathophysiological and electrophysiological/information processing levels actually interact, and how anatomy may in many ways be a product rather than a cause of physiology.

B. Time Courses of Mechanisms

For the most part, researchers have looked for causes of autism in mechanisms that occur early and create permanent change or damage. This approach is logical if one assumes that genetic influences are overwhelmingly predominant, and 'autism' is a fixed lifelong trait. However evidence is emerging that ASDs may in many respects be more state-like and variable than trait-like and fixed.

1. Plasticity

One of the remarkable shifts in conceptual thinking about ASDs is an appreciation of its brain plasticity (Helt et al. 2008). Growing numbers of reports of improvement and loss of diagnosis, reversal of neurological symptoms in a growing number of mouse models of genetic syndromes that in humans prominently feature autism (Cobb, Guy and Bird 2010; Ehninger et al. 2008; Goebel-Goody et al. 2012; Henderson et al. 2012; Kaphzan et al. 2012; Liu, huang, and Smith 2012; Mehta, Gandal, and Siegel 2011; Paylor et al. 2008; Rotschafer et al. 2012; Sato et al. 2012; Suvrathan et al. 2010), short-term pharmaceutically induced improvement in brain connectivity (Narayanan et al. 2010), and transient reversal or abeyance of symptomatology under various circumstances (including fever, fluid-only diet, and certain antibiotic treatments (Sandler et al. 2000; Curran et al. 2007)) – all of these throw into question the long-standing assumption that we are simply dealing with a 'broken brain.' Indeed, how could a 'broken brain' produce markedly improved function with such a short turnaround time? (Herbert 2009) Such a time frame cannot possibly be accounted for by remodeling of the brain's anatomical substrate. 'Brain waves' and their synchronization, on the other hand, could easily vary over short time periods. Looking into physiological and environmental modulators not only of brain development but also of everyday brain function becomes increasingly imperative.

In addition, documentation of average to superior intelligence in most people with autism (Edelson 2006; Dawson et al. 2007), as well as of domains of perceptual superiority (Soulieres, Zeffiro, et al. 2011; Soulieres, Dawson et al. 2011; Samson et al. 2011; Soulieres et al. 2010; Soulieres et al. 2009; Mottron et al. 2006; Mottron 2004; Bertone et al. 2005; Perreault et al. 2011), call into question the long-standing assumption that ASDs are intrinsically or for the most part associated with cognitive deficits – another strike against the outdated 'deficit' or 'broken brain' model.

2. Mechanisms that operate actively throughout the lifecourse

One particularly valuable lesson about ASDs that can be learned from looking at how EMF/RFR affects underlying biology is that these impacts are by no means confined to early development. We already have clinical reports of 'intermittent autism' – for example, some children with mitochondrial disease who have ups and downs of their bioenergetics status 'have autism' on their bad days but don't display autistic features on their good days (Korson 2007). These children with their vulnerable, barely compensated mitochondria seem to be teetering right at the brink of the interface of metabolic and electrophysiological dysfunction, tipping back and forth on this knife edge. It makes one wonder what everyday exposures – allergens, infection, pesticide on the school playground, even perchance EMF/RFR – might contribute to the bad days (with their loss of electrophysiological optimization, probably on account of insufficient energy to drive fully integrated brain function), and conversely how many choices exist in everyday life that could tilt things in the direction of more good days (by helping to stabilize more optimal nervous system performance) (Herbert and Weintraub 2012).

The short time course needed for biologically effective EMF/RFR 'doses' to lead to observable impacts reflects that these exposures can affect cells without obstruction (unlike many chemical agents), and create impacts within minutes. This type of mechanism may also give us fresh and important ways of understanding the short-term variability – the good days and the bad days – that are so common in ASD even in those who do not have a formal diagnosis of mitochondrial disease.

3. Pathophysiology and allostatic load

Based on these considerations, the strategy to be pursued in this examination of a potential EMF/RFR - ASD link is to review the many parallels between underlying biology, or pathophysiology, in ASDs and the impacts of EMF/RFR on living organisms. EMF/RFR exposures have demonstrated impacts at just about every level at which biology and physiology have been shown to be disrupted in ASDs. EMF/RFR has been shown to potentiate the impact of various toxicants when both exposures occur together (Juutilainen, Kumlin, and Naarala 2006); this may be additive or more than additive. This suggests that EMF/RFR may synergize with other contributors and make things worse. With many different environmental factors piling on to a much smaller number of environmentally vulnerable physiological mechanisms (Herbert 2010), one must consider that the model of 'allostatic load' – the sum total of stressors and burdens – may be central to understanding how the many risk factors interact to create autism – and to create a spectrum of levels of severity across so many of ASD's associated features. A cascade of exposures interacting with vulnerabilities can potentially lead to a tipping point for an individual, such as the phenomenon of autistic regression experienced by a substantial subset of people with ASDs. When exposures increase at the population

level, we are likely to see trends of increase in the number of people passing that tipping point and getting diagnosed. EMF/RFR exposures have increased several thousand-fold or more in the past two decades from wireless technology innovations that have unplanned side effects from pulsed RFR, a newly classified human carcinogen (Baan et al, 2011). Nearly six billion people globally own wireless phones, for example. Many hundreds of thousands more are exposed to wireless whole-body transmissions from wireless antenna facilities (Sage and Carpenter, BioInitiative 2012 Report, Section 24). For this as well as for physiological reasons allostatic loading as a viable concept for the study of ASDs should reasonably address EMF/RFR as one of the collection of exposures of relevance to the overall stress load, since it is now a chronic and unremitting exposure in daily life at environmentally relevant levels shown to cause bioeffects from preconception and pregnancy through infancy, childhood and the whole lifecourse.

In an article entitled "Unrelenting Stress is Toxic,: The New Scientist (28 July 2012) describes stress in an eloquent way:

> "*Unrelenting stress is toxic because it can turn the body's defense system against itself. Neuroendocrinologist Bruce McEwen at Rockefeller University in New York says the stress response that evolved to protect us from harm can be hijacked and actually cause harm when the stress level never abates. In a normal situation, the introduction of stress causes the body to deliver a boost of energy – by sending a surge of glucose to the muscles – and to increase heart rate, blood pressure and breathing to get oxygen to the muscles in hurry. At the same time, blood vessels constrict and clotting factors increase – ready to slow bleeding in case you are wounded. These responses are a part of a fight-or-flight survival kit, and once the stress has passed, these should subside. But for people under unrelenting stress, this response never quite switches off – leaving sugar levels unregulated, high blood pressure, increate risk of blood clots, depressed sex drive and an immune system buckling under the strain. Prolonged exposure to stress hormones can have other effects as well, including affecting the brain by altering the structure of the neurons and their connections, which in turn can influence behaviour and hormonal processes."*

This passage refers to effects on the hypothalamo-pituitary-adrenal axis (Aldad, 2012), but as will be discussed in the Part II, equally important is cellular stress from stress proteins (heat shock protein HSP) and from oxidative stress generated at very low-intensity EMF and RFR levels as detailed in the BioInitiative 2012 Update, Section 7 by Martin Blank, PhD; Blank, 2012). Both are significant kinds of stress that can add body-burdens via allostatic loading.

II. PARALLELS IN PATHOPHYSIOLOGY

This section will review parallels in pathophysiology between ASDs and impacts of EMF/RFR. It will begin with a review of mechanisms of direct impact at the level of molecules, cells, tissues and genes. It will then move on to consider how these levels of damage lead to degradation of the integrity of functional systems including mitochondrial bioenergetics, melatonin, immune function and nervous system physiology. The review of parallels will conclude with a discussion of electromagnetic signaling and synchronized oscillation from membranes to nervous system, treating 'aberrant' neural systems and somatic function and behaviors as consequences or 'outputs' of disturbed underlying physiology to which EMF/RFR is a plausible contributor.

A. Damage: Means and Domains

ASDs have been conceptualized as 'neurodevelopmental' which has focused attention on how genes and environment could alter brain development. This leads to the unstated presumption that virtually everything important about the brain in ASDs has to do with differences in the way it was formed. In genetics this has led to a hunt for neurodevelopmental genes. There is no question that environmental impacts can alter brain development, and impact brain function across the lifespan. This chapter begins the work to systematically rectify the omission of EMF/RFR as one environmental contributor in ASDs.

However the influence of the environment on neurodevelopmental conditions such as ASDs does not stop there. Evidence is accumulating showing that increased expression of genes associated with physiological dysregulation, as well as single-nucleotide polymorphisms (SNPs) associated with these issues, may be if anything more prominent than alterations of 'neurodevelopmental' genes (Lintas, Sacco, and Persico 2012). In a study of gene expression in ASDs, Down syndrome and Rett syndrome, these authors state, *"Our results surprisingly converge upon immune, and not neurodevelopmental genes, as the most consistently shared abnormality in genome-wide expression patterns. A dysregulated immune response, accompanied by enhanced oxidative stress and abnormal mitochondrial metabolism seemingly represents the common molecular underpinning of these neurodevelopmental disorders."* Others have also found pathophysiology-related genes as figuring most prominently in alterations of gene expression in ASD (Kong et al. 2012; Jung, Kohane, and Wall 2011; Voineagu et al. 2011; Waly et al. 2012). SNPs associated with methylation abnormalities, impaired

glutathione synthesis and mitochondrial dysfunction also have been identified as significant risk factors.

Genetics may create risk, but the actual nervous system and health consequences probably come from dysfunction at the physiological level. Evidence for pathophysiological dysfunction in ASDs increasingly abounds. In particular, a growing body of literature documents immune aberrations, low total and reduced glutathione levels, lower activity of the anti-oxidative stress system and mitochondrial dysfunction. These phenomena may be both genetically and environmentally modulated. As will be discussed further below, they are certainly pertinent to the neurodevelopment of the brain, which has been by far the dominant focus autism research, but it does not stop there as they can significantly modulate brain function in real time, as well as shape the function of the entire organism, including the autonomic system, the cardiovascular, endocrine, immune, gastrointestinal and reproductive systems and more.

1. Cellular Stress

Oxidative Stress

Autism (ASD) research indicates that oxidative stress may be a common attribute amongst many individuals with autism. In the past decade the literature on this has moved from a trickle to a flood. Studies document reduced antioxidant capacity, increased indicators of oxidative stress and free radical damage, alterations in nutritional status consistent with oxidative stress, altered lipid profiles, and pertinent changes not only in blood but also in brain tissue. Associations of ASDs with environmental exposures such as air pollution and pesticides are indirectly supportive as well, since such exposures are linked in other literature to oxidative stress (Kanthasamy et al. 2012; Roberts et al. 2010; Knox 2010; Rose, Melnyk, Trusty, et al. 2012; Rose, Melnyk, Pavliv, et al. 2012; Ghanizadeh et al. 2012; Frustaci et al. 2012; Rossignol and Frye 2011; Adams et al. 2011, 2011; Mostafa et al. 2010; Zecavati and Spence 2009; Yao et al. 2006; Naviaux 2012; Chauhan and Chauhan 2006; Chauhan, Chauhan, and Brown 2009).

Reactive oxygen species are produced as a normal consequence of mitochondrial oxidative metabolism as well as other reactions, but when their number exceeds the cell's antioxidant capacity a situation of oxidative stress develops. It is certainly the case that oxidative stress can be a consequence of exposures to chemical toxicants, or of the interactive impacts of toxicants, nutritional insufficiencies and genetic vulnerabilities. This set of risk factors has received considerable attention for the potential roles each component and various possible combinations could play in causing or exacerbating autism.

Less often mentioned in the ASD pathophysiology literature is that it is also well established that EMF/RFR exposures can be associated with oxidative damage.

Published scientific papers that demonstrate the depth of EMF and RFR evidence reporting oxidative damage in human and animal models are profiled in Section 6 (Genotoxicity) of this BioInitiative 2012 Report and in the BioInitiative Report (2007), both by Henry Lai, PhD (Lai, 2012; Lai, 2007). These cellular effects can occur at low-intensity, legal levels of exposure that are now 'common environmental levels' for pregnant women, the fetus, the infant, the very young child, and the growing child as well as for adults. Electromagnetic fields (EMF) can enhance free radical activity in cells (Lai and Singh 2004; De Iuliis et al. 2009) particularly via the Fenton reaction, and prolonging the effect causes a larger increase, indicating a cumulative effect. The Fenton reaction is a catalytic process of iron to convert hydrogen peroxides, a product of oxidative respiration in the mitochondria, into hydroxyl free radical, which is a very potent and toxic free radical (Lai, in the BioInitiative Report 2007; Lai, 2007). Free radicals damage and kill organelles and cells by damaging macromolecules, such as DNA, protein and membrane components.

Further indications of a link to oxidative stress are findings that EMF and RFR at very low intensities can modulate glutamate, glutathione and GABA, and affect mitochondrial metabolism. Alterations in all these substances and processes have been documented in ASDs (Bristot Silvestrin et al. 2012; Brown et al. 2012; Choudhury, Lahiri, and Rajamma 2012; Essa et al. 2012; Oberman 2012; Yang and Pan 2012; Chauhan, Audhya, and Chauhan 2012; Frustaci et al. 2012; Main et al. 2012; Pecorelli et al. 2012; Rose, Melnyk, Pavliv, et al. 2012; Rose, Melnyk, Trusty et al. 2012; Waly et al. 2012; Banerjee et al. 2012; Coghlan et al. 2012; Enticott et al. 2012; Kang and Barnes 2013; Mendez et al. 2012; Piton et al. 2012; Anitha, Nakamura, Thanseem, Matsuzaki, et al. 2012; Anitha, Naamura, Thanseem, Yamada, et al. 2012; Gargus 2008; Giulivi et al. 2010; Hadjixenofontos et al. 2013; Napolioni et al. 2011; Rossignol and Frye 2011). Campisi et al (2010) report that increased glutamate levels from 900 MHz cell phone frequency radiation on primary rat neocortical astroglial cell cultures induced a significant increase in ROS levels and DNA fragmentation after only 20 min with pulsed RFR at non-thermal levels (Campisi et al. 2010).

Fragopoulou et al (2012) conducted proteomics analysis of proteins involved in brain regulation in mice as a consequence of prolonged exposure to EMF (Fragopoulou et al. 2012). They identified altered expression of 143 proteins, ranging from as low as 0.003 fold downregulation up to 114 fold overexpression with affected proteins including neural function-related proteins including Glial Fibrillary Acidic Protein (GFAP), alpha-synuclein, Glia Maturation Factor beta (GMF), apolipoprotein E (apoE)), heat shock proteins, and cytoskeletal proteins (i.e., neurofilaments and tropomodulin), as well as proteins of brain metabolism such as aspartate aminotransferase and glutamate dehydrogenase. The authors pointed out that oxidative stress was consistent with some of these changes.

Aberrations in glutathione metabolism and deficiencies in reserves of reduced glutathione are increasingly associated with ASDs, both systemically and in the brain. The parallel with EMF/RFR impacts here is strong, since glutathione reduction associated with EMF/RFR is reported in at least twenty three relevant research studies in both human and animal studies since 1998, including the following citations (Shapiro et al. 2012; Ozgur, Guler, and Seyhan et al. 2010; Ozguner et al. 2005; Moustafa et al. 2001; Kesari, Kumar, and Behari 2011; Jelodar, Akbari, and Nazifi 2012; Hoyto et al. 2008; Guney et al. 2007; Esmekaya et al. 2011; Atasoy et al. 2012)Al-Demegh, 2012; Kumar, 2010; Meral, 2007; Oktem et al. 2005; Ozguner et al. 2006). It is increasingly appreciated that glutathione is a final common pathway, a critical piece of environmentally vulnerable physiology, as glutathione reserves are compromised by an enormous number of environmental stressors, so that the cumulative impact upon glutathione may be far greater than could be predicted by the magnitude of any specific exposure (Lee, Jacobs, and Porta 2009), which supports an allostatic loading model.

Also of note are studies showing that the effects of EMF/RFR can be reduced by supplementation with antioxidants and radical scavengers. As an example, Vitamins E and C reduced adverse impacts on rat endometrium from 900MHz EMR exposure (Guney et al. 2007). Gingko biloba has also prevented mobile phone-induced increases in malondialdehyde and nitric oxide levels in brain tissue as well as decreases in brain superoxide dismutase and glutathione peroxidase activities and increases in brain xanthin oxidase and adenosine deaminase activities, and treated rats were spared the histopathological cell injury found in the untreated rats (Ilhan et al. 2004). Substantial further literature on antioxidants and radical scavengers is reviewed in Section 15 in Belyaev's contribution to the Bioinitiative 2012 Report (Belyaev 2012).

Stress protein (heat shock protein) responses

Another well-documented effect of exposure to low- intensity ELF and RFR is the creation of stress proteins (heat shock proteins) that signal a cell is being placed under physiological stress) (Weisbrot et al. 2003; Velizarov, Raskmark, and Kwee 1999; Leszczynski et al. 2004; Leszczynski et al. 2002; de Pomerai et al. 2000; Daniells et al. 1998; Blank and Goodman 2004). Heat shock proteins are in a family of inducible proteins that are initiated when any increased need for protection from stray electrons occurs (Padmini 2010; Bottoni, Giardina, and Scatena 2009). The HSP response is generally associated with heat shock, exposure to toxic chemicals and heavy metals, and other environmental insults. HSP is a signal of cells in distress. Plants, animals and bacteria all produce stress proteins to survive environmental stressors like high temperatures, lack of oxygen, heavy metal poisoning, and oxidative stress. It should also be noted that the generation of HSP stress proteins can have constructive medical applications, such as protection from reperfusion of the heart following ischemic injury (George et al. 2008). Another concomitant impact of cellular stress can be protein

misfolding, which has been documented in association with exposure to EMF/RFR. (Bohr and Bohr 2000; Mancinelli et al. 2004)

Although a number of papers have demonstrated increases in HSPs in people with ASDs (El-Ansary and Al-Ayadhi 2012; Evers, Cunningham-Rundles, and Hollander 2002; El-Ansary, Ben Bacha, and Kotb 2012; Walker, Segal, and Aschner 2006; Vojdani et al. 2004), it has been investigated far less often than oxidative stress. Part of the research needed to study possible influences of EMF/RFR on ASDs would be to study this more carefully.

2. Membranes and channels

Cell membranes and lipid peroxidation

Cell and organelle membranes play roles in partitioning cells from the extracellular milieu as well as in sustaining boundaries and regulating flow of materials between cellular compartments needing different metabolic parameters for their activities. They also play critical roles in maintaining electrical differences and the flow of electricity.

Adey (2002) summarized studies that report cell membranes as the site of initial field transductive coupling.

> *"Collective evidence points to cell membrane receptors as the probable site of first tissue interactions with both ELF and microwave fields for many neurotransmitters (Mironova et al. 1994), hormones (Liburdy 1995; Ishido, Nitta, and Kabuto 2001), growth- regulating enzyme expression (Byus, Pieper, and Adey 1987; Chen et al. 2000; Litovitz et al. 1993) (Penafiel et al. 1997), and cancer-promoting chemicals (Cain, Thomas, and Adey 1993; Mevissen, Haussler, and Loscher 1999). In none of these studies does tissue heating appear involved causally in the responses. Physicists and engineers have continued to offer microthermal, rather than athermal, models for these phenomena (Barnes 1996; Astumian, Weaver, and Adair 1995), with views that exclude consideration of cooperative organization and coherent charge states, but it is difficult to reconcile experimental evidence for factors such as modulation frequency-dependence and required duration of an amplitude-modulated signal to elicit a response (coherence time) (Litovitz et al. 1993) with models based on the equilibrium dynamics of tissue heating."* (Adey 2002)

Membranes are well-known targets of oxidative stress. Membrane damage is a major route through which free radical damage proliferates through the cellular system. Lipid peroxidation of membranes most often affects polyunsaturated fatty acids such as EPA and DHA which are the most abundant and vulnerable lipids in the brain where the damage they sustain can have serious impacts – DHA is 40% of brain tissue. Lipid

peroxidation of membranes has been identified as an effect of EMF/RFR in multiple studies (Desai, Kesari, and Agarwal 2009; Phelan et al. 1992). A variety of other mechanisms for membrane alteration related to EMF/RFR have been intimated in the literature. Physicochemical properties of membranes such as phase transition of phosphatidylcholine can be shifted by nonthermal effects of microwave radiation (Beneduci et al. 2012). Membrane potential and currents may also be impacted by pulsed radiofrequency fields (Linz et al. 1999). This has been observed graphically in altered cellular movement in Paramecium caudatum, with these cells becoming broader, with a broader-appearing cytopharynx, with their pulse vesicles having difficult in expelling their content outside the cell, and with less efficient movement of cilia (Cammaerts et al. (2011) which the authors suggested might be due to targeting of the cellular membrane. The impacts on this unicellular organism may help us imagine what the impact of EMF/RFR might be on cells with some structural similarities, such as columnar epithelial cells and ciliated cells in mucosal surfaces in the respiratory system, digestive tract, uterus and fallopian tubes and central spinal cord.

Indications of lipid peroxidation of membranes has been documented in ASDs, including malonaldehyde and isoprostanes, as well as alteration of membrane phospholipids and prostaglandins (Pecorelli et al. 2012; El-Ansary et al. 2010; El-Ansary, Ben Bacha, and Kotb 2012; Zhang, Sun, et al. 2012; Yao et al. 2006; Al-Gadani et al. 2009; Chauhan and Chauhan 2006; Ming, Stein, et al. 2005; Zoroglu et al. 2004) In one study the iosoprostane levels showed a biomodal distribution with the majority of ASD subjects showing moderate increase but a smaller group showing dramatic increases (Ming, Stein, et al. 2005). Thromboxane, reflecting platelet activation, was also elevated in one study (Yao et al. 2006). Given that this phenomenon has been identified in many people with ASDs, it is plausible that such individuals will likely be more vulnerable to having such cellular injuries caused, worsened or both by EMF/RFR exposures.

Calcium channels

Of particular prominence in the EMF/RFR physiological impact literature is the impact on calcium channels and signaling. Calcium signaling is ubiquitous in biological systems ranging from single-celled organisms to the most sophisticated functioning of our nervous and immune systems. This signaling takes place through a myriad of mechanisms within and between cells. The exquisite tuning of organisms is influenced by the precision of functioning of these systems, with even subtle disturbances having the potential to ramify in a nonlinear fashion through a system causing larger-scale disturbances elsewhere. EMF/RFR exposures have been shown to create disturbances in calcium signaling through a variety of mechanisms, including membrane leakage (Nesin et al. 2012), alteration of calcium-binding proteins and GFAP reactivity (Maskey et al. 2012; Maskey et al. 2010), and altered ultrastructural distribution of calcium and calcium-activated ATPases after exposure (Kittel et al. 1996). Adey (2002) provided an

overview of key studies on calcium efflux and the importance of calcium in cell signalling. *"Early studies described calcium efflux from brain tissue in response to ELF exposures (Bawin and Adey 1976; Blackman et al. 1985), and to ELF-modulated RF fields (Bawin and Adey 1976) (Blackman 1979) (Blackman et al. 1985; Dutta, Ghosh, and Blackman 1989). Calcium efflux from isolated brain subcellular particles (synaptosomes) with dimensions under 1.0 μm also exhibit an ELF modulation frequency-dependence in calcium efflux, responding to 16 Hz sinusoidal modulation, but not to 50 Hz modulation, nor to an unmodulated RF carrier (Lin-Liu and Adey 1982). In the same and different cell culture lines, the growth regulating and stress responsive enzyme ornithine decarboxylase (ODC) responds to ELF fields (Byus et al. 1988; Litovitz et al. 1993) and to ELF-modulated RF fields (Byus, Pieper, and Adey 1987) (Litovitz et al. 1993) (Penafiel et al. 1997) ."* (Adey 1994)

Dutta et al (1992) reported:

> *"Radio-frequency electromagnetic radiation (RFR) at 915 and 147 MHz, when sinusoidally amplitude modulated (AM) at 16 Hz, has been shown to enhance release of calcium ions from neuroblastoma cells in culture. The dose-response relation is unusual, consisting of two power-density "windows" in which enhanced efflux occurs, separated by power-density regions in which no effect is observed. To explore the physiological importance of these findings, we have examined the impact of RFR exposure on a membrane-bound enzyme, acetylcholinesterase (AChE), which is intimately involved with the acetylcholine (ACh) neurotransmitter system. Neuroblastoma cells (NG108), exposed for 30 min to 147-MHz radiation, AM at 16 Hz, demonstrated enhanced AChE activity, as assayed by a procedure using 14C-labeled ACh. Enhanced activity was observed within a time window between 7.0 and 7.5 h after the cells were plated and only when the exposure occurred at power densities identified in a previous report as being effective for altering the release of calcium ions. Thus RFR affects both calcium-ion release and AChE activity in nervous system-derived cells in culture in a common dose-dependent manner."* (Dutta et al. 1992)

The prominence of these calcium signaling impacts of EMF/RFR are striking when considered in relation to ASD pathophysiology, where such alterations have been proposed as of central importance. Calcium channels play an important role in regulating neuronal excitability, whose disturbance during development has been thought by many to be potentially contributory to the development of ASDs, as well as to the often associated vulnerability to seizures. Gene alterations have been identified associated with a number of voltage-gated calcium channels in ASDs (Smith, 2012; Krey and Dolmetsch 2007; Pasca et al. 2011; Gargus 2009; Lu et al. 2012). However, based on an examination of patient laboratory and phenotype data it has been argued that aberrant calcium signaling could be downstream: Palmieri and Persico (2010) suggest that *"an*

abnormal neuroimmune response as a relevant player in elevating intracellular Ca2+ levels, deranging neurodevelopment, driving oxidative stress, and ultimately affecting synaptic function and neural connectivity especially in long-range neuronal pathways physiologically responsible for integrated information processing." (Palmieri and Persico 2010) Peng and Jou (2010) have in turn shown how increased intracellular calcium can cause oxidative stress, and a vicious circle: *"...mitochondrial ROS [reactive oxygen species]rise can modulate Ca2+ dynamics and augment Ca2+ surge. The reciprocal interactions between Ca2+ induced ROS increase and ROS modulated Ca2+ upsurge may cause a feedforward, self-amplified loop creating cellular damage far beyond direct Ca2+ induced damage."* (Peng and Jou 2010*)*

Environmental as well as genetic routes to calcium signaling dysfunction have been identified (Pessah and Lein 2008) including chemicals such as the polyaromatic hydrocarbons. PCB-95 in particular modulates the calcium-dependent signaling pathway responsible for activity-dependent dendritic growth (Wayman, 2012; Wayman, 2012). In fact, once a genetic mutation has been associated with altering a critical signaling pathway and conferring risk for autism, chemicals or other environmental agents can be identified that target the same pathways and also confer ASD risk. Stamou et al. (2012) have reviewed this strategy of identifying multiple mechanisms converging on common signaling pathways regarding Ca(2+)-dependent mechanisms as well as extracellular signal-regulated kinases (ERK)/phosphatidylinositol-3-kinases (PI3K) and neuroligin-neurexin-SHANK (Stamou et al. 2012). From this point of view, there may be no particular reason to privilege genetic mutations in their contribution to a disturbance of calcium signaling, since whether this function becomes derailed due to a genetic mutation, from a chemical toxin or from EMF/RFR perturbation of calcium signaling, the functional effect is comparable. Moreover if a person is subject to multiple triggers all of which have calcium signaling impacts, the gene-environment interactions may lead to impacts that could be less, the same as or more than any one contributor alone might create.

3. Junctions and barriers

The damage discussed so far has been at the molecular and subcellular level. However impacts from this level reverberate up to larger scales in the system. Where membranes create boundaries between cells and subcellular compartments, barriers do this at a larger scale. Cells become capable of forming barriers between each other through tight junctions which block substances and cells from 'slipping through the cracks,' so to speak, between the cells. Conversely, gap junctions are subcellular structures providing openings that allow physical passage of materials between cells otherwise separated by membranes.

It appears that such connections between cells can also be altered by electromagnetic fields and radiofrequency exposures, at least under certain circumstances. High frequency magnetic fields have been observed to be associated with a sharp decrease in intercellular gap junction-like structures, in spite of increased gene expression for pertinent proteins (Cervellati, 2009). Changes in tight junctions have been observed upon exposure to microwave and x-ray irradiation {Palfia, 2001).

A number of papers in the ASD research field document problems pertinent to junctions. Connexin abnormalities have been documented in neuropathological studies (Fatemi et al. 2008). and MacFabe and colleagues identified lipid alterations associated with oxidative stress, membrane fluidity and the modulation of gap junction coupling (Thomas et al. 2012). Decrease in platelet endothelial cell adhesion molecule-1 were reduced and this reduction correlated with repetitive behavior and abnormal brain growth; achesion molecules modulate permeability and signaling at the blood-brain barrier as well as leukocyte infiltration into the central nervous system (Onore et al. 2012).

EMF and RFR might also compromise biologically important barrier structures that separate blood flow from organs like the brain (Salford et al, BioInitiative Report 2012, Section 10) (Salford, 2012). This raises important questions regarding whether other 'barriers' that keep blood flow separate from the gut (gut-blood barrier), or the placenta (blood-placenta barrier) or the eye (ocular-blood barrier) may also be rendered pathologically leaky, and allow albumin, toxins, pro-inflammatory cytokines and infectious agents to cross this barrier into the intestines (invoking immune responses) and impacting the developing fetus (Somosy, 1993). While there are a fair number of negative studies, there are also many studies showing and association between EMF/RFR and pathological leakage of the blood-brain barrier (BBB), as well as evidence in animal studies of damage to brain cells and damage to or death of neurons. Such leakage has been shown to be potentiated by physiological factors such as diabetes and insulin (Gulturk et al 2010) and has also potentiated viral lethality in a dose-dependent fashion (Lange et al, 1991). Many of the positive findings were associated with non-thermal exposures comparable to normal cell phone radiation exposure (Salford, 1994; Salford, 2003; Salford, 2007; Salford, 1992; Eberhardt, 2008; Nittby, 2009; Nittby, 2008). There are scattered reports of increased permeability across other membranes and barriers, such as the blood-testicle barrier in mice (Wang, 2008; Wang et al., 2010 and the rat liver canalicular membrane (Lange, 1993). A 1992 study by Kues et al. reported that *"studies in our laboratory have established that pulsed microwaves at 2.45 GHz and 10 mW/cm2 are associated with production of corneal endothelial lesions and with disruption of the blood-aqueous barrier in the non-human primate eye."* (Kues et al. 1992) A recent study showing impact of high-frequency electromagnetic fields on trophoblastic connexins (Cervellati et al. 2009) may indicate the vulnerability of the placenta and placental barrier function to electromagnetic fields. A thorough review and

methodological discussion of literature regarding EMF/RFR impacts on the BBB is provided by Salford in Section 10 of the BioIniative 2012 Report (Salford, 2012).

According to a review by Zlokovic, *"BBB breakdown, due to disruption of the tight junctions, altered transport of molecules between blood and brain and brain and blood, aberrant angiogenesis, vessel regression, brain hypoperfusion, and inflammatory responses, may initiate and/or contribute to a "vicious circle" of the disease process, resulting in progressive synaptic and neuronal dysfunction and loss in disorders such as Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, multiple sclerosis, and others."* (Zlokovic 2008). The integrity of the BBB can be compromised by oxidative stress which can lead to increased permeability (Parathath, Parathath, and Tsirka 2006). The resultant extravasation of albumin into brain parenchyma can be excitotoxic and neurotoxic (Hassel, Iversen, and Fonnum 1994; Eimerl and Schramm 1991).

The evidence suggesting possible existence of barrier function compromise in people with ASDs is largely indirect. The existence of brain neuroinflammation in ASDs has been documented in a growing number of studies (Boso et al. 2006; El-Ansary and Al-Ayadhi 2012; Young et al. 2011), and this is known to be associated with BBB permeability (Erickson, Dohi, and Banks 2012; Janigro 2012; Takeshita and Ransohoff 2012). In a review of clinical MRI findings in ASDs 19/59 showed white matter signal abnormalities (Boddaert et al. 2009), which in other settings have been associated with cerebral hypoperfusion, though not necessarily in the same locations as the hyperintensities (Vardi et al. 2011; Brickman, 2009). Blood flow abnormalities, predominantly hypoperfusion, documented in a few dozen PET and SPECT studies, could also be caused by and/or associated with physiological phenomena associated with vascular permeability as will be revisited below. Increased intestinal permeability has been documented (although its absence has also been documented) (de Magistris et al. 2010; Lucarelli et al. 1995; D'Eufemia et al. 1996; Horvath and Perman 2002; White 2003; Robertson et al. 2008; Souza et al. 2012) and discussed in the context of food exposures, particularly gluten (Silva et al. 2012; Sapone et al. 2011; Visser et al. 2009; Simpson et al. 2009; Fasano 2009; Lammers et al. 2008; De Angelis et al. 2006). The reactivity to large numbers of different foods clinically observed in many children with autism has been framed by some as a manifestation of indiscriminate exposure of the immune system and the brain to food proteins on account of intestinal permeability as well as BBB permeability (Theoharides and Doyle 2008). This reactivity could in turn feed in to aberrant immune responsivity which in turn could further amplify barrier vulnerability (Fasano, 2009).

A number of studies have made an association between an increased risk of having a child with autism and maternal infection during pregnancy. This phenomenon looks like it is a result of the maternal immune system response rather than being due to an impact

deriving from a specific infectious agent; but the potential for an accompanying compromise of the placental barrier is also conceivable in this setting. Under these circumstances the fetal risk of exposure to maternal blood toxins, cytokines and stress proteins in-utero could potentially be increased if placenta barrier (BPB) function were impaired. The integrity, or compromise thereto, of the maternal-fetal interface via the placenta is an important modulator of brain development (Hsiao and Patterson 2012).

4. Genetic alterations and reproductive impacts

Because of the high heritability of autism that was calculated from the concordance rates of monozygotic (identical) vs. dizygotic (fraternal) twins found in by a series of small twin studies performed some decades ago, the overwhelming emphasis in recent decades in autism research has been on genetics, and on finding linkages between genes, brain and behavior. As mentioned earlier, this point of view also promotes more of a structural/anatomical orientation than a bioelectric/physiological orientation. Along with this emphasis it has seemed obvious to people just looking at the stubborn persistence of symptoms in affected individuals that ASDs are inborn, lifelong brain defects. From this vantage point there would be no reason to think about the transduction of pathophysiology – whether acquired or genetic or some combination – to brain and hence behavior (or, more broadly, neurocognitive function). Thus the research agenda of looking for gene-brain-behavior correlations has seemed both self-evident and sufficient.

In recent years the genetic premises of this seemingly obvious framing of autism as overwhelmingly genetic have been undermined at several levels. (The undermining of the brain premises will be discussed beyond what was covered in Part I in later sections.) First the number of reported cases is increasing, making it more difficult to maintain that ASDs are purely genetic because these increases can only be partly explained away by greater awareness or other data artifacts (King and Bearman 2009; Hertz-Picciotto and Delwiche 2009). Second, the complexity of the ways we understand how genes might relate to autism has grown, from an expectation a decade ago that a small number of genes (even less than a dozen) would explain everything to an identification of close to a thousand genes associated with autism, as well as ‘de novo’ mutations present in ASD children but not their parents and even ‘boutique’ mutations not shared beyond an individual family. Out of over a hundred genetic syndromes in which autism commonly occurs, it is unclear what the pertinent genetic mutations and rearrangements have in common to account for the shared association with ASDs (Anney et al. 2010; Betancur 2011). Moreover, a recent twin study that was much larger than any of the prior such studies identified a modest genetic role but a substantial environmental role (Hallmayer et al. 2011). Also of interest, a Swedish study of identical twins and schizophrenia grouped into monochorionic (shared placenta) and dichorionic (each had its own placenta) showed 60% concordance for schizophrenia diagnosis for monochorionic twins but only 10.7%

concordance for dichorionic twins (Davis, Phelps, and Bracha 1995); though this work has not yet been replicated in ASD twins, in principle it opens the door to non-genetic interpretations of any concordance figures that have generally been assumed to be indicators of heritable genetics. The authors of this study interpreted their findings as consistent with data on viral infection as a contributor to schizophrenia risk (a possibility also entertained in ASDs (Patterson 2012; Teixeira and Barichello 2012; Atladottir et al. 2012, 2012; Hornig et al. 1999), but one could also consider the possibility of differences in the dichorionic cases in the integrity of the placental barrier.

All of this calls into question the idea that genetics can be presumed to be the 'cause' of autism simply based upon heritability calculations, and upgrades the importance of looking not only at the environment and environmentally vulnerable physiology, but also at acquired mutations. There is certainly progress being made through genetic research to the identification of networks of genes and mechanisms on which genes converge (Voineagu et al. 2011), but environmental mechanisms converge on these mechanisms too (Stamou et al. 2012), and the mechanisms are what drive the impacts.

Genotoxicity

One route through which environmental impacts may influence an organism's status is by changing genes through mutation – that is, by genotoxicity. This has been proposed as a mechanism for the generation of 'de novo' mutations (found in children but not their parents) being found in ASDs (Kinney et al. 2010) and increasingly in other settings as well, making mutations something that needs to be accounted for rather than simply assuming tey are associated with normal, stable variation. Reviews and published scientific papers on genotoxicity and EMF report that both ELF-EMF and RFR exposures can be considered genotoxic – i.e., damaging to DNA – under certain conditions of exposure, including under conditions of intermittent and/or chronic ELF and RFR exposure that are of low-intensity and below current world safety standards (Ruediger 2009; Ivancsits et al. 2005; Diem et al. 2005; Blank and Goodman 2011; Phillips, Singh, and Lai 2009; REFLEX 31 May 2004; Sage and Carpenter 2009; Lai and Singh 2004). Types of genetic damage reported have included DNA fragmentation and single- and double-strand DNA breaks, micronucleation and chromosome aberrations, all of which indicate genetic instability. Genotoxic impacts of EMF/RFR are further reviewed in the BioInitiative Working Group 2007 contribution by Lai as well as in Section 6 of the present Bioinitiative Report {Lai, 2007; Lai, 2012).

The European research program REFLEX (Risk Evaluation of Potential Environmental Hazards From Low-Energy Electromagnetic Field Exposure Using Sensitive in vitro Methods – a 5FP EU project) documented many changes in normal biological functioning in tests on DNA at exposure levels below existing public safety standards(REFLEX 31 May 2004). Some of the key findings included:

- Gene mutations, cell proliferation and apoptosis which are caused by or result in altered gene and protein expression profiles. The convergence of these events is required for the development of all chronic diseases.
- Genotoxic effects and a modified expression of numerous genes and proteins after EMF exposure could be demonstrated with great certainty.
- Genotoxic effects produced by RF-EMF in fibroblasts, HL- 60 cells, granulosa cells of rats and neural progenitor cells derived from mouse embryonic stem cells.
- Response of cells to RF exposure between SAR levels of 0.3 and 2 W/Kg with a significant increase in single- and double-strand DNA breaks and in micronuclei frequency.
- A clear demonstration of increase in intracellular generation of free radicals in HL-60 cells accompanying RF-EMF exposure.
- The observation that the induced DNA damage was not based on thermal effects, which raises concerns about the thermal-based environmental safety limits for ELF-EMF exposure.

These impacts could be contributors to a role for genetics in ASDs that does not derive from only inheritance but also from environmental and epigenetic influences. Moreover, in the light of the great heterogeneity of genetic findings in ASD alongside the documented impacts of EMF/RFR upon many other levels of pathophysiology than simply genetics, it becomes worth reflecting whether genetics might not be the primary problem but instead, in many cases at least, just one of many levels of collateral damage from environmental impacts. Whatever genetic variants a person carries may bias their system toward specific vulnerability, or may contribute more generically by increasing entropy and molecular disorder; in either capacity they may aggravate the situation but may not be part of the main cause.

Contributors to Genotoxicity

Oxidative stress and free radical damage to DNA

Oxidative stress and excessive free radical production are very well known to be potentially genotoxic. They can be a consequence of myriad environmental factors, including but by no means limited to EMF/RFR. The DNA damage that can result could very well be one cause of 'de novo' mutations. Although there is not a consensus at this time about the rates or causes of *de novo* mutations in ASDs, and using present methods of detection are only found in a small percentage of individuals with ASDs, given the potential contribution of environmentally triggered oxidative stress and free radical damage that we know is present in at least large numbers of people with ASDs, a serious investigation of the potential contribution of EMF and RFR to de novo mutations in ASD seems warranted, given the large increase in exposure to these phenomena accompanying the massively increased non-ionizing radiation exposures in daily life due to

electrification and the global saturation of RFR from wireless technologies (BioInitiative 2012 Report, Section 24, Public Health Implications, Sage and Carpenter, 2012).

Challenge to DNA repair mechanisms

Reduced DNA repair may contribute to increased risk of cancers, but it may also contribute to a variety of other diseases and disturbances of growth and development. When the rate of damage to DNA exceeds the rate at which DNA can be repaired, there is the possibility of retaining mutations and initiating pathology. Failure to trigger DNA damage repair mechanisms, or incomplete or failed repair, may be a consequence of a variety of commonplace stressors, including EMF/RFR exposure. A decrease in DNA repair efficiency has been reported to result from exposure to low-intensity RFR in human stem cells, and other cells. Mobile phone frequency GSM exposure at the frequency of 915 MHz consistently inhibited DNA repair foci in lymphocytes (Markova et al. 2005; Belyaev et al. 2005; Belyaev, Markova, and Malmgren 2009). Belyaev, Markova and colleagues (2005) and Markova et al. (2009) reported that very low-intensity microwave radiation from mobile phones inhibits DNA repair processes in human stem cells. A significant reduction in 53BP1 ((tumor suppressor p53 binding protein 1) foci was found in cells exposed to microwave radiofrequency radiation within one hour of exposure. Fibroblast cells were impacted in this fashion but adapted over time, whereas stem cells were similarly affected (inhibited 53BP1 foci) but did not adapt to microwave radiation during chronic exposure (Markova et al. 2005; Belyaev et al. 2005). Additional challenges to DNA repair mechanisms include not only toxicants and other damaging inputs but also nutritional insufficiencies of substances important to the proper functioning of DNA repair mechanisms, including Vitamin D, essential fatty acids, and minerals such as selenium and molybdenum (Christophersen and Haug 2011). The high possibility that various such contributors may combine supports an 'allostatic load' model of environmental injury and genotoxicity. Also note the overlap between nutritional risk factors for oxidative stress and for impaired DNA repair mechanisms. This supports a vicious circle model where the more oxidative damage to the genome, the less the cells will be prepared to deal with it successfully. It can also work the other way around – nutrients can attenuate the degree of damage; instances of this will be discussed in the Melatonin section below.

Chromatin condensation

Chromatin condensation is another hallmark of damage from EMF and RFR. Orderly chromatin condensation is a normal part of cell division, but it can also be provoked pathologically. The work of Markova, Belyaev and others has repeatedly shown that RFR exposure can cause chromatin condensation. Belyaev (1997) reported that super-low intensity RFR resulted in changes in genes, and chromatin condensation of DNA at intensities comparable to exposures from cell towers (typically at RFR levels of 0.1 to 1.0 uW/cm2) (Belyaev, Alipov, and Harms-Ringdahl 1997). Significant microwave-induced

changes in chromatin conformation were observed when rat thymocytes were analyzed in-between 30-60 min after exposure to MW (Belyaev and Kravchenko 1994). This effect nearly disappeared if the cells were incubated more than 80 min between exposure and analysis.

In recent studies, human lymphocytes from peripheral blood of healthy and hypersensitive to EMF persons were exposed to non-thermal microwave radiation NT MW) from the GSM mobile phones (Belyaev et al. 2005; Markova et al. 2005). NT MW induced changes in chromatin conformation similar to those induced by heat shock, which remained up to 24 h after exposure. The same group has reported that contrary to human fibroblast cells, which were able to adapt during chronic exposure to GSM/UMTS low intensity RFR exposure, human stem cells did not adapt (Belyaev, Markova, and Malmgren 2009).

Researchers have recently identified large numbers of "spontaneous genetic glitches," or de novo mutations, more likely to be transmitted by fathers than by mothers to their children (Neale et al. 2012; O'Roak et al. 2012; Sanders et al. 2012). These glitches are widely distributed across the genome, with their location rather than their size conferring risk. The Eichler team at the University of Washington found that 39% of the 126 most severe or disruptive mutations map to a network associated with chromatin remodeling that has already been ranked as significant amongst autism candidate genes (O'Roak et al. 2012). Whether the prominence of chromatin-related gene mutations can be related in any meaningful way to the impacts of EMF/RFR on chromatin condensation is not possible to say at this point in time and this apparent parallel between ASDs and EMF/RFR may be a pure coincidence, though an intriguing one worth looking into further, including regarding how these mutations and the chromatin-remodeling impacts of EMF/RFR exposure may interact.

Gonadal and germline impacts

De novo mutations have been shown to be more of a problem related to paternal age (O'Roak et al. 2012; Paul, Nagano, and Robaire 2011; Iossifov et al. 2012; Cantor et al. 2007; Alter et al. 2011), and this may be related to the impact of environmental factors such as EMF/RFR on the stem cell genome, particularly in sperm which have no DNA repair capacity. Vulnerability of testes and ova, and of sperm and egg cells, relates to the tissue milieu in which damage to the germline can take place, as well as on the greater vulnerability of stem cells. Several international laboratories have replicated studies showing adverse effects on sperm quality, motility and pathology in men who use and particularly those who wear a cell phone, PDA or pager on their belt or in a pocket (Agarwal et al. 2008; Agarwal et al. 2009; Wdowiak, Wdowiak, and Wiktor 2007; De Iuliis et al. 2009; Fejes et al. 2005; Aitken et al. 2005) Kumar, 2012). Other studies conclude that usage of cell phones, exposure to cell phone radiation, or storage of a

mobile phone close to the testes of human males affect sperm counts, motility, viability and structure (Aitken et al. 2004; Agarwal et al. 2007; Erogul et al. 2006). Animal studies have demonstrated oxidative and DNA damage, pathological changes in the testes of animals, decreased sperm mobility and viability, and other measures of deleterious damage to the male germ line (Dasdag et al. 1999; Yan et al. 2007; Otitoloju et al. 2010; Salama et al. 2009) Behari et al. 2006; Kumar et al. 2012). Of note, altered fatty acids consistent with oxidative stress have been found in sperm cells in male infertility (Zalata et al. 1998; Zalata, Hafez, and Comhaire 1995).

There are fewer animal studies that have studied effects of cell phone radiation on female fertility parameters. Panagopoulous et al. 2012 report decreased ovarian development and size of ovaries, and premature cell death of ovarian follicles and nurse cells in *Drosophila melanogaster* (Panagopoulos 2012). Gul et al (2009) report rats exposed to stand-by level RFR (phones on but not transmitting calls) caused decrease in the number of ovarian follicles in pups born to these exposed dams (Gul, Celebi, and Ugras 2009). Magras and Xenos (1997) reported irreversible infertility in mice after five (5) generations of exposure to RFR at cell phone tower exposure levels of less than one microwatt per centimeter squared (μW/cm2) (Magras and Xenos 1997).

Implications of genotoxicity

The issue of genotoxicity puts the contribution of genetic variation into a different light – as something that needs to be accounted for, not necessarily assumed as the starting point. In this regard it has been speculated that the apparent higher rates of autism in Silicon Valley, discussed in the past as related to 'geek genes' (Silberman 2001), might be conditioned by higher levels of exposure to EMF/RFR. The relationship between the greater vulnerability of male sperm than of female eggs to adverse effects of EMF/RFR exposure and the marked (4:1) predominance of paternal origin of de novo point mutations (4:1 bias), also deserves further careful attention (O'Roak et al. 2012).

5. Implications of Damage

We have reviewed parallels between ASD and EMF/RFR in molecular, cellular and tissue damage, including cellular stress (oxidative stress, the heat shock response and protein misfolding), injury of membranes, aberrant calcium signaling, and compromise of junctions and barriers. The genotoxicity of EMF/RFR was reviewed in relation to issues of environmental contributions to autism and of the phenomenon of de novo mutations. The compromise of the tissue substrate appears to have many commonalities in ASDs and in EMF/RFR exposures. Also notable was the possibility of attenuating some of the damage through increasing antioxidant status.

These commonalities come to mind in considering the implications of a recent study documenting arrest of symptomatology in a mouse model of Rett syndrome through a

bone marrow transplant of wild-type microglia (Derecki et al. 2012; Derecki, Cronk, and Kipnis 2012). The introduction of these competent microglia cells did not directly target the neuronal defect associated with the MECP2 gene mutation; instead the benefits of the transplant were diminished through inhibition of phagocytosis. Phagocytosis involves removing debris. This suggests that while research has focused on how specific molecular defects, particularly in the synapse, may contribute to Rett pathophysiology, there may also be an important contribution from cellular debris, misfolded proteins and other disordered cellular structure and function. Such disorder could be accumulating in cells under the conditions of pathophysiological disarray reviewed above. This has potentially broad implications for other genetic disorders, as well as for conditions like ASDs which are for the most part idiopathic. Based on this study as well as on the levels of damage just reviewed, problems in cells that are pertinent to ASDs most likely go beyond any specific defect introduced by a mutation. Additionally it is conceivable that many of the mutations may be not part of normal background variation but instead collateral damage from the same environmental factors that are also driving the damage to the pathophysiology. It is also encouraging that at least some of the damage and dysfunction was reversible by a generic cellular mechanism (phagocytosis), and this could have broad significance for idiopathic ASDs as well, along with other conditions involving related pathophysiological challenges.

B. Degradation of System Integrity

In the setting of molecular, cellular and tissue damage, one would predict that the organization and efficiency of a variety of organelles, organs and systems would also be degraded. EMF/RFR exposures yield a stressful situation of chronically interrupted homeostasis. Here we will review disturbances from EMF/RFR in systems (including include oxidative and bioenergetics metabolism, immune function and electrophysiological oscillations) that include molecular and cellular components subject to the kinds of damage discussed in the previous section. We will review disturbances that have been associated with EMF/RFR, and consider the parallel disturbances that have been documented in ASDs.

1. Mitochondrial dysfunction

Mitochondria are broadly vulnerable, in part because the integrity of their membranes is vital to their optimal functioning – including channels and electrical gradients, and their membranes can be damaged by free radicals which can be generated in myriad ways. Moreover, just about every step in their metabolic pathway can be targeted by environmental agents, including toxicants and drugs, as well as mutations (Wallace and Starkov 2000). This supports an allostatic load model for conditions in which mitochondrial dysfunction is an issue, which includes ASDs as well as myriad other chronic conditions.

Mitochondria are commonly discussed in terms of the biochemical pathways and cascades of events by which they metabolize glucose and generate energy. But in parallel with this level of function there also appears to be a dimension of electromagnetic radiation that is part of the activity of these organelles. For example, electromagnetic radiation can be propagated through the mitochondrial reticulum, which along with the mitochondria has a higher refractive index than the surrounding cell and can serve to propagate electromagnetic radiation within the network (Thar and Kuhl 2004). It is also the case that *"The physiological domain is characterized by small-amplitude oscillations in mitochondrial membrane potential (delta psi(m)) showing correlated behavior over a wide range of frequencies…. Under metabolic stress, when the balance between ROS [reactive oxygen species, or free radicals] generation and ROS scavenging [as by antioxidants] is perturbed, the mitochondrial network throughout the cell locks to one main low-frequency, high-amplitude oscillatory mode. This behavior has major pathological implications because the energy dissipation and cellular redox changes that occur during delta psi(m) depolarization result in suppression of electrical excitability and Ca2+ handling…"* (Aon, Cortassa, and O'Rourke 2008). These electromagnetic aspects of mitochondrial physiology and pathophysiology could very well be impacted by EMF/RFR.

There are also a variety of types of mitochondrial damage that have been documented in at least some of the studies that have examined the impacts of EMF/RFR upon mitochondria. These include reduced or absent mitochondrial cristae (Khaki et al. 2006; Lahijani, Tehrani, and Sabouri 2009; Esmekaya et al. 2011), mitochondrial DNA damage (Xu et al. 2010), swelling and crystallization (Lahijani, Tehrani, and Sabouri 2009), alterations and decreases in various lipids suggesting an increase in their use in cellular energetics (Chernysheva 1987), damage to mitochondrial DNA (Xu et al. 2010), and altered mobility and lipid peroxidation after exposures (Wang et al. 2002). Also noted has been enhancement of brain mitochondrial function in Alzheimer's transgenic mice and normal mice (Dragicevic et al. 2011). The existent of positive as well as negative effects gives an indication of the high context dependence of exposure impacts, including physical factors such as frequency, duration, and tissue characteristics; these are

intensively reviewed in Belyaev's contribution to BioInitiative 2012 in Section 15 (Belyaev 2012).

The idea that mitochondrial dysfunction might be common in ASDs met with a fair bit of consternation, and many professionals have preferred to limit their consideration to mitochondrial disorders with proven genetic mutations. However the concept of mitochondrial dysfunction is better established in other areas of medicine, with thousands of papers and hundreds of reviews carrying "mitochondrial dysfunction" in their titles. By now there is a large amount of evidence for biochemical and other abnormalities in a large portion of children with autism that are consistent with mitochondrial dysfunction (Giulivi et al. 2010; Palmieri et al. 2010; Pastural et al. 2009). Recently published postmortem brain tissue studies that have added a new dimension of evidence for mitochondrial abnormalities in ASDs will be reviewed in the section on alteration of brain cells below.

Some have called the mitochondrial issues most commonly seen in ASDs 'secondary mitochondrial dysfunction' (Zecavati and Spence 2009; Rossignol and Frye 2011) to indicate that it results from environment insults and/or other pathophysiological dysfunction rather than directly from genetics (Hadjixenofontos et al. 2012); the already discussed potential for EMF/RFR to damage channels, membranes and mitochondria themselves could contribute in a number of ways to degrading mitochondrial function without a basis in genetic mutation, as could toxicant exposures and immune challenges. In a meta-analysis of studies of children with ASD and mitochondrial disorder, the spectrum of severity varied, and 79% of the cases were identified by laboratory not associated with genetic abnormalities (Rossignol and Frye 2011). "*Substantial percentages of autistic patients display peripheral markers of mitochondrial energy metabolism dysfunction, such as (a) elevated lactate, pyruvate, and alanine levels in blood, urine and/or cerebrospinal fluid, (b) serum carnitine deficiency, and/or (c) enhanced oxidative stress……In some patients, these abnormalities have been successfully explained by the presence of specific mutations or rearrangements in their mitochondrial or nuclear DNA. However, in the majority of cases, abnormal energy metabolism cannot be immediately linked to specific genetic or genomic defects."* (Palmieri and Persico 2010)

2. Melatonin dysregulation

Melatonin, mitochondria, glutathione, oxidative stress

Melatonin is well-known for its role in regulation of circadian rhythms, but it also plays important metabolic and regulatory roles in relation to cellular protection, mitochondrial malfunction and glutathione synthesis. (Leon et al. 2005; Luchetti et al. 2010; Limon-Pacheco and Gonsebatt 2010) *"It is known that melatonin scavenges oxygen and*

nitrogen-based reactants generated in mitochondria. This limits the loss of the intramitochondrial glutathione and lowers mitochondrial protein damage, improving electron transport chain (ETC) activity and reducing mtDNA damage. Melatonin also increases the activity of the complex I and complex IV of the ETC, thereby improving mitochondrial respiration and increasing ATP synthesis under normal and stressful conditions." (Leon et al. 2005) It also helps prevent the breakdown of the mitochondrial membrane potential, decrease electron leakage, and thereby reduce the formation of superoxide anions. (Hardeland 2005) Pharmacological doses of melatonin not only scavenge reactive oxygen and nitrogen species, but enhance levels of glutathione and the expression and activities of some glutathione-related enzymes. (Limon-Pacheco and Gonsebatt 2010; Gupta, Gupta, and Kohli 2003)

Melatonin can attenuate or prevent some EMF/RFR effects

Melatonin may have a protective effect in the setting of some EMF/RFR exposures, apparently in relation to these functions just described. EMF/RFR can impact melatonin; one example is exposure to 900-MHz microwave radiation promoted oxidation, which reduced levels of melatonin and increased creatine kinase and caspase-3 in exposed as compared to sham exposed rats (Kesari, Kumar, and Behari 2011).

Further types of adverse impacts can be seen in the next set of examples, but what is interesting is that melatonin can attenuate or prevent them. In an experiment exposing rats to MW from a GSM900 mobile phone with and without melatonin treatment to study renal impacts (Oktem et al. 2005), the untreated exposed rats showed increases of lipid peroxidation markers as reduction of the activities of superoxide dismutase, catalase and glutathione peroxidase indicating decrement in antioxidant status. However these negative effects were inhibited in the exposed rats treated with melatonin. Melatonin also inhibited the emergence of preneoplastic liver lesions in rats exposed to EMFs (Imaida et al. 2000). The development of DNA strand breaks was observed in RFR exposed rats; this DNA damage was blocked by melatonin (Lai and Singh 1997). Exposure of cultured cortical neurons to EMF led to an increase in 8-hydroxyguanine in neuronal mitochondria, a common biomarker of DNA oxidative damage, along with a reduction in the copy number of mitochondrial DNA and the levels of mitochondrial RNA transcripts; but these effects could all be prevented by pretreatment with melatonin (Xu et al. 2010). In a study of skin lesion induced by exposure to cell phone radiation, the skin changes in the irradiated group (which included thicker stratum corneum, epidermal atrophy, papillamatosis, basil cell proliferation, increased epidermal granular cell layer and capillary proliferation, impaired collagen tissue distribution and separation of collagen bundles in dermis) were prevented (except for hypergranulosis) by melatonin treatment (Ozguner et al. 2004). Melatonin as well as caffeic acid phenyethyl ester (an antioxidant) both protected against retinal oxidative stress in rates exposed long-term to mobile phone irradiation (Ozguner, Bardak, and Comlekci 2006). Nitric oxide (NO) was increased in

nasal and sinus mucosa in rats after EMF exposure, with this NO possibly acting as a defense mechanism suggesting tissue damage; but this was prevented by pretreatment with melatonin (Yariktas et al. 2005). Melatonin treatment significantly prevented the increase in the MDA (malondyaldehyde, a marker of lipid peroxidation) content and XO (xanthine oxidase) activity in rat brain tissue after 40 days of exposure, but it was unable to prevent the decrease of CAT activity and increase of carbonyl group contents (Sokolovic et al. 2008).

Of note, the melatonin production of infants in isolettes in neonatal intensive care units appears to be impacted by the high ELF-EMF environment, in that when infants were removed from those exposures they showed an increase in melatonin levels (Bellieni, Tei, et al. 2012). There is an increased prevalence of ASDs in children who were born prematurely (Indredavik et al. 2010; Indredavik et al. 2008; Johnson et al. 2011; Johnson et al. 2010; Johnson and Marlow 2011; Lampi et al. 2012; Limperopoulos 2009, 2010; Limperopoulos et al. 2008; Matson, Matson, and Beighley 2011; Pinto-Martin et al. 2011). There are many potential prematurity-associated factors that could contribute to increased risk for ASDs, but electromagnetic exposure might be one of them worthy of further consideration, as it could be modified; conversely, such exposures in vulnerable infants are likely to have much broader impacts beyond reducing melatonin synthesis.

Melatonin and autism

Based on the commonality of both sleep disorders and low melatonin levels, Bourgeron (2007) proposed that synaptic and clock genes are important in ASDs, and that future studies should investigate the circadian modulation of synaptic function (Bourgeron 2007). A number of melatonin-related genetic variants have been identified as associated with ASDs. Polymorphisms, deletions and polymorphisms in the ASMT gene, which encodes the last enzyme of melatonin synthesis, have been found (Pagan et al. 2011; Jonsson et al. 2010; Melke et al. 2008), and variations have been found as well for melatonin receptor genes (Chaste et al. 2010; Pagan et al. 2011; Jonsson et al. 2010). CYP1A2 polymorphisms have been found in slow melatonin metabolisers, in whom melatonin levels are aberrant and initial response to melatonin for sleep disappeared in a few weeks (Braam et al. 2012).

Regarding melatonin status in people with ASDs, a recent meta-analysis summarized the current findings as indicating that *"1) Physiological levels of melatonin and/or melatonin derivatives are commonly below average in ASD and correlate with autistic behavior, 2) Abnormalities in melatonin-related genes may be a cause of low melatonin levels in ASD, and 3) … treatment with melatonin significantly improves sleep duration and sleep onset latency in ASD."* (Rossignol and Frye 2011) The meta-analysis also showed that polymorphisms in melatonin-related genes in ASD could contribute to lower melatonin

concentrations or an altered response to melatonin, but only in a small percentage of individuals, since pertinent genes were found in only a small minority of those screened.

Autism AND Melatonin AND Glutathione

Whereas PubMed searches for "autism AND melatonin" and "autism AND glutathione" each coincidentally yielded 72 citations, and "melatonin AND glutathione" yielded 803 citations, the search for "autism AND melatonin AND glutathione" yielded zero citations. This is interesting given the strong connection of melatonin and glutathione metabolically, as discussed above, alongside of the strongly established interest in both glutathione and melatonin in ASD research and increasingly in clinical practice. Hopefully one contribution of an investigation of EMF/RFR links to ASDs will be to help bring attention to this relationship, which may help identify potential environmental and physiological causes for low melatonin in those without pertinent mutations. Of pertinence, tryptophan hydroxylase (TPH2) – the rate limiting enzyme in the synthesis of serotonin, from which melatonin is derived – is extremely vulnerable to oxidation, and tends to misfold when its cysteine residues are oxidized, with the enzyme being converted to a redox-cycling quinoprotein (Kuhn and Arthur 1999; Kuhn and Geddes 1999; Kuhn et al. 2011; Kuhn and Arthur 1997).

3. Disturbed immune function

There is by now a broad appreciation of the presence of immune disturbances in ASDs, to the point where there is an emerging discussion of ASDs as neuroimmune disorders (Bilbo, Jones, and Parker 2012; Persico, Van de Water, and Pardo 2012). Research identifying immune features in ASDs spans from genetics where risk genes have been identified to epigenetics where altered expression of immune genes is being reported as prominent in ASD epigenetics (Kong et al. 2012; Waly et al. 2012; Lintas, Sacco, and Persico 2012), and also includes prenatal infectious and immune disturbances as risk factors for autism as well as other neurodevelopmental and neuropsychiatric diseases as well as other conditions such as asthma (Patterson 2011; Smith et al. 2007; Fox, Amaral, and Van de Water 2012). Immune disturbances in infants and children with ASD are heterogeneous, with some but not all manifesting autoimmunity (Soumiya, Fukumitsu, and Furukawa 2011; Martin et al. 2008). Anecdotally, recurrent infection is common while on the other hand some get sick less often than their peers. It is common for people with autism to have family members with immune or autoimmune diseases (Croen et al. 2005). The immune system is turning out to have an important role in brain development (Bilbo and Schwarz 2012; Schwarz and Bilbo 2012; Boksa 2010). As mentioned, glial activation associated with brain immune response has been identified in a growing number of studies. Whether or not EMF/RFR contributes to these features of ASDs causally, based on the evidence below regarding immune impacts of EMF/RFR exposure (which is also reviewed much more thoroughly by Johansson in Section 8 of the present

Bioinitiative Report) (Blank 2012), it is certainly plausible that such exposures could serve as aggravating factors.

Low-intensity exposures

It is clear that the body's immune defense system responds to very low-intensity exposures. Chronic exposure to factors that increase allergic and inflammatory responses on a continuing basis is likely to be harmful to health, since the resultant chronic inflammatory responses can lead to cellular, tissue and organ damage over time. We are increasingly appreciating the extent to which many chronic diseases are related to chronic immune system dysfunction. Disturbance of the immune system by very low-intensity electromagnetic field exposure is discussed as a potential underlying cause for cellular damage and impaired healing (tissue repair), which could lead to disease and physiological impairment (Johansson 2009; Johannson 2007).

Both human and animal studies report that exposures to EMF and RFR at environmental levels associated with new technologies can be associated with large immunohistological changes in mast cells as well as other measures of immune dysfunction and dysregulation. Mast cells not only can degranulate and release irritating chemicals leading to allergic symptoms; they are also widely distributed in the body, including in the brain and the heart, which might relate to some of the symptoms commonly reported in relation to EMF/RFR exposure (such as headache, painful light sensitivity, and cardiac rhythm and palpitation problems).

Consequences of immune challenges during pregnancy

As mentioned, infection in pregnancy can also increase the risk of autism and other neurodevelopmental and neuropsychiatric disorders via maternal immune activation (MIA). Viral, bacterial and parasitic infections during pregnancy are thought to contribute to at least 30% of cases of schizophrenia (Brown and Derkits 2010). The connection of maternal infection to autism is supported epidemiologically, including in a Kaiser study where risk was associated with psoriasis and with asthma and allergy in the second trimester (Croen et al. 2005), and in a large study of autism cases in the Danish Medical registry (Atladottir et al. 2010) with infection at any point in pregnancy yielding an adjusted hazard ration of 1.14 (CI: 0.96-1.34) and when infection occurred during second trimester the odds ratio was 2.98 (CI: 1.29-7.15). In animal models, while there is much variation in study design, mediators of the immune impact appear to include oxidative stress, interleukin-6 and increased placental cytokines (Smith et al. 2007; Patterson 2009; Boksa 2010). Garbett et al. (2012) commented on several mouse models of the effects of MIA on the fetal brain that *"The overall gene expression changes suggest that the response to MIA is a neuroprotective attempt by the developing brain to counteract environmental stress, but at a cost of disrupting typical neuronal differentiation and axonal growth."* (Garbett et al. 2012). Maternal fetal brain-reactive

autoantibodies have also been identified in some cases (Braunschweig et al. 2012; Braunschweig and Van de Water 2012; Fox, Amaral, and Van de Water 2012; Goines et al. 2011; Wills et al. 2009; Wills et al. 2011; Zimmerman et al. 2007).

Although we have evidence of immune impacts of EMF/RFR, the impact of repeated or chronic exposure to EMF and RFR during pregnancy is poorly studied; could this trigger similar immune responses (cytokine production) and stress protein responses, which in turn would have effects on the fetus? Although this has been poorly studied, we do have data that very low cell phone radiation exposures during both human and mouse pregnancies have resulted in altered fetal brain development leading to memory, learning, and attention problems and behavioral problems (Aldad et al. 2012).

Potential immune contributions to reactivity and variability in ASDs

Immune changes in ASDs appear to be associated with behavioral change (Shi et al. 2003; Ashwood et al. 2008; Ashwood et al. 2011; Breece et al. 2012; Heuer et al. 2008), but the mechanisms are complex and to date poorly understood (Careaga and Ashwood 2012) and likely will need to be elucidated through systems biology methods that capture multisystem influences on the interactions across behavior, brain and immune regulation (Broderick and Craddock 2012), including electrophysiology.

Two of the particularly difficult parts of ASDs are the intense reactivity and the variability in assorted symptoms such as tantrums and other difficult behaviors. Children with ASDs who also have gastrointestinal symptoms and marked fluctuation of behavioral symptoms have been shown to exhibit distinct innate immune abnormalities and transcriptional profiles of peripheral blood monocytes (Jyonouchi et al. 2011). It is worth considering EMF/RFR exposures could be operating through related mechanisms so as to add to allostatic loading in ways that exacerbate behavior. In Johansson 2006 and 2007 a foundation is provided for understanding how chronic EMF/RFR exposure can compromise immune function and sensitize a person to even small exposures in the future (Johannson 2007; Johansson et al. 2006). Johansson discusses alterations of immune function at environmental levels resulting in loss of memory and concentration, skin redness and inflammation, eczema, headache, and fatigue. Mast cells that degranulate under EMF and RFR exposures and substances secreted by them (histamine, heparin and serotonin) may contribute to features of this sensitivity to electromagnetic fields (Johansson et al. 2006). Theoharides and colleagues have argued that environmental and stress related triggers might activate mast cells, causing inflammatory compromise and leading to gut-blood-brain barrier compromise, seizures and other ASD symptoms (Theoharides et al. 2012, 2010), and that this cascade of immune response and its consequences might also be triggered in the absence of infection by mitochondrial fragments that can be released from cells in response to stimulation by IgE/anti-IgE or by the proinflammatory peptide substance P (Zhang, Asadi, et al. 2012).

Seitz et al. (2005) reviewed an extensive literature on electromagnetic hypersensitivity conditions reported to include sleep quality, dizziness, headache, skin rashes, memory and concentration impairments related to EMF and RFR (Seitz, 2005). Some of these symptoms are common in ASDs, whether or not they are due to EMF/RFR exposure, and the experience of discomfort may be hard to document due to difficulties with self-reporting in many people with ASDs.

Johansson (2007, 2009) also reports that benchmark indicators of immune system allergic and inflammatory reactions occur under exposure conditions of low-intensity non-ionizing radiation (immune cell alterations, mast cell degranulation histamine-positive mast cells in biopsies and immunoreactive dendritic immune cells) (Johannson 2007; Johansson 2009). In facial skin samples of electro- hypersensitive persons, the most common finding is a profound increase in mast cells as monitored by various mast cell markers, such as histamine, chymase and tryptase (Johansson et al. 2001). In ASDs, infant and childhood rashes, eczema and psoriasis are common, and they are common in family members as well (Bakkaloglu et al. 2008).

4. Alteration of and damage to cells in the brain

Brain cells have a variety of ways of reacting to environmental stressors, such as shape changes, metabolic alterations, upregulation or downregulation of neurotransmitters and receptors, other altered functionality, structural damage, production of un-metabolizable misfolded proteins and other cellular debris, and apoptosis; these range along a spectrum from adaptation to damage and cell death. These types of alterations can be looked at in animals under controlled conditions, but in human beings direct cellular examination can only be done on surgical biopsy tissue – which is hardly ever available in people with ASDs – or after death, at which point there has been a whole lifetime of exposures that are generally impossible to tease apart if there were even motivation to do so. This complicates the comparison of brain cell and tissue-related pathophysiology between what is seen in ASDs and what is associated with EMF/RFR exposures.

Brain cells

Impact of EMF/RFR on cells in the brain has been documented by some of the studies that have examined brain tissue after exposure, although the interpretation of inconsistencies across studies is complicated by sometimes major differences in impact attributable to differences in frequencies and duration of exposure, as well as to differences in resonance properties of tissues and other poorly understood constraints on cellular response. These studies and methodological considerations have been reviewed in depth in Belyaev, 2012 in section 15 of the 2012 BioInitiatve Report (Belyaev 2012), as well as by Salford et al. (2012) in Section 10 (Salford, Nittby, and Persson 2012). A few examples of observations after exposure have included dark neurons (an indicator of neuronal damage), as well as alteration of neuronal firing rate (Bolshakov and Alekseev

1992), and upregulation of genes related to cell death pathways in both neurons and astrocytes (Zhao, Zou, and Knapp 2007). Astrocytic changes included increased GFAP and increased glial reactivity (Chan et al. 1999; Ammari et al. 2008; Ammari et al. 2010; Brillaud, Piotrowski, and de Seze 2007), as well as astrocyte-pertinent protein expression changes detected by Fragopoulou et al, 2012 as mentioned above. Also observed has been a marked protein downregulation of the nerve growth factor glial maturation factor beta (GMF) which is considered as an intracellular signal transduction regulator in astrocytes, which could have significant impact on neuronal-glial interactions as well as brain cell differentiation and tumor development. Diminution of Purkinje cell number and density has also been observed, (Ragbetli et al. 2010) including in two studies of the impacts of perinatal exposure (Albert, 1981; Albert, 1981). Promotion of pro-inflammatory responses in EMF-stimulated microglial cells has also been documented (Yang et al. 2010).

Neuropathology findings in ASDs have been varied and have been interpreted according to various frameworks ranging from a regionalized approach oriented to identifying potential brain relationships to ASD's behavioral features (Amaral, Schumann, and Nordahl 2008) to identifying receptor, neurotransmitter and interneuron abnormalities that could account for an increased excitation/inhibition ratio (Levitt 2009; Geschwind 2007; Anney 2010; Casanova 2006; Rubenstein 2003). Studies have documented a range of abnormalities in neurons, including altered cellular packing in the limbic system, reduced dendritic arborization, and reductions in limbic GABAergic systems. Over the past decade a shift has occurred from presuming that all pertinent brain changes occurred prior to birth, to an acknowledgement that ongoing cellular processes appear to be occurring not only after birth but well into adulthood (Bauman and Kemper 2005). One of the reasons for this shift was the observation that head size (as well as brain weight and size) was on average larger in children with autism, and the head sizes of children who became diagnosed with autism increased in percentile after birth (Herbert 2005).

Neuroinflammation, glial activation and excitotoxicity

Although much attention has been paid in ASD brain literature to specific regions manifesting differences in size and activity in comparison to those without ASDs, there are other observations that are not strictly regional in nature, such as more widely distributed scaling differences (e.g. larger brains, wider brains, increased white matter volume, along with altered functional connectivity and coherence to be discussed below). Recently more studies have appeared identifying pathophysiological abnormalities such as neuroinflammation, mitochondrial dysfunction and glutathione depletion in brain tissue. Neuroinflammation was first identified in a study of postmortem samples from eleven individuals aged 5-44 who had died carrying an ASD diagnosis, in which activated astrocytes and microglial cells as well as abnormal cytokines and chemokines were found. Other research has identified further astrocyte abnormalities include, altered

expression of astrocyte markers GFAP abnormalities including elevation, antibodies, and altered signaling (Laurence 2005; Singh 1997; Fatemi et al. 2008). Increased microglia activation and density as well as increased myeloid dendritic cell frequencies have also been documented. (Vargas et al. 2005; Breece et al. 2012; Tetreault et al. 2012), as has abnormal microglial-neuronal interactions (Morgan et al. 2012). Recently through use of the PET ligand PK11105 microglial activation was found to be significantly higher in multiple brain regions in young adults with ASDs (Suzuki et al. 2013). Genes associated with glial activation have been documented as upregulated. Garbett et al measured increased transcript levels of many immune genes, as well as changes in transcripts related to cell communication, differentiation, cell cycle regulation and chaperone systems (Garbett et al. 2008). Voineaugu and colleagues performed transcriptomic analysis of autistic brain and found a neuronal module of co-expressed genes which was enriched with genetically associated variants, and an immune-glial module showing no such enrichment for autism GWAS signals (Voineagu et al. 2011).

Neuroinflammation also does not appear to be strictly localized in a function-specific fashion, and it may contribute both to more broadly distributed and more focal features for tissue-based reasons. It may be that brain regions with particular prominence in ASDs may have distinctive cellular characteristics – e.g. the amygdala (Baron-Cohen et al. 2000; Dziobek et al. 2010; Hall et al. 2010; Mercadante et al. 2008; Nordahl et al. 2012; Otsuka et al. 1999; Schulkin 2007; Schumann and Amaral 2006; Schumann et al. 2009; Truitt et al. 2007; Zirlinger and Anderson 2003), which may have a larger or more reactive population of astrocytes (Johnson, Breedlove, and Jordan 2010) or the basal ganglia which may have greater sensitivity to even subtle hypoxia or perfusion abnormalities. In this case it may be the histology of these areas that makes them vulnerable to environmental irritants, and this may contribute to how environmental factors such as EMF/RFR might trigger or aggravate some of ASD's features. More widely distributed brain tissue pathology be part of what leads to differences in ASDs in brain connectivity. However these types of tissue-function relationships have been poorly investigated. The contribution of tissue differences is one of the physical considerations covered by Belyaev (2012) in Section 15 of the 2012 BioInitiative Report (Belyaev, 2012).

Various signs of mitochondrial dysfunction and oxidative stress have also been identified in the brain. Findings include downregulation of expression of mitochondrial electron transport genes (Anitha, Nakamura, Thanseem, Matsuzaki, et al. 2012) or deficit of mitochondrial electron transport chain complexes (Chauhan et al. 2011), brain region specific glutathione redox imbalance (Chauhan, Audhya, and Chauhan 2012), and evidence of oxidative damage and inflammation associated with low glutathione redox status (Rose, Melnyk, Pavliv, et al. 2012). Oxidative stress markers were measured as increased in cerebellum (Sajdel-Sulkowska, Xu, and Koibuchi 2009).

Additional support for the presence of tissue pathophysiology-based changes in brains of people with ASDs comes from the various studies documenting reduction in Purkinje cell numbers (Whitney et al. 2009; Whitney et al. 2008; Bauman and Kemper 2005; Shi et al. 2009; Blatt and Fatemi 2011; Fatemi et al. 2002; Fatemi et al. 2012), possibly due to oxidative stress and an increased excitation/inhibition ratio that could potentially be acquired (Fatemi et al. 2012). Also of note are changes in the glutamatergic and GABAergic systems, which when imbalanced can disturb the excitation/inhibition ratio and contribute to seizure disorders; reductions in GABA receptors as well as in GAD 65 and 67 proteins that catalyse the conversion of glutamate into GABA have been measured. (Yip, Soghomonian, and Blatt 2007, 2008, 2009) A consensus statement on the cerebellum in ASDs stated that, *"Points of consensus include presence of abnormal cerebellar anatomy, abnormal neurotransmitter systems, oxidative stress, cerebellar motor and cognitive deficits, and neuroinflammation in subjects with autism."* (Fatemi et al. 2012)

Some indirect corroboration for these findings has come from neuroimaging, where the initial hypothesis regarding the tissue basis of the larger size of brains in so many people with autism – that it was due to a higher density of neurons and more tightly packed axons – came under question with the emergence of contradictory findings, well reviewed a few years ago by Dager and colleagues (Dager et al. 2008). These include reduced rather than increased density of NAA (n-acetylaspartate, a marker of neuronal integrity and density that is produced in the mitochondria), reduced rather than increased fractional anisotropy suggesting less tightly packed axonal bundles (Bode et al. 2011; Cascio et al. 2012; Mak-Fan et al. 2012; Travers et al. 2012; Walker et al. 2012; Wolff et al. 2012); Sundaram, 2008) and greater rather than lower diffusivity, all of which may be more consistent with lower density of tissue and tissue metabolites and more fluid, which could be consistent with neuroinflammation and/or oxidative stress. The early postnatal development of such lower fractional anisotropy and increased diffusivity was measured in the process of occurring recently, in the first large prospective longitudinal imaging study of infants, who trended from 6 months to 2 years in the direction of these findings becoming more pronounced – but still with substantial overlap with those infants who did not develop autism (Wolff et al. 2012). This trend was consistent with prior studies showing increase in head size after birth, and added some information about what was happening in the brain to drive this size increase, although due to its methods it could only indirectly address the possibilty that emergence during the first few years of life of tissue pathophysiology disturbances such as neuroinflammation might be contributing to these trends (Herbert 2012).

There is also substantial variability across many different types of brain findings. Of interest is that a number of functional brain imaging and electrophysiology studies have identified greater heterogeneity in response to stimuli between individuals in the ASD

group than individuals in the neurotypical control group (Muller et al. 2003; Dinstein et al. 2012). This may make more sense from the point of view of non-linear response – i.e. a disproportionality between output and input (as well as state and context sensitivity), in a pathophysiologically perturbed brain system. Nonlinearity has also been a significant methodological issue in EMF/RFR research because linear methods of study design and data analysis have often been insensitive to effects, whereas nonlinear methods have been argued to show greater sensitivity (Carrubba and Marino 2008; Marino, Wolcott, Chervenak, Jourd'heuil, Nilsen, Frilot, et al. 2001; Marino and Frilot 2003; Carrubba et al. 2006; Carrubba et al. 2012; Marino, Nilsen, and Frilot 2003; Marino, Wolcott, et al. 2001, 2001; Carrubba et al. 2007; Marino et al. 2000; Bachmann, 2005).

The presence of various types of tissue pathophysiology both in findings in postmortem tissue from individuals with ASDs and in documented impacts of EMF/RFR exposure are intriguing and suggest overlap in processes involved. But it is not really possible to infer any specific agent of injury from cellular responses since for the most part these are not specific but rather are stress or repair responses generic to a variety of triggers. It is important to entertain how environmental agents could contribute to brain changes in ASDs, and how these changes may develop over progress over time after the earliest periods in brain development. EMF/RFR exposures could be preconceptional, prenatal or postnatal – or all of the above; it is conceivable that this could be the case in ASDs as well.

Altered development

There is some evidence for altered brain and organism development in relation to EMF/RFR exposure. Aldad et al. 2012 exposed mice in utero to cellular telephone radiation, with resultant aberrant miniature excitatory postsynaptic currents, dose-responsive impaired glutamatergic synaptic transmission onto layer V pyramidal neurons of the prefrontal cortex (Aldad et al. 2012). Lahijani exposed preincubated chicken embryos to 50 Hz EMFs, and made the following morphological observations: *"exencephalic embryos, embryos with asymmetrical faces, crossed beak, shorter upper beak, deformed hind limbs, gastroschesis, anophthalmia, and microphthalmia. H&E and reticulin stainings, TEMS, and SEMs studies indicated EMFs would create hepatocytes with fibrotic bands, severe steatohepatitis, vacuolizations, swollen and extremely electron-dense mitochondria, reduced invisible cristae, crystalized mitochondria with degenerated cristae, myelin-like figures, macrophages engulfing adjacent cells, dentated nuclei, nuclei with irregular envelopes, degenerated hepatocytes, abnormal lipid accumulations, lipid droplets pushing hepatocytes' nuclei to the corner of the cells, abundant cellular infiltrations cellular infiltrations inside sinusoid and around central veins, disrupted reticulin plexus, and release of chromatin into cytosol,, with partially regular water layers,"* and attributed cell damage to elevated free radical induced cell membrane disruptions (Lahijani, Tehrani, and Sabouri 2009).

Although it is of great interest to characterize the changes in development associated with ASDs, it is also difficult to do in human beings because at present diagnosis is not possible until at least 2-3 years after birth. By now there have been a lot of prospective studies of infants at high risk for autism, but the in vivo brain imaging and electrophysiology data from these studies is only starting to be published, and so the for now the main sources of information are still inference backwards from post-mortem or imaging data, and animal models, both of which have clear limitations. Thus it is impossible to seek precise parallels here between what we know about the development of ASDs compared with the impacts of EMF/RFR exposures.

Nevertheless it is of real concern that such exposures have elicited some of the brain tissue changes that have been documented, both in early development and subsequently. Already noted above is the question of whether high exposures of neonates to monitoring equipment may affect the melatonin levels of neonates (Bellieni, Tei, et al. 2012); these exposures also impact heartrate variability . There are no studies yet on infants exposed to baby surveillance monitors or DECT wireless phones. However there are good laboratory testing studies yielding actual measurements of these devices that conclude: "*Maximum incident field exposures at 1m can significantly exceed those of base stations (typically 0.1 - 1 V/m). At very close distances the derived or reference exposure limits are violated" for baby surveillance monitors and DECT phones.* Further, the authors conclude that, based on very strictly controlled laboratory testing of everyday devices like baby monitors and some cordless phones *"(W)orse case peak spatial SAR values are close to the limit for the public or uncontrolled environments, e.g., IEEE802.11b and Bluetooth Class I".*(Kuhn et al. 2012) Even exposure of the fetus to laptop computer wireless emissions through the pregnant mother's use of them may on her lap involve induction of strong intracorporeal electric current densities from the power supply possibly even more than the device itself (Bellieni, Pinto, et al. 2012).

Brain blood flow and metabolism

Cerebral perfusion and metabolism abnormalities have been identified in close to 2 dozen papers studying autistic cohorts. Cerebral perfusion refers to the quantity of blood flow in the brain. Abnormal regulation of cerebral perfusion is found in a range of severe medical conditions including tumors, vascular disease and epilepsy. Cerebral hypoperfusion has also been found in a range of psychiatric disorders (Theberge 2008). Neurocognitive hypotheses and conclusions, as well as localization of perfusion changes, have been heterogeneous across these papers. Hypoperfusion or diminished metabolism has been identified in frontal regions (George, 1992; Gupta, 2009; Degirmenci, 2008; Wilcox, 2002; Galuska, 2002; Ohnishi, 2000; temporal lobes (Boddaert, 2002 ; Burroni, 2008 ; Degirmenci, 2008, Galuska, 2002, George, 1992 ; Hashimoto, 2000, Ohnishi, 2000, Ryu, 1999, Starkstein, 2000, Zilbovicius, 2000), as well as a variety of subcortical regions including basal ganglia (Degirmenci, 2008; Ryu, 1999; Starkstein, 2000),

cerebellum (Ryu, 1999), limbic structures (Ito, 2005, Ohnishi, 2000) and thalamus (Ito, 2005, Ryu, 1999, Starkstein, 2000) – i.e., in a widely distributed set of brain regions. It is interesting to note that even with this regional variation in localization, most of these publications showed that cerebral perfusion was *reduced*; in the only one of those studies reporting some areas of localized hyperfusion, these areas were found in the middle of areas in the frontal pole and temporal lobe that were hypoperfused (McKelvey 1995), Only one study showed no difference in perfusion between autistic and control subjects (Herold 1988). Possibly because virtually all of these studies were oriented toward testing neuropsychological rather than pathophysiological hypotheses, there were no probes or tests reported to unearth the tissue level alterations that might be underlying these reductions in blood flow in these brains.

While a large number of animal studies have documented BBB abnormalities from EMF/RFR exposures, only a few PET studies have been performed evaluating EMF exposure effects upon brain glucose metabolism. Volkow et al. performed PET scans both with and without EMF exposure (50 min of GSM-900 with maximum SAR of 0.901 W/kg), and the participants were blinded to the exposure situation (Volkow et al. 2011). A 7% increase in metabolism in the exposure situation compared to controls was identified regionally on the same side of the head as where the mobile phone was placed, in the right orbitofrontal cortex and in the lower part of the right superior temporal gyrus . The strength of the E-field from the phones correlated positively with the brain activation, which the authors hypothesized was from an increase in brain neuron excitability. . A subsequent smaller study by Kwon et al. demonstrated not increased but decreased brain ^{18}FDG uptake after GSM-900 exposure, this time in the temporoparietal junction (Kwon et al. 2011).

Many possible mechanisms could be involved in the metabolic and perfusion abnormalities identified, ranging from altered neuronal activity that was hypothesized in the Volkow et al. (2011) ^{8}FDG PET study to narrowing of vascular lumen in the setting of reduced perfusion. Underlying tissue pathophysiology-based phenomena could influence the measurable metabolism and perfusion abnormalities, via mechanisms such as excitotoxicity, cell stress response, constriction of capillary lumen by activated astrocytes, volume effects of vascular extravasation, subtle alterations in blood viscosity due to immune or oxidative stress-associated blood chemical changes, with other possibilities as well. Given the types of damage at the cellular level covered in this pathophysiology section so far – including oxidative stress, membrane and barrier function damage and poorly functioning channels, which occur both in ASDs as a consequence of EMF/RFR exposure, and given the heterogeneity of localization of abnormalities in the autism perfusion papers as well as considerations of nonlinearity, it may not be so surprising that the results in the two PET studies of human impacts of EMF exposure were not consistent.

6. Electrophysiology perturbations

At this stage the argument we hit a key pivot point, where we look at how the alterations in molecular, cellular and systems physiological function, which occur in the brain as well as in the body, impact the transduction into the electrical signaling activities of the brain and nervous system. Certainly the cells and tissues whose physiological challenges we have already discussed provide the material substrate for the electrical activity. Although ASD behaviors are influenced by many factors, they must in principle be mediated through nervous system electrophysiology.

If the cells responsible for generating synapses and oscillatory signaling are laboring under cellular and oxidative stress, lipid peroxidation, impaired calcium and other signaling system abnormalities, then mitochondrial metabolism will fall short, all the more so because of the challenges from the immune system which in turn be triggered to a major extent by environment. How well will synapses be generated? How well will immune-activated and thereby distracted glial cells be able to modulate synaptic and network activity? (Tasker et al. 2012; Eroglu and Barres 2010; Bilbo and Schwarz 2009; Fields 2006)

At present we are in the early stages of being able to formulate these questions well enough to address them. We do know that microglial activation can impact excitatory neurotransmission mediated by astrocytes (Pascual et al. 2012). We do know that the cortical innate immune response increases local neuronal excitability and can lead to seizures (Rodgers et al. 2009; Gardoni et al. 2011). We do know that inflammation can play an important role in epilepsy (Vezzani et al. 2011). We know less about lower levels of chronic or acute pathophysiological dysfunction and how they may modulate and alter the brain's electrophysiology.

Seizures and Epilepsy

EEG signals in ASDs are abnormal on a variety of levels. At the most severe level, EEGs show seizure activity. In addition to the association of some severe epilepsy syndromes (e.g. Landau Kleffner, tuberous sclerosis) with autism, the risk of epilepsy is substantially higher in people with ASDs than in the general population, with a large subset of these individuals experiencing seizure onset around puberty, likely in relation to aberrations in the dramatic and brain-impactful hormonal shifts of that phase of life. Although less than 50% of people clearly have seizures or epilepsy, a much larger number have indications of epileptiform activity, and an even larger percent have subclinical features that can be noted by a clinical epileptologist though not necessarily flagged as of clinical concern.

Epileptic seizures can be both caused by and cause oxidative stress and mitochondrial dysfunction. Seizures can cause extravasation of plasma into brain parenchyma (Mihaly

and Bozoky 1984; Librizzi et al. 2012; Marchi et al. 2010; van Vliet et al. 2007; Yan et al. 2005) which can trigger a vicious circle of tissue damage from albumin and greater irritability, as discussed above. Evidence suggests that if a BBB is already disrupted, there will be greater sensitivity to EMF/RFR exposure than if the BBB were intact (Tore et al. 2002; Tore et al. 2001), suggesting that such exposures can further exacerbate vicious circles already underway.

The combination of pathophysiological and electrophysiological vulnerabilities has been explored in relation to the impact of EMF/RFR on people with epilepsy – which, as discussed above, is a lot more common in ASDs than in the general population.. EMF/RFR exposures from mobile phone emissions have been shown to modulate brain excitability and to increase interhemispheric functional coupling (Vecchio et al. 2012; Tombini et al. 2012). In a rat model the combination of picrotoxin and microwave exposure at mobile phone-like intensities led to a progressive increase in neuronal activation and glial reactivity, with regional variability in the fall-off of these responses three days after picrotoxin treatment (Carballo-Quintas et al. 2011), suggesting a potential for interaction between a hyperexcitable brain and EMF/RFR exposure.

One critical issue here is nonlinearity and context and parameter sensitivity of impact. In one study, rat brain slices exposed to EMF/RFR showed reduced synaptic activity and diminution of amplitude of evoked potentials, while whole body exposure to rats led to synaptic facilitation and increased seizure susceptibility in the subsequent analysis of neocortical slices (Varro et al. 2009). Another study unexpectedly identified enhanced rat pup post-seizure mortality after perinatal exposure to a specific frequency and intensity of exposure, and concluded that apparently innocuous exposures during early development might lead to vulnerability to stimuli presented later in development (St-Pierre et al. 2007)

Sleep

Sleep involves a profound change in brain electrophysiological activity, and EEG abnormalities including disrupted sleep architecture figure in sleep challenges in ASD. Sleep symptoms include bedtime resistance, sleep onset delay, sleep duration and night wakings, and sleep architecture can involve significantly less efficient sleep, less total sleep time, prolonged sleep latency, and prolonged REM latency (Buckley et al. 2010; Giannotti et al. 2011), with these sleep problems being worse in children with ASDs who regressed than in those who did not regress into their autism (Giannotti, 2011). EEG abnormalities have also been associated with EMF/RFR exposure, including disrupted sleep architecture as well as changes in sleep spindles and in the coherence and correlation across sleep stages and power bands during sleep (Borbely, 1999; Huber, 2003).

Sleep disturbance symptoms are also common in both situations. Insomnia is commonly reported in people who are chronically exposed to low-level wireless antenna emissions. Mann (1996) reported an 18% reduction in REM sleep, which is key to memory and learning functions in humans. In ASDs sleep difficulties are highly pervasive and disruptive not only to the affected individual but also to their whole family due to the associated problems such as noise and the need for vigilance.

The multileveled interconnections involved in the modulation of sleep exemplify the interconnectedness of the many levels of pathophysiology reviewed here: *"Extracellular ATP associated with neuro- and glio-transmission, acting via purine type 2 receptors, e.g., the P2X7 receptor, has a role in glia release of IL1 and TNF. These substances in turn act on neurons to change their intrinsic membrane properties and sensitivities to neurotransmitters and neuromodulators such as adenosine, glutamate and GABA. These actions change the network input-output properties, i.e., a state shift for the network."* (Clinton et al. 2011) With disturbance simultaneously at so many of these levels, it is not surprising that sleep dysregulation is nearly universal in ASDs, and common in the setting of EMF/RFR exposures.

Quantitative electrophysiology

While clinical reading of EEG studies is done visually, a growing number of studies are examining EEG and MEG data using digital signal processing analysis, and often using data collected in controlled research settings with high density array equipment and carefully designed stimuli paradigms. In these settings a variety of abnormalities have been identified other than epileptic. These include abnormalities in the power spectrum, i.e. the distribution of power over the different frequencies present, with some studies showing impaired or reduced gamma-and activity (Sun et al. 2012; Rojas et al. 2008; Rippon, 2007) and others 8) showing reduction of spectral power across all bands (Tierney et al. 2012) while still others showed increased high-frequency oscillations. (Orekhova et al. 2007) Abnormalities in coherence and synchronization between various parts of the brain have been found (Muller 2008; Muller et al. 2011; Wass 2011), comparable to abnormal functional connectivity measured by fMRI (Just et al. 2004) but measurable using EEG or MEG with higher temporal resolution (Duffy, 2012; Isler, 2010; Murias, 2007; Murias, 2007; Coben, 2008). Several studies have identified reduced complexity and increased randomness in EEGs of people with autism (Lai et al. 2010; Catarino et al. 2011), as well as an increase in power but a reduction in coherence (Isler et al. 2010; Mathewson et al. 2012). Some electrophysiological metrics are emerging as potential discriminators between brain signal from individuals with ASDs and those who are neurotypical, such as a wavelet-chaos-neural network methodology applied to EEG signal (Ahmadlou, Adeli, and Adeli 2010).

EMF/RFR also has impacts at levels of brain function measurable by these techniques. At various frequencies and durations of exposure it has been noted to impact alpha and beta rhythms (Hinrikus et al. 2008), to increase randomness (Marino, Nilsen, and Frilot 2003; Marino and Carrubba 2009), to alter power, to modulate interhemispheric synchronization (Vecchio et al. 2007), to alter electrical activity in brain slices (Tattersall et al. 2001) and to alter the patterns of coordination (spectral power coherence) across the major power bands (Hountala et al. 2008). Bachman et al. (2006) showed statistically significant changes in EEG rhythms and dymanics occurred in between 12% and 20% of healthy volunteers (Bachmann, 2006). In children, exposures to cell phone radiation have resulted in changes in brain oscillatory activity during some memory tasks.

Sensory processing

At the symptomatic level issues with sensory processing are highly prevalent in ASDs. Phenomenology can include hypersensitivity to external stimuli, hyposensitivity to internal sensations and difficulty localizing sensation including pain, and difficulty processing more than one sensory channel at one time. (Robledo, Donnellan, and Strandt-Conroy 2012; Perry et al. 2007; Sacco et al. 2010) There is now electrophysiological evidence of abnormalities at early (brainstem) stages of sensory processing, as well as in later stages of processing that occur in the cortex. Some studies have shown lower and some longer latencies of response to an auditory stimulus. Domains of perception where the performance of people with ASDs is superior to that of neurotypical individuals have been identified. (Marco et al. 2011) *"It is obvious…that sensory processing abnormalities in ASD are distributed rather than localized; sensory abnormalities in ASD obviously span multiple dimensions of latency, adaptation, magnitude and behavior abnormalities, with both enhanced and impaired behavior associated with aberrant cortical responses. Given this diversity in findings, the heterogeneity of ASD, and broad variability seen over and over again in the ASD groups almost irrespective of the study, it is hard to imagine that one single theory could account for all of these observations…. It is therefore probable that several mechanisms and neuronal abnormalities, most likely at multiple levels (from single neurons through to inter-area connections), all contribute to varying degrees to the abnormal sensory processing observed in ASD. It is also likely that no single mechanism is unique to one sensory modality, which is why we see such a widely distributed range of abnormalities across modalities."* (Kenet 2011)

It is also possible that the mechanisms may not simply be neural – they may also be modulated by glial, metabolic, immune, perfusional and other physiological processes and physical properties as well. Yet although there is some consideration of the pathophysiology-sensory function interaction (Kern et al. 2010), it has basically not been fleshed out in studies of ASDs with experimental designs integrating pathophysiological and electrophysiology.

Kenet et al. (2010) demonstrated environmental vulnerability of sensory processing in the brain by the exposure of rat dams to noncoplanar polychlorinated biphenyls (PCBs), during gestation and for three subsequent weeks of nursing (Kenet, 2011). *"Although the hearing sensitivity and brainstem auditory responses of pups were normal, exposure resulted in the abnormal development of the primary auditory cortex (A1). A1 was irregularly shaped and marked by internal nonresponsive zones, its topographic organization was grossly abnormal or reversed in about half of the exposed pups, the balance of neuronal inhibition to excitation for A1 neurons was disturbed, and the critical period plasticity that underlies normal postnatal auditory system development was significantly altered. These findings demonstrate that developmental exposure to this class of environmental contaminant alters cortical development."* (Kenet et al. 2007). This study may be particularly relevant for EMF/RFR exposures, as the noncoplanar PCBs were discussed above as targeting calcium signaling as do EMF/RFR exposures – i.e. they both converge upon a common cellular mechanism (Pessah and Lein 2008; Stamou et al. 2012), justifying exploring the hypothesis that the outcomes one might expect from EMF/RFR could be similar.

Autonomic dysregulation

Although there are a fair number of negative studies regarding the impact of EMF/RFR exposure on the autonomic nervous system, increased HRV and autonomic disturbances have been documented (Andrzejak et al. 2008; Szmigielski et al. 1998; Bortkiewicz et al. 2006; Graham et al. 2000; Saunders and Jefferys 2007). Buchner and Eger (2010), in a study in rural Germany of the health impacts of exposures from a new base station yielding novel exposure to EMF/RFR, saw a significant elevation of the stress hormones adrenaline and noradrenaline during the first six months with a concomitant drop in dopamine, with a failure to restore the prior levels after a year and a half. These impacts were felt by the young, the old and the chronically ill, but not by healthy adults (Buchner and Eger 2011).

Effects on the neonate are also evident. Bellieni et al (2008) found that heart rate variability is adversely affected in infants hospitalized in isolettes or incubators where ELF-EMF levels are in the 0.8 to 0.9 μT range (8 to 9 mG). Infants suffer adverse changes in heart rate variability, similar to adults (Bellieni et al. 2008). This electromagnetic stress may have lifelong developmental impacts, based on a study showing that in utero beta 2 agonist exposure can potentially induce a permanent shift in the balance of sympathetic-to-parasympathetic tone (Witter et al. 2009).

Meanwhile clinical observation and a growing body of literature support a major role for stress in ASDs (Anderson and Colombo 2009; Anderson, Colombo, and Unruh 2012; Daluwatte et al. 2012; Ming et al. 2011), with variability amongst individuals in the severity of the stress response but a tendency to have high tonic sympathetic arousal at

baseline (Hirstein, Iversen, and Ramachandran 2001; Toichi and Kamio 2003; Ming, Julu, et al. 2005; Mathewson et al. 2011; Cheshire 2012; Chang et al. 2012).

The impact of EMF/RFR exposure can also be greatly influenced by the stress system status of the individual being exposed. Tore et al sympathecotomized some of his rats before exposure to GSM, to simulate cell phone exposure (Tore et al. 2002; Tore et al. 2001). Salford et al. (2012) reviewed the results:

> *"Comparing the animals, which had been subjected to ganglionectomy, to the other animals, Töre et al. made an interesting observation: as expected, albumin extravasation was more prominent in the sympathectomised sham-exposed rats as compared to normal exposed rats. This was due to the fact that the sympathectomised rats were in a chronic inflammation-prone state with hyper-development of pro-inflammatory structures, such as the parasympathetic and sensory inputs as well as mast cells, and changes in the structure of the blood vessels. Such an inflammation-prone state has a well-known effect on the BBB leakage. However, when comparing sham-exposed sympathectomised rats to GSM-exposed sympathectomised rats, a remarkable increase in albumin leakage was present in the GSM exposed sympathectomised rats compared to the sham rats.* ***In the GSM-exposed sympathectomised rats, both brain areas and the dura mater showed levels of albumin leakage resembling those observed in positive controls after osmotic shock****.[emphasis added] Indeed, more attention should be paid to this finding, since it implicates that the sensitivity to EMF-induced BBB permeability depends not only on power densities and exposure modulations, but also on the initial state of health of the exposed subject."* (Salford, Nittby, and Persson 2012)

This dramatically greater impact on an autonomically and immunologically vulnerable set of animals raises concerns since the vulnerabilities of these animals bear some resemblance to the pathophysiological challenges of individuals with ASDs.

The interconnection between stress and brain connectivity (or coherence) in ASDs is brought out by Narayanan et al. (2010) n a pilot study testing the impact of the beta blocker propranolol on brain functional connectivity measured using functional MRI (Narayanan et al. 2010). A fairly immediate increase in functional connectivity was noted from propranolol – but not from nadolol which has the same vascular effects but does not cross the BBB. Propranolol decreases the burden of norepinephrine, thereby reducing the impact of stress systems on brain processing, and the authors interpreted these effects as creating an improvement of the brain's signal-to-noise ratio (Hasselmo, 1997), allowing it to utilize and coordinate more remote parts of its networks. This suggests that stressors such as EMF/RFR, by adding non-biologically meaningful noise to the system, might have the opposite effects, degrading coherent integration.

C. De-tuning of the Brain and Organism

1. Electromagnetic signaling, oscillation and synchrony are fundamental, and vulnerable

While electrophysiological activity is an intrinsic property of the nervous system, electromagnetic signaling are vital parts of every cell and of molecular structure.

> *"All life on earth has evolved in a sea of natural low-frequency electromagnetic (EM) fields. They originate in terrestrial and extraterrestrial sources. The ever-growing use of electric power over the last century has sharply modified this natural environment in urban environments. Exposure to power-frequency fields far stronger than the natural environment is now universal in civilized society."* (Adey 1994)

Adey published some of the earliest scientific studies on the "cooperativity" actions of cells in communication. Studies showing us that the flux of calcium in brain tissue and immune cells is sensitive to ELF-modulated radiofrequency fields is actually telling us that some of the most fundamental properties of cells and thus of our existence can be modulated by EMF/RFR.

> *"...in first detection of environmental EM fields in tissues, there appears to be a general consensus that the site of field action is at cell membranes. Strands of protein are strategically located on the surface of cells in tissue, where they act as detectors of electrical and chemical messages arriving at cell surfaces, transducing them and transmitting them to the cell interior. The structural basis for this transductive coupling by these protein strands is well known. Through them, cell membranes perform a triple role, in* ***signal detection, signal amplification, and signal transduction to the cell interior****."* (Adey 1994)

Communication between cells through gap junctions, which is a means of "metabolic cooperation," is also vulnerable to disruption, as discussed earlier.

Oscillation is also a universal phenomenon, and biological systems of the heart, brain and gut are dependent on the cooperative actions of cells that function according to principles of non-linear, coupled biological oscillations for their synchrony, and are dependent on exquisitely timed cues from the environment at vanishingly small levels (Buzsaki 2006; Strogatz 2003). The key to synchronization is the joint actions of cells that co-operate electrically - linking populations of biological oscillators that couple together in large arrays and synchronize spontaneously according to the mathematics described for Josephson junctions (Brian Josephson, the 1993 Nobel prize winner for this concept). This concept has been professionally presented in journal articles and also popularized in a book by Prof. Steven Strogatz, a mathematician at Cornell University who has written

about ‘sync’ as a fundamental organizing principle for biological systems (Strogatz 2001) (Strogatz 2003).

> *“Organisms are biochemically dynamic. They are continuously subjected to time-varying conditions in the form of both extrinsic driving from the environment and intrinsic rhythms generated by specialized cellular clocks within the organism itself. Relevant examples of the latter are the cardiac pacemaker located at the sinoatrial node in mammalian hearts and the circadian clock residing at the suprachiasmatic nuclei in mammalian brains. These rhythm generators are composed of thousands of clock cells that are intrinsically diverse but nevertheless manage to function in a coherent oscillatory state. This is the case, for instance, of the circadian oscillations exhibited by the suprachiasmatic nuclei, the period of which is known to be determined by the mean period of the individual neurons making up the circadian clock. The mechanisms by which this collective behavior arises remain to be understood.”* (Strogatz 2003)

The brain contains a population of oscillators with distributed natural frequencies, which pull one another into synchrony (the circadian pacemaker cells). Strogatz has addressed the unifying mathematics of biological cycles and external factors disrupt these cycles. This also applies to mitochondria:

> *“Organisation of mitochondrial metabolism is a quintessential example of a complex dissipative system which can display dynamic instabilities. Several findings have indicated that the conditions inducing instabilities are within the physiological range and that mild perturbations could elicit oscillations. Different mathematical models have been put forth in order to explain the genesis of oscillations in energy metabolism. One model considers mitochondria as an organised network of oscillators and indicates that communication between mitochondria involves mitochondrial reactive oxygen species (ROS) production acting as synchronisers of the energy status of the whole population of mitochondria. An alternative model proposes that extramitochondrial pH variations could lead to mitochondrial oscillations.”* (Iotti, Borsari, and Bendahan 2010)

The field of bioelectromagnetics has studied exposure to very low levels of electromagnetic frequencies.

These exposures can alter critical properties of chemical reactions. *“In a chemical reaction, the bond breaks and each partner reclaims its electron from the bond, moving away to encounter a new partner. It is now an unattached, highly reactive free radical. Reforming a bond requires a meeting between two radicals with opposite electron spins, the union producing a singlet pair. The lifetime of free radicals is typically short, in the*

range of microseconds to nanoseconds. It is in this brief period that imposed magnetic fields may alter the rate and amount of product of a chemical reaction. Since the effect is only on the kinetics of chemical reactions, they are known as magnetokinetic effects (Steiner and Ulrich, 1989). They occur only in nonthermal states of biomolecular systems, defined as an insensitivity to random thermal interactions during the brief period of their existence (Walleczek, 1994). They are a consequence of a coherent quantum-mechanical step which accompanies free radical formation." (Adey 1994)

Not just chemical reactions but synchronous biological oscillations in cells (pacemaker cells) can be disturbed and disrupted by artificial, exogenous environmental signals, whicn can lead to desynchronization of neural activity that regulates critical functions (including metabolism) in the brain, gut and heart and circadian rhythms governing sleep and hormone cycles (Strogatz, 1987). Buzsaki in his book *Rhythms of the Brain* (2006) says "*rhythms can be altered by a wide variety of agents and that these perturbations must seriously alter brain performance."* (Buzsaki 2006)

Disturbance can get increasingly disruptive as more damage occurs and more systems are thrown out of kilter and out of cooperativity. One can think of the kindling model in which repeated induction of seizures leads to longer and more sever seizures and greater behavioral involvement. The combination of disruptive and stimulatory effects of biologically inappropriate EMF/RFR exposures could contribute to disruption of synchronized oscillation and cooperativity at a myriad of levels but particularly in the brain, and this may contribute to the loss of coherence and complexity in the brain in autism, as well as dysregulation of multiple other bodily systems. Strogatz points out that there are many more ways of being desynchronized than being synchronized (Strogatz, 2003). It has even been suggested that autism itself could be due to brain desynchronization (Welsh, 2005).

2. Behavior as an "emergent property"

Although from a pathophysiological point of view one might hypothesize that a brain with greater indications of oxidative stress along with immune activation and mitochondrial dysfunction might generate different oscillatory activity than a brain in which those pathophysiological features were absent, to date almost no attention has been paid to testing this hypothesis in ASD or neurodevelopmental and neuropsychiatric conditions more generally. From this vantage point it would make sense to propose that the compromised whole body health status of at least many with ASDs would make it harder for them to maintain the resilience of their brain cells and brain activities in the face of potentially disruptive exposures. Yet the investigation of how this might occur remains a largely unexplored frontier. But from the point of view of making sense of the

brain impact of environmental challenges – including but not limited to EMF-RFR – this investigation is crucial.

The pathophysiological perspective that guides this review would suggest a move away from considering the behavioral manifestations of ASDs as core 'traits,' *Instead behaviors may be better understood as 'outputs' or emergent properties – what the brain and body produce – when their physiological attributes are altered* in these fashions for whatever reasons – be they genetic, environmental or many combinations of both (Anderson 2009, 2008; Sieb 2004; Smith and Thelen 2003; Custodio et al. 2007; Herbert 2012). Sleep and consciousness have also been considered 'emergent properties' (Krueger et al. 2008; Krueger and Obal 2003). Brain oscillatory activity is critical for organizing behavior, and it arises from cells and subcellular features that are shaped by the environment and can act differently based on their functional status as well as on account of external sensory or psychosocial stimuli.

In particular, a) brain oscillatory activity is intimately connected with underlying cellular, metabolic and immune status, b) EMF/RFR is capable of perpetrating changes at each of these levels, and c) problems at each of these levels can make other problems worse. And as mentioned earlier, EMF/RFR and various toxicants can co-potentiate damage (Juutilainen and Kumlin 2006; Juutilainen, Kumlin, and Naarala 2006; Verschaeve et al. 2006; Ahlbom et al. 2008; Hoyto et al. 2008; Juutilainen 2008; Luukkonen et al. 2009; Markkanen, Juutilainen, and Naarala 2008), amplifying allostatic load.

Put together, all of this implies that the combination of these EMF/RFR impacts may quite plausibly significantly contribute both to how ASDs happen in individuals and to why there are more reported cases of ASDs than ever before (with studies showing that not all of this increase can be written off as artifact (King and Bearman 2009; Hertz-Picciotto and Delwiche 2009).

The hopeful side of this framing of the problem comes from moving beyond the increasingly anachronistic idea that autism is determined overwhelmingly by genetic code about which we can do little or nothing. An emerging model that explains much more of what we now know frames ASDs as the dynamic, active outcomes of perturbed physiological processes – again, more like a chronic but changeable 'state' than a 'trait.' In the latter model, one is empowered to strongly reduce exposures and to make aggressive constructive environmental changes – particularly in diet and nutrition, given their protective potency discussed above (Herbert and Weintraub 2012). In this way allostatic load can be reduced, physiological damage can be repaired, homeostasis can be restored and resilience and optimal function can be promoted.

III. IMPLICATIONS

A. Summary

In the above review, the case has been made that ASDs involve physiological challenges at multiple levels, and that these challenges are paralleled in the physiological impacts of EMF/RFR exposure. Evidence has also been presented to suggest that the many levels of damage and degradation of physiological and functional integrity are profoundly related to each other. Although autism spectrum disorders (ASDs) are defined by problems with behavior, communication, social interaction and sensory processing, under the surface they also involve a range of disturbances of underlying biology that find striking parallels in the physiological impacts of electromagnetic frequency and radiofrequency exposures (EMF/RFR). At the cellular and molecular level many studies of people with ASDs have identified oxidative stress and evidence of free radical damage, evidence of cellular stress proteins, as well as deficiencies of antioxidants such as glutathione. Elevated intracellular calcium in ASDs can be associated with genetic mutations but more often may be downstream of inflammation or chemical exposures. Cell membrane lipids may be peroxidized, mitochondria may function poorly, and immune system disturbances of various kinds are common. Brain oxidative stress and inflammation as well as measures consistent with blood-brain barrier and brain perfusion compromise have been documented. Changes in brain and autonomic nervous system electrophysiology can be measured and seizures are far more common than in the population at large. Sleep disruption and high levels of stress are close to universal. In parallel, all of these phenomena have also been documented to result from or be modulated by EMF/RFR exposure. Moreover, some people with ASDs have de novo mutations (that their parents do not have), and EMF/RFR exposures could contribute to this due to their potential genotoxicity. EMF/RFR exposure during pregnancy may send spurious signals to developing brain cells during pregnancy, altering brain development during critical periods, and may increase oxidative stress and immune reactivity that can increase risk for later developmental impairments, with further disruption later in development increasing risk, physiological dysregulation and severity of outcome.

All of this does not prove that EMF/RFR exposures cause autism, but it does raise concerns that they could contribute by increasing risk, and by making challenging biological problems and symptoms worse in these vulnerable individuals. Placed alongside the dramatic rise in reported cases of ASDs, that parallels the dramatic rise in deployment of wireless technologies, a strong case can be made for aggressively investigating links between ASDs and EMR/RFR, and minimizing exposures for people with autism as well as families preconceptionally, during pregnancy, and around infants and children at home, at school, and in health care centers and hospitals.

These arguments have implications for how we understand what ASDs 'are' and how they work. These implications call upon us to take the environmental contribution very seriously, which involves on the one hand a sobering appreciation of the vast array of exposures that can contribute to risk via perturbed development and physiological degradation, and on the other hand a sense that there are powerful things we can do to improve the situation.

B. Exposures and their Implications

Several thousand scientific studies over four decades point to serious biological effects and health harm from EMF and RFR as are intensively reviewed in the many detailed sections of this BioInitiative Report. These studies report genotoxicity, single-and double-strand DNA damage, chromatin condensation, loss of DNA repair capacity in human stem cells, reduction in free-radical scavengers (particularly melatonin), abnormal gene transcription, neurotoxicity, carcinogenicity, damage to sperm morphology and function, effects on behavior, and effects on brain development in the fetus of human mothers that use cell phones during pregnancy. Cell phone exposure has been linked to altered fetal brain development and ADHD-like behavior in the offspring of pregnant mice.

1. Exposures have outpaced precautions

There is no question that huge new exposures to EMF/RFRs have occurred over the past few decades. As discussed extensively in other parts of this Bioinitiative 2012 update (Sage, 2012), there is much concern that regulations to date have been based on a very limited sense of the pertinent biology, and particularly that limiting concern to thermal impacts is no longer valid since there is a wealth of evidence by now that non-thermal impacts can be biologically very powerful.

Only in the last two decades have exposures to RFR and wireless technologies become so widespread as to affect virtually every living space, and affect every member of societies around the world. Even as some disease patterns like brain tumors from cell phone use have become 'epidemiologially visible', there are no comprehensive and systematic global health surveillance programs that really keep up to report EMF/RFR health trends (Fragopoulou et al. 2010).

> "*The deployment of new technologies is running ahead of any reasonable estimation of possible health impacts and estimates of probabilities, let alone a solid assessment of risk. However, what has been missing with regard to EMF has been an acknowledgement of the risk that is demonstrated by the scientific studies. There is clear evidence of risk, although the magnitude of the risk is*

uncertain, and the magnitude of doing nothing on the health effects cost to society is similarly uncertain. This situation is very similar to our history of dealing with the hazards of smoking decades ago, where the power of the industry to influence governments and even conflicts of interest within the public health community delayed action for more than a generation, with consequent loss of life and enormous extra health care costs to society." (Sage and Carpenter 2009).

2. The population's exposure has increased

Given the range of physiological impacts described in Part 2, the very rapid global deployment of both old and new forms of emerging wireless technologies in the last two decades needs aggressive evaluation from a public health perspective.

In the United States, the deployment of wireless infrastructure (cell tower sites) to support cell phone use has accelerated greatly in the last decades. The Cellular Telephone Institute of America (CTIA) estimated that in 1997 there were only 36,650 cell sites in the US; but increased rapidly to 131,350 in June 2002; 210,350 in June 2007 and 265,561 in June 2012 (Roche, 2012; Cellular Telephone Industry of America (CTIA) 2012). About 220,500 cell sites existed in 2008 (Reardon, 2007; Cellular Telephone Industry of America (CTIA) 2012; Anonymous, May 2005). These wireless facilities for cellular phone voice and data transmission produce RFR over broad areas in communities and are an involuntary and unavoidable source of radiofrequency radiation exposure. Other new RFR exposures that didn't exist before are from WI-FI access points (hotspots) that radiate 24/7 in cafes, stores, libraries, classrooms, on buses and trains, and from personal WI-FI enabled devices (iPads, tablets, PDAs, etc).

Not surprisingly, the use of cell phones has a parallel growth trend. In the late 1980s and early 1990's, only a few percent of the US population were cell phone users. By 2008, eighty-four percent (84%) of the population of the US owned cell phones [16]. CTIA reports that wireless subscriber connections in the US increased from 49 million in June 1997 to 135 million in June 2002 to 243 million in June 2007 to 322 million in June 2012 (Roche, 2012; Cellular Telephone Industry of America (CTIA), June 2012) This represents more than a 100% penetration rate in the US consumer market, up from just a few percent in the early 1990's. The number of wireless subscribers in June 1997 was 18%; in June 2002 it was 47%; in June 2007 it was 81% and in June 2012 it is 101%.

The annualized use of cell phones in the US was estimated to be 2.23 trillion minutes in 2008 and 2.296 trillion minutes in 2010 (CITA, 2012). There are 6 billion users of cell phones world- wide in 2011 up from 2.2 billion in 2008 and many million more users of cordless phones.

The number of US homes with *only* wireless cell phones has risen from 10.5% in 2007 to 31.6% in June of 2012 (Roche, 2012; Cellular Telephone Industry of America (CTIA),

June 2012). There are no statistics for June 1997 nor for June 2002, since landline (non-wireless) phone use predominated. The shift to wireless communications, more minutes of use, and reliance on cell and cordless phones rather than corded phones is an extremely revealing measure of new EMF and RFR exposures for both adults and children.

3. Infants, children and childbearing families are highly exposed and vulnerable

With regard to children, the spread of cell towers in communities, often placed on pre-school, church day-care, and school campuses, means that young children may have hundreds of thousands of times higher RF exposures in home and school environments than existed even 20-25 years ago. In addition, the nearly universal switch to cordless and cell phones, and away from corded landline phones, means close and repetitive exposures to both EMF and RFR in the home. Wireless laptops and wireless internet in schools, and home offices and for homework mean even more chronic exposures to RFR, a designated IARC 2B Possible Human Carcinogen (International Agency for Research on Cancer of the World Health Organization, May 2011; Baan, 2011) The great utility of handheld devices as communication aids and sources of information and satisfaction for people on the autism spectrum may come with a concerning underbelly.

Exposures prior to conception or during pregnancy and infancy are also important to consider. These exposures can come from faulty wiring, proximity to power lines, or high-frequency transients from a proximate transformer on a utility pole, or internal sources of pulsed RFR in the home (examples include an electronic baby monitor in the crib, a wireless router in the next room, a DECT phone that pulses high emissions of RFR on a continuous basis 24/7, or conversion to all compact fluorescent bulbs that produce significant 'dirty electricity' for occupants due to low-kilohertz frequency fields on electrical wiring and in ambient space. Sick and vulnerable infants in neonatal intensive care units are heavily exposed from being surrounded by equipment, with negative metabolic and autonomic consequences documented and other likely consequences needing further investigation (Bellieni et al. 2008; Bellieni, Tei, et al. 2012).

Wireless phones and laptops exposures produce extremely low frequency pulses from the battery of the wireless device (Sage, 2007; Sage and Carpenter 2009) and the exposures to pulsed radiofrequency microwave radiation when the wireless device is transmitting or receiving calls and emails.

Especially since EMF/RFR exposures are already classified as IARC 2B Possible Human Carcinogens, we should be actively investigating these sources of damage to DNA that could reasonably result in 'de novo mutations' but also be aware that common environmental exposures from EMF and RFR might play a role in the higher rates of concordance for autism (ASD) among twins and siblings.

Researchers also should be aware that common environmental exposures from EMF and RFR might play a role in the higher rates of autism (ASD) among twins and siblings, not solely because of maternal use of wireless devices during pregnancy and paternal sperm exposure to wireless devices peri-conception; but also because such oxidative damage to DNA can occur at levels introduced into the world of the fetus, and young developing infant and child via baby surveillance monitoring devices in the crib and wireless devices in the home. The deployment of technologies poses risks to human fertility and reproduction capacity, to the fetus, to children and adults (Sage and Carpenter 2009).

4. ASD risk and genomic damage to future generations

Barouki and Grandjean (2012) make a persuasive case that public health interventions are critically needed in early childhood development to prevent adult diseases that appear decades later (Barouki et al. 2012). Although they do not include EMF or RFR but only chemicals, they do say that physiological stressors, which EMF and RFR certainly have been established to be, should be reduced during critical development windows. They say: "*The current pandemic of non-communicable diseases and the increased prevalence of important dysfunctions demand an open interrogation of why current interventions appear insufficient. We now know that disease risk can be induced very early in the life course and that it is modifiable by nutrients and environmental chemical exposures (along with drugs. infections, and other types of stresses)".*

Part II of this chapter documents the detailed scientific basis for considering EMF/RFR exposures to be of significance to the ASDs crisis. Public health interventions are warranted now to protect the genetic heritage of humans, as well as the other stocks of genetic material in wildlife and plants in the face of what appears to be on-going impairment of these genomes. The risk of genomic damage for future generations is sufficiently documented to warrant strong preventative action and new public safety limits that observe EMF/RFR levels shown to cause adverse effects.

5. De-tuning the organism

Genetic mutations may lead to cancer and other diseases in the present and future generations, but the exposures that are capable of creating genotoxic impacts also compromise physiological function Even genotoxicity can have not only specific but also non-specific effects due to inefficiencies, misfolded proteins, and cellular debris, as discussed in the section "Implications of Damage" at the end of the first part of Part II, regarding the rescue of a mouse model of Rett syndrome through enabling a probably generic process of microglial phagocytosis, critical to debris removal, rather than through correcting some specific molecular defect of the synapse (Derecki et al. 2012; Derecki, Cronk, and Kipnis 2012).

In the present setting, where the argument about the pertinence of the cascade of physiological and genotoxic compromises to autism includes the degradative impact on oscillatory synchronization, it is also worth considering that oscillation is a property of living and even physical systems much more generally, and not just of brain oscillatory networks (Strogatz 2003). Under certain circumstances, phase transitions occur and synchronization emerges, often rather quickly rather than gradually – more like a state change than a gradual trend. On the other hand, as mentioned, synchronization can be lost, and there are an enormous number of ways for a system to be de-synchronized, which may relate to the heterogeneity amongst people with ASD that so vexes researchers.

In the setting of autism, a baby gestated or developing as a neonate in a milieu with excessively elevated EMF/RFR exposures is bound to have interference with the normal development processes, including the organization of information and experience in the brain. This baby's environment also often nutritional insufficiencies (processed denatured pesticide-laden food low in antioxidants, minerals and essential fatty acids essential to cellular protection). The baby's gestational period may have been complicated by the mother's own health issues such as conditions like obesity and diabetes (Krakowiak, 2012) which converge on inflammation, oxidative stress and other common forms of physiological dysregulation associated with or even just eating nutrient-depleted, pesticide-laden processed food. The exquisite 'tuning up' of the brain and body as it develops will integrate and respond to the environmental inputs it receives, and is particularly sensitive to environmental miscues (whether chemical like endocrine disruptors, EMF/RFR, or other hostile environmental conditions whether hostile or nurturing). To the extent that the baby is burdened with more disorganized or hostile cues than nurturing and organizing cues, that baby may lose resiliency and become more physiologically vulnerable –perhaps approaching a tipping point into decompensation.

From a systems point of view, the phenomenon of 'autistic regression' may occur after an accumulation of multisystem signaling interference leading to a tipping point of loss of some vital systems synchronization and increase in randomization. EMF/RFR exposures could plausibly contribute both to this vulnerability and to the decompensation/desynchronization process – as could other stressors such as infection, toxicity, acute stress. The vulnerability, then, is the 'allostatic load' – the total burden of stressors pressing toward disorganization. The tipping point may come in a variety of ways but upon investigation one is likely to find that unless it is a severe stressor it is not triggered simply by a single source of stress in an otherwise blissfully healthy child, but rather is the "straw that breaks the camel's back' laid atop a prior accumulation of 'allostatic load.'

C. Conclusions and Recommendations

1. Change our deployment of EMF/RFR

The deployment of RFR from wireless technologies has incredible momentum, and it has made many things easier and many other things possible for the first time. On the other hand this momentum can interfere with setting up the technology in a fashion truly respectful of biological tolerances. Other sections in the Bioinitiative 2012 update will address recommendations and guidelines for increasing the safety profile. This will undoubtedly provoke controversy. The problems will not get settled immediately, and transformation to healthier arrangements will take time.

> *"There is no question that global implementation of the safety standards proposed in the Bioinitiative Report, if implemented abruptly and without careful planning, have the potential to not only be very expensive but also disruptive of life and the economy as we know it. Action must be a balance of risk to cost to benefit. The major risk from maintaining the status quo is an increasing number of cancer cases, especially in young people, as well as neurobehavioral problems at increasing frequencies. The benefits of the status quo are expansion and continued development of communication technologies. But we suspect that the true costs of even existing technologies will only become much more apparent with time. Whether the costs of remedial action are worth the societal benefits is a formula that should reward precautionary behavior*." (Sage and Carpenter 2009)

2. Encourage precautions right now based on present knowledge

In the meantime many people have already started taking precautionary measures, and more will wish to do so. Physicians and health care people should raise the visibility of EMF/RFR as a plausible environmental factor in clinical evaluations and treatment protocols. Reducing or removing EMF and wireless RFR stressors from the environment is a reasonable precautionary action given the overall weight of evidence.

- Children with existing neurological problems that include cognitive, learning, attention, memory, or behavioral problems should as much as possible be provided with wired (not wireless) learning, living and sleeping environments,
- Special education classrooms should aim for 'no wireless' conditions to reduce avoidable stressors that may impede social, academic and behavioral progress.
- All children should reasonably be protected from the physiological stressor of significantly elevated EMF/RFR (wireless in classrooms, or home environments).
- School districts that are now considering all-wireless learning environments should be strongly cautioned that wired environments are likely to provide better learning and teaching environments, and prevent possible adverse health consequences for both students and faculty in the long-term.

- Monitoring of the impacts of wireless technology in learning and care environments should be performed with sophisticated measurement and data analysis techniques that are cognizant of the non-linear impacts of EMF/RFR and of data techniques most appropriate for discerning these impacts.
- There is sufficient scientific evidence to warrant the selection of wired internet, wired classrooms and wired learning devices, rather than making an expensive and potentially health-harming commitment to wireless devices that may have to be substituted out later, and
- Wired classrooms should reasonably be provided to all students who opt-out of wireless environments.

Undoubtedly risks and the above recommendations will be dismissed by those poised to benefit from the sale of these new systems. Many people also feel that new possibilities have opened up to themselves and the world through wireless technologies. But the public needs to know that these risks exist, that transition to wireless should not be presumed safe, and that it is very much worth the effort to minimize exposures that still provide the benefits of technology in learning, but without the threat of health risk and development impairments to learning and behavior in the classroom.

Broader recommendations also apply, related to reducing the physiological vulnerability to exposures, reduce allostatic load and build physiological resiliency through high quality nutrition, reducing exposure to toxicants and infectious agents, and reducing stress (Herbert and Weintraub 2012), all of which can be implemented safely based upon presently available knowledge.

3. Build an environmentally physiologically centered research program in ASDs as a platform for investigating the EMR/RFR-ASD linkage

This review has been structured around the physiological parallels between ASDs and the impacts of EMF/RFR. What is missing from the autism research agenda is some cross-study of these two bodies of research evidence. To do this we will need both a recognition of the importance of these risks, and a collaborative multi-site research program centered around a "middle-out" physiological approach that can incorporate the the gene-brain-behavior agenda that has dominated ASD research into a broader framework (Herbert 2013). While the middle-out approach is an emerging framework in systems biology that can incorporate complexity and nonlinear, multileveled modeling (Cristofolini et al. 2008; de Graaf et al. 2009; Majumder and Mukherjee 2011; Vinga et al. 2010; Walker and Southgate 2009), the gene-brain-behavior approach has been based on an expectation of linear mapping across the levels on which it focuses, but instead the systems involved appear to be much more complex, and the physiological levels largely

left out of this linear approach are critically important to helping people with ASDs because they will help not only with understanding how environment impacts function but also with identifying leverage points.

4. Take the evidence as a call to action

Both EMF and RFR exposures are already classified as IARC 2B Possible Human Carcinogens. The substantial scientific literature on EMF and RFR effects on DNA, on immune and blood-brain barrier disruption, on stress proteins, on circadian rhythms and hormone disregulation, and on cognition, sleep, disruption of neural control and altered brainwave activity all argue for reduction of exposures now, and better coordinated research in these areas.

All relevant environmental conditions should be given weight in defining and implementing prudent, precautionary actions to protect public health, including EMF and RFR. Evidence is sufficient to add EMF/RFR prominently to the list of exposures that can degrade the human genome, and impair normal development, health and quality of our physiology. With the rising numbers people with ASDs and other childhood health and developmental disorders, we cannot afford to ignore this component of risk to our children and vulnerable populations. When the risk factors are largely avoidable or preventable, ignoring clear evidence of large-scale health risks to global populations poses unnecessary and unacceptable risks. Taking this evidence as a call to action will be challenging and disruptive in the short term, but constructive in the longer term as we learn to use EMF/RFR in healthier ways.

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SECTION 22

Precaution in Action – Global Public Health Advice Following BioInitiative 2007

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I. INTRODUCTION

This section highlights some major milestones in documentation of potential health effects of low-intensity electromagnetic fields and radiofrequency radiation, and subsequent national and international actions taken to address the problem. The categories of response are divided into Publications and Health Agency Advisories, Local and National Country Actions, Expert Research Group and Physicians' Advisories and the formal classification by the World Health Organization International Agency for Research on Cancer for RFR as a 2B Possible Human Carcinogen.

II. PUBLICATIONS AND HEALTH AGENCY ADVISORIES (2007 – 2012)

The BioInitiative Report (2007)

The BioInitiative Report (1) is a 650+ page report documenting the evidence for bioeffects and adverse health effects (the science and public health consequences of that body of scientific evidence) from electromagnetic field and radiofrequency (microwave) radiation. It was written by an independent international research group to give an overview of what is known of biological effects that occur at low-intensity EMFs exposures (for both radiofrequency radiation RFR and power-frequency ELF-EMF), and various forms of combined exposures that are now known to be bioactive). The Report examines the research and current standards and finds that these standards are far from adequate to protect public health. The report presents solid science on this issue, and makes recommendations to decision-makers and the public.

The BioInitiative Working Group was composed of scientists, researchers and public health policy professionals. In 2007, the Working Group documented information from over 2000 published scientific studies and reviews reporting bioeffects and adverse health impacts of electromagnetic fields and radiofrequency radiation at exposure levels far below current public safety standards that should be considered in the international debate about the adequacy (or inadequacy) of existing public exposure standards.

Eleven chapters documented key scientific studies and reviews identifying low-intensity effects of electromagnetic fields. Sections 16 and 17 were prepared by public health and policy experts. These sections discuss the standard of evidence which should be applied in public health and environmental planning, how the scientific information should be evaluated in the context of prudent public health policy, and the basis for taking precautionary and preventative actions that are proportionate given this evidence.

European Environment Agency (2007)

European Environmental Agency Executive Director Jacqueline McGlade, PhD provided early support for the BioInitiative Report (2007). The Agency's Head of Communications and Corporate Affairs issued a news release on the publication of the BioInitiative Report, and the EEA contributions to it on September 17, 2007, two weeks after the Report was published on the web. It stated (2):

> *"A new report raising concerns about the effects of electromagnetic fields (EMF) on human health calls for tougher safety standards to regulate radiation from mobile phones, power lines and many other sources of exposure in daily life. The report, 'Bioinitiative: A Rationale for a Biologically-Based Public Exposure Standard for Electromagnetic Fields' was compiled by the BioInitiative Working Group, an international group of scientists, researchers and public health policy professionals. The EEA has contributed to this new report with a chapter drawn from the EEA study 'Late lessons from early warnings: the precautionary principle 1896–2000' published in 2001."*
>
> *"The EEA study reviews the histories of a selection of public and environmental hazards, such as asbestos, benzene and PCBs, from the first scientifically based early warnings about potential harm, to subsequent precautionary and preventive measures. Cases on tobacco smoking and lead in petrol are forthcoming."*
>
> *"Although the EEA does not have specific expertise in EMF, the case studies of public hazards analyzed in the 'Late Lessons from Early Warnings' publication show that harmful exposures can be widespread before there is both 'convincing' evidence of harm from long-term exposures, and biological understanding of how that harm is caused."*
>
> *"There are many examples of the failure to use the precautionary principle in the past, which have resulted in serious and often irreversible damage to health and environments. Appropriate, precautionary and proportionate actions taken now to avoid plausible and potentially serious threats to health from EMF are likely to be seen as prudent and wise from future perspectives. We must remember that precaution is one of the principles of EU environmental policy*."
>
> Professor Jacqueline McGlade, Executive Director, EEA.

In the fall of 2007, the EEA Director responsed to strong media and industry attention to the BioInitiative Report, defending the EEA's position to declare 'early warnings' appropriate with respect to the evidence on mobile phone radiofrequency radiation and possible health hazards. The Director defended EEA recommendations for prudent public health action, based on the scientific evidence presented in the BioInitiative Report. (3)

> *"The BioInitiative report draws attention to some of the emerging evidence of potential harm from the long term effects of non-ionising radiations from electro and magnetic fields (EMF), particularly from the radio frequency (RF) exposures that arise from mobile phone telecommunications."*
>
> *"The Bioinitiative report, however, is only one of several reports reviewing the risks from the*

thermal and non-thermal effects of EMF that have been published over recent years."

"These include reports from the NIEHS, the EU, the WHO, the UK National Radiological Protection Board and others The EEA's contribution to the BioInitiative report was a chapter on the history and general application of the precautionary principle to a number of well known hazards for which there had been, and in some cases still is, much scientific uncertainty. The chapter summarised the main messages from our report, "Late Lessons from Early Warnings: the Precautionary Principle 1896-2000", (EEA 2001)."

"The point of our chapter for the BioInitiative report was to illustrate how past uncertainties had been dealt with so as to provide lessons that may be helpful in dealing with current hazards for which there is both scientific uncertainty and high stakes, both health and economic."

"It is because this accumulating evidence on RF is of increasing scientific concern, and because the exposure of the public, particularly vulnerable groups, is widespread and generally rising, that we judged it was timely to draw wider attention to the possibly serious hazards from EMF".

"In our judgement, the human and experimental evidence, taken together, is "clear" enough to support using the precautionary principle to justify reducing exposures, where feasible, and to review the evidence for the existing exposure limits, which, as you know, are based on thermal effects only."

EEA Director Jacqueline McGlade to Wolfram Konig, Nov 27, 2007

<u>*European Parliament (2007)*</u>

In September 26, 2007 Carolyn Lucas, MEP, introduced the topic of the BioInitiative Report recommendations to the European Parliament (4) and asked the European Commission what action the Commission is taking in response to the report, its conclusions and endorsement by the European Environment Agency.

"As the Commission will be aware, on 31 August 2007 the international BioInitiative Working Group of renowned scientists and public health policy experts published a report called "A Rationale for a Biologically-Based Public Exposure Standard for Electromagnetic Fields (ELF and RF)".

"This report documents evidence that ELFs are a risk factor for both childhood and adult cancers, and sets out how wireless technologies which rely on RF to send emails and voice communications are thousands of times stronger than levels reported to cause sleep disorders, headaches, problems with memory and concentration and other physical symptoms. It notes the unprecedented levels of exposure to ELFs being created by the "explosion of new sources" and raises serious scientific concerns over the health risks posed by long-term and cumulative exposure."

"The report concludes that current safety limits regulating the levels of ELF permitted from power lines, mobile phones and other sources are highly inadequate, and that a much more cautious approach should be taken to further deployment of risky technologies."

"The European Environment Agency (EEA) contributed a chapter to the report, concerning the consequences of previous failures to apply the precautionary principle in the face of public and environmental hazards. Following publication of the study the EEA's Executive Director has publicly stressed the importance of precaution where potentially serious future consequences may be involved, and called for actions to reduce exposures to ELF, particularly where vulnerable groups are concerned."

"What action is the Commission taking in response to this report, its conclusions and endorsement by the EEA? Does the Commission agree that the balance of evidence points to the need to revise public safety standards regulating radiation levels from sources of day-to-day ELF exposure, as well as policies on the testing and deployment of new telecommunications technologies?"

European Parliament 2008

The European Parliament issued advice on the Communication from the Commission to the Council, the European Parliament and the European Economic and Social Committee regarding the mid-term review of the European Environment and Health Action Plan 2004-2010 (COM(2007)0314). See Appendix A for full text, but in part, it stated:

21. Is greatly concerned at the Bio-Initiative international report (8) concerning electromagnetic fields, which summarises over 1500 studies on that topic and which points in its conclusions to the health risks posed by emissions from mobile-telephony devices such as mobile telephones, UMTS, Wifi, Wimax and Bluetooth, and also DECT landline telephones;

22. Notes that the limits on exposure to electromagnetic fields which have been set for the general public are obsolete, since they have not been adjusted in the wake of Council Recommendation 1999/519/EC of 12 July 1999 on the limitation of exposure of the general public to electromagnetic fields (0Hz to 30 GHz) (9, obviously take no account of developments in information and communication technologies, of the recommendations issued by the European Environment Agency or of the stricter emission standards adopted, for example, by Belgium, Italy and Austria, and do not address the issue of vulnerable groups, such as pregnant women, newborn babies and children;

23. Calls, consequently, upon the Council to amend its Recommendation 1999/519/EC in order to take into account the Member States' best practices and thus to set stricter exposure limits for all equipment which emits electromagnetic waves in the frequencies between 0.1 MHz and 300 GHz

Pathophysiology Journal Publication - Special Issue on EMF (2009)

As a direct result of the BioInitiative Report, a special, peer-reviewed issue of Pathophysiology (6) was published in March 2009 and contained most of the BioInitiative content (some chapters updated from 2006 to 2009 published works) including a chapter on public health implications of wireless technologies (7). It also extended the scope of coverage to include RF impacts on the blood-brain barrier, effects of cell towers on wildlife, and reproduction effects in animal studies. It provided assurance of the high scientific quality of the BioInitiative Report analysis and conclusions, and buttressed the need for new EMF safety standards in a respected, peer-reviewed scientific journal.

"Bioelectromagnetics, the study of biological effects of electromagnetic fields (EMF), is an interdisciplinary science with a technical literature that is not easily accessible to the non-specialist. To increase access of the public to the technical literature and to the health implications of the scientific findings, the Bioinitiative Report was organized by an international group of scientists and published online at www.bioinitiative.org on August 31, 2007. The report has been widely read, and was cited in September 2008 by the European Parliament when it voted overwhelmingly that the current EMF safety standards were obsolete and needed to be reviewed. "

"DNA shows biological effects at the sub-cellular level that occur at very low EMF thresholds and across frequency ranges of the EM spectrum. Interactions with DNA may account for many of the effects of EMF, and they raise the possibility that genetic damage due to EMF can lead to cancer."

"The brain is exposed to radiation from mobile phone antennas, and laboratory studies show that the radiation causes leakage of the protective blood–brain barrier, as well as the death of neurons in the brain. Radiation emitted from base stations can affect all who are in the vicinity. Epidemiological studies have shown a relation between exposure to mobile phones, base-stations and the development of brain tumors. Some epidemiological studies have significant flaws in design, and the risk of brain cancer may be greater than reported in the published results."

"In addition to the risk of brain cancer, EMF in the environment may contribute to diseases like Alzheimer's dementia and breast cancer in humans, as well as reproductive and developmental effects in animals in the wild. EMF affects the biochemical pathways and immunological mechanisms that link the different organ systems in our bodies and those of animals. The human body can act as an antenna for RF signals, and a small percentage of the population appears to be so sensitive to EMF that it interferes with their daily lives. In addition to the growing presence of EMF signals in the environment, the complexity of the signals may be important in altering biological responses. These are among the many factors that must be considered in approaching EMF safety issues."

Preface, Pathophysiology, Guest Editor Martin Blank, PhD

Media coverage of the Pathophysiology Journal in 2009 highlighted the everyday problems of EMF and wireless exposures in society. For the typical person on the street, the message of the BioInitiative Report and its subsequent contributions to a scientific journal were broken down into examples more familiar to them (8).

"Public health concerns and scientific evidence for risks from cell phones and other wireless devices is published today in the journal Pathophysiology. International researchers have urged quick precautionary action to address a possible epidemic of brain tumors and many other health risks. Over four billion people around the world now use cell phones. They are rapidly eliminating the use of traditional land-line phones throughout the world. Health researchers from six countries give findings in fifteen (15) chapters covering health risks to humans and wildlife from electromagnetic fields and radiofrequency radiation."

"The global rollout of wireless technologies and devices like cell phones, cordless phones, cell towers (masts) and many other sources greatly increases our EMF exposure in daily life. The enormous popularity of new communication devices that allow email, texting, and access to the Internet from any city street has placed the issue squarely before government agencies like the FDA and the FCC, and also parents and school administrators. Parents must decide whether possible health risks to their children outweigh the convenience of keeping track of them. School officials and teachers care because of disruption and distraction in the classroom from cell phone use. National safety officials in the US face public criticism about highway collisions and road deaths from cell phone use while driving. Federal railway officials are

still coping with the problem of illicit texting by US railroad personnel that lead to the catastrophic collision of two trains in Chatsworth, California in 2008 killing 24 and injuring 135 more."

Reba Goodman, PhD (Columbia University) commented: "*cells in the body react to EMFs as potentially harmful, just like to other environmental toxins including heavy metals and toxic chemicals. The DNA in living cells recognizes electromagnetic fields at very low levels of exposure, and produces a biochemical stress response."*

David O. Carpenter, MD, Co-Editor of the BioInitiative Report and Director of the University of Albany, Institute of Health and the Environment concluded: "*the existing FCC and international limits do not do enough to protect people, especially children, from daily exposures to electromagnetic fields and radiofrequency radiation. The existing safety limits did not anticipate these new kinds of technologies affecting the health of people living with and using wireless devices on a daily basis. These effects are now widely reported to occur at exposure levels significantly below most current national and international limits."*

Brain tumor specialist Dr. Lennart Hardell, MD, PhD works as both an oncologist and a researcher at Orebro University Hospital in Sweden. He is an expert on cell phones and brain tumors.

"The evidence for risks from prolonged cell phone and cordless phone use is quite strong. For people who have used these devices for 10 years or longer, and when they are used mainly on one side of the head, the risk of malignant brain tumor is doubled for adults and is even higher for persons with first use before the age of 20 years."

Swedish researcher Olle Johansson, PhD (Karolinska Institute) said: "*most worrisome to me are the constant and unavoidable EMF exposures (from cell and DECT phones, power lines, new wireless technologies like WIMAX and WI-FI, etc.) everywhere in our daily life that may affect the overall health of this and coming generations. I worry especially about the impacts on the immune system, our only real line of defense against disease."*

Wildlife biologist Alfonso Balmoro, PhD of Valladolid, Spain voiced his concern that: *"electromagnetic radiation is a form of environmental pollution which may hurt wildlife. Phone masts located in their living areas are irradiating continuously some species that could suffer long-term effects, like reduction of their natural defenses, deterioration of their health, problems in reproduction and reduction of their useful territory through habitat deterioration. Therefore microwave and radiofrequency pollution constitutes a potential cause for the decline of animal populations and deterioration of health of plants living near phone masts."*

Co-Editor of the BioInitiative Report Cindy Sage observed: *"Prolonged exposure to radiofrequency and microwave radiation from cell phones, cordless phones, cell towers, WI-FI and other wireless technologies has been linked to interference with short-term memory and concentration, sleep disruption, headache and dizziness, fatigue, immune disruption, skin rashes and changes in cardiac function."*

"*these effects can happen with even very small levels of exposure if they occur on a daily basis. Cell phone use is likely to be more harmful in children whose brain and nervous system development can last into late adolescence*"

"The public health implications of billions of people who are exposed makes this a matter of critical concern to policy-makers around the world."

The European Environment Agency Director's Statement (2009)

Two years following the publication of the BioInitiative Report, and just months after publication of the special issue of Pathophysiology on EMF, the EEA updated its comments on potential health

risks of EMF and concern over the adequacy of public safety limits for emerging wireless technologies. The EEA issued a Statement on Mobile Phones for the September, 2009 conference 'Cell Phones and Health: Science and Public Policy Questinos, Washington DC. In part, the comments read (9):

> *"This event and the related Senate Hearings yesterday, have been, in part, stimulated by the BioIntiative Report, (2007), which helped increase public awareness of the potential hazards of electromagnetic fields, not least from mobile phones. The European Parliament responded to this debate with its resolution earlier this year which, among other things, called for lowering exposure to electromagnetic fields and for new exposure limits that would better protect the public. We fully share these recommendations."*

The EEA provides data, information and knowledge on the environment, including its impacts on public health, to EU institutions (the European Parliament, European Commission, and European Council of Ministers), to the 32 Member Countries of the EEA, and to the general public.

> *"The intention of the EEA to promote the use of mobile telephony in this way increases its responsibility to provide information that can help ensure the safety of the public when using mobile phones, especially vulnerable groups such as children, the elderly, and the immuno- compromised. This is the reason why the EEA issued an early warning about the potential hazards of EMF on 17 September 2007."*
>
> *"In this we drew attention to the BioInitiative report and to the other main references relevant to this debate (from the EU, the WHO, and the UK National Radiological Protection Board) which, taken together, provided the basis for our early warning on EMF."*
>
> *"Specifically, we noted that there are many examples of the failure to use the precautionary principle in the past, which have resulted in serious and often irreversible damage to health and environments. Appropriate, precautionary and proportionate actions taken now to avoid plausible and potentially serious threats to health from EMF are likely to be seen as prudent and wise from future perspectives".*
>
> *"This is the reason why the EEA issued an early warning about the potential hazards of EMF on 17 September 2007."*

EEA Recommendations based on current evidence (2009)
The evidence is now strong enough, using the precautionary principle, to justify the following steps:

1. *For governments, the mobile phone industry, and the public to take all reasonable measures to reduce exposures to EMF, especially to radio frequencies from mobile phones, and particularly the exposures to children and young adults who seem to be most at risk from head tumours. Such measures would include stopping the use of a mobile phone by placing it next to the brain. This can be achieved by the use of texting; hands free sets; and by the use of phones of an improved design which could generate less radiation and make it convenient to use hands free sets.*
2. *To reconsider the scientific basis for the present EMF exposure standards which have serious limitations such as reliance on the contested thermal effects paradigm; and simplistic assumptions about the complexities of radio frequency exposures.*
3. *To provide effective labeling and warnings about potential risks for users of mobile phones.*
4. *To generate the funds needed to finance and organise the urgently needed research into the health effects of phones and associated masts. Such funds could include grants from industry and possibly a small levy on the purchase and or use of mobile phones. This idea of a research levy is*

a practice that we think the US pioneered in the rubber industry with a research levy on rubber industry activities in the 1970s when lung and stomach cancer was an emerging problem for that industry. The research funds would be used by independent bodies.

European Parliament 2009

On April 2, 2009, the European Parliament adopted the "European Parliament resolution of 2 April 2009 on health concerns associated with electromagnetic fields (2008/2211(INI))" (10). The Document was based on the "Report on health concerns associated with electromagnetic fields", Rapporteur: Frederique Ries (11) Committee on the Environment, Public Health and Food Safety. See Appendix B for full text. It part, the resolution says:

H. (W)hereas, however, there are some points that appear to be the subject of general agreement, in particular the idea that reactions to microwave exposure vary from one person to another, the need, as a matter of priority, to conduct exposure tests under actual conditions in order to assess the non-thermal effects associated with radio-frequency (RF) fields, and the fact that children exposed to EMFs are especially vulnerable (9) ,

1. Urges the Commission to review the scientific basis and adequacy of the EMF limits as laid down in Recommendation 1999/519/EC and report to the Parliament; calls for the review to be undertaken by the Scientific Committee on Emerging and Newly Identified Health Risks;

2. Calls for particular consideration of biological effects when assessing the potential health impact of electromagnetic radiation, especially given that some studies have found the most harmful effects at lowest levels; calls for active research to address potential health problems by developing solutions that negate or reduce the pulsating and amplitude modulation of the frequencies used for transmission;

5. Invites the Member States and local and regional authorities to create a one-stop shop for authorisation to install antennas and repeaters, and to include among their urban development plans a regional antenna plan

6. Urges the authorities responsible for authorising the siting of mobile telephony antennas to reach agreement, jointly with the operators in that sector, on the sharing of infrastructure, in order to reduce the volume thereof and the exposure of the public to EMFs;

15. Draws attention in this context to the appeal for caution from the coordinator of the Interphone study, Elisabeth Cardis, who, in the light of existing knowledge, recommends, as far as children are concerned, that mobile phones should not be used beyond reasonable limits and that landlines should be preferred;

21. Calls on the Commission, in recognition of the public concern in many Member States, to work with all relevant stakeholders, such as national experts, non-governmental organisations and industrial sectors, to improve the availability of, and access to, up-to-date information understandable to non-specialists on wireless technology and protection standards;

24. Proposes that the EU's indoor air quality policy should encompass the study of "wireless" domestic appliances, which, like Wi-Fi for Internet access and digital enhanced cordless telecommunications (DECT) telephones, have been widely adopted in recent years in public places and in the home, with the result that citizens are being continuously exposed to microwave emissions;

29. Instructs its President to forward this resolution to the Council, the Commission, the

This revision essentially neutralized the chance for an independent and unbiased review of health effects and assessment of the adequacy of the ICNIRP/FCC thermally-based public health standards by designating the SCENIHR Committee to be the arbiter. The SCENIHR Committee ignored the non-thermal science and public health issues on EMF in past reviews. Appointing SCENIHR to provide the 'official' report to Parliament on health effects of EMF essentially guaranteed the outcome would be ineffectual for precautionary action, that the standard of evidence for judging would be "causal" evidence; and a public health standard for judging the evidence would not prevail. Reaching the very high bar of establishing 'causal evidence of risk' is not in line with precautionary, prudent public health decision-making. It will delay necessary actions for avoidance long past the 'early warning' stage when such actions may reasonably prevent substantial health harm.

However many points adopted in the resolution are in favour of public health and must not be dismissed.

Seletun Statement 2009

In November, 2009, a scientific panel met in Seletun, Norway, for three days of intensive discussion on existing scientific evidence and public health implications of the unprecedented global exposures to artificial electromagnetic fields (EMF). The Scientific Panel recognized that the body of evidence on EMF requires a new approach to protection of public health; the growth and development of the fetus, and of children; and argues for strong preventative actions. The study concluded that "new, biologically-based public exposure standards are urgently needed to protect public health worldwide" (12).

The Seletun Statement was published in 2010 in the journal Reviews on Environmental Health. It was titled *Scientific panel on electromagnetic field health risks: Consensus points, recommendations, and rationales*. Scientific Meeting: Seletun, Norway, November 17-21, 2009. (12).

Specific Recommendations from the Seletun Scientific Panel are:

"Extremely Low Frequency (Fields from Electrical Power)

- *Based on the available evidence, the Seletun Scientific Panel recommends a 0.1 uT (1 mG) exposure limit for all new installations based on findings of risk for leukemia, brain tumours,*

Alzheimer's, ALS, sperm damage and DNA strand breaks. This exposure limit does not include a safety margin;

- *For all newly installed, or newly upgraded electrical power distribution, the Panel recommends a 0.1 uT (1 mG) set-back distance, from residences, hospitals, schools, parks, and playgrounds schools (and similar locations occupied by children) [A 0.1 uT (1 mG) time-weighted average (TWA) using peak loading for transmission lines to ensure that average is about half of this for typical exposures; or equivalent for long-term exposure in interior EMF environments (wiring, trans-formers, appliances, others).];*

- *For all newly constructed residences, offices, schools (and other facilities with children), and hospitals there shall be a 0.1 uT (1 mG) max. 24 hour average exposure limit;*

- *For all new equipment (e.g. transformers, motors, electronic products), where practical, the Panel recommends a 0.1 uT (1 mG) max. 24 hour average exposure limit. Where not practical (e.g. large power transformers), there should be a fence, or boundary marker, with clearly written warning labels that states that within the boundary area the 0.1 uT (1 mG) maximum, 24 hour average exposure limit is exceeded;*

- *The Panel recommends all countries should adopt electrical code requirements to disallow conduction of high-frequency voltage transients back into electrical wiring systems;*

- *All new electronic devices including compact fluorescent lamps (CFLs) should be constructed with filters to block high-frequency voltage transients from being conducted back onto electrical wiring systems;*

- *The Panel recommends electric field reductions from electrical wiring in buildings based on evidence of increased cancer risk from prolonged or repetitive electric field exposure. The United States National Electrical Code (NEC) and other govern-mental codes relating to building design and construction should be revised so that all new electrical wiring is enclosed in a grounded metal shield;*

- *The United States NEC and other govern-mental codes that disallow net current on electrical wiring should be better enforced, and ground fault interrupters (GFIs) should be installed on all electrical circuits in order to reduce net current.*

<u>*Radiofrequency/Microwave Radiation Exposure Limit Recommendations*</u>

- *Present guidelines, such as IEEE, FCC, and ICNIRP, are not adequate to protect humans from harmful effects of chronic EMF exposure. The existing scientific knowledge is, however, not sufficient at this stage to formulate final and definite science-based guidelines for all these fields and conditions, particularly for such chronic exposure as well as contributions of the different parameters of the fields, e.g. frequency, modulation, intensity, and window effects. The values suggested below are, thus, provisional and may be altered in the future.*

- *For whole-body (in vivo experiments) or cell culture-based exposure, the Seletun Scientific Panel finds sufficient evidence to establish a scientific benchmark for adverse health effect at 0.0166 W/kg based on at least 32 scientific studies reporting low-intensity effects (defined as studies reporting effects at exposures of 0.1 W/kg or lower) /8-39/.*

- *The Panel recommends a provisional whole-body limit of 0.00033 W/kg by incorporation of an additional 50-fold safety margin applied to the scientific benchmark of 0.0166 W/kg. This is consistent with both ICNIRP and IEEE/FCC safety factors. An additional 10-fold reduction is applied to take prolonged exposure into account (because 29 of the 32 studies are acute exposure only), giving a final whole-body limit of 0.000033 W/kg (33 μW/kg). No further safety margin or provision for sensitive populations is incorporated. This may need to be lowered in the future.*

- *Based on power density measurements, the Seletun Scientific Panel finds sufficient evidence for a whole-body scientific bench-mark for adverse health effect exists down to 85 mW/m^2 (0.0085 mW/cm^2 or 8.5 μW/cm^2) based on at least 17 scientific studies reporting low-intensity effects on humans. Taking more recent human studies conducted near base stations, or at base-station RF levels, Kundi and Hutter /57/ report that the levels must exceed 0.5-1.0 mW/m^2 (0.05 to 0.1 uW/cm^2) for effects to be seen; /40-57/.*

- *The Panel recommends a provisional whole-body (far-field) limit of 1.7 mW/m^2 (also = 0.00017 mW/cm^2 = 0.17 μW/cm^2) by incorporation of an additional 50-fold safety margin applied to the scientific benchmark of 85 mW/m^2. This is consistent with both ICNIRP and IEEE/FCC safety factors. This may need to be lowered in the future.*

- *It can be argued that a further 10-fold reduction is not justified since 13 of the 17 studies are already testing for long-term RF exposure. However, considering that the latest human population studies as reported by Kundi & Hutter (2009) do not show effects below 0.5-1.0 mW/m2, it can also then be argued that an additional 10-fold reduction on precautionary grounds is justified. If another 10-fold reduction is applied, the recommended level would then be 0.17 mW/m^2 (also 0.000017 mW/cm^2 = 0.017 μW/cm^2);*

- *The Seletun Scientific Panel recommends these numeric limits to governments and health agencies for adoption in place of ICNIRP, IEEE/FCC and other outdated public safety guidelines and limits in use around the world. This approach is based on traditional public health principles that support taking actions to protect public health when sufficient evidence is present. Sufficient scientific evidence and public health concern exist today based on increased risk for cancer, adverse fertility and reproductive outcomes, immune disruption, neurological diseases, increased risk of road collisions and injury-producing events, and impairment of cognition, behaviour, performance, mood status, and disruption of sleep;*

- *Numeric limits recommended here do not yet take into account sensitive populations (EHS, immune-compromised, the fetus, developing children, the elderly, people on medications, etc). Another safety margin is, thus, likely justified further below the numeric limits for EMF exposure recommended here;*

- *The Scientific Panel acknowledges that numeric limits derived here for new biologically-based public exposure standards are still a billion times higher than natural EMF levels at which all life evolved.*

<u>Specific Recommendations for mobile (cell) and cordless phone use</u>

- *The Seletun Scientific Panel recommends that users keep mobile (cell) phones away from head and body;*

- *The Seletun Scientific Panel recommends that users keep mobile (cell) phones and PDAs* switched off if worn or carried in a pocket or holster, or on a belt near the body. *PDA is generic for any type of Personal Digital Assistant or hand-held computer device;*

- *The Panel strongly recommends against the use of mobile (cell) and cordless phones and PDAs by children of any age;*

- *The Panel strongly recommends against the use of mobile (cell) and cordless phones and PDAs by pregnant women;*

- *The Panel recommends that use of mobile (cell) and cordless phones and PDAs be curtailed near children or pregnant women, in keeping with preventative and precautionary strategies. The most vulnerable members of society should have access to public places without fear of harm to health;*

- *Public access to public places and public transportation should be available without undue risk of*

EMF exposure, particularly in enclosed spaces (trains, airplanes, buses, cars, etc) where the exposure is likely to be involuntary;

- *The Panel recommends wired internet access in schools, and strongly recommends that schools do not install wireless internet connections that create pervasive and prolonged EMF exposures for children;*

- *The Panel recommends preservation of existing land-line connections and public telephone networks;*

- *The Panel recommends against the use of cordless phones (DECT phones) and other wireless devices, toys and baby monitors, wireless internet, wireless security systems, and wireless power transmitters in SmartGrid-type connections that may produce unnecessary and potentially harmful EMF exposures;*

- *The Panel recognizes that wired internet access (cable modem, wired Ethernet connections, etc) is available as a substitute;*

- *The Panel recommends use of wired headsets, preferably with hollow-tube segments;*

- *The Panel recommends avoidance of wireless (Bluetooth-type) headsets in general;*

- *The Panel encourages the removal of speakers from headsets on wireless phones and PDAs;*

- *The Panel encourages _auto-off switches' for mobiles (cells) and PDAs that automatically turn off the device when placed in a holster;*

- *The Panel strongly discourages the technology that allows one mobile (cell) phone to act as a repeater for other phones within the general area. This can increase exposures to EMF that are unknown to the person whose phone is ―piggy-backed upon without their knowledge or permission;*

- *The Panel recommends the use of telephone lines (land-lines) or fiber optic cables for SmartGrid type energy conservation infra-structure. Utilities should choose options that do not create new, community-wide exposures from wireless components of SmartGrid-type projects. Future health risks from prolonged or repetitive wireless exposures of SmartGrid-type systems may be avoided by using telephone lines or fiber-optic cable. The Panel endorses energy conservation but not at the risk of exposing hundreds of millions of families in their homes to a new, involuntary source of wireless radiofrequency radiation."*

<u>Ten Key points had been identified:</u>

- *"The global populations are insufficiently protected, thus currently at risk;*

- *Sensitive Populations are extra vulnerable;*

- *Government actions are urgently warranted now, based on evidence of serious disruption to biological systems;*

- *The Burden of Proof for the safety of radiation-emitting technologies should fall on Producers and Providers, not Consumers;*

- *EMF Exposures should be reduced in advance of complete understanding of mechanisms of action;*

- *The current operative measure of Radiation Risk - the specific absorption rate (SAR) - is inadequate, and misguides on safety and health risks;*

- *An international Disease Registry is needed to track Time Trends of the incidence of Illnesses to correlate the illnesses with exposures;*

- *Pre-market health testing and safety demonstration is needed for all radiation-emitting technologies;*
- *Parity is needed for occupational exposure standards, compared to those for the general public;*
- *Persons with Electrohypersensitivity need the classification Functionally Impaired.*
- *The scientists recommend specific exposure limits for different frequency fields, including microwaves, used in wireless communications, and ELF electric fields and magnetic fields."*

Collegium Ramazzini Publication (2010)

The 400 page review of non-thermal EMF effects by the Ramazzini Institute, and sponsored by the International Commission for Electromagnetic Safety, and the National Institute for the Study and Control of Cancer and Environmental Diseases 'Bernardino Ramazzini' in 2010 provided a substantial evidence foundation for the relationship between low-intensity EMF (ELF-EMF and RFR) exposure and potential health risks (13). Taken as a whole, the two-volume report provides a compelling scientific basis on which to take precautionary, prudent public health actions. The EEA relied heavily on the Collegium Ramazzini publication to buttress their Statement on Mobile Phones, when addressing the Council of Europe the following year.

European Environment Agency (2011)

Dr. Jacqueline McGlade, Executive Director of the European Environment Agency provided key guidance to the Council of Europe in her *Statement on Mobile Phones and the Potential Head Cancer Risk for EMF* to the Council of Europe, Paris, February 25th 2011 (14). It read:

> *"The European Parliament[1] has responded to this public concern with a resolution on EMF in 2009 which, among other things, called for lowering exposure to electromagnetic fields and for lower exposure limits that would better protect the public from health hazards. We share these recommendations."*

[1] European Parliament resolution of 2 April 2009 on health concerns associated with electromagnetic fields (2008/2211(INI))

Further, she urged the Council of Europe take interim actions to protect public health, particularly for children, with the following:

> *"The EU Commission and the EEA sees the precautionary principle as central to public policymaking where there is scientific uncertainty and high health, environmental and economic costs in acting, or not acting, when faced with conflicting evidence of potentially serious harm."*
>
> *"This is precisely the situation that characterises EMF at this point in its history. Waiting for high levels of proof before taking action to prevent well known risks can lead to very high health and economic costs, as we have seen with asbestos, leaded petrol and smoking."*

Council of Europe 2011

[1] European Parliament resolution of 2 April 2009 on health concerns associated with electromagnetic fields (2008/2211(INI))

On May 27, 2011 the Standing Committee, acting on behalf of the Parliamentary Assembly of the Council of Europe (PACE), adopted the Resolution 1815 (2011) "The potential dangers of electromagnetic fields and their effect on the environment" (15) based on the Doc. 12608, report of the Committee on the Environment, Agriculture and Local and Regional Affairs, rapporteur: Mr Huss (16). The Parliamentary Assembly of the Council of Europe come from the national parliaments of the Organization's 47 member states and speak for the 800 million Europeans who elected them. The texts adopted by PACE – recommendations, resolutions and opinions – serve as guidelines for the Committee of Ministers, national governments, parliaments and political parties (17).

Recommendations given by the PACE Resolution 1815:

> *"8. In light of the above considerations, the Assembly recommends that the member states of the Council of Europe:*
>
> ***8.1. in general terms:***
>
> *8.1.1. take all reasonable measures to reduce exposure to electromagnetic fields, especially to radio frequencies from mobile phones, and particularly the exposure to children and young people who seem to be most at risk from head tumours;*
>
> *8.1.2. reconsider the scientific basis for the present standards on exposure to electromagnetic fields set by the International Commission on Non-Ionising Radiation Protection, which have serious limitations, and apply ALARA principles, covering both thermal effects and the athermic or biological effects of electromagnetic emissions or radiation;*
>
> *8.1.3. put in place information and awareness-raising campaigns on the risks of potentially harmful long-term biological effects on the environment and on human health, especially targeting children, teenagers and young people of reproductive age;*
>
> *8.1.4. pay particular attention to "electrosensitive" people who suffer from a syndrome of intolerance to electromagnetic fields and introduce special measures to protect them, including the creation of wave-free areas not covered by the wireless network;*
>
> *8.1.5. in order to reduce costs, save energy, and protect the environment and human health, step up research on new types of antenna, mobile phone and DECT-type device, and encourage research to develop telecommunication based on other technologies which are just as efficient but whose effects are less negative on the environment and health;*
>
> ***8.2. concerning the private use of mobile phones, DECT wireless phones, WiFi, WLAN and WIMAX for computers and other wireless devices such as baby monitors:***
>
> *8.2.1. set preventive thresholds for levels of long-term exposure to microwaves in all indoor areas, in accordance with the precautionary principle, not exceeding 0.6 volts per metre, and in the medium term to reduce it to 0.2 volts per metre;*
>
> *8.2.2. undertake appropriate risk-assessment procedures for all new types of device prior to licensing;*

8.2.3. introduce clear labelling indicating the presence of microwaves or electromagnetic fields, the transmitting power or the specific absorption rate (SAR) of the device and any health risks connected with its use;

8.2.4. raise awareness on potential health risks of DECT wireless telephones, baby monitors and other domestic appliances which emit continuous pulse waves, if all electrical equipment is left permanently on standby, and recommend the use of wired, fixed telephones at home or, failing that, models which do not permanently emit pulse waves;

8.3. concerning the protection of children:

8.3.1. develop within different ministries (education, environment and health) targeted information campaigns aimed at teachers, parents and children to alert them to the specific risks of early, ill-considered and prolonged use of mobiles and other devices emitting microwaves;

8.3.2. for children in general, and particularly in schools and classrooms, give preference to wired Internet connections, and strictly regulate the use of mobile phones by schoolchildren on school premises;

8.4. concerning the planning of electric power lines and relay antenna base stations:

8.4.1. introduce town planning measures to keep high-voltage power lines and other electric installations at a safe distance from dwellings;

8.4.2. apply strict safety standards for the health impact of electrical systems in new dwellings;

8.4.3. reduce threshold values for relay antennae in accordance with the ALARA principle and install systems for comprehensive and continuous monitoring of all antennae;

8.4.4. determine the sites of any new GSM, UMTS, WiFi or WIMAX antennae not solely according to the operators' interests but in consultation with local and regional government authorities, local residents and associations of concerned citizens;

8.5. concerning risk assessment and precautions:

8.5.1. make risk assessment more prevention oriented;

8.5.2. improve risk-assessment standards and quality by creating a standard risk scale, making the indication of the risk level mandatory, commissioning several risk hypotheses to be studied and considering compatibility with real-life conditions;

8.5.3. pay heed to and protect "early warning" scientists;

8.5.4. formulate a human-rights-oriented definition of the precautionary and ALARA principles;

8.5.5. increase public funding of independent research, in particular through grants from industry and taxation of products that are the subject of public research studies to evaluate health risks;

8.5.6. create independent commissions for the allocation of public funds;

8.5.7. make the transparency of lobby groups mandatory;

8.5.8. promote pluralist and contradictory debates between all stakeholders, including civil society (Århus Convention)."

European Environment Agency 2011

In October 12 2011, the European Environment Agency (EEA), an agency of the European Union. based in Copenhagen, Denmark, recommends again to take a precautionary approach to policy making in the EMF area (18). The Agency notes:

"The precautionary principle.

Because the evidence on mobile phones and cancer presents a mixed picture, the EEA recommends using the precautionary principle (PP), as recommended in the EU Treaty, to better manage the risk. There is no clear legal definition of the PP so the EEA has produced a working definition:

The precautionary principle provides justification for public policy actions in situations of scientific complexity, uncertainty and ignorance, where there may be a need to avoid, or reduce, potentially serious or irreversible threats to health and the environment, using an appropriate strength of scientific evidence, and taking into account the pros and cons of action and inaction.

The PP requires us to weigh evidence in a different way. This is not new - societies are used to using different strengths of evidence for different reasons, based on the costs of being wrong.
For example, criminals must be found guilty 'beyond all reasonable doubt' before they are convicted; injured people in compensation cases need only show a balance of evidence in order to win compensation for negligence; while doctors only need slight evidence of a serious illness to prescribe treatment. Such precautionary approaches are justified where it is not yet possible to establish causality beyond reasonable doubt.

Implications for policy makers and the mobile phone industry.

Citizens could be better informed about the risks of mobile phone use, as recommended by the EEA in September 2007. There is sufficient evidence of risk to advise people, especially children, not to place the handset against their heads: text messaging, or hands-free kits lead to about ten times lower radiation levels, on average, than when the phone is pressed to the head.

Governments may also wish to label mobile handsets as a 'possible carcinogen', in line with the IARC decision. In addition, more independent research is needed. The cost of these measures is very low, but the potential costs of inaction may be very high."

US Government Accountability Office (2012)

The US Government Accountability Office published a report in 2012 urging the US Federal Communications Commission to revisit the outdated safety standards for the exposures from wireless devices. (19)

The rapid adoption of mobile phones has occurred amidst controversy over whether the technology poses a risk to human health as a result of long-term exposure to RF energy from mobile phone use.

FCC and FDA share regulatory responsibilities for mobile phones. GAO was asked to examine several issues related to mobile phone health effects and regulation. Specifically, this report addresses:

1. *(1) what is known about the health effects of RF energy from mobile phones and what are current research activities,*
2. *(2) how FCC set the RF energy exposure limit for mobile phones, and*
3. *(3) federal agency and industry actions to inform the public about health issues related to mobile phones, among other things.*
4. *GAO reviewed scientific research; interviewed experts in fields such as public health and engineering, officials from federal agencies, and representatives of academic institutions, consumer groups, and the mobile phone industry; reviewed mobile phone testing and certification regulations and guidance; and reviewed relevant federal agency*
websites and mobile phone user manuals.

The Report noted that the FCC's RF energy exposure limit may not reflect the latest research. Redundant and overlapping jurisdiction over the setting of public safety limits is highlighted where the GAO Report notes:

> *"FCC told GAO that it relies on the guidance of federal health and safety agencies when determining the RF energy exposure limit, and to date, none of these agencies have advised FCC to change the limit. However, FCC has not formally asked these agencies for a reassessment. By not formally reassessing it's current limit, FCC cannot ensure it is using a limit that reflects the latest research on RF energy exposure. FCC has also not reassessed it's testing requirements to ensure that they identify the maximum RF energy exposure a user could experience. Some consumers may use mobile phones against the body, which FCC does not currently test, and could result in RF energy exposure higher than the FCC limit." (US GAO, 2012)*

The GAO Report recommends to the FCC that it formally reassess, and, if appropriate, change it's current RF energy exposure limit and mobile phone testing requirements related to likely usage configurations, particularly when phones are held against the body. FCC noted that a draft document that is now under consideration by the FCC has the potential to address GAO's recommendations. (US GAO, 2012)

European Environment Agency: Late Lessons II - Mobile Phone Chapter (2012)

The European Environment Agency (EEA) has Late Lessons from Early Warnings: Science, Precaution, Innovation (20). It includes a new chapter on Mobile Phone Use and Brain Tumor Risk (Hardell et al., 2012 (21). It addresses the early 'lessons' learned about carcinogenicity of EMF hazards from power lines and visual display units or VDUs. ELF-EMF was classified in 2001 by IARC as a 2B Possible Human Carcinogen. It provides a chronology of the publication of studies,

including the Final Interphone Report, the combined Hardell et al. papers (1999-2011) on brain tumor risks, and finally the classification in 2011 by IARC of radiofrequency radiation also to be a Group 2B Possible Human Carcinogen. The paper includes a section on risks to children. It shows that for children who start using a mobile phone in their early teenage years, by the time these children are in the 20-29 age group, they have a 500%+ increased risk of glioma and a 600%+ increased risk of acoustic neuroma when they are young adults. The risks for adults (ipsilateral, 10+ years of mobile phone use are roughly 200% or doubled.

III. EXPERT RESEARCH GROUP AND PHYSICIANS' ADVISORIES (2007 – 2012)

American Academy of Environmental Medicine Statement

In a landmark statement adopted early 2012, the American Academy of Medicine (AAEM) signaled it's opposition to the California Public Utilities Commission proposal to install wireless utility meters in California that create new sources of elevated radiofrequency radiation wherever buildings have electrical meters (22 and Appendix C). The letter stated:

> *"The American Academy of Environmental Medicine opposes the installation of wireless 'smart meters' in homes and schools based on a scientific assessment of the current medical literature (references available on request). Chronic exposure to wireless radiofrequency radiation is a preventable environmental hazard that is sufficiently well-documented to warrant immediate preventative public health action."*

The American Academy of Environmental Medicine was founded in 1965, and is an international association of physicians and other professionals interested in the clinical aspects of humans and their environment. The Academy is interested in expanding the knowledge of interactions between human individuals and their environment, as these may be demonstrated to be reflected in their total health. The AAEM provides research and education in the recognition, treatment and prevention of illnesses induced by exposures to biological and chemical agents encountered in air, food and water. This represents the first national physician's group to look in-depth at wireless health risks; and to advise the public and decision-makers about preventative public health actions that are necessary. The AAEM based its opinion in part on the established scientific evidence, and on the recent classification by the WHO International Agency for Research on Cancer (IARC) that radiofrequency radiation, like ELF-EMF is a Group 2B Possible Human Carcinogen. The rationale for widespread public exposure to a new source of radiofrequency radiation in every home and classroom, after being designated a Possible Human Carcinogen, is clearly unacceptable from a medical and public health standpoint. The full text of the letter is Appendix A.

International Doctors´ Appeal (2012)

In 2002 more than 1000 physicians signed the "Freiburg Appeal" (23). It was translated into many languages. As many as 36,000 people from all over the world support its warning about the dangers of wireless communication. Ten years later, in October 2012 the 'International Doctors´ Appeal 2012' was published (24).

"As physicians and scientists, we hereby call on our colleagues and the wider global community to support us with their signature in our fight for the protection of life. However, we also appeal to the politicians to ensure that the people are protected by the following precautionary measures, which also include fundamental human rights:

- *Protect the inviolability of the home by minimizing radio-frequency exposure levels, which penetrate through the walls of one's own home.*
- *Considerably lower radio-frequency radiation exposures as well as exposure limits to a level that reliably protects humans and nature from adverse biological effects of electromagnetic fields.*
- *Convert devices/transmitters that transmit continuously (e.g. cordless phones, wireless Internetaccess (Wi-Fi), and wireless meters) to technologies that only emit radio-frequency radiation on demand when being used.*
- *Children and adolescents need special protection: Children below the age of 8 should not use cell phones and cordless phones; children and adolescents between the ages 8 and 16 should not use cell phones or only use them in the case of an emergency.*
- *Attach clearly visible warning labels and safety guidelines for lowering the radiation exposure on cell phones and other wireless devices, including instruction manuals. An important reminder: Try not to carry a cell phone right next to your body when it is turned on.*
- *Identify and clearly mark protected zones for electrohypersensitive people; establish public areas without wireless access or coverage, especially on public transport, similar to smoke-free areas for nonsmokers.*
- *Promote the development of communication technologies and electricity use that is more compatible with health. Prefer wired solutions for home use and public facilities. Expand fiberoptic networks as the foundation of a modern, sustainable, and performance-based technology that meets the ever-increasing demand for higher data transmission rates.*
- *Provide government funding for industry-independent research and education that do not dismiss strong scientific and medical findings of potential risks, but rather work to clarify those risks.*

We also call on you as an individual: Prefer wired communication technologies. Inform yourself and pass this information on to your family, neighbors, friends, and politicians. You can make a difference by sharing information and making precautionary choices so that the protection of human health and the environment is not left to and limited by commercial interests."

American Academy of Pediatrics (July 2012)

The American Academy of Pediatrics (AAP), a non-profit professional organization of 60,000 primary care pediatricians, pediatric medical subspecialists, and pediatric surgical specialists in the

United States dedicated to the health, safety and well-being of infants, children, adolescents, and young adults strongly supports the proposal for a formal inquiry into radiation standards for cell phones and other wireless products. The Academy encourages the Federal Communications Commission (FCC) to vote to move forward with it's proposed inquiry into the adequacy of the existing FCC public safety limits (25 and Appendix D).

> *"The FCC has not assessed the standard for cell phone radiation since 1996. According to industry groups, approximately 44 million people had mobile phones when the standard was set; today, there are more than 300 million mobile phones in use in the United States. While the prevalence of wireless phones and other devices has sky-rocketed, the behaviors around cell phone uses have changed as well. The number of mobile phone calls per day, the length of each cell phone call, and the amount of time people use mobile phones has increased, while cell phone and wireless technology has undergone substantial changes. Many more people, especially adolescents and young adults, now use cell phones as their only phone line and they begin using wireless phones at much younger ages."*
>
> *"The AAP believes the inquiry to reassess the radiation standard presents an opportunity to review its impacts on children's health and well-being. In the past, such standards have generally been based on the impact of exposure on an adult male. Children, however, are not little adults and are disproportionately impacted by all environmental exposures, including cell phone radiation. In fact, according to IARC, when used by children, the average RF energy deposition is two times higher in the brain and 10 times higher in the bone marrow of the skull, compared with mobile phone use by adults. While the Academy appreciates that the FCC is considering investigating whether the emission standards should be different for devices primarily used by children, it is essential that any new standard for cell phones or other wireless devices be based on protecting the youngest and most vulnerable populations to ensure they are safeguarded throughout their lifetimes."*
>
> *"Finally, in reviewing the SAR standard, the FCC has the opportunity to highlight the importance of limiting media use among children. The Academy has found potentially negative effects and no known positive effects of media use by children under the age of two, including television, computers, cell phones, and other handheld wireless devices. In addition, studies consistently show that older children and adolescents utilize media at incredibly high rates, which potentially contributes to obesity and other health and developmental risks. In reviewing the SAR limit, the FCC has the opportunity to improve the health of our nation by highlighting the importance of limiting screen time and media use for children and adolescents."*

IV. LOCAL AND NATIONAL COUNTRY ACTIONS (2007 – 2012)

City of Brussels

The order of 1 March 2007 on the protection of the environment against the potentially harmful effects and nuisances caused by non-ionizing radiation, established a new regional framework legislation. Installations emitting electromagnetic radiation in the Brussels-Capital Region need environmental permits to be issued by Brussels Environment (26). The ordinance defines a standard of 3 V/m (also ~ 24 mW/m² ~ 2.4 µW/cm²) is not exceeded by the transmitting mobile phone antennas. Compliance with this standard is applied since 14 March 2009.

"Environmental permit for antennas: The steps of the procedure (27)

1. *Introduction of the permit application*
   The application of the *environment permit is introduced by the operator of the antenna to Brussels Environment includes a technical dossier containing plans from a simulation of the electromagnetic field in a radius of influence of 200 meters from the transmitting antenna.*
   This simulation takes into account the technical characteristics of the antenna and the surrounding environment (presence of buildings ...). It aims to ensure that 25% of the 3 V/m standard (also ~ 24 mW/m² ~ 2.4 µW/cm²) [given as power density = 1.5 V ~ 6 mW/m² ~ 0.6 µW/cm²/m] *is not exceeded in any place accessible to the public.*
2. *Site visit and review of the record*
   A Brussels Environment agent reviews the application and conducts a site visit to see if the simulation is correct and if the environmental situation close to the antenna described in the application file corresponds reality given. If this is the case, the file is submitted to public inquiry.
3. *Public Inquiry*
   The application is submitted to a 15 days public inquiry to notify you and allow you to give your opinion. Public inquiry was announced by red posters usual affixed near the place of the antenna location. Any citizen can go to municipal services concerned to take note of the case.
4. *Decision*
   The environmental permit is granted or refused by Brussels Environment. This license ensures that all measures for safety and protection of the environment and residents are provided."

Principality of Liechtenstein

In 2008 in the Principality of Liechtenstein a new environmental law came into effect including regulations and legal limits for cellular transmitters (28). The complete text for article 31 and 34 is given below. Article 31 defines locations with sensitive use where site specific limits have to be applied. However article 34, paragraph 4 (0.6 V/m limit) had been repealed in 2009 after business associations had initiated a national referendum (29).

Article 31 - Places of Sensitive Use

Regarded as places of sensitive use:

a) rooms in buildings where people stay regularly over a long period;
b) playgrounds and rest places of schools, kindergartens and nursery schools operated by the public;
c) fixed outdoor workplaces where work-related to the same person is shown during more than 800 hours a year. Including, in particular fixed sales stands and Jobs at permanently installed equipment, but not outside areas of restaurants and construction sites;
d) those areas of undeveloped land in construction zones on which uses are permitted by letters a and b.

Article 34 transmitters for cellular and wireless local loops

Site specific limits

1) For transmitters of mobile cellular networks and transmitters for wireless local loops with a total effective radiated power of at least 6 watts, the site specific limits under paragraph 2 and 4 apply. They do not apply for radio relay systems, the wireless network security "Polycom" and other radio networks of security and rescue organizations.
2) The site specific limit for the effective value (rms) of the electric field strength is:
a) for installations transmitting exclusively in the frequency range of 900 MHz: 4.0 V/m (also =

42 mW/m² = 4.2 µW/cm²);
b) for facilities that broadcast exclusively in the frequency range of 1800 MHz or in a higher frequency range: 6.0 V/m (also ~ 100 mW/m² = 10 µW/cm²).;
c) for facilities that broadcast in both frequency ranges specified in letters a and b: 5.0 V/m (also = 66 mW/m² = 6.6 µW/cm²).

3) *Whereas the operative mode and the maximum call and data traffic is at maximum transmission power.*
4) *Holder of a broadcast system are required to reduce the actual electric filed strength to the lowest technically feasible value, using appropriate measures and to accomplish by the end of 2012 an actual electric field strength of 0.6 V/m (also ~ 1 mW/m² ~ 0,1 µW/cm²) on average.*
5) *The Government shall provide further details by ordinance.*

Italy – Autonomous Province of Bolzano - South Tyrol (2009)

In a Decree dated April 29, 2009, the governor of the Autonomous Province Bolzano issued Regulation No. 24 concerning telecommunications infrastructure. In the autonomous province of Bolzano radio- and cellular transmitter sites have to be operated that take health aspects into account (30, 31). In practice e.g. radio transmitters had been aggregated on tall mast sites preferably outside residential areas on mountains. The population exposure from cellular antenna sites is calculated with help of predictive software and the best possible sites are evaluated. Each site has to be approved by a communications commission. The national limit for the sum of all RF sources in Italy is 6 V/m (also ~ 100 mW/m² ~ 10 µW/cm²). In the autonomous province of Bolzano the competent authority - State Agency for Environment - negotiates each cellular site with the relevant operator(s) in order to achieve a site specific exposure of 3 V/m (also ~ 24 mW/m² ~ 2.4 µW/cm²) and lower (32).

Austria – Ministry of Health 2010

In December 2010 the document "Aspects of the current health assessment of mobile communications - Recommendation of the Supreme Health Council" was published (33). Some of the recommendations are listed below.

"... Radio equipment, which leads to a prolonged exposure of people should be set up using a precautionary target value, since long-term effects can not be excluded with sufficient certainty. This target value should be set for high-frequency effects at least a factor of 100 below the limit for the power density of the ÖNORM E 8850 (note by the author: similar to ICNIRP 1998). In addition, legal measures should be taken, that
a) in case that various electromagnetic fields acting simultaneously, all relevant frequencies of different emitters are not to exceed the limits and
b) operators are encouraged to minimize exposure from electromagnetic fields well below the limit values during planning and operation."

,, ... In view of the many pending issues, the rational use of mobile phones should be taken generally, which seeks to have meaningful use and avoid unnecessary exposure. This is especially true for children and adolescents, since they will be predictable more exposed over their lifetime and

the organ-specific exposure through anatomical and developmental differences in certain tissues may be higher than in adults."

Nine specific recommendations were given by the Austrian Supreme Health Council:

1. *"If possible, do not call, when the reception is poor.*
2. *Keep calls short.*
3. *In situations where you can choose between mobile and fixed-line, use the landline.*
4. *Make calls in the car as little as possible.*
5. *With GSM (2 G) phones, wait a little time while connecting, before you run the phone to your head. Exposure by UMTS (3 G) mobile phones is usually much lower. Make sure to set the connection in multi-band-mobiles preferably via UMTS (3 G)*
6. *Use headsets or speakerphones.*
7. *When buying a cell phone mind low SAR values.*
8. *Wear the mobile not directly on the body.*
9. *Send an SMS instead of calling."*

France (2010)

In 2010 in France the Environmental Law some regulations concerning EMF issues had been supplemented (34, 35). Some excerpts are given below:

Article 183

- *Wireless terminals that are intended to be connected with a public telephone network may not be placed on the market without additional equipment, which allows to limit the exposure of the head during communication.*
- *The Higher Audiovisual Council shall ensure that the development of the sector of audiovisual communication goes along with an increased level of protection of the environment and the health of the population.*
- *Any advertising, about what aid whatsoever, with the direct aim to promote the sale, the provision or the use of a mobile phone by children under 14 is prohibited.*
- *The payment or free circulation of goods which contain a radio equipment and their use is specifically designed for children under six may be banned by decree of the Minister of Health, in order to avoid excessive exposure of children.*
- *Individuals who are responsible for the transport of electrical energy have to carry out a regular control of the electromagnetic fields, which are induced by power lines. The result of these measurements is to report annually to the French Agency for Sanitary Safety of environment and labor, which will publish them.*
- *In kindergarten (pre-), in the primary schools and in secondary schools (secondary) the use of a mobile phone is prohibited by a student during the entire lesson and at the designated places given in the house rules.*

Article 184

For any mobile telephone that is offered for sale [in France], the specific absorption rate is legible and in French. It must also provide a recommendation for the use of additional equipment, by means

of which the radio exposure of the head can be limited during the communication, as in the fifth Paragraph of point I of Article 183 of this law provided.

Austria – Austrian Medical Association (2012)

In 2012 the Austrian Medical Association published the "Guideline of the Austrian Medical Association for the diagnosis and treatment of EMF-related health problems and illnesses (EMF syndrome)"(36). The guideline is recommended to doctors of all disciplines in Austria. The guideline says in part:

"There has been a sharp rise in unspecific, often stress-associated health problems that increasingly present physicians with the challenge of complex differential diagnosis. A cause that has been accorded little attention so far is increasing electrosmog exposure at home, at work and during leisure activities, occurring in addition to chronic stress in personal and working life. It correlates with an overall situation of chronic stress that can lead to burnout.

How can physicians respond to this development?

The Austrian Medical Association has developed a guideline for differential diagnosis and potential treatment of unspecific stress-related health problems associated with electrosmog. Its core element is a patient questionnaire consisting of a general assessment of stress symptoms and a specific assessment of electrosmog exposure. The guideline is intended as an aid in diagnosing and treating EMF-related health problems."

Key elements of the guideline are:

1. *History of health problems and EMF exposure*
2. *Examination and findings*
3. *Measurement of EMF exposure*
4. *Prevention or reduction of EMF exposure*
5. *Diagnosis*
6. *Treatment*

Russian National Committee on Non-Ionizing Radiation (2011 and 2012)

On March 3, 2011 the Russian National Commitee on Non-Ionizing Radiation Protection approved the "Resolution: Electromagnetic Fields from Mobile Phones: Health Effects on Children and Teenagers" (37 and Appendix E). Parts of the resolution are given below.

"The Resolution evolved from scientific statements adopted by RNCNIRP in 2001, 2004, 2007, 2008 and 2009, taking into account contemporary views and actual scientific data. The Resolution represents a viewpoint of the professional scientific community and is meant for public dissemination, for the consumers of the mobile telecommunications services, as well as for the legislative and executive authorities who develop and implement health protection, environmental, communication, scientific and safety policies."

In 2012, the RCNIRP issued an update to this Resolution, calling on all countries to halt the use of wireless technologies in the school classrooms, and to move quickly to replace wireless with wired internet and teaching technologies (38 and Appendix F).

V. INTERNATIONAL HEALTH AGENCY ACTION

WHO International Agency for Research On Cancer – Formal Classification (2011)

On May 31, 2011 the WHO/International Agency for Research on Cancer (IARC) classified radiofrequency electromagnetic fields as possibly carcinogenic to humans (Group 2B), based on an increased risk for glioma, a malignant type of brain cancer, associated with wireless phone use (39, 40).

A group of 30 researchers, scientists and medical doctors were invited to participate in an assessment of the scientific literature on radiofrequency radiation carcinogenicity in Lyon, France. Under the auspices of IARC, this IARC Monograph Working Group on RFR conducted a comprehensive scientific assessment of RF studies and determined:

> *"In view of the limited evidence in humans and in experimental animals, the Working Group classified RF- EMF as "possibly carcinogenic to humans" (Group 2B). This evaluation was supported by a large majority of Working Group members."*
>
> *"The Working Group concluded that the (Interphone Final Report) findings could not be dismissed as reflecting bias alone, and that a causal interpretation between mobile phone RF-EMF exposure and glioma is possible. A similar conclusion was drawn from these two studies for acoustic neuroma, although the case numbers were substantially smaller than for glioma."*

It is important to recognize that the IARC RF Working Group did not find the evidence insufficient to classify (Group 3) or not a carcinogen (Group 4). Both of these possible outcomes to the scientific assessment could have rendered a substantially weaker conclusion. Where there has been the necessity of a virtual scientific paradigm shift to accommodate ANY consideration of both ELF-EMF and RFR to the status where legitimate scientific attention is achieved is a notable achievement. There is a very high bar set to show that non-chemical carcinogens warrant IARC carcinogenicity evaluation - it greatly exceeds that necessary for chemicals and other toxins.

The WHO press release No° 208 states

> *"The IARC Monograph Working Group discussed the possibility that these exposures might induce long-term health effects, in particular an increased risk for cancer. This has relevance for public health, particularly for users of mobile phones, as the number of users is large and growing,*

particularly among young adults and children."

The corresponding monograph has not been published as of October 2012. On request, IARC clarified the frequency range covered by the monograph (41).

> *"The IARC Monographs classification of Radiofrequency Electromagnetic Fields (RF-EMF) covers the entire radiofrequency segment of the electromagnetic spectrum (30 kHz-300 GHz). Within this spectrum, the electromagnetic fields around (or the radiation emitted by) mobile telephones represent the most intense and most wide-spread exposure situation, for which a small increase in risk for glioma and acoustic neuroma has been found in the group of 'heavy users'. Other devices that emit the same type of RF radiation - base-station antennas, radio/tv antennas, WiFi stations, smart meters - fall under the same evaluation. However, because the exposure levels for many of these other devices and exposure situations are so much lower than the exposure to someone who has a functioning cell phone against her/his ear, the risk will be considerably less (although the hazard still exists)."*

VI. CONCLUSIONS

1) The European Environmental Agency (2007) concludes that: "(*T)here are many examples of the failure to use the precautionary principle in the past, which have resulted in serious and often irreversible damage to health and environments. Appropriate, precautionary and proportionate actions taken now to avoid plausible and potentially serious threats to health from EMF are likely to be seen as prudent and wise from future perspectives. We must remember that precaution is one of the principles of EU environmental policy*."

2) The European Parliament, the Council of Europe and various governmental agencies in Europe, Scandinavia, Israel, North America, India and Asia have called for better warnings, to reduce or eliminate exposures from wireless devices, to label devices with health warnings, to develop new, lower public safety standards, to protect sensitive subgroups (children, people who are sensitized to EMF and wireless radiation already (electrosensitivity), and to inform and protect pregnant women and their young from unnecessary exposures. The countries of France, Italy, Belgium, the Principality of Liechtenstein, Switzerland, Austria, the United Kingdom, and others have led in proposing new restrictions on wireless exposures, based on scientific and public health reviews of the evidence. The US Government Accountability Office has called for review of American (FCC) safety limits for wireless devices.

3) Physicians and health advisory groups around the world have called for prudent public health actions that include reducing or eliminating ELF and RFR exposures, especially for pregnant women and for the developing fetus, and children, and particularly where other options are available (in the case of wireless exposures in particular). Some of these groups include the Austrian Ministry of Health, the Russian National Committee on Non-Ionizing Radiation, the American Academy of Environmental Medicine, the American Academy of Pediatrics, the British Chief Medical Officer, and many more governmental agencies across Europe, Scandinavia, North America, India and Asia.

4) Physicians and researchers who have published in-depth reviews on the science and public health policy implications of ELF and RFR risks to health include Pathophysiology, Vol 16 (2,3); 2009; the two-volume *Non Thermal effects and Mechanisms of interaction between Electromagnetic Fields and Living Matter*. eds Giuliani L and Soffritti, M, ICEMS, Ramazzini Institute, Bologna, Italy., 2010; the World Health Organization INTERPHONE Final Report, 2010; and the WHO International Agency for Research on Cancer RFR Monograph (Baan et al, 2011) designating RFR

as a Group 2B Possible Human Carcinogen.

5) Overall, these provide support for warnings and advice to consumers and the public that the body of evidence for bioeffects from daily exposure levels of ELF and RFR can reasonably be presumed to result in adverse health impacts with chronic exposure. The studies on which these warnings rely establish that bioeffects from exposure to ELF and RFR are established, not speculative or weak. Further, they establish that existing ICNIRP and FCC public safety limits are inadequate to protect public health; and underscore the need for new, biologically-based public exposure standards.

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VIII. APPENDICES

APPENDIX A Full Text of European Parliament Statement - 2008

"The European Parliament ,

– having regard to the Communication from the Commission to the Council, the European Parliament and the European Economic and Social Committee on the mid-term review of the European Environment and Health Action Plan 2004-2010 (COM(2007)0314),

– having regard to its resolution of 23 February 2005 on the European Environment and Health Action Plan 2004-2010(1) ,

– having regard to the World Health Organisation (WHO) report of 27 July 2007 entitled 'Principles for evaluating health risks in children associated with exposure to chemicals',

– having regard to Articles 152 and 174 of the EC Treaty targeting a high level of protection for human health and the environment,

– having regard to Decision No 1350/2007/EC of the European Parliament and of the Council of 23 October 2007 establishing a second programme of Community action in the field of health (2008-13)(2) ,

– having regard to Rule 45 of its Rules of Procedure,

– having regard to the report of the Committee on the Environment, Public Health and Food Safety (A6-0260/2008),

A. noting with interest the fact that, since 2003, the EU has based its health-protection policy on closer cooperation between the health, environment and research sectors, so that it may be hoped that a coherent and integrated European environmental health strategy will eventually be introduced,

B. whereas the courses of action currently being followed by the EU as part of its first environment and health action plan (2004-2010) (COM(2004)0416) - namely, the preparation of indicators, the development of integrated monitoring, the collection and evaluation of relevant data as well as an increase in the volume of research - will allow greater insight into the interactions between sources of pollution and health effects but are known to be inadequate as a means of reducing the growing number of diseases related to environmental factors,

C. whereas it is virtually impossible to establish a mid-term assessment of the aforementioned action plan, since the latter pursues no clear, quantified objective and the total budget allocated to it is difficult to determine and definitely insufficient for its efficient promotion,

D. whereas the main objective of the 2008-2013 health programme is to act upon the factors which traditionally determine health (diet, smoking, alcohol consumption and the use of drugs); whereas this 2004-2010 action plan should focus on certain new health challenges and in addition address the determining environmental factors which affect human health, such as indoor and outdoor air quality, electromagnetic waves, nanoparticles and chemicals which are a cause for serious concern (substances classed as carcinogenic, mutagenic or toxic to reproduction [CMR], endocrine disruptors), as well as risks to health arising from climate change,

E. whereas respiratory illnesses rank second as a cause of death and in terms of incidence, prevalence and cost within the EU, whereas they constitute the main cause of death amongst children under the age of five

and whereas such diseases are continuing to progress on account of - in particular - indoor and outdoor air pollution,

F. whereas atmospheric pollution caused, in particular, by fine particles and ground-level ozone, is a significant threat to human health which is affecting the proper development of children and reducing life expectancy in the EU(3) ,

G. whereas, with reference to the issue of urban environmental health, particularly the quality of indoor air, the Community - in accordance with the subsidiarity and proportionality principles - should do more to combat domestic pollution, since Europeans spend on average 90% of their time inside buildings,

H. whereas at the 2004 and 2007 WHO ministerial conferences on health and the environment, attention was drawn to the links between the complex combined influence of chemical pollutants and a number of chronic illnesses and disorders (affecting children in particular); whereas those concerns are also expressed in official documents issued in connection with the United Nations Environment Programme (UNEP) and by the Intergovernmental Forum on Chemical Safety (IFCS),

I. whereas there is increasing scientific evidence that certain cancers, such as cancer of the bladder, bone cancer, lung cancer, skin cancer, breast cancer and others are caused not only by the effects of chemical substances, radiation and airborne particles but also by other environmental factors,

J. whereas these problematic developments in environmental health have been accompanied in recent years by the emergence of new diseases or syndromes, such as multiple chemical hypersensibility, dental-amalgam syndrome, hypersensitivity to electromagnetic radiation, sick-building syndrome and attention-deficit and hyperactivity syndrome in children,

K. whereas the precautionary principle has been enshrined in the Treaty since 1992 and whereas the European Court of Justice has repeatedly specified the substance and the scope of that principle in Community law, which constitutes one of the cornerstones of the protection policy pursued by the Community in the field of health and the environment(4) ,

L. having regard to the highly restrictive - if not to say impracticable - nature of the criteria adopted by the Commission in its 2 February 2000 Communication on the precautionary principle (COM(2000)0001),

M. having regard to the importance of human biological monitoring as a tool for assessing the European population's degree of exposure to the effects of pollution and the determination (repeatedly expressed by Parliament in Paragraph 3 of its aforementioned resolution of 23 February 2005 and in the conclusions issued at the end of the 20 December 2007 Council meeting of Environment Ministers) to expedite the introduction of a biological-monitoring programme at EU level,

N. whereas it is readily acknowledged that climate change can play an important role in increasing the severity and incidence of certain diseases and in particular that heat-wave frequency, flooding and wildfires as the most frequent natural disasters in the EU can lead to additional diseases, poor sanitation and deaths, while at the same time recognising the beneficial effects on health of measures to alleviate climate change,

O. whereas climate change will have significant effects on human health, inter alia by encouraging the development of certain infectious and parasitic diseases mainly because of changes in temperature and humidity and their impact on ecosystems, animals, plants, insects, parasites, protozoa, microbes and viruses,

P. whereas Directive 2000/60/EC of the European Parliament and of the Council of 23 October 2000 establishing a framework for Community action in the field of water policy(5) and its daughter directives contain clear provisions concerning the preservation and restoration of healthy waters,

Q. whereas environmental medicine is a new medical discipline based on university teaching which is still too fragmentary and unevenly distributed amongst the Member States and which thus deserves to be supported and promoted within the EU,

R. whereas the number of persons suffering as a result of environmental factors is increasing and epidemiologies should be developed in order to obtain a full picture of diseases which are caused wholly or in part by environmental factors,

1. Acknowledges the efforts made by the Commission since the action plan was launched in 2004, particularly in terms of improving the chain of information concerning health and the environment, integrating and expanding European research in this area and cooperating with specialist international organisations such as the WHO;

2. Considers, however, that such an action plan is bound to fail at least in part, since it is designed solely to accompany existing Community policies, it is not based upon a preventive policy intended to reduce illnesses linked to environmental factors, and it pursues no clear, quantified objective;

3. Draws the Commission's attention to the fact that a programme has already been carried out under the aegis of the WHO as part of which the WHO Member States established their own national and local environmental health action plans comprising specific objectives and implementation plans; recommends to the Commission therefore that it review this WHO programme as a possible model which could also serve as a useful example to the Union in the future;

4. Deeply regrets the fact that the Commission (and in particular its Research DG) has not provided sufficient funding for human biological monitoring in 2008 to enable it (as it had promised Parliament and the Member States) to introduce a consistent approach to biological monitoring within the EU;

5. Calls upon the Commission to respond by 2010 to two essential objectives which the Commission set itself in 2004 and to establish and carry out a practicable communication strategy for these objectives, namely to make members of the general public aware of environmental pollution and the impact thereof on their health, and to reconsider and adapt European risk-reduction policy;

6. Strongly recommends that the Commission and Member States meet their obligations as regards implementation of Community legislation;

7. Stresses that, when it comes to assessing the impact of environmental factors on health, consideration should be given first and foremost to vulnerable groups such as pregnant women, newborn babies, children and the elderly;

8. Calls for special attention to be given to vulnerable groups, who are the most susceptible to pollutants, by introducing measures to reduce exposure to indoor environmental contaminants in healthcare facilities and schools through the adoption of sound indoor air quality management practices;

9. Urges the Commission, when drafting proposals for the revision of existing laws, not to weaken those laws under pressure from lobbies or regional or international organisations;

10. Points that the EU needs to apply a continuous dynamic and flexible approach to the Action Plan; considers that it is therefore of paramount importance to acquire specific expertise on the subject of environmental health, to be based on transparency and on a multidisciplinary and adversarial approach which would thus enable the general public's distrust of official agencies and committees of experts to be countered; points to the importance of improving the training of health experts by means, in particular, of exchanges of best practice at Community level;

11. Points out that in recent years there have been genuine advances in environmental policy in the form of (for example) a reduction in air pollution, an improvement in water quality, the collection and recycling of waste, the monitoring of chemicals and a ban on leaded petrol, but notes at the same time that EU policy still lacks a comprehensive preventive strategy and fails to apply the precautionary principle;

12. Calls, therefore, on the Commission to revise the criteria laid down in its aforementioned Communication as regards recourse to the precautionary principle pursuant to European Court of Justice case-law, in order to ensure that an action and security principle based on the adoption of provisional and proportionate measures lies at the heart of Community health and environment policies;

13. Considers that shifting the burden of proof onto producers or importers and requiring them to demonstrate that a product is harmless would make it possible for a policy based on prevention to be promoted (as provided for in European Parliament and Council Regulation (EC) No 1907/2006 of 18 December 2006 concerning the registration, evaluation, authorisation and restriction of chemicals (REACH) and establishing a European Chemicals Agency(6)), and encourages the Commission to extend that obligation to Community legislation concerning all products; considers that any increase in animal testing under the Action Plan should be avoided and full regard should be paid to the development and use of alternative methods;

14. Calls once again upon the Commission to come forward as soon as possible with concrete measures on indoor air quality which would ensure a high level of protection of health and safety indoors to be established, in particular when revising Council Directive 89/106/EEC of 21 December 1988 on the approximation of laws, regulations and administrative provisions of the Member States relating to construction products(7) , and to propose measures to increase the energy efficiency of buildings and the safety and the harmlessness of chemical compounds used in equipment and furnishings;

15. Recommends that, in order to reduce damaging effects of the environment on health, the Commission should call upon Member States, by means of tax concessions and/or other economic incentives, to interest market operators in improving the quality of indoor air and reducing exposure to electromagnetic radiation in their buildings, branch establishments and offices;

16. Recommends that the Commission draft appropriate minimum requirements to guarantee the quality of indoor air in buildings to be newly built;

17. Recommends that, in awarding individual European Union support, the Commission bear in mind its impact on the quality of indoor air, exposure to electromagnetic radiation and the health of particularly endangered sections of the population in the projects concerned in a similar way to that in which attention is devoted to environmental protection criteria;

18. Calls for environmental quality standards for priority substances in water to be laid down in accordance with the latest scientific knowledge and regularly brought into line with current scientific thinking;

19. Points out that certain Member States have successfully introduced mobile analysis laboratories (or "green ambulances") to enable habitat pollution in public and private places to be diagnosed swiftly and reliably; considers that the Commission could promote such a practice within the Member States which have not yet acquired such a means of direct intervention at a polluted site;

20. Is concerned about the lack of specific legal provisions to ensure the safety of consumer products containing nanoparticles and the relaxed attitude of the Commission with regard to the need to review the regulatory framework for the use of nanoparticles in consumer products in light of the increasing number of consumer products containing nanoparticles being put on the market;

21. Is greatly concerned at the Bio-Initiative international report(8) concerning electromagnetic fields, which summarises over 1500 studies on that topic and which points in its conclusions to the health risks posed by emissions from mobile-telephony devices such as mobile telephones, UMTS, Wifi, Wimax and Bluetooth, and also DECT landline telephones;

22. Notes that the limits on exposure to electromagnetic fields which have been set for the general public are obsolete, since they have not been adjusted in the wake of Council Recommendation 1999/519/EC of 12 July 1999 on the limitation of exposure of the general public to electromagnetic fields (0Hz to 30 GHz)(9) , obviously take no account of developments in information and communication technologies, of the recommendations issued by the European Environment Agency or of the stricter emission standards adopted, for example, by Belgium, Italy and Austria, and do not address the issue of vulnerable groups, such as pregnant women, newborn babies and children;

23. Calls, consequently, upon the Council to amend its Recommendation 1999/519/EC in order to take into account the Member States' best practices and thus to set stricter exposure limits for all equipment which emits electromagnetic waves in the frequencies between 0.1 MHz and 300 GHz;

24. Takes a very serious view of the multiple health risks created by global warming on EU territory and calls for enhanced cooperation between the WHO, the Member States" monitoring authorities, the Commission and the European Centre for Disease Prevention and Control in order to bolster the early-warning system and thus to curb the harmful effects which climate change has on health;

25. Highlights that this Action Plan would benefit from being extended to cover negative impacts of climate change on human health by elaborating on effective adaptation measures necessary at Community level, such as:

- *systematic public education programmes and awareness-raising;*
- *integration of climate change adaptation measures into public health strategies and programmes, such as communicable and non-communicable diseases, workers' health and animal diseases hazardous to health;*
- *proper surveillance aiming at the early detection of disease outbreaks;*
- *health-related early warning systems and response;*
- *coordination of existing environmental data monitoring networks with disease outbreak networks;*

26. Calls on Member States and the Commission to respond adequately to the new threats posed by climate change such as the increased presence of emerging viruses and undetected pathogens and therefore implement new existing pathogen reduction technologies that reduce known and undetected viruses and other pathogens transmitted by blood;

27. Regrets that the current cost benefit impact assessment of the '20 20 by 2020 Europe's Climate Change Opportunity' (COM(2008)0030) only considers the health benefits of reduced air pollution at a 20% reduction of greenhouse gas emissions by 2020; calls on the Commission to ensure that the (ancillary) co-benefits to health of various levels of ambition, in line with the International Panel on Climate Change recommendations of domestic 25% to 40% as well as possibly 50% or more of greenhouse gas emission reduction by 2020, are urgently investigated and modelled into an impact assessment by the Commission;

28. Calls on the Commission to pay attention to the serious problem of mental health, considering the number of suicides in the EU, and to devote more resources to the development of adequate prevention strategies and therapies;

29. Reiterates that the Commission and the Member States should support the WHO Children's Environment and Health Action Plan in Europe, to encourage it both through EU and bilateral development policy, and to encourage similar processes outside the WHO Europe Region;

30. Calls on the Commission to reincorporate into its second action plan the initiative SCALE (Science, Children, Awareness, Legal instruments, Evaluation) relating to the reduction of exposure to pollution, as set out in the European Environment and Health Strategy (COM(2003)0338);

31. Urges the Commission to work on and provide instruments that would foster the development and promotion of innovative solutions, as stressed within the Lisbon agenda framework, in order to minimise major health risks from environmental stressors;

32. Urges the Council to take a decision without delay on the proposal for a regulation establishing the Union Solidarity Fund, as Parliament adopted its position as long ago as 18 May 2006(10) ; considers that the new regulation, which, together with other measures, will lower thresholds for the entry into force of the Union Solidarity Fund, will make it possible to alleviate more effectively, flexibly and quickly damage caused by natural or man-made disasters; stresses that such a financial instrument is very important, particularly because it is assumed that natural disasters will occur more frequently in future, partly on account of climate change;

33. Recommends, as SMEs are of decisive economic importance in Europe, that the Commission should provide technical support to SMEs to make it possible, and help them, to comply with binding environmental health regulations and encourage them to make other changes which are positive from the point of view of environmental health and affect the operation of enterprises;

34. Advises the Commission to envisage (by 2010 and under the "second cycle" of the health and environment action plan) refocusing its initiatives on vulnerable populations and to devise new methods of risk assessment, taking into account the fundamental fact that children, pregnant women and older people are particularly vulnerable;

35. Urges the Commission and Member States therefore to acknowledge the advantages of the prevention and precautionary principles and to develop and implement tools enabling potential environmental and health threats to be anticipated and countered; recommends that the Commission cost the 'second cycle' of this action plan and make provision for appropriate funding covering a larger number of practical measures to reduce environmental impact on health and to implement prevention and precautionary measures;

36. Instructs its President to forward this resolution to the Council, the Commission, the governments and parliaments of the Member States and the WHO.

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(2) OJ L 301, 20.11.2007, p. 3.

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(5) OJ L 327, 22.12.2000, p. 1.

(6) OJ L 396, 30.12.2006, p. 1; corrected version in OJ L 136, 29.5.2007, p. 3.

(7) OJ L 40, 11.2.1989, p. 12.

(8) Published by a group of independent scientists on 31 August 2007. For details, see: www.bioinitiative.org.

(9) OJ L 199, 30.7.1999, p. 59.

(10) OJ C 297 E, 7.12.2006, p. 331.

APPENDIX B Full Text of European Parliament Resolution – 2009

European Parliament 2009

On April 2, 2009, the European Parliament adopted the "European Parliament resolution of 2 April 2009 on health concerns associated with electromagnetic fields (2008/2211(INI))" (10). The Document was based on the "Report on health concerns associated with electromagnetic fields", Rapporteur: Frederique Ries (11) Committee on the Environment, Public Health and Food Safety.

A. whereas electromagnetic fields (EMFs) exist in nature and have consequently always been present on earth; whereas, however, in recent decades, environmental exposure to man-made sources of EMFs has risen constantly, driven by demand for electricity, increasingly more specialised wireless technologies, and changes in the organisation of society; whereas the end effect is that every individual is now being exposed to a complex mixture of electric and magnetic fields of different frequencies, both at home and at work,

B. whereas wireless technology (mobile phones, Wi-Fi/WiMAX, Bluetooth, DECT landline telephones) emits EMFs that may have adverse effects on human health,

C. whereas most European citizens, especially young people aged from 10 to 20, use a mobile phone, an object serving a practical purpose and as a fashion accessory, and whereas there are continuing uncertainties about the possible health risks, particularly to young people whose brains are still developing,

D. whereas the dispute within the scientific community regarding the potential health risks arising from EMFs has intensified since 12 July 1999, when exposure limits for fields in the 0 Hz to 300 GHz range were laid down in Recommendation 1999/519/EC,

E. whereas the fact that the scientific community has reached no definite conclusions has not prevented some national or regional governments, in China, Switzerland, and Russia, as well as in at least nine EU Member States, from setting what are termed "preventive" exposure limits, that is to say, lower than those advocated by the Commission and its independent scientific committee, the Scientific Committee on Emerging and Newly Identified Health Risks(7) ,

F. whereas actions to limit the exposure of the general public to EMFs should be balanced against improvements to quality of life, in terms of safety and security, brought about by devices transmitting EMFs,

G. whereas among the scientific projects arousing both interest and controversy is the Interphone epidemiological study, financed by an EU contribution of EUR 3 800 000, primarily under the Fifth RTD Framework Programme(8) , the findings of which have been awaited since 2006,

H. whereas, however, there are some points that appear to be the subject of general agreement, in particular the idea that reactions to microwave exposure vary from one person to another, the need, as a matter of priority, to conduct exposure tests under actual conditions in order to assess the non-thermal effects associated with radio-frequency (RF) fields, and the fact that children exposed to EMFs are especially vulnerable(9) ,

I. whereas the EU has laid down exposure limits to protect workers from the effects of EMFs; whereas on the basis of the precautionary principle such measures should also be taken for the sections of population concerned, such as residents and consumers,

J. whereas the Special Eurobarometer report on Electromagnetic Fields (No 272a of June 2007) indicates that the majority of citizens do not feel that the public authorities inform them adequately on measures to protect them from EMFs,

K. whereas it is necessary to continue investigations into intermediate and very low frequencies so that conclusions can be drawn as to their effects on health,

L. whereas the use of Magnetic Resonance Imaging (MRI) must not be threatened by Directive 2004/40/EC as MRI technology is at the cutting edge of research, diagnosis and treatment of life-threatening diseases for patients in Europe,

M. whereas the MRI safety standard IEC/EN 60601-2-33 establishes limit values for EMFs which have been set so that any danger to patients and workers is excluded.

1. Urges the Commission to review the scientific basis and adequacy of the EMF limits as laid down in Recommendation 1999/519/EC and report to the Parliament; calls for the review to be undertaken by the Scientific Committee on Emerging and Newly Identified Health Risks;

2. Calls for particular consideration of biological effects when assessing the potential health impact of electromagnetic radiation, especially given that some studies have found the most harmful effects at lowest levels; calls for active research to address potential health problems by developing solutions that negate or reduce the pulsating and amplitude modulation of the frequencies used for transmission;

3. Maintains that as well as, or as an alternative to, amending European EMFs limits, the Commission, working in coordination with experts from Member States and the industries concerned (electricity companies, telephone operators and manufacturers of electrical appliances including mobile phones), should draw up a guide to available technology options serving to reduce exposure to EMFs;

4. Notes that industry stakeholders as well as relevant infrastructure managers and competent authorities can already influence certain factors, for example setting provisions with regards to the distance between a given site and the transmitters, the height of the site in relation to the height of the base station, or the direction of a transmitting antenna in relation to living environments, and, indeed, should obviously do so in order to reassure, and afford better protection to, the people living close to such facilities; calls for optimal placement of masts and transmitters and further calls for the sharing of masts and transmitters placed in this way by providers so as to limit the proliferation of poorly positioned masts and transmitters; calls on the Commission and Member States to draw up appropriate guidance;

5. Invites the Member States and local and regional authorities to create a one-stop shop for authorisation to install antennas and repeaters, and to include among their urban development plans a regional antenna plan

6. Urges the authorities responsible for authorising the siting of mobile telephony antennas to reach agreement, jointly with the operators in that sector, on the sharing of infrastructure, in order to reduce the volume thereof and the exposure of the public to EMFs;

7. Acknowledges the efforts of mobile communications and other EMF-transmitting wireless technologies to avoid damaging the environment, and in particular to address climate change;

8. Considers that, given the increasing numbers of legal actions and measures by public authorities having the effect of a moratorium on the installation of new EMF-transmitting equipment, it is in the general interest to encourage solutions based on negotiations involving industry stakeholders, public

authorities, military authorities and residents" associations to determine the criteria for setting up new GSM antennas or high-voltage power lines, and to ensure at least that schools, crèches, retirement homes, and health care institutions are kept clear, within a specific distance determined by scientific criteria, of facilities of this type;

9. Calls on the Member States to make available to the public, jointly with the operators in the sector, maps showing exposure to high-voltage power lines, radio frequencies and microwaves, and especially those generated by telecommunications masts, radio repeaters and telephone antennas. Calls for that information to be displayed on an internet page so that it can easily be consulted by the public, and for it to be disseminated in the media;

10. Proposes that the Commission consider the possibility of using funding from the Trans-European Energy Networks to investigate the effects of EMFs at very low frequencies, and particularly in electrical power lines,

11. Calls on the Commission, during the 2009-2014 parliamentary term, to launch an ambitious programme to gauge the electromagnetic compatibility between waves created artificially and those emitted naturally by the human body with a view to determining whether microwaves might ultimately have undesirable consequences for human health;

12. Calls on the Commission to present a yearly report on the level of electromagnetic radiation in the EU, its sources, and actions taken in the EU to better protect human health and the environment;

13. Calls on the Commission to find a solution enabling Directive 2004/40/EC to be implemented more rapidly and thus ensure that workers are properly protected against EMFs, just as they are already protected under two other Community acts against noise(10) and vibration(11) and to introduce a derogation for MRI under Article 1 of that Directive.

14. Deplores the fact that, as a result of repeated postponements since 2006, the findings of the Interphone study have yet to be published, the purpose of this international epidemiological study being to establish whether there is a link between use of mobile phones and certain types of cancer, including brain, auditory nerve, and parotid gland tumours;

15. Draws attention in this context to the appeal for caution from the coordinator of the Interphone study, Elisabeth Cardis, who, in the light of existing knowledge, recommends, as far as children are concerned, that mobile phones should not be used beyond reasonable limits and that landlines should be preferred;

16. Believes in any event that it is up to the Commission, which has an important contribution to the financing of this global study, to ask those in charge of the project why no definitive findings have been published and, should it receive an answer, to inform Parliament and the Member States without delay;

17. Also suggests to the Commission, to make for efficiency in policy and budget terms, that the Community funding earmarked for studies on EMFs be partly switched to finance a wide-ranging awareness campaign to familiarise young Europeans with good mobile phone techniques, such as the use of hands-free kits, keeping calls short, switching off phones when not in use (such as when in classes) and using phones in areas that have good reception;

18. Considers that such awareness-raising campaigns should also familiarise young Europeans with the health risks associated with household devices and the importance of switching off devices rather than leaving them on stand-by;

19. Calls on the Commission and Member States to increase research and development funding for the evaluation of potential long-term adverse effects of mobile telephony radio frequencies; calls also for an increase in public calls for proposals for investigation of the harmful effects of multiple exposure to different sources of EMFs, particularly where children are concerned;

20. Proposes that the European Group on Ethics in Science and New Technologies be given the additional task of assessing scientific integrity in order to help the Commission forestall possible cases of risk, conflict of interests, or even fraud that might arise now that competition for researchers has become keener;

21. Calls on the Commission, in recognition of the public concern in many Member States, to work with all relevant stakeholders, such as national experts, non-governmental organisations and industrial sectors, to improve the availability of, and access to, up-to-date information understandable to non-specialists on wireless technology and protection standards;

22. Calls on the International Commission on Non-Ionising Radiation Protection and the World Health Organisation (WHO) to be more transparent and open to dialogue with all stakeholders in standard setting;

23. Condemns certain particularly aggressive marketing campaigns by telephone operators in the run-up to Christmas and other special occasions, including for example the sale of mobile phones designed solely for children or free call time packages aimed at teenagers;

24. Proposes that the EU's indoor air quality policy should encompass the study of "wireless" domestic appliances, which, like Wi-Fi for Internet access and digital enhanced cordless telecommunications (DECT) telephones, have been widely adopted in recent years in public places and in the home, with the result that citizens are being continuously exposed to microwave emissions;

25. Calls, given its constant concern to improve consumer information, for the technical standards of the European Committee for Electrotechnical Standardisation to be amended with a view to imposing labelling requirements whereby the transmitting power would have to be specified and every wireless-operated device accompanied by an indication that it emitted microwaves;

26. Calls on the Council and Commission, in coordination with the Member States and the Committee of the Regions, to encourage the introduction of a single standard designed to ensure that local residents are subjected to as low a degree of exposure as possible when high-voltage grids are extended;

27. Is greatly concerned about the fact that insurance companies are tending to exclude coverage for the risks associated with EMFs from the scope of liability insurance policies, the implication clearly being that European insurers are already enforcing their version of the precautionary principle;

28. Calls on Member States to follow the example of Sweden and to recognise persons that suffer from electrohypersensitivity as being disabled so as to grant them adequate protection as well as equal opportunities;

29. Instructs its President to forward this resolution to the Council, the Commission, the governments and parliaments of the Member States, the Committee of the Regions, and the WHO.

(1) OJ L 199, 30.7.1999, p. 59.
(2) OJ L 159, 30.4.2004, p. 1.

(3) OJ L 91, 7.4.1999, p. 10.

(4) OJ L 374, 27.12.2006, p. 10.

(5) Texts adopted, P6_TA(2008)0410.

(6) OJ C 175, 21.6.1999, p. 129.

(7) Opinion of 21 March 2007 adopted at the 16th plenary meeting of the Committee.

(8) Quality of life programme, contract No QLK4-1999-01563.

(9) March 2001 STOA study on "The physiological and environmental effects of non-ionising EMR", PE297.574.

(10) Directive 2003/10/EC of the European Parliament and of the Council of 6 February 2003 on the minimum health and safety requirements regarding the exposure of workers to the risks arising from physical agents (noise) (OJ L 42, 15.2.2003, p. 38).

(11) Directive 2002/44/EC of the European Parliament and of the Council of 25 June 2002 on the minimum health and safety requirements regarding the exposure of workers to the risks arising from physical agents (vibration) (OJ L 177, 6.7.2002, p. 13).

APPENDIX C American Academy of Environmental Medicine

American Academy of Environmental Medicine

6505 E Central • Ste 296 • Wichita, KS 67206
Tel: (316) 684-5500 • Fax: (316) 684-5709
www.aaemonline.org

January 19, 2012

Decision Proposed Decision of Commissioner Peevy (Mailed 11/22/2011)
BEFORE THE PUBLIC UTILITIES COMMISSION OF THE STATE OF CALIFORNIA
On the proposed decision 11-03-014

Dear Commissioners:

The Board of the American Academy of Environmental Medicine opposes the installation of wireless "smart meters" in homes and schools based on a scientific assessment of the current medical literature (references available on request). Chronic exposure to wireless radiofrequency radiation is a preventable environmental hazard that is sufficiently well documented to warrant immediate preventative public health action.

As representatives of physician specialists in the field of environmental medicine, we have an obligation to urge precaution when sufficient scientific and medical evidence suggests health risks which can potentially affect large populations. The literature raises serious concern regarding the levels of radio frequency (RF - 3KHz – 300 GHz) or extremely low frequency (ELF – 300Hz) exposures produced by "smart meters" to warrant an immediate and complete moratorium on their use and deployment until further study can be performed. The board of the American Board of Environmental Medicine wishes to point out that existing FCC guidelines for RF safety that have been used to justify installation of "smart meters" only look at thermal tissue damage and are obsolete, since many modern studies show metabolic and genomic damage from RF and ELF exposures below the level of intensity which heats tissues. The FCC guidelines are therefore inadequate for use in establishing public health standards. More modern literature shows medically and biologically significant effects of RF and ELF at lower energy densities. These effects accumulate over time, which is an important consideration given the chronic nature of exposure from "smart meters". The current medical literature raises credible questions about genetic and cellular effects, hormonal effects, male fertility, blood/brain barrier damage and increased risk of certain types of cancers from RF or ELF levels similar to those emitted from "smart meters". Children are placed at particular risk for altered brain development, and impaired learning and behavior. Further, EMF/RF adds synergistic effects to the damage observed from a range of toxic chemicals. Given the widespread, chronic, and essentially inescapable ELF/RF exposure of everyone living near a "smart meter", the Board of the American Academy of Environmental Medicine finds it unacceptable from a public health standpoint to implement this technology until these serious medical concerns are resolved. We consider a moratorium on installation of wireless "smart meters" to be an issue of the highest importance.

The Board of the American Academy of Environmental Medicine also wishes to note that the US NIEHS National Toxicology Program in 1999 cited radiofrequency radiation as a potential Carcinogen. Existing safety limits for pulsed RF were termed 'not protective of public health' by the Radiofrequency Interagency Working Gropu (a federal interagency working group includeing the FDA, FCC, OSHA, the EPA and others). Emissions given off by 'smart meters' have been classified by the World Health Organization International Agency for Research on Cancer (IARC) as a Possible Human Carciongen.

Hence, we call for:

- An immediate moratorium on "smart meter" installation until these serious public health issues are resolved. Continuing with their installation would be extremely irresponsible.
- Modify the revised proposed decision to include hearings on health impact in the second proceedings, along with cost evaluation and community wide opt-out.
- Provide immediate relief to those requesting it and restore the analog meters.

Members of the Board
American Academy of Environmental Medicine

APPENDIX D American Academy of Pediatrics Statement

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

AAP Headquarters
141 Northwest Point Blvd
Elk Grove Village, IL 60007-1019
Phone: 847/434-4000
Fax: 847/434-8000
E-mail: kidsdocs@aap.org
www.aap.org

Reply to
Department of Federal Affairs
Homer Building, Suite 400 N
601 13th St NW
Washington, DC 20005
Phone: 202/347-8600
Fax: 202/393-6137
E-mail: kids1st@aap.org

July 12, 2012

The Honorable Julius Genachowski
Commissioner
Federal Communications Commission
445 12th Street SW
Washington, DC 20554

Dear Chairman Genachowski:

The American Academy of Pediatrics (AAP), a non-profit professional organization of 60,000 primary care pediatricians, pediatric medical sub-specialists, and pediatric surgical specialists dedicated to the health, safety and well-being of infants, children, adolescents, and young adults strongly supports the proposal for a formal inquiry into radiation standards for cell phones and other wireless products. The Academy encourages the Federal Communications Commission (FCC) to vote to move forward with this inquiry in an expeditious manner.

The FCC has not assessed the standard for cell phone radiation since 1996. According to industry groups, approximately 44 million people had mobile phones when the standard was set; today, there are more than 300 million mobile phones in use in the United States. While the prevalence of wireless phones and other devices has sky-rocketed, the behaviors around cell phone uses have changed as well. The number of mobile phone calls per day, the length of each cell phone call, and the amount of time people use mobile phones has increased, while cell phone and wireless technology has undergone substantial changes. Many more people, especially adolescents and young adults, now use cell phones as their only phone line and they begin using wireless phones at much younger ages.

The FCC standard for maximum radiation-exposure levels are based on the heat emitted by mobile phones. These guidelines specify exposure limits for hand-held wireless devices in terms of the Specific Absorption Rate (SAR), which measures the rate the body absorbs radiofrequency (RF). The current allowable SAR limit is 1.6 watts per kilogram (W/kg), as averaged over one gram of tissue. Although wireless devices sold in the United States must ensure that they do not exceed the maximum allowable SAR limit when operating at the device's highest possible power level, concerns have been raised that long-term RF exposure at this level affects the brain and other tissues and may be connected to types of brain cancer, including glioma and meningioma.

In the past few years, a number of American and international health and scientific bodies have contributed to the debate over cell phone radiation and its possible link to cancer. The International Agency for Research on Cancer (IARC), part of the

United Nations' World Health Organization, said in June 2011 that a family of frequencies that includes mobile-phone emissions is "possibly carcinogenic to humans." The National Cancer Institute has stated that although studies have not demonstrated that RF energy from cell phones definitively causes cancer, more research is needed because cell phone technology and cell phone use are changing rapidly. While a definitive link between cell phone radiation and brain cancer has not been established, these studies and others clearly demonstrate the need for further research into this area and highlight the importance of reassessing the current SAR to determine if it is protective of human health.

The AAP believes the inquiry to reassess the radiation standard presents an opportunity to review its impacts on children's health and well-being. In the past, such standards have generally been based on the impact of exposure on an adult male. Children, however, are not little adults and are disproportionately impacted by all environmental exposures, including cell phone radiation. In fact, according to IARC, when used by children, the average RF energy deposition is two times higher in the brain and 10 times higher in the bone marrow of the skull, compared with mobile phone use by adults. While the Academy appreciates that the FCC is considering investigating whether the emission standards should be different for devices primarily used by children, it is essential that any new standard for cell phones or other wireless devices be based on protecting the youngest and most vulnerable populations to ensure they are safeguarded throughout their lifetimes.

Finally, in reviewing the SAR standard, the FCC has the opportunity to highlight the importance of limiting media use among children. The Academy has found potentially negative effects and no known positive effects of media use by children under the age of two, including television, computers, cell phones, and other handheld wireless devices. In addition, studies consistently show that older children and adolescents utilize media at incredibly high rates, which potentially contributes to obesity and other health and developmental risks. In reviewing the SAR limit, the FCC has the opportunity to improve the health of our nation by highlighting the importance of limiting screen time and media use for children and adolescents.

The AAP supports the proposal for a formal inquiry into radiation standards for cell phones and other wireless products and the Academy encourages the FCC to vote in favor of moving forward with this investigation. If you have questions or concerns, please contact Kristen Mizzi in the AAP's Washington Office at 202/347-8600.

Sincerely,

Robert W. Block, MD FAAP President

Appendix E RCNIRP Resolution: Electromagnetic Fields from Mobile Phones: Health Effects on Children and Teenagers

"The Resolution evolved from scientific statements adopted by RNCNIRP in 2001, 2004, 2007, 2008 and 2009, taking into account contemporary views and actual scientific data. The Resolution represents a viewpoint of the professional scientific community and is meant for public dissemination, for the consumers of the mobile telecommunications services, as well as for the legislative and executive authorities who develop and implement health protection, environmental, communication, scientific and safety policies."

" ... Thus, for the first time in the human history, children using mobile telecommunications along with the adult population are included into the health risk group due to the RF EMF exposure. A situation has emerged that cumulative EMF exposure of children may be comparable to adult exposure and may be equal to the levels of occupational exposure of workers. At the same time, the society, with all its administrative and social structures, remain in a "waiting" position."

"Priority measures aimed at protection of children and teenagers

Taking into account the RNCNIRP position and the precautionary measures suggested by WHO, the Committee considers that urgent measures must be taken because of the inability of children to recognize the harm from the mobile phone use and that a mobile phone itself can be considered as an uncontrolled source of harmful exposure.

1. *It is required that the information that a mobile phone is a source of RF EMF is clearly shown on the phone's body (or any other telecommunication device).*
2. *It is required that the "User's Guide" contains information that a mobile phone (personal wireless communication tool using electromagnetic communication method, etc.) is a source of harmful RF EMF exposure. Usage of a mobile phone by children and adolescents under 18 years old is not recommended by the Sanitary Rule SanPiN 2.1.8/2.2.4.1190-03, and mobile phone use requires implementation of precautionary measures in order to prevent health risks. Mobile phone use by pregnant women is not recommended in order to prevent risk for a fetus.*
3. *The easiest way to reduce RF EMF exposure is to move the mobile phone away from one's head during the phone call which may be achieved by using the hands-free sets (protection by distance). Shortening the call duration is another way to reduce the exposure (protection by time).*
4. *The RNCNIRP considers it is reasonable to develop mobile phones with reduced EMF exposure (with hands-free sets, included limitation functions, such as limitation of the number of daily phone calls, possibility of forced limitation of phone call duration, etc.).*
5. *It is required to include courses on mobile phones use and issues concerning EMF exposure in the educational program in schools.*
6. *It is reasonable to set limits on mobile telecommunications use by children and adolescents, including ban on all types of advertisement of mobile telecommunications for children (teenagers) and with their participation.*
7. *The RNCNIRP is ready to assist the mass-media in their awareness-raising work and educational activities in the area of EMF and, in particular, to provide information about the newest research of the impact of EMF on human health and the measures to curb the negative impact of this physical agent.*
8. *Better safety criteria for children and teenagers are required in the nearest term. Features of the developing organism should be taken into account, as well as the significance of bioelectric processes for human life and activities, present and future conditions of EMF, prospects of technological and technical development should be addressed in a document of legal status.*
9. *Development of a funded national program for studying possible health effects from chronic EMF exposure of the developing brain is necessary."*

Appendix F RCNIRP Resolution to Regulate the Use of WI-FI in Schools

RUSSIAN NATIONAL COMMITTEE
ON NON-IONIZING RADIATION PROTECTION

June 19, 2012 *Moscow, Russia*

Recommendations

of the Russian National Committee on Non-Ionizing Radiation Protection of the necessity to regulate strictly the use of Wi-Fi in kindergartens and schools

Mobile cellular communication is getting more popular among children of different ages. Children excel adult population in the mobile phone calls use. At the same time, there is a daily brain exposure of EMF RF. In addition, all children are constantly exposed of EMF RF from base stations. The problem of the children's health maintenance in the development of wireless communications was set up as priority by World Health Organization.

Electromagnetic radiation from Wi-Fi creates an additional burden for the child brain, whose body is in a state of development and the formation of mental activity. During this period, children are most susceptible to adverse environmental factors (WHO, publication number 3, April 2003).

It is necessary to note that the existing standards have been developed, without consideration of this additional exposure of EMF.

RussCNIRP consider necessary:

1. Ministry of Health and other organizations, responsible for the population safety (including children), should pay attention to the regulation of Wi-Fi use in kindergartens and schools; to the strengthening of sanitary control of the Wi-Fi using and to the development of an appropriate regulatory framework.
2. To recommend the usage of wired networks in schools and educational institutions, rather than a network using wireless broadband systems, including Wi-Fi.

Chairman of RussCNIRP,
Professor

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SECTION 23

The Precautionary Principle

"Late Lessons from Early Warnings: Towards Realism and Precaution with EMF?"

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Disclaimer.: The views expressed are those of the author and do not represent the views of the EEA or its Management Board. The author has no competing financial interest in the matters dealt with.

Prepared for the BioInitiative Working Group

2007

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I. INTRODUCTION

The histories of selected public and environmental hazards, from the first scientifically based early warnings about potential harm, to the subsequent precautionary and preventive measures, have been reviewed by the European Environment Agency.("Late Lessons from Early Warnings: the Precautionary Principle 1896-2000", EEA,2001). This paper summarises some of the definitional and interpretative issues that arise from the report and subsequent debates, such as the contingent nature of knowledge; the definitions of precaution, prevention, risk, uncertainty, and ignorance; the use of differential levels of proof; and the nature and main direction of the methodological and cultural biases within the environmental health sciences. These issues are relevant to EMF.

II. THE TWELVE "LATE LESSONS FROM EARLY WARNINGS

The paper does not address the specifics of EMF hazards, leaving it to the reader to apply, or not, the "Twelve late Lessons" that conclude the report. These lessons attempt to synthesise the fourteen historical experiences from the very different case study chapters into generic knowledge that can help inform policy-making on current issues such as GMO,, nanotechnologies, mobile phones, and endocrine disrupting substances where the luxuries of hindsight are not yet available but where exposures are already widespread and rising.

The idea of the twelve late lessons is to make the most of past experience to help anticipate future surprises whilst recognising that history never exactly repeats itself. When adopted alongside the best available science the lessons aim to help minimize hazards without compromising innovation. The "lessons" are reproduced below.

A. "Identify/Clarify the Framing and Assumptions"

1. Manage "risk", "uncertainty" and "ignorance"
2. Identify/reduce "blind spots" in the science
3. Assess/account for all pros and cons of action/inaction
4. Analyse/evaluate alternative options

5. Take account of stakeholder values
6. Avoid "paralysis by analysis" by acting to reduce hazards via the precautionary principle.

B. "Broaden Assessment Information"

7. Identify/reduce interdisciplinary obstacles to learning
8. Identify/reduce institutional obstacles to learning
9. Use "lay", local as well as specialist knowledge
10. Identify/anticipate "real world" conditions
11. Ensure regulatory and informational independence
12. Use more long-term (ie. decades) monitoring and research

III. EARLY USE OF PRECAUTION

The Vorsorgeprinzip, or "foresight" principle, only emerged as a specific policy tool during the German debates on the possible role of air pollution as a cause of "forest death" in the 1970-80s. However, John Graham, one of Bush's science policy advisors, and trenchant critic of the precautionary principle, has noted that:

> *"Precaution, whether or not described as a formal principle, has served mankind well in the past and the history of public health instructs us to keep the spirit of precaution alive and well"*. (Graham 2002).

Graham might have been thinking of the cholera episode of 1854 when precaution did indeed serve the people of London well. Dr. John Snow, a London physician, used the spirit of precaution to advise banning access to the polluted water of the Broad St. pump which he suspected was the cause of the cholera outbreak. He based his recommendation on the evidence he had been accumulating for some years including his study of S. London populations served by both piped and well water. Snow's views on cholera causation were not shared by The Royal College of Physicians who considered Snow's thesis and rejected it as 'untenable' as they and other "authorities" of the day believed that cholera was caused by airborne contamination. This particular scientific "certainty" soon turned out to be certainly mistaken, with the last remaining doubt being removed when Koch in Germany isolated the cholera vibrio in 1883.

From the *association* between exposure to water polluted with human faeces, and cholera, observed by Snow in 1854, to Koch's discovery of the *"mechanism of action"*, took 30 years of further scientific inquiry. Such a long time lag between acknowledging compelling associations and understanding their mechanisms of action is a common feature of scientific inquiry, as the histories of TBT, PCBs, DES, the Great Lakes pollution, beef hormones and the other cases in the EEA report illustrate.

IV. KNOWLEDGE AND IGNORANCE REQUIRES BOTH PREVENTION AND PRECAUTION

The Broad St. pump, TBT, DES, PCBs and Great Lakes Pollution examples described here also serve to illustrate the contingent nature of knowledge. Today's scientific certainties can be tomorrow's mistakes, and today's research can both reduce and increase scientific uncertainties, as the boundaries of the "known" and the unknown expand. Waiting for the results of more research before taking action to reduce threatening exposures may not only take decades but the new knowledge may identify previously unknown sources of both uncertainty and ignorance, as awareness of what we do not know expands, thereby supplying further reasons for inaction. "Paralysis by Analysis " can then follow.

"The more we know, the more we realise what we don't know" is not an uncommon scientific experience. Socrates observed some time ago:
"I am the wisest man alive, for I know one thing, and that is that I know nothing". (Plato's Apology 1.21).

This was an early lesson in humility that has been lately forgotten by many scientists and politicians, who often put what turns out to be "misplaced certainty" in today's scientific knowledge: or assume that uncertainty can only be reduced, and not increased, by further research.

The distinction between uncertainty and ignorance is important. (Stirling, 1999) Ignorance is knowing that today's knowledge is very limited: it is the source of scientific surprises, such as the hole in the ozone layer, the mesothelioma cancer from asbestos, imposex in sea snails etc. It is distinct from the uncertainties that arise from

gaps in knowledge and from variances in sampling and monitoring; parameter variability; model assumptions; and from the other attempts to approximate, model and predict unfolding realities.

Foreseeing and preventing hazards in the context of ignorance presents particular challenges to decision-makers. At first sight it looks impossible to do anything to avoid or mitigate "surprises". And ignorance ensures that there will always be surprises. However, some measures that could help limit the consequences of ignorance and the impacts of surprises are:

- using intrinsic properties as generic predictors for unknown but possible impacts e.g. the persistence, bioaccumulation and spatial range potential of chemical substances. (Stroebe et al., 2004)
- reducing specific exposures to potentially harmful agents on the basis of credible 'early warnings' of *initial* harmful impacts, thus limiting the size of any other 'surprise' impacts from the same agent, such as the asbestos cancers that followed asbestosis; and the PCB neurotoxicological effects that followed its wildlife impacts.
- promoting a diversity of robust and adaptable technological and social options to meet needs, which limits technological 'monopolies' (such as those like asbestos, CFCs, PCBs etc.), and therefore reduces the scale of any 'surprise' from any one technological option.
- using more long-term research and monitoring of what appear to be "surprise sensitive sentinels", such as frogs and foetuses.

A. Prevention and Precaution

The distinction between *prevention* and *precaution* is also important. Preventing hazards from "known" risks is relatively easy and does not require precaution. Banning smoking, or asbestos, today requires only acts of prevention to avoid the well-known risks. However, it would have needed precaution, (or foresight, based on a sufficiency of evidence), to have justified acts to avoid exposure to the then uncertain hazards of asbestos in the 1930s –50s, or of tobacco smoke in the 1960's). Such precautionary acts then, if implemented successfully, would have saved many more lives in Europe than today's bans on asbestos and smoking are doing. As

Cogliano has recently pointed out, the difference between prevention and precaution can be further illustrated by showing that *prevention* is used to justify the restriction of exposure to an IARC Category 1 carcinogen whereas *precaution* is necessary to justify restricting exposure to a Category 2A or B carcinogen, where the evidence is less strong. The section below. on different levels of proof , further elaborates this point.
For EMF, the question is, does the existing strength of evidence justify *precautionary* actions now? Or will exposure reduction be delayed until the evidence is clear enough to justify the more belated and overall less protective *prevention* of "known" causes, so that EMF replicates the fate of asbestos ,smoking and most of the other cases in the EEA report?

Some commentators, who have a long and distinguished history in preventing occupational and environmental risks, have queried the added value of the precautionary principle in the field of public health, with its long traditions of prevention. (Goldstein, 2007).

The key to understanding the added value of the PP requires a) acknowledging the distinction between prevention and precaution described above; b) an appreciation of the further distinctions between the primary, secondary and tertiary preventative *measures* that have long between adopted in public health, and the prior *justification* for any such measure, which the PP brings; and c) a recognition of the increased legitimacy and transparency that arises from the articulation and adoption of the PP in legal texts, international agreements and conventions, as opposed to being merely part of general practice.

More empirically, the evidence that many scientific disciples, legal scholars (de Sadeleer, 2007),and international policymakers, have, since the 1970s, recognised the need for legitimising the PP as a new policy tool that is better able to deal with systems complexities, ignorance and uncertainties, suggests that the PP brings added value to the protection of the environment and the public.

There is much discussion generated by the different meanings often attached to the common terms “prevention”, “precaution”, “risk”, “uncertainty” and “ignorance”. **Table 1** attempts to clarify these so as to help reduce unnecessary argumentation.

Table 1: Clarification of Key Terms

Situation	***State and dates of knowledge***	***“Nature of the justification for Action”***
Risk	**‘Known’ impacts; ‘known’ probabilities e.g. asbestos**	**Prevention: action taken to reduce known hazards e.g. eliminate exposure to asbestos dust**
Uncertainty	**‘Known’ impacts; ‘unknown’ probabilities e.g. antibiotics in animal feed and associated human resistance to those antibiotics**	**Precautionary prevention: action taken to reduce exposure to potential hazards**
Ignorance	**‘Unknown’ impacts and therefore ‘unknown’ probabilities eg the ‘surprises’ of chlorofluorocarbons (CFCs), pre 1974**	**Precaution: action taken to anticipate, identify and reduce the impact of ‘surprises’**

Source: Reproduced, with amendment, from the Late Lessons Report, EEA 2001.

V. THE PRECAUTIONARY PRINCIPLE: DEFINITIONS AND INTERRPRETATIONS

There are some relatively rare but successful acts of “precautionary prevention” in the EEA report such as on cholera in1854, on TBT in France in the 1980s, and on CFCs in the 1970s. Together with the many other examples of the failure to use the precautionary principle in the other case studies (EEA, 2001), these illustrate the wisdom of taking appropriate precautionary actions to avoid plausible and serious threats to health or environments, especially when the impacts are irreversible and likely to be much more costly to society than the precautionary measures.

Some commentators have stressed the need for policymakers to take account of the foreseeable, or plausible, countervailing (secondary) costs of otherwise genuine precautionary attempts to protect the environment and health. (Rushton, 2007). This

consideration of countervailing costs has long been recognised by the better policymakers, even if it is difficult in practice to anticipate and account for all consequences of actions. And of course there are the secondary benefits of precautionary actions as well, which tend to be less stressed, such as the benefit of reduced respiratory and cardiovascular disease from the reduced combustion of fossil fuels: a large and early secondary benefit of that climate change measure.

The outcomes of some controversial actions based on the PP, such as the EU ban on antibiotics as growth promoters, which is a Late Lessons case study, have since been scrutinised, and have been considered sound ,or unsound, depending on the science used and its interpretation by different interests. (Cox, 2007, Angulo et al., 2004).

Any policy effectiveness analysis of measures taken to deal with such multi-causal and long term hazards as antibiotics as growth promoters is fraught with methodological difficulties and is hampered by long latencies and complex biological systems: untangling the causal impact of one stressor amongst many inter-dependent ones is virtually impossible. The value of applying more probabilistic and value of information data to such conundrums is recognised by many risk managers. However, this cannot remove the need for scientific and political judgment about how to take appropriate and proportionate action in the face of irreducible uncertainties, ignorance and plausible hazards which could have serious, widespread and irreversible impacts and for which probabilities are not possible at the time when they are most needed. This is the current case with many EMF exposures.

A. Some Definitions and Interpretations of the Precautionary Principle

The increasing awareness of complexity and uncertainty during the 1980/90's led to the German debates on the Vorsorgeprinzip shifting to the international level, initially in the field of conservation (World Charter for Nature UN 1982), but then particularly in marine pollution, where an overload of data accompanied an insufficiency of knowledge. (Marine Pollution Bulletin, 1997). This generated the need to act with precaution to reduce the large amounts of chemical pollution entering the North Sea. Since then many international treaties have included the PP (including the often cited version from the Third North Sea Ministerial Conference, 1990, have included

reference to the precautionary principle, or, as they refer to it in the USA, the precautionary approach.

The N.Sea declaration called for *"action to avoid potentially damaging impacts of substances, even where there is no scientific evidence to prove a causal link between emissions and effects"*.

This definition has often, and sometimes mischievously, been used to deride the precautionary principle by claims that it appears to justify action even when there is "no scientific evidence" that associates exposures with effects. However, the N. Sea Conference definition clearly links the words "no scientific evidence" with the words. "to prove a causal link". We have already seen with the Broad St. pump and TBT examples that there is a significant difference between evidence about an "association" and evidence that is robust enough to establish a "causal" link. (Hill, 1965).

The Treaty of the European Union also cites the precautionary principle, as well as the other key principles of sound public policy on health:

> "*Community policy on the environment … shall be based on the precautionary principle and on the principles that preventive action should be taken, that environmental damage should, as a priority, be rectified at the source and the polluter should pay*" (Treaty on European Union, 1992).

Other parts of the EU Treaty ,and cases taken at the European Court of Justice, make it clear that these principles also apply to environmental and consumer protection issues.

These principles, as well as the important and legally required *proportionality principle*, which limits disproportion between the costs and benefits of prevention, are not defined in the Treaty but are illuminated by their practical application in case law. However, all serious applications of the precautionary principle require some scientific evidence of a plausible association between exposures and current, or potential, impacts.

There is still much disagreement and discussion about the interpretation and practical application of the precautionary principle, due, in part, to this lack of clarity and consistency over its definition. For example, many definitions in the Treaties and Conventions use a double negative to define the precautionary principle: that is, they

identify reasons that cannot be used to justify not acting, but without specifying that a sufficiency of evidence is needed to justify taking action.

B. Reasonable Grounds for Concern?

The Communication from the EU on the precautionary principle (European Commission 2000) does specify that "reasonable grounds for concern" are needed to justify action under the precautionary principle, but it does not make explicit that these grounds will be case specific: nor does it explicitly distinguish between risk, uncertainty and ignorance. Since the EC Communication, the EU Council of Misisters, EU case law, and the regulation establishing the new European Food Safety Authority, EFSA, (General Food Law Regulation, EC No 178/2002), have further clarified the circumstances of use and application of the precautionary principle.
For example, the judgement of the European Court of Justice in the BSE case contained a general definition which authoritative commentators think contain many of the necessary elements of the precautionary principle that are applicable in all areas of the EC law:

> "*Where there is uncertainty as to the existence or extent of risks to human health, the institutions may take protective measures without having to wait until the reality and seriousness of those risks become fully apparent*" (Christoforou, 2002).

The WHO Declaration from the Fourth Ministerial Conference on Environment and Health (WHO, 2004a) refers explicitly to the precautionary principle with the recommendation:

> *"that it should be applied where the possibility of serious or irreversible damage to health or the environment has been identified and where scientific evaluation, based on available data, proves inconclusive for assessing the existence of risk and its level but is deemed to be sufficient to warrant passing from inactivity to policy alternatives"* (WHO, 2004b).

The American Public Health Association (APHA) affirmed endorsement of the precautionary principle as a cornerstone of public health for the protection of children's health. In a 2000 policy statement, the APHA encouraged governments, the private sector and health professionals to promote and use the precautionary principle to protect the health of developing children (APHA, 2001).

C. The EEA working definition of the Precautionary Principle.

The working definition used in the European Environment Agency that has been developed during debates since 2001 is explicit about specifying both uncertainty and ignorance, as contexts for applying the principle, and in acknowledging that a case-specific sufficiency of scientific evidence is needed to justify public policy actions:

> '*The Precautionary Principle provides justification for public policy actions in situations of scientific complexity, uncertainty and ignorance, where there may be a need to act in order to avoid, or reduce, potentially serious or irreversible threats to health or the environment, using an appropriate level of scientific evidence, and taking into account the likely pros and cons of action and inaction*' (Gee, 2006).

The definition is also explicit about the trade off between action and inaction, and widens the conventionally narrow, and usually quantifiable, interpretation of costs and benefits to embrace the wider and sometimes unquantifiable, "pros and cons". Some of these wider issues, such as loss of the ozone layer, or of public trust in science, are unquantifiable, but they can sometimes be more damaging to society than the quantifiable impacts: and they need to be included in any comprehensive risk assessment. The EEA definition is proving to be useful in clarifying the use and interpretation of the PP, especially in emerging issues such as EMF.

VI. DIFFERENT LEVELS OF PROOF FOR DIFFERENT PURPOSES

The level of proof (or strength of scientific evidence) that would be appropriate to justify public action in each case varies with the pros and cons of action or inaction. These include the nature and distribution of potential harm; the justification for, and the benefits of the agent or activity under suspicion; the availability of feasible alternatives; and the overall goals of public policy. Such policy goals can include the achievement of the "high levels of protection" of public health, of consumer safety, and of the environment, required by the EU Treaty.

The use of different levels of proof is not a new idea: societies often use different levels of proof like for different purposes.

For example, a high level of proof (or strength of evidence) such as “beyond all reasonable doubt” is used to achieve good science where A is seen to cause B only when the evidence is very strong. Such a high level of proof is also used to minimise the costs of being wrong in the criminal trial of a suspected murderer, where it is usually regarded as better to let several guilty men go free than it is to wrongly convict an innocent man. However, in a different, civil trial setting, where, say, a citizen seeks compensation for neglectful treatment at work, which has resulted in an accident or ill health, the court often uses a lower level of proof commensurate with the costs of being wrong in this different situation. I n compensation cases an already injured party is usually given the benefit of the doubt by the use of a medium level of proof, such as “balance of evidence or probability”. It is seen as being less damaging (or less costly in the wider sense) to give compensation to someone who was *not* treated negligently than it is to *not* provide compensation to someone who was treated negligently. The “broad shoulders” of insurance companies are seen as able to bear the costs of mistaken judgements rather better than the much narrower shoulders of an injured citizen. In each of these two illustrations it is the nature and distribution of the costs of being wrong that determines the level of proof (or strength of evidence) that is “appropriate” to the particular case.

Bradford Hill, cited above, was very concerned about the social responsibility of scientists and he concluded his classic 1965 paper on association and causation in environmental health , which was prepared at the height of the smoking controversy, with a “call for action” in which, *inter alia*, he also proposed the concept of case specific and differential levels of proof. His three examples ranged from “relatively slight” to “very strong” evidence, depending on the nature of the potential impacts and of the pros and cons in each specific case, i.e., possibly teratogenic medicine for pregnant women; a probable carcinogen in the workplace; and government restrictions on public smoking or diets. (Bradford Hill 1965).

Identifying an appropriate level of proof has also been an important issue in the climate change debates. The International Panel on Climate Change (IPCC) discussed

at length this issue before formulating their 1995 conclusion that “on the balance of evidence” mankind is disturbing the global climate. They further elaborated on this issue in their 2001 report where they identified 7 levels of proof (or strengths of evidence) that can be used to characterise the scientific evidence for a particular climate change hypothesis.

Table 2 provides the middle 5 of these levels of proof from the IPPC and illustrates their practical application to a variety of different societal purposes. In the cancer field the International Agency for Research on Cancer also uses several strengths of evidence to characterise the scientific evidence on carcinogens. (Cogliano, 2007)

Different Levels of Proof for Different Purposes: Some Examples and Illustrations

Probability	Quantitative descriptor (Probability bands based on IPCC 2001)	Qualitative Descriptor	Illustrations
100 % probability	Very likely (90-99 %)	• "Statistical significance"	• Part of strong scientific evidence for "causation"
		• "Beyond all reasonable doubt"	• Most criminal law. And the Swedish Chemical law, 1973, for evidence of "safety" of substances under suspicion-burden of proof on manufacturers
90 %	Likely (66-90 %)	• "Reasonable certainty"	• Food Quality Protection Act, 1996 (US)
		• "Sufficient scientific evidence"	• To justify a trade restriction designed to protect human, animal or plant health under World Trade Organisation Sanitary and Phytosanitary (SPS) Agreement, Art. 2.2, 1995
50 %	Medium Likelihood (33-66 %)	• "Balance of evidence"	• Intergovernmental Panel on Climate Change 1995 & 2001
		• "Balance of probabilities"	• Much Civil and some administrative law
		• "Reasonable grounds for concern"	• European Commission Communication on the Precautionary Principle 2000
		• "Strong possibility"	• British Nuclear Fuels occupational radiation compensation scheme, 1984 (20-50% probabilities triggering different awards up to 50% +, which then triggers full compensation)
	Low Likelihood (10-33 %)	• "Scientific suspicion of risk"	• Swedish Chemical law, 1973, for sufficient evidence to take precautionary action on potential harm from substances-burden of proof on regulators
0 %		• "Available pertinent information"	• To justify a provisional trade restriction under WTO SPS Agreement, Art. 5.7 where "scientific information is insuffiicient"
	Very Unlikely (1-10 %)	• Low risk	• Household fire insurance
0 % probability		• "Negligible and insignificant"	• Food Quality Protection Act, 1996 (US)

Source: EEA, 2001

VII. FALSE NEGATIVES AND FALSE POSITIVES.

All of the 14 case studies (tributylin or TBT, benzene, PCBs, CFCs, MTBE, SO_2. Great Lakes pollution. DES, and beef hormones. asbestos. medical x-rays, BSE and Fisheries are all examples of "false negatives" in the sense that the agents or activities were regarded as not harmful for some time before evidence showed that they were indeed hazardous.

We tried to include a "false positive" case study in the report (i.e., where actions to reduce potential hazards turned out to be unnecessary), but failed to find either authors or sufficiently robust examples to use. Providing evidence of "false positives" is more difficult than with "false negatives" (Mazur, 2004). How robust, and over what periods of time, does the evidence on the absence of harm have to be before concluding that a restricted substance or activity is without significant risk?

Volume 2 of "Late Lessons", which the EEA intends to publish in 2008, will explore the issues raised by false positives. including lessons to be learned from such apparent examples as the EU ban on food irradiation and hazardous labelling on saccharin in the US. The Y2K computer bug story may also carry some interesting lessons.

Why are there so many "false negatives" to write about, and how might this be relevant to EMF? Conclusions based on the first Late lessons volume of case studies point to two main answers: the bias within the health and environmental sciences towards avoiding "false positives", thereby generating more "false negatives", and the dominance within decision-making of short-term, specific, economic and political interests over the longer term, diffuse, and overall welfare interests of society.

The latter point needs to be further explored, particularly within the political sciences. Researchers could examine the ways in which society's long-term interests can be more effectively located within political and institutional arrangements that have, or could have, an explicit mandate to look after the longer term welfare of society, and thereby to better resist the short-term pressures of particular economic or political interests. The judiciary in democracies can play part of this role, as can long running

and independent advisory bodies, such as the Royal Commission on Environmental Pollution (UK), or the German Advisory Council on Global Change.

The current and increasing dominance of the short-term in markets and in parliamentary democracies makes this an important issue. The experiments we are conducting with planet earth, its eco-systems and the health of its species, including humans, require, *inter alia*, more long-term monitoring of "surprise-sensitive" parameters which could, hopefully, give us early warnings of impending harm. Such long-term monitoring requires long-term funding, via appropriately designed institutions: such funding and institutions are in short supply. The case studies in Vol. 1 of "Late Lessons" illustrate both the great value, (e.g. in the TBT, DES, Great Lakes and CFCs stories), yet relative paucity, of long-term monitoring of both health and environments. Such monitoring can contribute to the "patient science" that slowly evolving natural systems require for their better understanding.

Since the publication of "Late Lessons" we have further explored the second cause of "false negatives" i.e. the issue of bias within the health and environmental sciences. Table 3 lists sixteen common features of methods and culture in the environmental and health sciences and shows their main directions of error. Of these, only three features tend towards generating "false positives" whereas twelve tend towards generating "false negatives". (Clearly, the weighting of these different biases would be the next step but has not yet been tried).

Table 3

ON BEING WRONG:
Environmental and Health Sciences and Their Directions of Error

SCIENTIFIC STUDIES	SOME METHODOLOGICAL FEATURES	MAIN[1] DIRECTIONS OF ERROR-INCREASES CHANCES OF DETECTING A:
Experimental	• High doses	• False positive
Studies	• Short (in biological terms) range of doses	• False negative
(Animal	• Low genetic variability	• False negative
Laboratory)	• Few exposures to mixtures	• False negative
	• Few Foetal-lifetime exposures	• False negative
	• High fertility strains	• False negative (Developmental/reproductive endpoints)
Observational	• Confounders	• False positive
Studies	• Inappropriate controls	• False positive/negative
(Wildlife &	• Non-differential exposure misclassification	• False negative
Humans)	• Inadequate follow-up	• False negative
	• Lost cases	• False negative
	• Simple models that do not reflect complexity	• False negative
Both	• Publication bias towards positives	• False positive
Experimental And	• Scientific cultural pressure to avoid false positives	• False negative
Observational Studies	• Low statistical power (e.g. From small studies)	• False negative
	• Use of 5 % probability level to minimise chances of false positives	• False negative

Source: Gee, 2006

[1] Some features can go either way (e.g. inappropriate controls) but most of the features mainly err in the direction shown in the table

The general bias towards the null helps to produce robust science, basing it on strong foundations of knowledge, but this bias can encourage poor public health or environmental policy. The goals of science and public policy-making on health and environmental hazards are different: science puts a greater priority on avoiding "false positives" by accepting only very high levels of proof of "causality", whereas public policy tries to prioritize the avoidance of "false negatives" on the basis of a sufficiency of evidence of potential harm.

Table 3 is derived from papers presented to a conference on the precautionary principle organised by the Collegium Ramazzini, the EEA, the WHO and NIEHS in 2002. (Grandjean et al., 2003). It provides a first and tentative step in trying to capture and communicate the main directions of this bias within the environmental and health sciences, a bias which decision makers and the public should be aware of. As they debate the evidence on emerging hazards such as EMF.

The appropriate balance between false negatives and positives was addressed at a JRC/EEA workshop on the precautionary principle and scientific uncertainty which was held during the "Bridging the Gap" Conference, 2001, organised by the Swedish Presidency of the EU, in partnership with the EEA and DG Research. It drew the following conclusion:

> *"Improved scientific methods to achieve a more ethically acceptable and economically efficient balance between the generation of "false negatives" and "false positives" are needed"*. (Swedish EPA 2001).

VIII. SOME CRITERIA FOR ESTABLISHING CAUSATION

Bradford Hill established nine criteria for helping to move from association to causation in environmental health which have been, and still are, widely used in debates on issues such as EMF

Two of the apparently more robust of the "criteria" may not be so robust in the context of multi-causality, complexity and gene/host variability.

For example, ***"consistency"*** of study findings is not always to be expected. As Prof. Needleman, who provided the first of what could be called the second generation of early warnings on lead in petrol in 1979 has observed:

> *"Consistency in nature does not require that all or even a majority of studies find the same effect. If all studies of lead showed the same relationship between variables, one would be startled, perhaps justifiably suspicious"* (Needlemann , 1995).

It follows that the *presence* of consistency of results between studies on the same hazard can provide robust evidence for a causal link, but the *absence* of such consistency may not provide very robust evidence for the absence of a real association. In other words, the "criterion" of consistency is asymmetrical, like most of the other Bradford Hill "criteria".

Similarly, the criterion of ***"temporality",*** which says that the putative cause X of harm Y must come before Y appears, is robust in a simple, uni-causal world. In a multi-causal, complex world of common biological end points that have several chains of causation this may not necessarily be so. For example, falling sperm counts can have multiple, co-causal factors, some of which may have been effective at increasing the incidence of the biological end point in question in advance of the stressors in focus, thereby confusing the analysis of temporality. The resulting overall sperm count trends could then be rising, falling or static, depending on the combined direction and strengths of the co-causal factors and the time lags of their impacts. It follows that say, chlorine chemicals, may or may not be co-causal factors in falling sperm counts: but the use of the "temporality" argument by the WHO, who observed that sperm counts began to fall before chlorine chemistry production took off, does not provide robust evidence that they are not causally involved.

The presence of "temporality", like "consistency" may be robust evidence *for* an association being causal, but its *absence* may not provide robust evidence *against* an association. Bradford Hill was explicitly aware of the asymmetrical nature of his "criteria": his followers have not always been so aware.
During 2005, the 40th anniversary year of the Bradford Hill "criteria", the EEA convened a panel of experts to review the "criteria" and their use in light of advances in knowledge, particularly multi-causality, since 1965. A report will be published in 2007.

How this goal can be achieved without compromising science remains to be explored, (Grandjean 2004; Grandjean et al., 2004). It is clearly necessary, particularly when dealing with EMF, for scientific methods to not only take account of thisfalse negative/positive bias in methodologies but also to more clearly reflect other realities such as multi-causality; thresholds; timing of dose; sensitive sub-populations, such as children, (Jarosinska and Gee, 2007); sex, age, and immune conditions of the host; information physics; effects below the thresholds of "acute" impacts, such as tissue heating; non-linear dose/response relationships; "low dose" effects; and the effects arising from disturbing the balance between opposing elements in complex biological systems. The evidence on EMF needs to take full account of these realities, as well as of the methodological biases of Table 3.

1X. PUBLIC PARTICIPATION IN RISK ANALYSIS

Choosing an appropriate level of proof for a particular case is clearly based, *inter alia*, on value judgements about the acceptability of the costs, and of their distribution, of being wrong in both directions, i.e. of acting or not acting to reduce threatening exposures. This is why it is necessary to involve the public in decisions about serious hazards and their avoidance: and to do so for all stages of the risk analysis process.

Three of the "twelve late lessons" (number 5, number 9 and number 10) explicitly invite early involvement of the public and other stakeholders at all stages of risk analysis, a development which has been actively encouraged in many other influential reports during the last decade. (NRC 1994; US Presidential Commission on Risk Assessment and Risk Management 1997; Royal Commission on Environmental Pollution 1998; CEC Communication on the Precautionary Principle 2000; German Advisory Council on Global Change 2001).

The best available science is therefore only a necessary but not a sufficient condition for sound public policy making on potential threats to health and the environment. Where there is scientific uncertainty and ignorance "it is primarily the task of the risk managers to provide risk assessors with guidance on the science policy to apply in their risk assessments." (Christoforou, 2003). The content of this science policy advice, as well as the nature and scope of the questions to be addressed by the risk

assessors, need to be formulated by the risk managers and relevant stakeholders at the initial stages of the risk analysis.

Involving the public in not only all stages of risk analysis, but also in helping to set research agendas and technological trajectories, (Wilsdon and Willis, 2004) is not easy. Many experiments, in both Europe and the USA, with focus groups, deliberative polling, citizens' juries, and extended peer review, (Funtovicz and Ravetz, 1990/92) are exploring appropriate ways forward.

The issue of time is also a critical issue for risk analysis and application of the precautionary principle. For example, the time from the first scientifically based early warnings (1896 for medical X rays, 1897 for benzene, 1898 for asbestos) to the time of policy action that effectively reduced damage was often 30-100 years. Some consequences of the failures to act in good time (e.g. on CFCs or asbestos) continue to cause damage over even longer time periods. For example, the ozone hole will cause many thousands of extra skin cancers in today's children but the cancers will only peak around the middle of this century because of the long latent period between exposure and effect. Such long-term but foreseeable impacts raise liability and compensation issues, including appropriate discount rates (if any) on future costs and benefits, which being value-laden choices. need also to be discussed by stakeholder groups. Again, experience in the climate change field with these long-term issues may be helpful in managing them with respect to electromagnetic fields (ELF and RF).

The wider involvement of stakeholders has also been recognised more recently by the International Risk Governance Council (IRGC, 2005) and the EU report on Science and Governance, (Wynne et al., 2007). Whether wider involvement of stakeholders results in better and more acceptable decisions needs to studied: early indications (Beierle, 2002), and lessons from history, suggests that is. In many cases several decades will be necessary to confidently judge outcomes, given latencies and complexities.

X. SOME EXAMPLES OF EARLY WARNINGS

The 14 case studies in the Late Lessons Report (EEA 2001) include examples some chemicals (tributylin or TBT, benzene, PCBs, CFCs, MTBE, SO_2 and Great Lakes pollution); two other pharmaceuticals (DES, and beef hormones); two physical agents (asbestos and medical x-rays); one pathogen (BSE); and Fisheries (overfishing).

The main issues discussed so far, such as the contingent nature of knowledge; ignorance and "surprises"; appropriate levels of evidence for policy actions; and public participation in risk analysis are critical to the successful application of both scientific knowledge and the precautionary principle to public policy-making. They are therefore relevant to discussions about the potentially new hazards that are now emerging e.g. from nanotechnology, (Royal Society 2003); from the non-ionising radiations arising from the use of mobile phones, (Stewart Reports 2000, 2004), and from endocrine disrupting substances or EDSs. (WHO, 2002).

With such newly emerging hazards it can be helpful to use historical examples to illustrate what a scientifically based early warning looks like as it is often difficult to properly recognise such warnings at the time they occur. A good example is that provided by the UK Medical Research Council's Swann Committee in 1969. They were asked to assess the evidence for risks of resistance to antibiotics in humans following the prolonged ingestion of trace amounts of antibiotics arising from their use as growth promoters in animal feed. (Edqvist and Pedersen 2001). They concluded that:

> *"Despite the gaps in our knowledge .. we believe … on the basis of evidence presented to us, that this assessment is a sufficiently sound basis for action .. The cry for more research should not be allowed to hold up our recommendations'….'sales/use of AFA should be strictly controlled via tight criteria, despite not knowing mechanisms of action, nor foreseeing all effect"*. (Swann 1969).

A. Antibiotics in Animal Feed

The Swann Committee also concluded that it would be more rewarding and innovative to improve animal husbandry as a means of encouraging disease free animal growth rather than to the cruder approach of diets containing antimicrobials. Despite the gaps in knowledge, the need for much more research, and considerable ignorance about the mechanisms of action, a sufficiency of evidence was identified and described by the Swann Report that justified the need for public authorities to restrict the possibility of exposures to antibiotics from animal growth promoters. This early warning was initially heeded, but was then progressively ignored by the pharmaceutical companies and regulatory authorities, who wanted more scientific justification for restricting anti-microbial growth promoters. However, in 1985 in Sweden, and then in the EU in 1999, the use of antibiotics as growth promoters was finally banned. Pfizer, the main supplier of such antibiotics in Europe, appealed against the European Commission banning decision, pleading, *inter alia*, an insufficiency of scientific evidence. They lost this case at the European Court of Justice (Case T-13/99-Pfizer 2002), a case which further clarified the proper use and application of the precautionary principle in circumstances of scientific uncertainty and of widespread, if low, public exposures to a potentially serious threat.

B. Lead in Gasoline

A US example of an early warning comes from the lead in gasoline story: a warning that was largely ignored for over 50 years, resulting in much damage to the intelligence and behaviour of children in America, Europe and the rest of the motorised world. Yandell Hendersson, Chair of the Medical Research Board, US Aviation Service, who had been asked to look at the scientific evidence on the possible hazards of tetraethyl lead during the temporary ban on lead in petrol, in 1925, concluded:

> *"It seems likely that the development of lead poisoning will come on so insidiously that leaded gasoline will be in nearly universal use … before the public and the government awakens to the situation"*. (Rosner and Markowitz, 2002).

Motorised societies would have gained much in dollars, brainpower and social cohesion had they heeded this foresight.

C. Tributylin (TBR) – A Marine Antifoulant for Ships

The case study on tributylin (TBT) and DES illustrate the surprises that arise from real life complexities and which may carry some lessons for the EMF debate. For example, the unfolding of the TBT story was accompanied by an increased appreciation of scientific complexity arising from the discoveries that adverse impacts were caused by very low doses (i.e. in parts/trillion); that high exposure concentrations were found in unexpected places e.g. in the marine micro-layer; and that bioaccumulation in higher marine animals, including sea-food for human consumption, was greater than expected. The early actions on exposure reduction in France and the UK in 1982-85 were based on a 'strength of evidence' for the 'association' only: knowledge about 'causality', **'**mechanisms of action' and other the complexities above came much later.

We were lucky in some ways with the TBT story: a highly specific, initially uncommon impact (imposex) was quickly linked to one chemical, TBT. This relatively easily identified linkage is not likely to be repeated for the more common and multi-causal impacts where, for example, neurodevelopmental diseases and dysfuntions, or common cancers, are the impacts under suspicion.

D. Diethylstilbestrol (DES)

Key lessons from the DES story are also instructive, as it provides the clearest example of endocrine disruption in humans. Diethylstilbestrol, commonly referred to as DES, is a synthetic estrogen . It was originally prescribed to prevent miscarriage, but did not. Later, sons and daughters of mothers given DES to prevent miscarriage developed cancers, reproductive tract anomalies, and had more pre-term babies themselves as a result. The effects of DES include the absence of visible and immediate teratogenic effects **not** being robust evidence for the absence of reproductive toxicity; and the **'**timing of the dose clearly determining the poison', in contrast to the 'dose determines the poison' dictum of Paracelsus. Timing is also relevant to other biological end points:

> *"the time of life when exposures take place may be critical in defining dose-response relationships of EDSs for breast cancer as well as for other health effects",* (WHO/IPCS, 2002).

Although the exposure levels were higher than the usual environmental levels of other EDSs, the DES story provides a clear warning about the potential dangers of perturbing the endocrine system with synthetic chemicals.

With over 20,000 publications, DES is now a well-studied compound, yet many doubts persist about its mechanisms of action. Since no dose-effect relationship has been found in humans, it cannot be excluded that DES could have been toxic at low doses, and that other less potent xenoestrogens could have similar effects.

If we still have few certainties about DES after so much time and research, what should our attitude be towards emerging hazards, such as other endocrine disrupting substances (EDSs) and EMF?

XI. CONCLUSION

The lessons of history from the EEA report, and subsequent debates and events, indicate that they have much relevance to the EMF issue, as well as to other emerging issues such as nanotechnology, (Royal Society, 2003) and endocrine disrupting substances or EDSs (WHO, 2002). The public health assessment of EMF could apply these lessons, approaches, terms of discussion and interpretations to the precautionary and preventative actions on the different parts of the EMF exposure problem.

There are of course large differences between smoking and EMF. The smoking hazard had at least 10 times the relative risk increase in the exposed population compared to the leukaemia risk from power line exposure; and the size of the smoking exposed population, and its exposure above that needed to generate a doubling of the risk, are both very much greater than with power lines. The larger relative risk for smoking and lung cancer seems to arise from comparing smokers with non, or never, smokers whilst the relative risk of 2 to 3 that arises between moderate and heavy smokers, or between second hand smokers and non smokers, is more relevant to the EMF issue,

where there is an absence of unexposed controls. The lower relative risks of 2 or 3 for EMF are biased towards the null to unknown extent by the absence of such controls (Milham, 1998). However, the parallel between the slow recognition of the smoking hazard and power line EMF hazard is interesting.

The parallel with the history of X rays is also pertinent. The initial discovery, by Alice Stewart in the early 50s, that a few x rays of a pregnant woman in the sensitive period of her pregnancy gave a 2 fold excess of leukaemia, was greeted with much strident disbelief, particularly from the male doctors whose latest toy was under threat. It took another 20 years or so before her result became generally accepted, and only after several negative studies that were conducted in the early response to her study. Many studies of X rays in pregnant women now exist, and, as with the power line studies, the relative risk remains at about 2. (EEA, 2001) What will the history of EMF look like in 2020?

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SECTION 23

The Precautionary Principle

2012 Supplement

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Disclaimer.: The views expressed are those of the author and do not represent the views of the EEA or its Management Board. The author has no competing financial interest in the matters dealt with.

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I. INTRODUCTION

In 2007, the evidence for EMF, and in particular radiofrequency radiation (RFR) from the use of mobile phones, was a focus for discussion in the BioInitiative Report (2007). It arose from growing scientific evidence of possible health risks, with a very large global population that could presumably be affected by the outcome.

Illustrating the importance of observing 'early warnings' of environmental and public health risks arising from emerging scientific studies and direct observation of impacts to peoples' health, this author wrote about the importance of applying 'lessons learned' from the histories of selected public and environmental hazards, from the first scientifically based early warnings about potential harm, to the subsequent precautionary and preventive measures, as reviewed by the European Environment Agency in Late Lessons from Early Warnings: the Precautionary Principle 1896-2000 (EEA, 2001). In considering the evidence on mobile phones and head cancers the EEA concluded that it would be prudent and timely to issue an "early warning" on the issue, in September, 2007. Five years on, this note briefly updates our opinion on this issue.

II. NEED FOR PRECAUTIONARY ACTIONS ON MOBILE PHONES

The communication leaflet for publication of "Late Lessons from Early Warnings 2: Science, Precaution, Innovation." (EEA, 2012) includes this message:

> *"In the context of scientific uncertainty and ignorance, the decision-makers responsible for incentivising and regulating innovation face a significant challenge in balancing opportunities against risks. The precautionary principle can help to better manage such choices. It requires actions to prevent potentially serious harm before the likelihood or severity of an innovation's impacts become all too clear."*

Volume 2 of 'Late Lessons' includes a chapter on mobile phones and brain tumour risk by Hardell, Carlberg and Gee. Inclusion of a full chapter on the science and public health implications of the mobile phone-brain cancer issue underscores the importance to the European Environmental Agency that mobile phone radiation is a possible health threat. This position is supported by the 2011 classification by the World Health

Organization International Agency for Research on Cancer (IARC) of radiofrequency radiation as a Group 2B Possible Human Carcinogen (Baan et al, 2011).

The evidence in 2012 is stronger than in 2007, and based essentially on two large population studies, the Hardell group in Sweden and the Interphone Study Group which involved 13 countries (WHO Interphone Final Report, 2010; Cardis & Radetski 2010? Hansson Mild et al, 2007; Hardell et al, 2006a, 2006b, 2006c; Hardell et al, 2008; Hardell et al, 2009a, 2009b; Hardell et al, 2010; Hardell et al, 2011a, 2011b; Hardell et al, 2012a in press; Hardell et al, 2012b in press). Are all 12 refs from Hardell needed? Looks like overkill…how about those from 2009?

Some researchers have identified in the last five years "*a consistent pattern of increased risk of glioma and acoustic neuroma associated with use of mobile phones and cordless phones.*" (Hardell et al, 2012b in press), a view that is essentially supported by the leader of the Interphone study. (Cardis & Radetski)

The European Environmental Agency's view on the need for precautionary measures on mobile phones is more warranted in 2012, than it was in 2007, or even early 2011, prior to the IARC decision, when we last reviewed the evidence for a presentation to the Council of Europe (EEA, 2011).

Precautionary actions that can be taken to reduce exposures to RFR would be consistent with actions that have been recommended for other emerging environmental and health issues, for example some uses of the common plastic, BPA, some nanotechnologies, and some food chain additives or contaminants, such as antibiotics, beef hormones, and GMOs. The 25 or so more historical case studies in the 'Late Lessons' volumes such as those on the Minamata Bay disaster, asbestos, leaded petrol, and tobacco illustrate the huge costs of not taking robust early warnings seriously.

Precautionary measures are of particular importance in regard to children, who are generally more biologically sensitive, may be unable to protect themselves; and for whom such exposures may carry greater life-time health risks than they do for adults.

The evidence for a brain tumour risk from mobile phones is still not well established

amongst all researchers in the field and there is much scientific controversy about what the current evidence means. The debate is not helped by what might be termed 'trial by media' where some scientific advocates leap into the lay press to argue their own case just as, or even before, their research is published. The effects of this behaviour would be minimized if the results of genuine differences of scientific opinion were made transparent when they were published, with clear explanations about the origins of divergent views, such as the scientific paradigms used ("tissue heating" or "information physics" ?); assumptions made; evidence rejected; and values chosen. This does not tend to happen. Divergent scientific views are often smoothed over with the use of what one respected commentator on the reporting of the Interphone results called "oracular " sentences (Saracci & ?? 2010 ?) which thereby give the media and others the opportunity to report quite opposite conclusions from the same study,as was the case with the Interphone study.

We note that countries including France, Germany, Belgium, Austria, Italy, Russia, India and others have moved toward cautionary warnings and some have revised some target exposure levels for new wireless facilities in line with recommendations issued in 2007. Further actions appear now to be warranted, especially in light of the authoritative 2011 IARC cancer classification.

The IARC, and the EEA , may be wrong to suggest there could be a brain tumour risk from the extensive use of mobile phones, and we dearly hope we are wrong. However, it is worth noting that during over 30 years of classifying cancer risks, covering around 900 agents, IARC very rarely downgrades its judgements: in most cases tentative carcinogens become more certain carcinogens as time since first exposures and further research accumulates. Is it not worth gambling that mobile phones will be one of those very rare cases where IARC has over-classified an agent? We think not. The human cost of getting such a gamble wrong would be too great, especially in light of the relatively low cost of reducing exposures significantly.

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SECTION 24

Key Scientific Evidence and Public Health Policy Recommendations

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I. KEY SCIENTIFIC EVIDENCE

Exposure to electromagnetic fields (EMF) has been linked to a variety of adverse health outcomes. The health endpoints that have been reported to be associated with ELF and/or RF include childhood leukemia, adult brain tumors, childhood brain tumors, genotoxic effects (DNA damage and micronucleation), neurological effects and neurodegenerative disease, immune system disregulation, allergic and inflammatory responses, breast cancer in men and women, miscarriage and some cardiovascular effects.

Effects are not specifically segregated for ELF or RF, since many overlapping exposures occur in daily life; and because this is an artificial division based on frequencies as defined in physics that has little bearing on the biological effects. Both ELF and RF, for example have been shown to cause cells to generate stress proteins, a universal sign of distress in plant, animal and human cells.

The number of people exposed to elevated levels of EMF has been estimated in various studies, and there is general agreement among them. In the United States, few people have chronic or prolonged exposures over 4 mG (0.4 μT) (Kheifets et al, 2005b). Section 20 has information on average residential and occupational ELF levels. The highest exposure category in most all studies is $\geq$ 4 mG ($\geq$ 0.4 μT). Many people have daily exposures to ELF in various ways, some of them up to several hundred milligauss for short periods of time, but relatively few people with the exception of some occupational workers habitually experience ELF exposures greater than 1-2 mG (0.2 – 0.3 μT - App. 20-A).

The exposure of children to EMF has not been studied extensively; in fact, the FCC standards for exposure to radiofrequency radiation are based on the height, weight and stature of a 6-foot tall man, not scaled to children or adults of smaller stature. They do not take into account the unique susceptibility of growing children to exposures (SCENIHR, 2007; Jarosinska and Gee, 2007), nor are there studies of particular relevance to children.

Differences in exposure patterns between infants, children and adults; 2) special susceptibilities of infants and children to the effects of EMF; and 3) interactions between chemical contaminants

and EMF are lacking; as are studies on chronic exposure for both children and adults. There is reason to believe that children may be more susceptible to the effects of EMF exposure since they are growing, their rate of cellular activity and division is more rapid, and they may be more at risk for DNA damage and subsequent cancers. Growth and development of the central nervous system is still occurring well into the teenage years so that neurological changes may be of great importance to normal development, cognition, learning, and behavior. Prenatal exposure to EMF have been identified as possible risk factor for childhood leukemia. Children are largely unable to remove themselves from exposures to harmful substances in their environments. Their exposure is involuntary.

Like second-hand smoke, EMF is a complex mixture, where different frequencies, intensities, durations of exposure(s), modulation, waveform and other factors is known to produce variable effects. Many years of scientific study has produced substantial evidence that EMF may be considered to be both carcinogenic and neurotoxic. The weight of evidence is discussed in this report, including epidemiological evidence and studies on laboratory animals.

Relative risk estimates associated with some of these endpoints are small and the disease is fairly rare (for childhood leukemia, for example), For other diseases, the risk estimates are small but the diseases are common and EMF exposures at levels associated with increased risks are widespread and chronic so the overall public health impacts may be very large.

A. Weight of Evidence Assessment and Criteria for Causality

A weight-of-evidence approach has been used to describe the body of evidence between health endpoints and exposure to electromagnetic fields (ELF and RF).

The number and quality of epidemiological studies, as well as other sources of data on biological plausibility are considered in making scientific and public health policy judgments. Methodological issues that were considered in the review of the epidemiological literature include 1) quality of exposure assessment. 2) sample size of the study, which detects the power to detect an effect, 3) extent to which the analysis or design takes into account potential

confounders or other risk factors, 4) selection bias, 5) the potential for bias in determining exposure. Assessment of the epidemiological literature is consistent with guidelines from Hill (1971), Rothman and Greenland (1998) and the Surgeon General's Reports on Smoking (US DHHS, 2004), and California Air Resources Board (2005). Factors that were considered in reaching conclusions about the weight of evidence overall included strength of the association, consistency of association, temporality, biological plausibility, dose-response and issues with non-linear dose-response, specificity and experimental evidence.

There is a relatively large amount of human epidemiological information with real world exposures, including data from occupational studies. There is less animal data in most cases, except for the genotoxicity studies. Human epidemiological evidence has be given the greatest weight in making judgments about weight-of-evidence, where the results across high quality studies give relatively consistent positive results. Meta-analyses of childhood leukemia, adult leukemia, adult brain tumors, childhood brain tumors, male and female breast cancer and Alzheimer's disease were relied upon in assessing the overall strength of epidemiological study results. Sections 5 – 15 provide analysis of the relevant scientific studies that are key evidence in making public health policy recommendations with respect to exposure to electromagnetic fields (both ELF and RF).

B. Summary of Evidence

1. Childhood Leukemia

Several meta-analyses have been conducted to assess risks of childhood leukemia from exposure to ELF. The results of these studies that combine or pool results of many individual studies (including studies that report both effects and no effects) consistently report increased risks.

Meta-Analysis: Studies of Childhood Leukemia and EMF

Greenland et al., (2000) reported a significantly elevated risk of 1.68 [95% CI 1.23-2.31] based on pooled results from 12 studies using a time-weighted average of exposure greater than 3 mG (0.3 μT). This is a 68% increased risk of childhood leukemia.

Ahlbom et al., (2000) reported a doubling of risk based on a meta-analysis of nine (9) studies. The results reported an elevated risk of 2.0 [95% CI 1.27-3.13] for EMF exposures equal to or greater than 4 mG (0.4 μT) as compared to less than 1 mG (0.1 μT)

Other Relevant Evidence

In 2002, the International Agency for Cancer Research (IARC) designated EMF as a "possible human carcinogen" or Group 2B Carcinogen based on consistent epidemiological evidence. The exposure levels at which increased risks of childhood leukemia are reported in individual studies range from above 1.4 mG or 0.14 μT (Green et al., 1999)for younger children to age six (6) to 4 mG (0.4 μT). Many individual studies with cutpoints of 2 mG or 3 mG (0.2-0.3 μT)) report increased risks. Plausible biological mechanisms exist that may reasonably account for a causal relationship between EMF exposure and childhood leukemia.

Recurrence of Childhood Leukemia and Poorer Survival Rates with Continued EMF Exposure

Foliart reported more than a four-fold (450% increased risk) of adverse outcome (poorer survival rate) for children with acute lymphoblastic leukemia (ALL) who were recovering in EMF environments of 3 mG (0.3 μT) and above (OR 4.5, CI 1.5-13.8). Svendsen reported a poorer survival rate of children with acute lymphoblastic leukemia (ALL) in children exposed to 2 mG (0.2 μT) and above. These children were three times more likely (300% increased risk) to die than children recovering in fields of less than 1 mG (OR 3.0, CI 0.9.8). Children recovering in EMF environments between 1- 2 mG (0.1-0.2 μT) also had poorer survival rates, where the increased risk was 280% (OR 2.8, CI 1.2-6.2).

Higher Lifetime Cancer Risks with Childhood EMF Exposure

Lowenthal (2007) reported that children raised for the first five years in home environments exposed to EMF within 300 meters of a high voltage power line have a five-fold (a 500 percent increased risk of developing some kinds of cancers sometime in later life. For children from newborn to 15 years of age; it is a three-fold risk of developing cancer later in life (Lowenthal et al., 2007). There is suggestive evidence for a link between adult leukemia and EMF exposure.

Attributable Risk

Wartenberg estimates that 8% to 11% of childhood leukemia cases may be related to ELF exposure. This translates into an additional 175 to 240 cases of childhood leukemia based on 2200 US cases per year. The worldwide total of annual childhood leukemias is estimated to be 49,000, giving an estimate of nearly 4000 to 5400 cases per year. Other researchers have estimated higher numbers that could reach to 80% of all cases (Milham, 2001).

2. Childhood Brain Tumors

Childhood Brain Tumors

There is suggestive evidence that other childhood cancers may be related to EMF exposure. The meta-analysis by Wartenberg et al., (1998) reported increased risks for childhood brain tumors. Risks are quite similar whether based on calculated EMF fields (OR = 1.4, 95% CI = 0.8 – 2.3] or based on measured EMF fields (OR = 1.4, 95% CI = 0.8 – 2.4).

3. Adult Brain Tumors

Brain Tumors in Electrical Workers and in Electrical Occupations (Meta-analysis)

A significant excess risk for adult brain tumors in electrical workers and those adults with occupational EMF exposure was reported (Kheifets et al., 1995). This is about the same size risk for lung cancer and second hand smoke (US DHHS, 2006). A total of 29 studies with populations from 12 countries were included in this meta-analysis. The relative risk was reported as 1.16 (CI = 1.08 – 1.24) or a 16% increased risk for all brain tumors. For gliomas, the risk estimate was reported to be 1.39 (1.07 – 1.82) or a 39% increased risk for those in electrical occupations. A second meta-analysis published by Kheifets et al., ((2001) added results of 9 new studies published after 1995. It reported a new pooled estimate (OR = 1.16, 1.08 – 1.01) that showed little change in the risk estimate overall from 1995.

4. Brain Tumors and Acoustic Neuromas in Cell Phone and Cordless Phone Users (Meta-Analysis)

Glioma and Acoustic Neuroma

Hardell et al., (2007) reported in a meta-analysis statistically significant increased risk for glioma with exposure of 10 years or greater in persons using cell phones. Risks were estimated to be 1.2 (0.8 – 1.9) for all use; but when ipsilateral use was assessed (mainly on same side of head) it increased the risk of glioma to 2.0 (1.2 – 3.4) for 10 years and greater use.

For acoustic neuromas, Hardell et al., (2007) reported the increased risk with 10 years or more of exposure to a cell phone at 1.3 (0.6 – 2.8) but this risk increased to 2.4 (1.1 – 5.3) with ipsilateral use (mainly on the same side of the head). There is a consistent pattern of increased risk for brain tumors (glioma) and acoustic neuromas at 10 years and greater exposure to cell phones.

The meta-analysis by Lakhola et al., (2006) reported that brain tumor risk was 1.3 (0.99 – 1.9) for ipsilateral use of a cell phone, but no data was given for exposures at 10 years or greater (all exposures were of shorter duration).

The meta-analysis by Kan et al., (2007) reported "no overall risk" but found elevated risk of brain tumors (RR = 1.25, CI 1.01 – 1.54) $\geq$ 10 years, reinforcing the findings of other pooled

estimates of risk. No estimates of increased risk with ipsilateral use were provided, which would have likely increased reported risks.

5. Neurodegenerative Diseases

Alzheimer's Disease and ALS

Evidence for a relationship between exposure and the neurodegenerative diseases, Alzheimer's and amyotrophic lateral sclerosis (ALS), is strong and relatively consistent. While not every publication shows a statistically significant relationship between exposure and disease, ORs of 2.3 (95% CI = 1.0-5.1 in Qio et al., 2004), of 2.3 (95% CI = 1.6-3.3 in Feychting et al., 2003) and of 4.0 (95% CI = 1.4-11.7 in Hakansson et al., 2003) for Alzheimer's Disease.

Hakansson et al., report more than a doubling of risk for ALS 2.2 (95% CI = 1.0-4.7).

Savitz et al., (1998) reports more than a tripling of risk for ALS (3.1, CI = 1.0 – 9.8).

6. Breast Cancer (Men and Women)

A meta-analysis by Erren (2001) on EMF and breast cancer reported pooled relative risks based on studies of both men and women. A total of 38 publications were reviewed; there were 23 studies on men; 25 studies on women; and 10 studies on both men and women. The pooled relative risk for women exposed to EMF was 1.12 (CI 1.09 – 1.15) or a 12% increased risk, Erren observed that variations between the contributing results are not easily attributable to chance (P = 0.0365). For men and breast cancer, he reported a fairly homogeneous increased risk (a pooled relative risk of 1.37 [CI 1.11 – 1.71]).

This analysis is well conducted. The results were stratified according to measured or assumed intensity of exposure to EMF; and the estimate of risk for the most heavily exposed group was extracted. Independent estimates of RRs were grouped according to gender, type of study (case-control and cohort), country where the study was conducted and method used to assess exposure. Pooled estimates of RRs and their 95% confidence intervals (CI) referring to various combinations of these factors were calculated according to appropriate statistical methods (Greenland, 1987). Misclassification possibilities were thoroughly assessed, and whether the results were sole endpoints or there were multiple endpoints in each study did not affect the RRs.

Erren qualifies his findings by discussing that latencies for cancers can be 20 to 30 years, Further, he notes that studies of total EMF exposures from both home, travel and workplace are rarely available, and these EMF sources are ubiquitous. Both could result in underestimation of risks. Another way in which risks might be masked is by variations in age of study participants. Forssen and colleagues (2000) reported no increased RRs for breast cancer in women of all ages

when they combined residential and occupational EMF exposures (RR = 0.9, CI 0.3 – 2.7). However, when risks for the women younger than 50 years of age were separated out and calculated, the RR increased to 7.3 (CI 0.7 – 78.3) although with wide confidence intervals based on only four cases. Erren notes

"When possibly relevant exposures to EMF in the whole environment are assessed only partially, errors in the categorization of exposure status are likely to occur. If such misclassification is random and thus similar in subrgroups being compared (nondifferential), then the error will tend to introduce bias towards the null. Substantial random misclassification of exposures would then tend to generate spurious reports of 'little or no effect'. Note for example that estimates of smoking-associated lung cancer risks in the early 1950's could have been seriously distorted if exposure assessment had not considered smoking either at work or at home."

"Collectively, the data are consistent with the idea that exposures to EMF, as defined, are associated with some increase in breast cancer risks, albeit the excess risk is small." Erren (2001)

7. Combined Effects of Toxic Agents and ELF

ELF and Toxic Chemical Exposures

There is also the issue of what weight to give the evidence for synergistic effects of toxic chemical exposure and EMF exposure. Juuilainen et al., (2006) reported that the combined effects of toxic agents and ELF magnetic fields together enhances damage as compared to the toxic exposure alone. In a meta-analysis of 65 studies; overall results showed 91% of the *in vivo* studies and 68% of the *in vitro* studies had worse outcomes (were positive for changes indicating synergistic damage) with ELF exposure in combination with toxic agents. The percentage of the 65 studies with positive effects was highest when the EMF exposure preceded the other exposure. The radical pair mechanism (oxidative damage due to free radicals) is cited as a good candidate to explain these results. Reconsideration of exposure limits for ELF is warranted based on this evidence.

II. FALLACIES AND ANSWERS IN THE DEBATE OVER EMF EVIDENCE

There are several arguments (false, in our view) that have been presented by those who minimize the strength of the relationship between exposure to both 50-60Hz ELF and RF EMFs. These are as follows:

A. "Only a small number of children are affected."

This argument is not correct because we do not know precisely how many children are affected. In 1988 Carpenter and Ahlbom attempted to answer this question based on the results of the New York State Powerlines Project and the results of the study of Savitz et al. (1988), and concluded that if the magnetic fields homes in the US were similar to those in Denver, Colorado fully 10 to 15% of US childhood leukemia (about 1,000 cases) could be associated with residential magnetic field exposure. They then concluded that exposure to magnetic fields from non-residential sources (particularly appliances) must be at least equal in magnitude, and that if so these two sources of exposure would account for 20-35% of childhood leukemia.

There have been several meta-analyses of the childhood leukemia data (Wartenberg, 1998; Greenland et al., 2000; Ahlbom et al., 2000). All have concluded that there is a significant association between residential exposure to magnetic fields and elevated risk of leukemia in children. Greenland et al. (2000) performed a meta-analysis of 15 studies of magnetic field or wire code investigations of childhood leukemia, and calculated the attributable fraction of cases of childhood leukemia from residential magnetic field exposure in the US was 3%. Ahlbom et al. (2000) conducted a different meta-analysis that concluded there was a significant 2-fold elevation of risk at exposure levels of 4 mG (0.4 μT) or greater. Kheifets et al. (2006) attempted to calculate the attributable fraction of worldwide childhood leukemia due to EMFs, based on the meta-analyses of Ahlbom et al. (2000) and Greenland et al., (2000). They concluded that the attributable fraction of leukemia was between <1% to 4%. The recent WHO Environmental Health Criteria ELF Monograph #238 (2007) states "(A)ssuming that the association is causal, the number of cases of childhood leukaemia worldwide that might be attributable to exposure can be estimated to range from 100 to 2,400 cases per year. However this represents 0.2 to 4.9% of the total annual incidence of leukaemia cases, estimated to be 49,000 worldwide in 2000. Thus, in a global context, the impact on public health, if any, would be limited and uncertain."

These reports are important, in that they show consistency in there being a clearly elevated risk of leukemia in children with EMF exposure from power line fields in homes. These meta-analyses lead to the conclusion, reflected in the WHO report, that there is an association between childhood cancer and exposure to elevated magnetic fields in homes. We strongly disagree, however, with the overall conclusion that these calculations indicate that the fraction of childhood leukemia attributable to EMFs is so small as to not have serious public health implications.

There are several reasons why the WHO ELF Environmental Health Criteria Monograph conclusion is not justified. These studies all considered either only measured magnetic fields in homes or wire codes from power lines, ignoring exposure from appliances, wireless devices and all exposures outside of the home. Thus these metrics do not come close to accounting for any individual's cumulative exposure to EMFs. If residential magnetic fields cause cancer, then those from other sources will add to the risk. The failure to measure total EMF exposure would tend to obscure the relationship and lead to

gross underestimation of the true relationship between exposure and disease. While the evidence for a relationship between exposure and childhood leukemia may be considered to be definitive at exposure levels of 3 or 4 mG (0.3 or 0.4 μT) or higher; there is evidence from some (but not all) of the other studies for an elevated risk at levels not greater than 2 mG (0.2 μT) (Savitz et al., 1988; Green, 1999). There is absolutely no evidence that exposures at lower levels are "safe", since persons with these exposures are usually the "control" group. Therefore this WHO statement fails to acknowledge the true magnitude of the problem, even when considering only childhood leukemia. The global attributable risk of childhood leukemia as a result of exposure to EMFs must be significantly greater than that calculated from consideration of only residential 50/60 Hz magnetic fields in studies where there is no unexposed control.

As detailed in other chapters in this report (Chapter 10), there is some evidence for a relationship between EMF exposure and brain cancers in children. We have almost no understanding of the mechanisms behind the development of brain cancers, and any cancer in a child is a tragedy. While evidence for a relationship between EMF exposure and childhood brain cancer is not as strong as for leukemia, it is of concern and deserves more study. Of even greater concern, given the clear evidence for elevated risk of childhood leukemia upon exposure to 50/60 Hz EMFs, is the relative lack of a comparable body of information on the effects of radiofrequency EMFs on the health of children. A recent study of South Korean children (1,928 with leukemia, 956 with brain cancer and 3,082 controls) living near to AM radio transmitters reports an OR of 2.15 (95% CI = 1.19-2.11) for risk of leukemia in children living within 2 km of the nearest AM transmitter as compared to those living more than 20 km from it (Ha et al., 2007). No relation was found for brain cancer. This study is consistent with the hypothesis that radiofrequency EMFs have similar effects to 50/60 Hz EMFs, but more study is needed. Since radiofrequency EMFs have higher energy than do power line frequencies, one might expect that they would be even more likely to cause disease. The enormous and very recent increase in use of cell phones by children is particularly worrisome. However there is little information at present on the long-term consequences of cell phone use, especially by children.

B. "There is insufficient evidence that adult diseases are secondary to EMF exposure."

It is correct that the level of evidence definitively proving an association between exposure to EMFs and various adult diseases is less strong that the relationship with childhood leukemia. However there are multiple studies which show statistically significant relationships between occupational exposure and leukemia in adults (see Chapter 11), in spite of major limitations in the exposure assessment. A very recent study by Lowenthal et al. (2007) investigated leukemia in adults in relation to residence near to high-voltage power lines. While they found elevated risk in all adults living near to the high voltage power lines, they found an OR of 3.23 (95% CI = 1.26-8.29) for individuals who spent the first 15 years of life within 300 m of the power line. This study provides support for two important conclusions: adult leukemia is also associated with

EMF exposure, and exposure during childhood increases risk of adult disease. Thus protecting children from exposure should be a priority.

The evidence for a relationship between exposure and breast cancer is relatively strong in men (Erren, 2001), and some (by no means all) studies show female breast cancer also to be elevated with increased exposure (see Chapter 12). Brain tumors and acoustic neuromas are more common in exposed persons (see Chapter 10). There is less published evidence on other cancers, but Charles et al. (2003) report that workers in the highest 10% category for EMF exposure were twice as likely to die of prostate cancer as those exposed at lower levels (OR 2.02, 95% CI = 1.34-3.04). Villeneuve et al. (2000) report statistically significant elevations of non-Hodgkin's lymphoma in electric utility workers in relation to EMF exposure, while Tynes et al. (2003) report elevated rates of malignant melanoma in persons living near to high voltage power lines. While these observations need replication, they suggest a relationship between exposure and cancer in adults beyond leukemia.

Evidence for a relationship between exposure and the neurodegenerative diseases, Alzheimer's and amyotrophic lateral sclerosis (ALS), is strong and relatively consistent (see Chapter 12). While not every publication shows a statistically significant relationship between exposure and disease, ORs of 2.3 (95% CI = 1.0-5.1 in Qio et al., 2004), of 2.3 (95% CI = 1.6-3.3 in Feychting et al., 2003) and of 4.0 (95% CI = 1.4-11.7 in Hakansson et al., 2003) for Alzheimer's Disease, and of 3.1 (95% CI = 1.0-9.8 in Savitz et al., 1998) and 2.2 (95% CI = 1.0-4.7 in Hakansson et al., 2003) for ALS cannot be simply ignored.

In total the scientific evidence for adult disease associated with EMF exposure, given all of the difficulties in exposure assessment, is sufficiently strong that preventive steps are appropriate, even if not all reports have shown exactly the same positive relationship. While there are many possible sources of false positive results in epidemiological studies, there are even more possible reasons for false negative results, depending on sample size, exposure assessment and a variety of other confounders. It is inappropriate to discount the positive studies just because not every investigation shows a positive result. While further research is needed, with better exposure assessment and control of confounders; the evidence for a relationship between EMF exposure and adult cancers and neurodegenerative diseases is sufficiently strong at present to merit preventive actions to reduce EMF exposure.

C. "The risk is low."

This argument is incorrect because at present it is not possible to determine the magnitude of the risk. Clearly as far as EMFs are concerned there is no unexposed population. Therefore one can only compare groups with different levels of exposure. We can perhaps say with confidence that the elevated risk of leukemia from residential exposure of children to magnetic fields is "low" (meaning ORs in the range of 2-4), but this does not consider the child's exposure to appliances, exposure in automobiles and at

daycare or school, exposures in playgrounds and at all of the other places that a child spends time. Even if the risk to one individual is low, the societal impact when everyone is exposed may be very significant.

In addition the exposure assessment is grossly inadequate, even in the best of studies. Most reports deal only with either characterization of the fields within residences or with job titles in occupational settings. Some studies attempt to quantitate other sources of exposure, such as frequency of cell phone usage or use of other appliances, but these studies almost always do not consider residential exposure from power lines. In no investigation has it been possible to follow the exposures of a large number of people over a number of years with accurate monitoring of total exposure to EMFs. This would of course be almost impossible to do for the very good reason that as a person moves through his or her environment the exposures vary from place to place and from moment to moment. However to truly and objectively determine the risk of exposure to EMFs it is essential to consider residential, occupational (or school) and recreational exposures to the full range of the electromagnetic spectrum, including appliances and wireless devices. This has not been accomplished in any study, and without such information it is not possible to determine the overall magnitude of the risk. It is possible, indeed likely, that upon consideration of both childhood and adult diseases that the risk is not low.

D. "There is no animal evidence".

It is correct that there is no adequate animal model system that reproducibly demonstrates the development of cancer in response to exposure to EMFs at the various frequencies of concern. McCann et al. (1997) reviewed the animal studies, and while they found most to be negative there were several that showed suggestive positive results. They also clearly identified issues that need to be improved in further animal carcinogenesis investigations. However Kheifets et al. (2005a) in a policy review noted that "even consistent negative toxicological data cannot completely overcome consistent epidemiological studies. First, a good animal model for childhood leukemia has been lacking. Second, particularly for ELF, the complex exposures that humans encounter on a daily basis and a lack of understanding of the biologically relevant exposure calls into question the relevance of exposures applied in toxicology. Another limitation of toxicologic studies is that animals cannot be exposed to fields that are orders of magnitude more powerful than those encountered by humans, decreasing their power to detect small risks." Further, they conclude that "(A)lthough the body of evidence is always considered as a whole, based on the weight of evidence approach and incorporating different lines of scientific enquiry, epidemiologic evidence, as most relevant, is given the greatest weight."

One positive animal study is that by Rapacholi et al. (1997), who demonstrated that lymphoma-prone transgenic mice developed significantly more lymphoma after exposure to 900 MHz fields (lymphoma being the animal equivalent of human leukemia) than did unexposed animals. More striking is the report from Denver, Colorado using the wire-code characterization originally developed by Wertheimer and Leeper (1979) showing

that pet dogs living in homes characterized as having high or very high wire codes, as compared to those with low or very low wire codes or buried power lines, showed a OR of 1.8 (95% CI = 0.9-3.4) for development of lymphoma after adjustment for potential confounders, whereas dogs that lived in homes with very high wire codes had an OR of 6.8 (95% CI = 1.6-28.5) (Reif et al., 1995). This study is impressive because the exposure of the dogs reflects the environment in which exposure has been associated with elevated risk of human cancer in two independent investigations (Wertheimer and Leeper, 1979: Savitz et al., 1988).

It is curious that in many legal situations the courts are reluctant to accept only evidence that substance X causes cancer in animals without corresponding evidence in humans. In the case of EMFs we have strong evidence that EMFs cause cancer in human, but much less evidence from animal models. The US Supreme Court, in the case of Daubert vs. Merrell Dow Pharmaceuticals, effectively ruled that animal studies were not relevant to human health, and that the only admissible evidence must be from human epidemiological studies! While this is certainly not a justifiable conclusion, the situation with regards to EMF health effects is that we have strong evidence for human cancer from epidemiological studies, but do not have good evidence for cancer in experimental animals. But it is humans that we should be concerned about, not the laboratory rats.

E. "We do not know a mechanism."

We do not know the mechanism of cancer in general, although we know a lot about cancer. It came as a major surprise to most scientists when Lichtenstein et al., (2000) reported that genetic factors play a minor role in causing most types of cancer, since it was commonly assumed that genetics was the major cause. However Lichtenstein et al. concluded from their study of identical twins that environmental factors were the initiating event in the great majority of cancers. This does not, of course, mean that genetic susceptibility to environmental contaminants is unimportant, but only that genetic factors alone do not result in cancer. We know mechanisms of action for some carcinogenic substances, but for most cancers we know neither the environmental trigger nor the mechanism of action. So there is no reason to negate the evidence that EMFs cause cancer just because we do not know a single mechanism to explain it's mode of action.

We do not know the mechanism or cause for development of Alzheimer's Disease or ALS. We do know that both are more common in individuals in certain occupations, and that exposure to certain metals appears to be associated with increased risk (Kamel et al., 2002; Shcherbatykh and Carpenter, 2007). In the case of Alzheimer's Disease there are abnormalities of amyloid β and tau protein (Goedert and Spillantini, 2006), but very limited understanding of why or how they form. Neither the association with metals nor the presence of abnormal proteins constitutes a mechanism for cause of disease. So rather than discounting the relationship between EMF exposure and neurodegenerative diseases we should be using this information as a tool to better understand the etiology of these diseases.

There is clear evidence from animal and cell culture studies that ELF and RFR have biological effects. Furthermore, these effects occur at intensities commonly experienced by humans. We know a number of ways in which EMFs alter cell physiology and function, as detailed in various chapters in this report. EMFs affect gene transcription (Chapter 5 and 6), cause the synthesis of stress proteins (Chapter 7) and cause breakage of DNA, probably through generation of reactive oxygen species (Chapter 6 and 9 - Lai and Singh, 2004). Any one of these actions might be responsible for the carcinogenic and neurodegenerative actions of EMFs. However, as with many environmental agents, it would be a mistake to assume that there is only one target or mechanism of action. It is unlikely, for example, that the effects on the nervous system and behavior are secondary to exactly the same cellular targets and actions that lead to cancer. It is likely that there are multiple mechanisms of action leading to disease. But the lack of complete understanding of basic mechanisms does not alter the importance of the relationships.

F. Vested Interests: How They Shape the Public Health Debate

There is no question but that global implementation of the safety standards proposed in this report has the potential to not only be very expensive but also could be disruptive of life and economy as we know it if implemented abruptly and without careful planning. Action must be a balance of risk to cost to benefit. However, "deny and deploy" strategies by industry should not be rewarded in future risk assessment calculations. For example, if significant economic investments in the roll-out of risky technologies persist beyond the time that there is reasonable suspicion of risk available to all who look, then such costs should not be borne by ratepayers (in the case of new powerlines) or by compensating industry for bad corporate choices. Such investments in the deployment of new sources of exposure for ELF and RF should not count toward the balance sheet when regulatory agencies perform risk assessments. Mistakes may be made, but industry should make mid-course corrections to inform and protect the public, rather than deny effects pending "proof". Whether the costs of remedial action are worth the societal benefits is a formula that should reward precautionary behavior. Prudent corporate policies should be expected to address and avoid future risks and liabilities. Otherwise, there is no market incentive to produce safe (and safer) products.

The deployment of new technologies is running ahead of any reasonable estimation of possible health impacts and estimates of probabilities, let alone a solid assessment of risk. However what has been missing with regard to EMF has been an acknowledgement of the risk that is demonstrated by the scientific studies. As discussed in earlier sections, in this case there is clear evidence of risk, although the magnitude of the risk is uncertain, and the magnitude of doing nothing on the health effects cost to society is similarly uncertain. This situation is very similar to our history of dealing with the hazards of smoking decades ago, where the power of the industry to influence governments and even conflicts of interest within the public health community delayed action for more than a generation, with consequent loss of life and enormous extra health care costs to society.

Just because a problem is difficult to solve is not a reason to deny that a problem exists. In fact solutions to difficult issues usually can't be expected until the issues are known and creative thinking is brought to bear to find a solution.

The most contentious issue regarding public and occupational exposures to ELF and RF involves the resolute adherence to existing ICNIRP and IEEE standards by many countries, in the face of growing scientific evidence of health risks at far lower levels. Furthermore there is widespread belief that governments are ignoring this evidence. There are two obvious factors that work against governments taking action to set exposure guidelines based on current scientific evidence of risk. These are: 1) contemporary societies are very dependent upon electricity usage and RF communications, and anything that restricts current and future usage potentially has serious economic consequences and 2) the electric power and communications industries have enormous political clout and even provide support for a significant fraction of what research is done on EMF. This results in legislation that protects the status quo and scientific publications whose conclusions are not always based on only the observations of the research. It hinders wise public health policy actions and implementation of prevention strategies because of the huge financial investments already made in these technologies.

In 1989, in an editorial for Science Magazine, Philip H. Abelson called for more research into low-frequency electromagnetic fields. At that time, he confirmed that a US Office of Technology Assessment (OTA) study had determined that *"(o)verall, the evidence is too weak to allow firm conclusions either way*" but a policy of prudent avoidance strategy was suggested, Abelson defined this as "*to systematically look for strategies which can keep people out of 60 Hz fields*". Both policy actions were developed in the midst of scientific uncertainty, but rising concern for possible health impacts to the public. At that time, with high level of unknowns, the appropriate level of policy action was prudent avoidance or precautionary action. Nearly two decades later, the level of action warranted is higher – based on many new scientific publications confirming risks may exist – and justifying prevention or preventative action.

III. EMF EXPOSURE AND PRUDENT PUBLIC HEALTH PLANNING

• *The scientific evidence is sufficient to warrant regulatory action for ELF; and it is substantial enough to warrant preventative actions for RF.*

• *The standard of evidence for judging the emerging scientific evidence necessary to take action should be proportionate to the impacts on health and well-being*

• *The exposures are widespread.*

• *Widely accepted standards for judging the science are used in this assessment.*

Public exposure to electromagnetic radiation (power-line frequencies, radiofrequency and microwave) is growing exponentially worldwide. There is a rapid increase in electrification in developing countries, even in rural areas. Most members of society now have and use cordless phones, cellular phones, and pagers. In addition, most populations are also exposed to antennas in communities designed to transmit wireless RF signals. Some developing countries have even given up running land lines because of expense and the easy access to cell phones. Long-term and cumulative exposure to such massively increased RF has no precedent in human history. Furthermore, the most pronounced change is for children, who now routinely spend hours each day on the cell phone. Everyone is exposed to a greater or lesser extent. No one can avoid exposure, since even if they live on a mountain-top without electricity there will likely be exposure to communication-frequency RF exposure. Vulnerable populations (pregnant women, very young children, elderly persons, the poor) are exposed to the same degree as the general population. Therefore it is imperative to consider ways in which to evaluate risk and reduce exposure. Good public health policy requires preventative action proportionate to the potential risk of harm and the public health consequence of taking no action.

IV. RECOMMENDED ACTIONS

A. Defining new exposure standards for ELF

This chapter concludes that new ELF limits are warranted based on a public health analysis of the overall existing scientific evidence. The public health view is that new ELF limits are needed now. They should reflect environmental levels of ELF that have been demonstrated to increase risk for childhood leukemia, and possibly other cancers and neurological diseases. ELF limits should be set below those exposure levels that have been linked in childhood leukemia studies to increased risk of disease, plus an additional safety factor. It is no longer acceptable to build new power lines and electrical facilities that place people in ELF environments that have been determined to be risky. These levels are in the 2 to 4 milligauss* (mG) range (0.2 – 0.4 μT), not in the 10s of mG or 100s of mG. The existing ICNIRP limit is 1000 mG (100 μT) and 904 mG (90.4 μT) in the US for ELF is outdated and based on faulty assumptions. These limits are can no longer be said to be protective of public health and they should be replaced. A safety buffer or safety factor should also be applied to a new, biologically-based ELF limit, and the conventional approach is to add a safety factor lower than the risk level.

While new ELF limits are being developed and implemented, a reasonable approach would be a 1 mG (0.1 μT) planning limit for habitable space adjacent to all new or upgraded power lines and a 2 mG (0.2 μT) limit for all other new construction. It is also recommended for that a 1 mG (0.1 μT) limit be established for existing habitable space for children and/or women who are pregnant (because of the possible link between childhood leukemia and *in utero* exposure to ELF). This recommendation is based on the assumption that a higher burden of protection is required for children who cannot protect themselves, and who are at risk for childhood leukemia at rates that are traditionally high enough to trigger regulatory action. This situation in particular warrants extending the 1 mG (0.1 μT) limit to existing occupied space. "Establish" in this case probably means formal public advisories from relevant health agencies. While it is not realistic to reconstruct all existing electrical distribution systems, in the short term; steps to reduce exposure from these existing systems need to be initiated, especially in places where children spend time, and should be encouraged. These limits should reflect the exposures that are commonly associated with increased risk of child hood leukemia (in the 2 to 5 mG (0.2 to 0.5 μT) range for all children, and over 1.4 mG (0.14 μT) for children age 6 and younger). Nearly all of the occupational studies for adult cancers and neurological diseases report their highest exposure category is

4 mG (0.4 μT) and above, so that new ELF limits should target the exposure ranges of interest, and not necessarily higher ranges.

Avoiding chronic ELF exposure in schools, homes and the workplace above levels associated with increased risk of disease will also avoid most of the possible bioactive parameters of ELF discussed in the relevant literature.

It is not prudent public health policy to wait any longer to adopt new public safety limits for ELF. These limits should reflect the exposures that are commonly associated with increased risk of childhood leukemia (in the 2 to 5 mG (0.2-0.5 μT) range for all children, and over 1.4 mG (0.14 μT) for children age 6 and younger). Avoiding chronic ELF exposure in schools, homes and the workplace above levels associated with increased risk of disease will also avoid most of the possible bioactive parameters of ELF discussed in the relevant literature.

B. Defining preventative actions for reduction in RF exposures

Given the scientific evidence at hand, the rapid deployment of new wireless technologies that chronically expose people to pulsed RF at levels reported to cause bioeffects, whicih in turn, could reasonably be presumed to lead to serious health impacts, is a public health concern. A public health action level that implements preventative action now is warranted, based on the collective evidence. There is suggestive to strongly suggestive evidence that RF exposures may cause changes in cell membrane function, cell communication, metabolism, activation of proto-oncogenes and can trigger the production of stress proteins at exposure levels below current regulatory limits. Resulting effects can include DNA breaks and chromosome aberrations, cell death including death of brain neurons, increased free radical production, activation of the endogenous opioid system, cell stress and premature aging, changes in brain function including memory loss, retarded learning, performance impairment in children, headaches and fatigue, sleep disorders, neurodegenerative conditions, reduction in melatonin secretion and cancers (Chapters 5, 6, 7, 8, 9, 10, and 12).

As early as 2000, some experts in bioelectromagnetics promoted a 0.1 μW/cm2 limit (which is 0.614 Volts per meter) for ambient outdoor exposure to pulsed RF, so generally in cities, the public would have adequate protection against involuntary exposure to pulsed radiofrequency (e.g., from cell towers, and other wireless technologies). The Salzburg Resolution of 2000 set a target of 0.1 μW/cm2 (or 0.614 V/m) for public exposure to pulsed radiofrequency. Since then, there are many credible anecdotal reports of unwellness and illness in the vicinity of wireless transmitters (wireless voice and data communication antennas) at lower levels. Effects include sleep disruption, impairment of memory and concentration, fatigue, headache, skin disorders, visual symptoms (floaters), nausea, loss of appetite, tinnitus, and cardiac problems (racing heartbeat), There are some credible articles from researchers reporting that cell tower -level RF exposures (estimated to be between 0.01 and 0.5 μW/cm2) produce ill-effects in populations living up to several hundred meters from wireless antenna sites,

This information now argues for thresholds or guidelines that are substantially below current FCC and ICNIPR standards for whole body exposure. Uncertainty about how low such standards might have to go to be prudent from a public health standpoint should not prevent reasonable efforts to respond to the information at hand. No lower limit for bioeffects and adverse health effects from RF has been established, so the possible health risks of wireless WLAN and WI-FI systems, for example, will require further research and no assertion of safety at any level of wireless exposure (chronic exposure) can be made at this time. The lower limit for reported human health effects has dropped 100-fold below the safety standard (for mobile phones and PDAs); 1000- to 10,000-fold for other wireless (cell towers at distance; WI-FI and WLAN devices). The entire basis for safety standards is called into question, and it is not unreasonable to question the safety of RF at any level.

A cautionary target level for pulsed RF exposures for ambient wireless that could be applied to RF sources from cell tower antennas, WI-FI, WI-MAX and other similar sources is proposed. The recommended cautionary target level is 0.1 microwatts per centimeter squared (μW/cm2)** (or 0.614 Volts per meter or V/m)** for pulsed RF where these exposures affect the general public; this advisory is proportionate to the evidence and in accord with prudent public health policy. A precautionary limit of 0.1 μW/cm2 should be adopted for outdoor, cumulative RF exposure. This reflects the current RF science and prudent public health response that would reasonably be set for pulsed RF (ambient) exposures where

people live, work and go to school. This level of RF is experienced as whole-body exposure, and can be a chronic exposure where there is wireless coverage present for voice and data transmission for cell phones, pagers and PDAs and other sources of radiofrequency radiation. An outdoor precautionary limit of 0.1 μW/cm2 would mean an even lower exposure level inside buildings, perhaps as low as 0.01 μW/cm2. Some studies and many anecdotal reports on ill health have been reported at lower levels than this; however, for the present time, it could prevent some of the most disproportionate burdens placed on the public nearest to such installations. Although this RF target level does not preclude further rollout of WI-FI technologies, we also recommend that wired alternatives to WI-FI be implemented, particularly in schools and libraries so that children are not subjected to elevated RF levels until more is understood about possible health impacts. This recommendation should be seen as an interim precautionary limit that is intended to guide preventative actions; and more conservative limits may be needed in the future.

Broadcast facilities that chronically expose nearby residents to elevated RF levels from AM, FM and television antenna transmission are also of public health concern given the potential for very high RF exposures near these facilities (antenna farms). RF levels can be in the 10s to several 100's of μW/cm2 in residential areas within half a mile of some broadcast sites (for example, Lookout Mountain, Colorado and Awbrey Butte, Bend, Oregon). Like wireless communication facilities, RF emissions from broadcast facilities that are located in, or expose residential populations and schools to elevated levels of RF will very likely need to be re-evaluated for safety.

For emissions from wireless devices (cell phones, personal digital assistant or PDA devices, etc) there is enough evidence for increased risk of brain tumors and acoustic neuromas now to warrant intervention with respect to their use. Redesign of cell phones and PDAs could prevent direct head and eye exposure, for example, by designing new units so that they work only with a wired headset or on speakerphone mode.

These effects can reasonably be presumed to result in adverse health effects and disease with chronic and uncontrolled exposures, and children may be particularly vulnerable. The young are also largely unable to remove themselves from such environments. Second-hand radiation, like second-hand smoke is an issue of public health concern based on the evidence at hand.

V. CONCLUSIONS

• We cannot afford 'business as usual" any longer. It is time that planning for new power lines and for new homes, schools and other habitable spaces around them is done with routine provision for low-ELF environments . The business-as-usual deployment of new wireless technologies is likely to be risky and harder to change if society does not make some educated decisions about limits soon. Research must continue to define what levels of RF related to new wireless technologies are acceptable; but more research should not prevent or delay substantive changes today that might save money, lives and societal disruption tomorrow.

• New regulatory limits for ELF based on biologically relevant levels of ELF are warranted. ELF limits should be set below those exposure levels that have been linked in childhood leukemia studies to increased risk of disease, plus an additional safety factor. It is no longer acceptable to build new power lines and electrical facilities that place people in ELF environments that have been determined to be risky (at levels generally at 2 mG (0.2 μT) and above).

• While new ELF limits are being developed and implemented, a reasonable approach would be a 1 mG (0.1 μT) planning limit for habitable space adjacent to all new or upgraded power lines and a 2 mG (0.2 μT) limit for all other new construction, It is also recommended for that a 1 mG (0.1 μT) limit be established for existing habitable space for children and/or women who are pregnant . This recommendation is based on the assumption that a higher burden of protection is required for children who cannot protect themselves, and who are at risk for childhood leukemia at rates that are traditionally high enough to trigger regulatory action. This situation in particular warrants extending the 1 mG (0.1 μT) limit to existing occupied space. "Establish" in this case probably means formal public advisories from relevant health agencies.

• While it is not realistic to reconstruct all existing electrical distributions systems, in the short term; steps to reduce exposure from these existing systems need to be initiated, especially in places where children spend time, and should be encouraged.

• A precautionary limit of 0.1 (μW/cm2 (which is also 0.614 Volts per meter) should be adopted for outdoor, cumulative RF exposure. This reflects the current RF science and prudent public health response that would reasonably be set for pulsed RF (ambient) exposures where people live, work and go to school. This level of RF is experienced as whole-body exposure, and can be a chronic exposure where there is wireless coverage present for voice and data transmission for cell phones, pagers and PDAs and other sources of radiofrequency radiation. Some studies and many anecdotal reports on ill health have been reported at lower levels than this; however, for the present time, it could prevent some of the most disproportionate burdens placed on the public nearest to such installations. Although this RF target level does not preclude further rollout of WI-FI technologies, we also recommend that wired alternatives to WI-FI be implemented, particularly in schools and libraries so that children are not subjected to elevated RF levels until more is understood about possible health impacts. This recommendation should be seen as an interim precautionary limit that is intended to guide preventative actions; and more conservative limits may be needed in the future.

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SECTION 24

Key Scientific Evidence and Public Health Policy Recommendations

(Supplement 2012)

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I. INTRODUCTION

In public health and environmental policy-making, asking the right questions is a highly evolved art form. It is necessary to periodically look for '*not-so-early-now warnings'* from new science and medical information. At some point it becomes '*old news'* in the real-world process of commercializing new technologies* and is ignored. Precious time is lost if the '*evidence curve'* does not come quickly enough to '*change the rollout curve*' and result in early enough interventions. EMF may be a highly preventable source of disease but not without early enough translation of the science into action. The time for arguing whether EMF health effects exist is over. We know they exist and that they result in human disease.

Asking the right questions and looking for proportionate responses necessarily involves make mid-course corrections guided by new evidence. This is particularly true when the consequences of doing nothing are too great to ignore – because they will affect billions of people in societies around the world. "*While there are many unanswered questions, the cost of doing nothing will result in an increasing number of people, many of them young, developing cancer*." (Carpenter, 2010).

What questions should be asked now, to move forward on the body of evidence? How much evidence do we need to act? Do we have enough? What standard of evidence should be used to judge (purely scientific vs precautionary public health). What is a relevant biological 'dose'? How long does a biological effect last? Are we accounting for differences among individuals or different types of cells?

Which of the studies are truly measuring chronic exposures (is a one-month or a one-year study really revealing chronic effects; if mid-length studies show no effect, does this tell us anything useful)? Why is it still considered reasonable to base safety standards on time-averaged radiofrequency exposures when the technologies today use pulsed RFR?

*Electronics, the internet, cellular telecommunications, wireless medical technologies, and wireless sensors for energy conservation, electric utilities management, transportation, education, banking and national security.

For example, the collective behavior of neurons is established through synchrony. "*Individual neurons have a time window of tens of milliseconds range for single neurons, but oscillatory coalitions of neurons can expand the effect window of synchronization from hundreds of milliseconds to many seconds"* (Buzsaki, 2006). This means the time span a bioeffect can last long enough to overlap with the next environmental provocation (pulsed RFR in this case) so that repetitive exposures may induce an unending cascade of neurological firing that eventually disrupts normal homeostasis and causes chronically abnormal function in cooperative assemblies of cells like neurons. RFR is bioactive and already classified as a Possible Human Carcinogen but the relevant RFR bursts are camouflaged and their relevant metrics are diluted away by time averaging. Why is it reasonable to use safety standards that were developed to guard against induced currents in tissue (ELF-EMF) or that heat or burn tissue (RFR)?

Briefly stated, here is what we knew in 2007.

- Bioeffects and adverse health effects of chronic exposure to low-intensity (non-thermal) non-ionizing radiation are established.
- Existing FCC and ICNIRP public safety limits are not sufficiently protective of public health.
- The World Health Organization has classified ELF-EMF as a Group 2B Possible Human Carcinogen (2001).
- New, biologically-based public exposure standards are critically needed.
- It is not in the public interest to wait.

Here is what we know in 2012. There is more evidence, over a broader range of studies. The levels of biological responses are extraordinarily low (down to the nanowatt and picowatt power density level).

New studies address fertility and reproduction, fetal and neonatal effects, cognitive and behavioral problems in children and neurological damage. There are more mobile phone base station studies with longer testing periods, much more information on genetic damage and confirmation of increased risk of brain cancers from not one or two

studies, but from many studies and many authors including the World Health Organization's massive 13-country INTERPHONE STUDY (Interphone Study Group, 2010).

There are many studies reporting effects of cell phone radiation (even on standby-mode), wireless laptop exposure, cell phone use by mothers resulting in altered fetal brain development in the offspring, and more evidence that the blood-brain barrier and memory are at risk from cell phone use. There is evidence from human and animal studies that key areas of the brain are negatively affected by RFR at legal levels.

There is better understanding of the important physical and biological factors that make ELF-EMF and RFR potent disruptors of living tissues and basic metabolic processes. More and more, EMF devices are being used for medical treatments in cancer, bone and wound healing and re-tuning the nervous system. Increased depth of evidence in many threads is presented in this report by well-regarded scientists and researchers from around the world. The number of good studies has grown. The exposure levels causing effects are documented to be much lower than in the past. The epidemiological evidence is now showing risks for a variety of adverse health outcomes. All this should be taken seriously by governments, and translated quickly into more protective safety standards, and in the interim, into strong preventative actions, warnings and substitution of safer technologies and redesigned devices.

Bioeffects are clearly established and occur at very low levels of exposure to electromagnetic fields and radiofrequency radiation. Bioeffects can occur in the first few minutes at levels associated with cell and cordless phone use. Bioeffects can also occur from just minutes of exposure to mobile phone masts (cell towers), WI-FI, and wireless utility 'smart' meters that produce whole-body exposure. Chronic base station level exposures can result in illness.

Many of these bioeffects can reasonably be expected to result in adverse health effects if the exposures are prolonged or chronic. This is because they interfere with normal body processes (disrupt homeostasis), prevent the body from healing damaged DNA, produce immune system imbalances, metabolic disruption and lower resistance to disease across multiple pathways. Essential body processes can eventually be disabled by incessant external stresses (from system-wide electrophysiological interference) and lead to pervasive impairment of metabolic and reproductive functions.

What does the WHO IARC Classification of ELF-EMF and RFR as Group 2B Possible Human Carcinogens Mean?

The World Health Organization International Agency for Cancer Research (IARC) designated ELF-EMF as a Group 2B (Possible) Carcinogen in 2001. This is the kind of exposure from power lines, battery switching in cell phone devices, laptop computers and appliances. The World Health Organization specifically reaffirmed its finding that EMF is classifiable as a Group 2B Possible Human Carcinogen in 2006 in their Health Criteria Monograph #238 (WHO, 2007).

World Health Organization International Agency for Research on Cancer (IARC) Cancer Classifications

Group 1	Known Carcinogen
Group 2A	Probable Carcinogen
Group 2B	Possible Human Carcinogen
Group 3	Insufficient Information
Group 4	Not a Carcinogen

In 2011, IARC determined that scientific evidence is sufficient now to classify radiofrequency radiation as a Group 2B Possible Human Carcinogen (Baan et al, 2011). This is the kind of exposure coming from cell and cordless phones, cell towers, WI-FI, wireless laptops, electronic baby monitors and wireless 'smart' utility meters.

So, what does this mean? According to the classification categories, it is again clear IARC did NOT find so little clear and consistent evidence that it should support a finding of "Not A Carcinogen". That would be the valid test that RFR is safe, as best public health experts can judge the evidence. Nor did IARC find that the evidence sufficient so as to make a stronger classification (Probably or Known Carcinogen). Rather, IARC found the evidence supports classification as a "Possible" cancer-causing

agent. That is not a weak or reckless judgment made with few facts. It should be a strong warning to governments to reconsider their safety standards, particularly in light of the billions of people at potential health risk from new wireless technologies. Studies of cell and cordless phones and of wireless whole-body RFR exposures consistently show human health impacts that have become 'epidemiologically visible' (Sections 11 and 21).

ELF-EMF AND RFR ARE CLASSIFIED AS POSSIBLE CANCER-CAUSING AGENTS – WHY ARE GOVERNMENTS NOT ACTING?

The World Health Organization International Agency for Research on Cancer has classified wireless radiofrequency as a Possible Human Carcinogen (May, 2011). The designation applies to low-intensity RFR in general, covering all RFR-emitting devices and exposure sources (cell and cordless phones, WI-FI, wireless laptops, wireless hotspots, electronic baby monitors, wireless classroom access points, wireless antenna facilities, etc). The IARC Panel could have chosen to classify RFR as a Group 4 – Not A Carcinogen if the evidence was clear that RFR is not a cancer-causing agent. It could also have found a Group 3 designation was a good interim choice (Insufficient Evidence). IARC did neither.

II. KEY SCIENTIFIC EVIDENCE (2006- 2012)

Many thousand scientific studies over four decades have provided warnings of serious biological effects and potential health harm from EMF and RFR. About 1800 new, scientific papers published in the last five years report more bioeffects and adverse health effects of EMF and RFR, and are presented in great detail in the BioInitiative Report 2012.

These studies since 2006 give critical support to the argument that current safety standards are grossly inadequate. They cannot be protecting public health if they do not prevent harm to a variety of types of human cells, human sperm and the developing fetus *in-utero*. These are all effects reported today due to cell phone radiation exposures that are both legal and common in daily home, business and school environments. These effects are shown to occur at very low-intensity permissible levels that have become 'typical' for pregnant women, the fetus, the infant, the child, and for adults. Such effects are occurring at hundreds to thousands of times lower intensity exposure levels than the current FCC public safety limits allow. These exposure levels are common in the

environment, but worst in close proximity to wireless devices like cell and cordless phones, 'smart' wireless utility meters, wireless routers, wireless classroom access points and laptops, to baby surveillance devices, and in the first few hundred meters of cell towers. WI-FI levels of RFR and cell phones-on-standby mode are sufficient to cause effects that, if chronic, may be damaging to the health of cellular DNA, reproductive germ cells (sperm) and the male reproductive organs.

Overall, these new studies report abnormal gene transcription (Section 5); genotoxicity and single-and double-strand DNA damage (Section 6); stress proteins because of the fractal RF-antenna like nature of DNA (Section 7); chromatin condensation and loss of DNA repair capacity in human stem cells (Sections 6 and 15); reduction in free-radical scavengers - particularly melatonin (Sections 5, 9, 13, 14, 15, 16 and 17); neurotoxicity in humans and animals (Section 9), carcinogenicity in humans (Sections 11, 12, 13, 14, 15, 16 and 17); serious impacts on human and animal sperm morphology and function (Section 18); effects on offspring behavior (Section 18, 19 and 20); and effects on brain and cranial bone development in the offspring of animals that are exposed to cell phone radiation during pregnancy (Sections 5 and 18). This is only a snapshot of the evidence presented in the BioInitiative 2014 updated report.

Many of these bioeffects are associated with disruption of normal biological functioning in the genes, and in the physiology of the nervous and cardiac systems of the body (brain, blood-brain barrier, heart, vascular system). Sleep disruption (insomnia) is a hallmark bioeffect of RFR. Hypersensitivity disorders like allergies and asthma are reported from exposure to environmental chemicals and to EMF. A pregnant woman's exposure to EMF has been linked to increased asthma and behavioral problems in the human child after *in-utero* exposure. Pregnant mice exposed to cell phone radiation give birth to baby mice with attention disorders, hyperactivity and impaired memory function, similar to effects seen in human babies as reported by Divan et al (2008).

A. Stress, Stress Proteins and DNA as a Fractal Antenna: The word stress invokes different concepts for people, but needs to be understood as a physiological response. BioInitiative author Martin Blank has described how both ELF-EMF and RFR produce stress proteins at very low exposure levels, and why this is only adaptive in the short-

term. Chronic exposures that trigger stress responses (stress proteins) regardless of their environmental cause are mal-adaptive if they go on too long. Any agent (EMF, ionizing radiation, chemicals, heavy metals, etc) that continuously generates stress proteins is not adaptive, and is harmful, if it is a constant provocation.

The work of Martin Blank and Reba Goodman of Columbia University has established that stress proteins are produced by ELF-EMF and RFR at levels far below current safety standards allow. Further, they think DNA is actually a very good fractal RF-antenna which is very sensitive to low doses of EMF, and may induce the cellular processes that result in chronic 'unrelenting' stress. That daily environmental levels of ELF-EMF and RFR can and do throw the human body into stress protein response mode (out of homeostasis) is a fundamental and continuous insult. Chronic exposures can then result in chronic ill-health**.**

B. Fetal Effects and Fetal Development Studies: Effects on the developing fetus from *in-utero* exposure to cell phone radiation have been observed in both human and animal studies since 2006. Divan et al (2008) found that children born of mothers who used cell phones during pregnancy develop more behavioral problems by the time they have reached school age than children whose mothers did not use cell phones during pregnancy. The July 2008 issue of Epidemiology reports that children whose mothers used cell phones during pregnancy had 25% more emotional problems, 35% more hyperactivity, 49% more conduct problems and 34% more peer problems (Divan et al, 2008).

Aldad et al (2012) showed that cell phone radiation significantly altered fetal brain development and produced ADHD-like behavior in the offspring of pregnant mice. Exposed mice had a dose-dependent impaired glutamatergic synaptic transmission onto Layer V pyramidal neurons of the prefrontal cortex. The authors conclude the behavioral changes were the result of altered neuronal developmental programming *in utero*. Offspring mice were hyperactive and had impaired memory function and behavior problems, much like the human children in Divan et al (2008).

A new study from Greece reports altered development of the cranial bones of the mouse fetus from low intensity (0.6 to 0.9 W/kg) *in-utero* 900 MHz cell phone radiation (Fragopoulou et al, 2009). They report *"our results clearly show that even modest exposure (e.g., 6-min daily for 21 days) is sufficient to interfere with the normal mouse developmental process."*

Other new studies by Fragopoulou et al report that brain astrocyte development followed by proteomic studies is adversely affected by DECT (cordless phone radiation) and mobile phone radiation (Fragopoulou et al, 2012); and that whole body exposure with GSM 900MHz affects spatial memory in mice (Fragopoulou et al, 2010).

FETAL BRAIN DEVELOPMENT MAY BE ALTERED

There is increasing evidence that fetal (*in-utero*) and early childhood exposures to cell phone radiation and wireless technologies in general is a risk factor for hyperactivity, learning disorders and behavioral problems in school.

Neonatal physician Carlo Bellieni of Italy found that heart rate variability is adversely affected in infants hospitalized in isolettes or incubators where ELF-EMF levels are in the 0.8 to 0.9 μT range (8 to 9 mG) (Bellieni, 2008). Infants suffer adverse changes in heart rate variability, similar to adults. He also reported that newborns cared for in the high ELF-EMF environments of isolettes have disrupted melatonin levels (Bellieni et al, 2012a).

C. Studies of Sperm: Several international laboratories have replicated studies showing adverse effects on sperm quality, motility and pathology in men who use and particularly those who wear a cell phone, PDA or pager on their belt or in a pocket (Agarwal et al, 2008; Agarwal et al, 2009; Wdowiak et al, 2007; De Iuliis et al, 2009; Fejes et al, 2005; Aitken et al, 2005; Kumar, 2012). Other studies conclude that usage of cell phones, exposure to cell phone radiation, or storage of a mobile phone close to the testes of human males affect sperm counts, motility, viability and structure (Aitken et al, 2004; Agarwal et al, 2007; Erogul et al., 2006). Animal studies have demonstrated oxidative and DNA damage, pathological changes in the testes of animals, decreased sperm mobility and viability, and other measures of deleterious damage to the male germ line

(Dasdag et al, 1999; Yan et al, 2007; Otitoloju et al, 2010; Salama et al, 2008; Behari et al, 2006; Kumar et al, 2012). There are fewer animal studies that have studied effects of cell phone radiation on female fertility parameters. Panagopoulous et al. 2012 report decreased ovarian development and size of ovaries, and premature cell death of ovarian follicles and nurse cells in *Drosophila melanogaster.* Gul et al (2009) report rats exposed to stand-by level RFR (phones on but not transmitting calls) caused decrease in the number of ovarian follicles in pups born to these exposed dams. Magras and Xenos (1997) reported irreversible infertility in mice after five (5) generations of exposure to RFR at cell phone tower exposure levels of less than one microwatt per centimeter squared (μW/cm2).

Agarwal et al (2009) evaluated the effect of cell phone radiation during talk mode on human sperm samples. The authors found "*radiofrequency electromagnetic waves emitted from cell phones may lead to oxidative stress in human semen. We speculate that keeping the cell phone in a trouser pocket in talk mode may negatively affect spermatozoa and impair male fertility.*"

Aitken et al (2005) studied the effect of 900 MHz cell phone radiation on mice (7 days, 12-hr per day at 0.09 W/kg). The authors found statistically significant damage to the mitochondrial genome of epididymal spermatozoa ($p<0.05$).

Avendano et al, 2012 provided evidence that a 4-hr exposure to WI-FI at exceeding low levels (0.5-1.0 μW/cm2) near a laptop computer caused decreased sperm viability and DNA fragmentation in human sperm samples. Avendado says "(*T)o our knowledge, this is the first study to evaluate the direct impact of a laptop use on human spermatozoa. Ex vivo exposure of human spermatozoa to a wireless internet-connected laptop decreased motility and induced DNA fragmentation by a nonthermal effect. We speculate that keeping a laptop connected wirelessly to the internet on the lap near the testes may result in decreased male fertility.*"

De Iuliis et al (2009) reported that "*RF-EMR in both the power density and frequency range of mobile phones enhances mitochondrial reactive oxygen species generation by human spermatozoa, decreasing the motility and vitality of these cells*

while stimulating DNA base adduct formation, and ultimately DNA fragmentation." They warned their findings *"have clear implications for the safety of extensive mobile phone use by males of reproductive age, potentially affecting both their fertility and the health and wellbeing of their offspring"* based on damage from a 6-hr exposure to 1800 MHz cell phone radiation in human sperm cells. This 6-hr exposure caused reduced sperm motility and viability and caused a significant increase in reactive oxygen species (free radicals that are associated with oxidative damage to DNA), and the effects were worse with more exposure (a significant dose-response was observed). Atasoy (2012) also questioned the safety of 2400 MHz exposure to those of reproductive age. This study reports that WI-FI internet access devices can damage DNA and reduce DNA repair when the exposures are very low(exposure level of 0.091 W/kg) and chronic; damage can occur even at levels that comply with 802.11 g WI-FI public safety limits.

Behari et al (2006) reported that chronic exposure of rats to cell phone radiation caused double-strand DNA breaks in sperm cells (35 days, 2-hr per day). This study also showed that the mobile radiation exposure at 900 MHz (at 0.9 W/kg) and at 2.45 GHz (at 0.1 W/kg) caused a statistically significant decrease in sperm count and the weight of testes.

Otitoloju et al., (2010) graphically describe sperm head abnormalities in mice exposed for six months to base-station level RF/MW at 70 to 100 nanowatts/cm2 (0.07 – 0.1 μW/cm2). Only 2% of controls but a stunning 39% to 46% of exposed mice had damaged sperm.

> *"The major abnormalities observed were knobbed hook, pin-head and banana-shaped sperm head. The occurrence of sperm head abnormalities was also found to be dose dependent. The implications of the observed increased occurrence of sperm head abnormalities on the reproductive health of humans living in close proximity to GSM base stations were discussed.*"

These studies taken together should provide a strong warning that 'normal' use of a cell phone presents risks that warrant strong preventative actions to protect the integrity of the human genome from de novo mutations and loss of fertility across entire male populations of cell phone users. Further, even the much lower exposure levels associated with mobile phone base station (cell tower) RFR levels are deleterious over time.

HUMAN SPERM AND THEIR DNA ARE DAMAGED

Human sperm are damaged by cell phone radiation at very low intensities (0.00034 – 0.07 μW/cm2). There is a veritable flood of new studies reporting sperm damage in humans and animals, leading to substantial concerns for fertility, reproduction and health of the offspring (unrepaired de novo mutations in sperm). Exposure levels are similar to those resulting from wearing a cell phone on the belt, or in the pants pocket, or using a wireless laptop computer on the lap. Sperm lack the ability to repair DNA damage.

D. Human Stem Cell Studies: Markova et al (2010) reported that 915 MHz microwave exposure significantly affects human stem cells. They found that very low-intensity microwave radiation from mobile phones can inhibit DNA repair processes in human stem cells. By placing a mobile phone at one meter distance from human stem cells in petri dishes (SAR = 0.037 W/Kg), they found a significant reduction in 53BP1 foci. These foci are a measure of DNA repair in cells with double strand DNA damage. The damage was greater to stem cells (derived from adipose tissue in humans) than in fibroblasts. Stem cells did not repair over time - and the damage was done within one hour of microwave exposure. Fibroblasts were similarly affected (inhibited 53BP1 foci) but repaired over time. The effects are carrier-frequency dependent. The effects occurred with GSM exposure at 915 MHz, but not at 905 MHz. The failure of DNA repair also occurred at the mobile phone UTMS carrier frequency of 1947 MHz. Analysis of the 53BP1 foci is a sensitive technique to measure double-strand DNA breaks in both unexposed cells and in cells exposed to cytotoxic agents. In the authors' words, *"this represents a direct mechanistic link to epidemiological data showing an association of MW exposure with increased cancer risk*." The data obtained from human stem cells is of "*utmost relevance for assessment of possible health risks of MW exposure from mobile phones."* Most, if not all adult tissues and organs including blood, skin and brain contain stem cells. Therefore, "*stem cells like blood cells and fibroblasts are always subjected to exposure from mobile phones*." With respect to children, because "*almost all organs and tissues possess stem cells and stem cells are more active in children, the possible relationship of chronic MW exposure and various types of tumors and leukemia especially in children should be investigated."*

Czyz et al (2004) reported that GSM cell phone exposure affected gene expression levels in embryonic stem cells (p53-deficient); and significantly increased heat shock protein HSP 70 production.

HUMAN STEM CELL DNA DOES NOT ADAPT OR REPAIR

Human adipose tissue stem cells lack the ability to repair DNA damage caused by chronic exposure to non-thermal microwaves. Damage to DNA in some other cells may be incompletely repaired.

E. Mobile Phone Base Station (Cell Tower) Studies

Human Studies: Hutter et al (2006) reported that short-term exposure to GSM cell phone radiation resulted in complaints of headache, neurological problems, sleep and concentration problems in adults with 0.01 - 0.05 μW/cm2 exposure levels. Kundi and Hutter (2009) reviewed human effects in fourteen (14) mobile phone base station studies and reported *"(F)rom available evidence it is impossible to delineate a threshold below which no effect occurs, however, given the fact that studies reporting low exposure were invariably negative it is suggested that power densities around 0.5–1 mW/m2 [*0.05 – 0.1 uW/cm2*] must be exceeded in order to observe an effect."*

Buchner and Eger (2012) conducted an eighteen (18) month study to assess changes in stress hormones in 60 persons exposed before and after a mobile phone base station went into operation in the Rimbach village in Germany. The study showed that chronic exposure to base station RF (whole-body) at 0.006 - 0.01 μW/cm2 in humans had significant impacts on stress hormones over time. In the beginning months, adrenaline levels first increased in a dose-dependent fashion according to exposure level ($p < 0.002$) and then decreased below normal levels ($p < 0.005$). Both the average as well as the median adrenaline values increased after the activation of the transmitter and decreased again after one year with exposure levels >0.006 μW/cm2. Chronically ill subjects and children showed especially strong responses; except for some "outliers," no effect was observed in healthy adults (Buchner and Eger, 2012). For dopamine, inverse effects to

those for adrenaline and noradrenaline were observed. The median dopamine levels decreased from 199 to 115 μg/g creatinine between January and July 2004. The fact that the dopamine levels of the study subjects decreased during this period is highly significant ($p<0.0002$). Thereafter, the median increased again: In January 2005, it was at 131 μg/g creatinine, in July of 2005. This increase is also significant between July 2004 and July 2005 ($p<0.05$).

Buchner (2012) indicates that the RFR transmitter induced changes in stress hormones that follow the classic stress syndrome of adaptation, then exhaustion established by Hans Seyle in the 1950's. *"After the stages of alarm and resistance, the last stage of exhaustion sets in. The parameters investigated in the Rimbach study follow this pattern"*.

A long-term 6-yr study assessed the role of exposure to radio frequency radiation (RFR) emitted either from mobiles or base stations and its relations with human's hormone profiles. The study revealed significant RFR effects on pituitary–adrenal axis, resulting in reduction of ACTH, cortisol, thyroid hormones, prolactin in young females, and testosterone levels in males (Eskander et al, 2012). But no direct measurements of RFR power density levels were made, only categories of distance from transmitter.

Oberfeld et al (2004) reported that populations exposed to base stations transmitting cell phone frequencies had more fatigue, depressive tendency, sleeping disorders, concentration difficulties, and cardio-vascular problems reported with exposure to GSM 900/1800 MHz cell phone signal.

Navarro et al (2003) reported that exposure levels of 0.01 - 0.11 μW/cm2 resulted in fatigue, headaches, sleeping problems in populations around mobile phone base stations.

Thomas et al (2008) reported an increase in adult complaints of headaches and concentration difficulties with short-term cell phone use at 0.005 to 0.04 μW/cm2 exposure levels.

Heinrich et al (2010) reported that children and adolescents (8-17 years old) with short-term exposure to base-station level RFR experienced headache, irritation, and concentration difficulties in school. RFR levels were 0.003 - 0.02 μW/cm2.

Thomas et al (2010) reported that RFR levels of 0.003 - 0.02 μW/cm2 resulted in conduct and behavioral problems in children and adolescents (8-17 years old) exposed to short-term cell phone radiation in school.

Mohler et al (2010) reported that adults exposed to 0.005 μW/cm2 cell phone radiation (base-station exposure levels) had sleep disturbances with chronic exposure, but this effect was not significantly increased across the entire population.

Human Studies at Base Station Exposure Levels (Cell Towers)

At least five new cell tower studies with base-station level RFR at levels ranging from 0.003 μW/cm2 to 0.05 uW/cm2 published since 2007 report headaches, concentration difficulties and behavioral problems in children and adolescents; and sleep disturbances, headaches and concentration problems in adults. This is highly consistent with studies done prior to 2007, but the 'effect levels' are significantly lower (dropping from the microwatt to the nanowatt range per square centimeter).

Public safety standards are 1,000 – 10,000 or more times higher than levels now commonly reported in mobile phone base station studies to cause bioeffects.

Sperm studies are showing DNA damage, impaired sperm quality, motility and viability from cell phones on standby mode and wireless laptop use at exposures of 0.00034 μW/cm2 to 0.07 μW/cm2. Several studies report sperm damage effects at 'standby model' cell phone emission levels, which are in the low nanowatt to picowatt per square centimeter range.

F. Electrohypersensitivity (EHS) Studies: McCarty et al (2011) studied electrohypersensitivity in a patient (a female physician). The patient was unable to detect the presence or absence of EMF exposure, largely ruling out the possibility of bias. In multiple trials with the fields either on or not on, the subject experienced and reported temporal pain, feeling of usease, skipped heartbeats, muscle twitches and/or strong headache when the pulsed field (100 ms, duration at 10 Hz) was on, but no or mild symptoms when it was off. Symptoms from continuous fields were less severe than with pulsed fields. The differences between field on and sham exposure were significant at the $p < 0.05$ level. The authors conclude that electromagnetic hypersensitivity is a neurological syndrome, and statistically reliable somatic reactions could be provoked in this patient by exposure to 60-Hz electric fields at 300 volts per meter (V/m). They

conclude *"EMF hypersensitivity can occur as a bona fide environmentally inducible neurological syndrome*." In their response to a letter to the editor of the journal, the authors say: *"(W)e followed an empirical approach and demonstrated a cause-and-effect relationship ($p < 0.05$) under conditions that permitted us to infer the existence of electromagnetic hypersensitivity (EHS), a novel neurological syndrome*." (Marino et al., 2012)

Further, the authors explain the significance of detecting EHS effects by non-linear methods.

> *"The important issue at this point is not whether EMF can produce symptoms (we empirically demonstrated that it can) but rather why this effect historically has been difficult to detect. It occurred to us that EHS has remained elusive because of the way it was studied. The experiments designed to detect EHS had been based on the assumption that if it existed, it was a linear phenomenon, whereas EHS is actually a nonlinear phenomenon." "Our study was designed to detect whether EHS was a linear or nonlinear phenomenon, and we were successful in showing a link between acute EMF exposure and somatic responses ($p < 0.05$). This finding – taken together with the unfailingly negative results of the linear studies – is good evidence that EHS is a nonlinear phenomenon, as we suspected."*

With the exception of the McCarty study there have not been clear demonstrations in controlled circumstances showing that persons reporting to be electrophypersensitive can distinguish whether or not RFR is being applied. There are, however, multiple reports of symptoms experienced by individuals exposed to EMFs in uncontrolled circumstances.

A. Johansson et al (2010) studied symptoms, personality traits and stress in people with mobile phone-related symptoms and electromagnetic hypersensitivity. They reported there is support for a difference between people with symptoms related to specific EMF sources and people with general EHS. The symptoms are anxiety, depression, somatization, exhaustion and stress. The EHS group reported more neurasthenic symptoms.

Two publications on electrohypersensitivity by O. Johansson (2007, 2009) provide an extensive overview of the relevant literature on electrohypersensitivity. Both

publications document symptoms and conditions giving rise to increased sensitivity to ELF-EMF and RFR. The need for new, biologically-based public exposure standards is recommended in both publications, in order to address electrohypersensitivity.

Landgrebe et al (2007) reported that their study of electrosensitive patients showed participants had a reduced intracortical facilitation as compared to two control groups. The EHS group of patients showed altered central nervous system function. In a follow-up study, the authors reported that EHS patients but not controls "*demonstrated significant cognitive and neurobiological alterations pointing to a higher genuine individual vulnerability of electromagnetic hypersensitive patients." (Landgrebe et al, 2008).*

The team of Sandstrom, Hansson Mild and Lyskov produced numerous papers between 1994 and 2003 involving people who are electrosensitive (Lyskov et al, 1995; Lyskov et al, 1998; Sandstrom et al, 1994; Sandstrom et al, 1995; Sandstrom et al, 1997; Sandstrom et al, 2003). Sandstrom et al (2003) presented evidence that heart rate variability is impaired in people with electrical hypersensitivity and showed a dysbalance of the autonomic nervous system. *"EHS patients had a disturbed pattern of circadian rhythms of HRF and showed a relatively 'flat' representation of hourly-recorded spectral power of the HF component of HRV"*. This research team also found that *"EHS patients have a dysbalance of the autonomic nervous system (ANS) regulation with a trend to hyper-sympathotonia, as measured by heart rate (HR) and electrodermal activity, and a hyperreactivity to different external physical factors, as measured by brain evoked potentials and sympathetic skin responses to visual and audio stimulation*." (Lyskov et al, 2001 a,b; Sandstrom et al, 1997). The reports referenced above provide evidence that persons who report being electrosensitive differ from others in having some abnormalities in the autonomic nervous system, reflected in measures such as heart rate variability. At present it remains unclear whether EHS is actually caused by RF/EMF exposure, or rather is a self-identifying syndrome of excessive responsiveness to a variety of stimuli. But given the relatively high percentage of persons reported to be electrosensitive (5% of the general population of Switzerland according to Schreier et al,

2006), with some being severely disabled as a consequence, it is critical that there be more study of this syndrome.

Tuengler and von Klitzing et al (2012) reported EHS people that were tested showed significant changes in regulation of the autonomic nervous system, including changes in capillary blood flow (microcirculation), heart rate variability, and electric skin potentials. The continuous detection of capillary blood flow is an important tool in analyzing the capacity of the autonomic nervous system. In EHS patients, von Klitzing finds that intestinal motility may also be disregulated and show no activity at all for some time after exposure.

G. Effects on the Blood-brain Barrier (BBB): The Lund University (Sweden) team of Leif Salford, Bertil Persson and Henrietta Nittby has done pioneering work on effects of very low level RFR on the human brain's protective lining – the barrier that protects the brain from large molecules and toxins that are in the blood.

THE BLOOD-BRAIN BARRIER IS AT RISK

The BBB is a protective barrier that prevents the flow of toxins into sensitive brain tissue. Increased permeability of the BBB caused by cell phone RFR may result in neuronal damage. Many research studies show that very low intensity exposures to RFR can affect the blood-brain barrier (BBB) (mostly animal studies). Summing up the research, it is more probable than unlikely that non-thermal EMF from cell phones and base stations do have effects upon biology. A single 2-hr exposure to cell phone radiation can result in increased leakage of the BBB, and 50 days after exposure, neuronal damage can be seen, and at the later time point also albumin leakage is demonstrated. *The levels of RFR needed to affect the BBB have been shown to be as low as 0.001 W/kg, or less than holding a mobile phone at arm's length. The US FCC standard is 1.6 W/kg; the ICNIRP standard is 2 W/kg of energy (SAR) into brain tissue from cell/cordless phone use. Thus, BBB effects occur at about 1000 times lower RFR exposure levels than the US and ICNIRP limits allow.* *(Salford, 2012)*

The consequence to modern life is that cell and cordless phone use may cause a pathological leakage of the BBB with very short use periods, and the damage may be long-lasting. Harmful substances may enter the brain. If the damage is ongoing (if cell and cordless phone use continues to occur over months and years), the potential for

harmful effects increases. There is already 'epidemiologically visible' evidence of increased brain cancer risk in humans (Section 11).

Volkow et al (2011a, b) reported increased glucose metabolism in the brain with cell phone use in humans. This important investigation of 47 human subjects used a randomized crossover design and labeled fluorodeoxyglucose to measure the metabolisms of the brain when the cell phone was activated but muted for 50 minutes as compared to not being activated. "*Our study showed that cell phone activation was associated with metabolic increases in brain regions closest to the antenna and that the increases showed a negative linear correlation with distance from the antenna. While the effect was small, the negative correlation of the effect with distance was statistically significant (R = −0.91; P <.001).* This study is particularly important in that it demonstrates definitively that an active cell phone, placed on the ear as one would normally be used, alters brain metabolic activity, but only in the region close to the cell phone.

H. Brain Cancer Studies: The Orebro University (Sweden) team led by Lennart Hardell, MD, an oncologist and medical researcher, has produced an extraordinary body of work on environmental toxins of several kinds, including the effects of radiofrequency/microwave radiation and cancer. Their 2012 work concludes:

> *"Based on epidemiological studies there is a consistent pattern of increased risk for glioma and acoustic neuroma associated with use of mobile phones and cordless phones. The evidence comes mainly from two study centres, the Hardell group in Sweden and the Interphone Study Group. No consistent pattern of an increased risk is seen for meningioma. A systematic bias in the studies that explains the results would also have been the case for meningioma. The different risk pattern for tumor type strengthens the findings regarding glioma and acoustic neuroma. Meta-analyses of the Hardell group and Interphone studies show an increased risk for glioma and acoustic neuroma. Supportive evidence comes also from anatomical localisation of the tumor to the most exposed area of the brain, cumulative exposure in hours and latency time that all add to the biological relevance of an increased risk. In addition risk calculations based on estimated absorbed dose give strength to the findings.*

In summary:

- *There is reasonable basis to conclude that RF-EMFs are bioactive and have a potential to cause health impacts.*

- *There is a consistent pattern of increased risk for glioma and acoustic neuroma associated with use of wireless phones (mobile phones and cordless phones) mainly based on results from case-control studies from the Hardell group and Interphone Final Study results.*
- *Epidemiological evidence gives that RF-EMF should be classified as a human carcinogen.*
- *Based on our own research and review of other evidence the existing FCC/IEE and ICNIRP public safety limits and reference levels are not adequate to protect public health.*
- *New public health standards and limits are needed.* (Hardell et al, 2012)

I**. Genetic Damage (Genotoxicity Studies):** There are at least several hundred published papers that report EMF affects cellular oxidative processes (oxidative damage). Increased free radical activity and changes in enzymes involved in cellular oxidative processes are the most consistent effects observed in cells and animals after EMF exposure. Aging may make an individual more susceptible to the detrimental effects of ELF EMF from oxidative damage, since anti-oxidants may decline with age. Clearly, the preponderance of genetic studies report DNA damage and failure to repair DNA damage.

Eighty six (86) new papers on genotoxic effects of RFR published between 2007 and mid-2012 are profiled. Of these, 54 (63%) showed effects and 32 (37%) showed no effects (Lai, 2012)

Forty three (43) new ELF-EMF papers and two static magnetic field papers that report on genotoxic effects of ELF-EMF published between 2007 and mid-2012 are profiled. Of these, 35 (81%) show effects and 8 (19%) show no effect (Lai, 2012).

J. Nervous System Damage: Factors that act directly or indirectly on the nervous system can cause morphological, chemical, or electrical changes in the nervous system that can lead to neurological effects. Both RF and ELF EMF affect neurological functions and behavior in animals and humans.

One hundred fifty five (155) new papers that report on neurological effects of RFR published between 2007 and mid-2012 are profiled. Of these, 98 (63%) showed effects and 57 (37%) showed no effects.

Sixty nine (69) new ELF-EMF papers (including two static field papers) that report on genotoxic effects of ELF-EMF published between 2007 and mid-2012 are profiled. Of these, 64 (93%) show effects and 5 (7%) show no effect. (Lai, 2012)

L. Children are More Vulnerable: Many studies demonstrate that children are more sensitive to environmental toxins of various kinds (Barouki et al, 2012; Preston, 2004; WHO, 2002; Gee, 2009; Sly and Carpenter, 2012).

> The Presidential Cancer Panel (2010) found that children '*are at special risk due to their smaller body mass and rapid physical development, both of which magnify their vulnerability to known carcinogens, including radiation.*'

> The American Academy of Pediatrics, in a letter to Congressman Dennis Kucinich dated 12 December 2012 states "*Children are disproportionately affected by environmental exposures, including cell phone radiation. The differences in bone density and the amount of fluid in a child's brain compared to an adult's brain could allow children to absorb greater quantities of RF energy deeper into their brains than adults. It is essential that any new standards for cell phones or other wireless devices be based on protecting the youngest and most vulnerable populations to ensure thay are safeguarded through their lifetimes."*

II. ISSUES AND ANSWERS IN THE EMF DEBATE

Much of the emphasis in the 2007 Bioinititative Report focused on cancer, which is still the best documented disease of concern from exposure to EMF/RF. The evidence that exposure to EMF/RF increases the risk of cancer has only gotten significantly stronger since then, and we have a better, albeit still incomplete, understanding of the mechanisms involved. However, in terms of threshold exposures that result in human disease, new research on male reproduction and neurobehavioral alterations provide evidence for harm at even lower exposure levels. RFR has been shown in this Report to act as an external synchronizer of neural activity, capable of disrupting sleep, circadian rhythms, diurnal hormone fluctuations, brain wave activity and heart rate variability by exposure to artificial electromagnetic signals (as opposed to natural evolutionary frequencies) and to do so at exceedingly low intensities.

Much of the debate over the body of EMF science ignores simple questions that would help to discriminate among studies with apparently conflicting results. Section 15 by Dr. Belyaev is helpful in identifying key factors which must be known and controlled for in experiments (biological variables and physical parameters include bandwidth, frequency, modulation, polarization, intermittence and coherence time of exposure, static

magnetic field, electromagnetic stray fields, sex, age, individual traits, and cell density during exposure). Dr. Andrew Marino emphasizes that detection of EMF/RFR effects require investigation of non-linear phenomena, a critical difference that if ignored, may miss important biological effects (Marino, 2012).

A unifying hypothesis for a plausible biological mechanism to account for very weak field EMF bioeffects other than cancer may lie with weak field interactions of pulsed RFR and ELF-modulated RFR as disrupters of synchronized neural activity. Electrical rhythms in our brains can be influenced by external signals. This is consistent with established weak field effects on coupled biological oscillators in living tissues. Biological systems of the heart, brain and gut are dependent on the cooperative actions of cells that function according to principles of non-linear, coupled biological oscillations for their synchrony, and are dependent on exquisitely timed cues from the environment at vanishingly small levels (Buzsaki, 2006; Strogatz, 2003). The key to synchronization is the joint actions of cells that co-operate electrically - linking populations of biological oscillators that couple together in large arrays and synchronize spontaneously according to the mathematics described for Josephson junctions (Brian Josephson, the 1993 Nobel prize winner for this concept). This concept has been professionally presented in journal articles and also popularized in print by Prof. Steven Strogatz, a mathematician at Cornell University who has written about 'sync' as a fundamental organizing principle for biological systems (Strogatz, 2001; 2003).

> *"Organisms are biochemically dynamic. They are continuously subjected to time-varying conditions in the form of both extrinsic driving from the environment and intrinsic rhythms generated by specialized cellular clocks within the organism itself. Relevant examples of the latter are the cardiac pacemaker located at the sinoatrial node in mammalian hearts and the circadian clock residing at the suprachiasmatic nuclei in mammalian brains. These rhythm generators are composed of thousands of clock cells that are intrinsically diverse but nevertheless manage to function in a coherent oscillatory state. This is the case, for instance, of the circadian oscillations exhibited by the suprachiasmatic nuclei, the period of which is known to be determined by the mean period of the individual neurons making up the circadian clock. The mechanisms by which this collective behavior arises remain to be understood."(Strogatz, 2003)*

Synchronous biological oscillations in cells (pacemaker cells) can be disrupted by artificial, exogenous environmental signals, resulting in desynchronization of neural

activity that regulates critical functions (including metabolism) in the brain, gut and heart and circadian rhythms governing sleep and hormone cycles (Strogatz, 1987). The brain contains a population of oscillators with distributed natural frequencies, which pull one another into synchrony (the circadian pacemaker cells). Strogatz has addressed the unifying mathematics of biological cycles and external factors disrupt these cycles. Buzsaki (2006) says "*rhythms can be altered by a wide variety of agents and that these perturbations must seriously alter brain performance. Rhythms are a robust phenomenon.*"

The heart's natural pacemaker center is the sinoatrial node, a cluster of about 10,000 cells that generate electrical rhythm that commands the rest of the heart to beat. Diseases related to disruption of that synchronization include epilepsy, chronic insomnia, and cardiac arrhythmias (Strogatz, 2003). Some EMF diseases are those where desynchronization of neural activity results in physiological changes that, if chronic, result in chronically disrupted homeostasis, and eventually ill-health and chronic diseases. Such a future burdens health care systems in an irreversible way.

The late Dr. Ross Adey in his last publication in Bioelectromagnetic Medicine (P. Roche and M. Markov, eds. 2004) concluded:

> "*There are major unanswered questions about possible health risks that may arise from exposures to various man-made electromagnetic fields where these human exposures are intermittent, recurrent, and may extend over a significant portion of the lifetime of the individual."*
>
> *"Epidemiological studies have evaluated ELF and radiofrequency fields as possible risk factors for human health, with historical evidence relating rising risks of such factors as progressive rural electrification, and more recently, to methods of electrical power distribution and utilization in commercial buildings. Appropriate models describing these bioeffects are based in nonequilibrium thermodynamics, with nonlinear electrodynamics as an integral feature. Heating models, based in equilibrium thermodynamics, fail to explain an impressive new frontier of much greater significance. Though incompletely understood, tissue free radical interactions with magnetic fields may extend to zero field levels."*

Our society appears determined to make everything wireless, and the consequence is to increase cumulative exposure to RFR. Many homes and almost every Starbucks or McDonalds has WiFi. Smart phones, tablets, video iPods and other wireless devices are even given to children as playthings. The result is a significant increase in cumulative RFR exposure of the whole population, but particularly of those who have and use wireless devices for prolonged periods of time. No national or international standard of RFR exposure considers cumulative effects, all being developed to avoid local tissue heating from acute exposures.

The issues around exposure of children to RFR is of critical importance. There is overwhelming evidence that children are more vulnerable than adults to many different exposures (Sly and Carpenter, 2012), including RFR, and that the diseases of greatest concern are cancer and effects on neurodevelopment. Yet parents place RFR baby monitors in cribs, provide very young children with wireless toys, and give cell phones to young children, usually without any knowledge of the potential dangers. A growing concern is the movement to make all student computer laboratories in schools wireless. A wired computer laboratory will not increase RFR exposure, and will provide safe access to the internet.

An urgent example for the need to address the lack of adequate public protection from inadequate safety standards for pulsed RFR exposures is the rapid, global rollout of wireless utility meters (‘smart’ meters for electricity, gas and water meters). Current safety standard calculations that rely on time-averaging of RFR almost entirely dilute out the power density of RFR levels that are delivered in millisecond bursts, but occur at intervals of every second, or multiple times per second when in use within a wireless mesh network. Said differently, the RFR power density levels are usually legal. While there have been no long term studies of adverse effects of smart meters on human health (primarily because they are so new), there are increasing reports from electrosensitive individuals of harm. Added together, these RFR pulses that now appear to be a highly bioactive agent but are essentially erased or made energetically invisible by time-averaging the pulses as current FCC safety rules mandate.

The wireless meters transmit RF signals like a mini-cell tower antennas in the cell phone radiation frequencies. Currently, they are being deployed in the US and are on the drawing boards around the world including many European countries. The 'smart meter' infrastructure represents the largest single commercial saturation of living space with pulsed RFR yet rolled out by industry. This program places a wireless device (like a mini-mobile phone base station) on the wall, replacing the electromechanical (spinning dial) meter. They will be installed on every home and classroom (every building with an electric meter). Utilities from California to Maine have installed tens of millions already, despite health concerns of experts who already are seeing thousands of health complaints. The wireless meters produce spikes of pulsed radiofrequency radiation on a continuous basis (24/7), and in typical operation, will saturate living space at levels that can be much higher than already reported to cause bioeffects and adverse health effects for some people. These meters, depending on where they are placed relative to occupied space in the home or classroom, can produce RFR exposure levels similar to that within the first 100 feet to 600 feet of a mobile phone base station (cell tower). In the not-so-distant future the plan is to have a wireless device implanted in every household appliance, which will communicate with the smart meter whenever electricity is being used. This will likely make the kitchen a major source of exposure to RFR.

The cumulative RFR burden within any community is largely unknown. Both involuntary sources (like cell towers, smart meters and second-hand radiation from the use of wireless devices by others) plus voluntary exposures from ones' personal use of cell and cordless phones, wireless routers, electronic baby surveillance monitors, wireless security systems, wireless hearing aids, and wireless medical devices like implanted insulin pumps all add up. No one is tallying up the combined exposure levels. Billions of new RFR transmitters from a global smart meter rollout will significantly add to the existing RFR body-burden of pulsed RFR for millions of people. The health concerns are the same as with all other sources of EMF/RFR. Cancer is a serious adverse effect, but damage to male reproduction and central nervous system effects may results from even lower levels of exposure. The work by Strogatz (2001, 2003) and Buzsaki (2006) on weak-field effects on non-linear biological oscillators (brain waves and synchronization of neural activities that regulate body processes) is directly relevant to an understanding

of the profound biological disruptions and health symptoms that continued exposures of pulsed RFR may produce.

The Commons of the Air

Turning to questions of social equity and the individuals' choice not to be exposed to harmful levels of environmental toxins, there has been little inclusion of the public in discussions of wireless radiofrequency exposure. Wireless technologies have become infused in daily habits of billions of people; often choices for wired equivalents are lacking (or those that exist are disappearing). Involuntary exposure to EMF and RFR is becoming more the norm, even where it runs counter to individual choice (second-hand radiation, like second-hand smoke is difficult to avoid).

> *"Wireless technologies drive electromagnetic energy through our air, into and through virtually all indoor and outdoor living environments. The protective air cushion around our planet holds breathable air, buffers us from space radiation, and supports and sustains life in tandem with the natural electromagnetic signature of the earth itself. We are changing this 'commons of the air' in major ways. Wireless signals from broadcast and communications technologies are crowding out and overpowering the natural background. The 'commons of the air' is being altered in unprecedented ways that have enormous consequences for life on earth."(Sage, 2010).*

The rush to 'buy the airwaves' and to market them for commercial purposes is loading '*the commons of the air*' with unsustainable levels of exposure (Sage, 2010). Commercial markets for wireless spectrum successfully lobby government regulators to allocate even more spectrum, once the existing frequencies are allocated. Sage (2010) asks:

> *"Who owns the 'commons of the air'? Who should be allowed to pollute it? What are the limits? On what basis should carrying capacity be defined? Who defines the limits? Do these limits conserve the resource for the future? Do they protect public health and welfare, and the health and well-being of other living things on earth? Who bears the burden of proof of safety or of harm? How should the 'new commons' be managed for the greater good? Do we know enough to act responsibly? Who decides? When should limits be placed on utilization?"*

With no regard to cumulative harm, this commercial rush to buy up wireless spectrum territorial rights has vast implications for public health and well-being. Environmental protections afforded to other natural resources under the National Environmental Policy Act have been ignored. The cumulative impacts and irretrievable commitments on humans, wildlife, and natural resources have never been assessed.

> *"Societies must now define carrying capacity for chronic electromagnetic and wireless exposures. Taking into account the large individual variability to withstand it, new limits must conserve and sustain the 'commons of the air' so that is sustainable for all—and this includes sensitive populations, the young, the elderly, and those with existing sensitivity. Some countries of the world already have surpassed sustainable wireless exposure levels as demonstrated by significant percentages that have already become electrosensitive." (Sage, 2010)*

Homeostasis and Human Health Rights

Chronic exposure to low-intensity RFR and to ELF-modulated RFR at today's environmental levels in many cities will exceed thresholds for increased risk of many diseases and causes of death (Sage and Huttunen, 2012). RFR exposures in daily life alter homeostasis in human beings. These exposures can alter and damage genes, trigger epigenetic changes to gene expression and cause de novo mutations that prevent genetic recovery and healing mechanisms. These exposures may interfere with normal cardiac and brain function; alter circadian rhythms that regulate sleep, healing, and hormone balance ; impair short-term memory, concentration, learning and behavior; provoke aberrant immune, allergic and inflammatory responses in tissues; alter brain metabolism; increase risks for reproductive failure (damage sperm and increase miscarriage risk); and cause cells to produce stress proteins. Exposures now common in home and school environments are likely to be physiologically addictive and the effects are particularly serious in the young (Sage and Huttunen, 2012). This declaration of human health rights below (Sage and Huttunen, 2012) is based on specific reference to health impacts of EMF and RFR that are reasonably well established to occur (Sage and Carpenter, 2009).

Human Health Rights Declaration
Fundamental Human Health Rights (Sage and Huttunen, 2012)

The right to homeostasis in our own bodies.
The right to normal central nervous system function.
The right to natural environmental cues that synchronize our circadian rhythms.
The right to sleep.
The right to heal.
The right to hear.
The right to reproduce.
The right to learn and retain memories.
The right to an intact genome.

If even one of these rights is compromised – placed at risk from involuntary wireless exposures in daily life, it is a breach of human health rights. When many of these human health rights are compromised without the consent of the individual, then the deployment of wireless technologies should be halted and existing exposures reduced or eliminated, in accord with the scientific and public health findings on chronic exposure to low-intensity radiofrequency radiation, and other forms of potentially harmful electromagnetic fields (Sage and Huttunen, 2012)

V. CONCLUSIONS FOR PRUDENT PUBLIC HEALTH PLANNING

Methodology and Approach for Precautionary Action Limits

In 2007, the BioInititive Report chapter on Key Scientific Evidence and Public Health Policy Implications, proposed a specific, interim radiofrequency radiation target level of 0.1 μW/cm2 for cumulative, outdoor RFR exposure (for AM, FM, TV and wireless). It was based on best-available scientific studies to that date. There were few studies prior to 2006 that reported effects at less than 0.1 to 1 μW/cm2 chronic RFR exposures.

In 2009, the journal Pathophysiology produced many peer-reviewed articles in a special two-volume edition on EMF (both ELF-EMF and RFR) essentially publishing the contents of the BioInitiative Report and updating some information. One of these 2009 Pathophysiology papers presented a review of mobile phone base station studies (Kundi and Hutter, 2009). It concluded that the overall studies did not detect effects (headache,

fatigue, tinnitus, concentration difficulties, sleep disruption, etc) at levels of RFR exposure below 0.05 to 0.1 μW/cm2.

New base station-level RFR studies are available in 2012 that can be analyzed to determine if new (and lower) RFR recommendations are warranted. The approach in this chapter relies on "lowest levels at which effects are not seen" akin to the “no observed effect level (NOEL)” used for chemical exposures, as a sufficient basis to establish scientific benchmarks for harm (or alternately, the lowest observed effects level of exposure). It is the province of the science and public health evaluation we do here to report the evidence regardless of what political or strategic complications it may create. An objective presentation of what the studies reveal for ‘effects levels’ is our goal; not to pre-judge or dilute the evidence because it may present strategic or political hurdles to achieve consensus on policy and regulatory changes. What this report does not intend to do is take into account“how could we do this” or “what would it mean”. The purpose is to lay out the science, and make some defensible reductions for factors that studies cannot or do not yet test for, and compensate with deductions for them (safety margins). As interim targets for precautionary action, they will serve as guides for decision-makers who will take up the issues of health, the quality of the future gene pool, social equity and cost.

There is no one study alone that meets impeccable standards for exposure assessment or totally eliminates all possibility for bias, but the constellation of studies together gives adequate support to delineate a ‘lowest observed effects level’, that in turn, with added safety margins, can serve as a guideline for precautionary action.

A reduction from the BioInitiative 2007 recommendation of 0.1 uW/cm2 (or one-tenth of a microwatt per square centimeter which is the same as 100 nanowatts/cm2) for cumulative outdoor RFR down to something three orders of magnitude lower (in the low nanowatt per square centimeter range) is justified on a public health basis. We use the new scientific evidence documented in this Report to identify ‘effect levels’ and then apply one or more reduction factors to provide a safety margin. We do note however, even a precautionary action level of several tenths of a nanowatt per square centimeter (or

several hundred picowatts per square centimeter) would still allow for cell phone transmissions (that can operate down to about 0.00003 V/m).

Even so, these levels may need to go lower in the future, as new and better studies are completed. This is what the authors said in 2007 (Carpenter and Sage, 2007, BioInitiative Report) and it remains true today in 2012. We leave room for future studies that may lower today's observed 'effects levels' and should be prepared to accept new information as a guide for new precautionary actions.

Establishing A Scientific Benchmark for 'Lowest Observed Effect Levels'

Studies that provide information at 'new levels of observed effect' have been identified. These serve as scientific benchmarks for possible risk to health and well-being. Next, we indentify reduction factors to compensate for sensitive subpopulations and apply them to the scientific benchmarks (lowest observed effect levels).

A ten-fold reduction factor is warranted (or higher) for studies that report effects from only short-term (i.e., acute) rather than chronic (i.e., long-term) exposures. Longer duration of exposure can cause bioeffects at lower exposures where these effects are NOT seen with shorter (acute) exposures (Belyaev, 1997; Belyaev, 2012). Chronic exposures with longer durations of weeks, months or years is what most populations face with respect to wireless classrooms, wireless offices and locations near base stations.

A second ten-fold reduction (or higher) is justified as a buffer for sensitive populations including children, the elderly and other adult groups that may be ill, already sensitized, in remission or suffer from ailments made worse by physiological stress and insomnia.

Studies which contribute together can reasonably contribute to delineating a new RFR lower effects level are primarily mobile phone (cell phone) base station studies of healthy human populations and studies of sperm damage in men who use and/or wear their wireless devices on or around the belt or pants pocket.

Power Density Studies (Mobile Phone Base Stations and Sperm/Fertility Studies)

A scientific benchmark of 0.003 uW/cm2 or three nanowatts per centimeter squared for 'lowest observed effect level' for RFR is based on mobile phone base station-level studies. The Thomas et al, (2008) study shows effects at a LOEL of 0.005 uW/cm2 on adults exposed to short-term cell phone radiation only (it is not a chronic exposure study). Other studies that are relevant are Thomas et al (2010) with a LOEL of 0.003 uW/cm2 and Heinrich et al (2010) with a LOEL of 0.003 uW/cm2. Both studied mixed child/adolescent populations of students, but have short-term test periods (are not chronic exposure studies) and have LOELs of 0.003 uW/cm2. Buchner et al (2012) shows a 0.006 uW/cm2 'effect level' and tests adult populations, but achieves 'chronic' exposure testing criterion (over 18 months). Applying a ten-fold reduction to compensate for the lack of long-term exposure (to provide a safety buffer for chronic exposure) or for children as a sensitive subpopulation yields a 300 to 600 picowatts per square centimeter precautionary action level. This is also equal to a 0.3 nanowatts to 0.6 nanowatts per square centimeter as a reasonable, precautionary action level.

Of the studies that deal with children and base-station level RFR exposures, none studied children exclusively, so the results may dilute out any apparent effects accruing to the younger test subjects. Thomas et al (2010) is a short-term exposure study of children and adolescents 8 to 17 years in age. Heinrich et al (2010) is a further study of the same population of 8 to 17 year olds over the short-term. A 100-fold reduction could be defended as reasonably conservative in this instance.

Behari et al (2006) provides the one sperm study expressed in power density units with a LOEL of 0.00034 uW/cm2. It is a chronic exposure study. The majority of sperm studies with good exposure information are expressed in SARs (W/kg). These range from LOELs of 0.014 (Kumar et al, 2012) to 0.091 W/kg (Atasoy et al, 2012) to 0.43 W/kg (Salama et al, 2008) to 0.795 W/kg (Panagopoulous et al, 2012) to 0.9 W/kg (Kesari et al, 2012). All the other sperm damage or ovarian damage studies have SARs

of greater than 1.0 W/kg (7 more studies). All are short-term studies. There are more sperm damage studies but without any measurements or other specific exposure information. These are studies that place sperm, or mice, or give prenatal exposures to animals close to sources of cell phone radiation. Such studies give weight to the argument that low-intensity RFR exposures can cause damage, but do not help in delineating LOELs because they have no specific exposure numbers, just distances.

Most of the sperm studies and base station studies which have exposures expressed power density (microwatts per square centimeter) have 'effect' levels in the nanowatt range (0.34 nanowatt/cm2 to 100 nanowatt/cm2)*. They include Behari and Kesari, 2006; Buchner and Eger, 2012; Oberfeld et al, 2004; Thomas et al, 2008, 2010; Heinrich et al, 2010; Navarro et al, 2003; and Otitoloju et al 2010. Avendano et al (2012) report that WI-FI exposure from a 4-hr laptop exposure decreased sperm viability and caused DNA fragmentation in human sperm samples (exposure in petri dishes) at 0.5 to 1.0 uW/cm2. The Kundi-Hutter 2009 Pathophysiology Journal review paper of base station studies through 2006 reports an overall NOEL below 0.05 to 0.1 uW/cm2. Overall, the new 2007-2012 power density studies are reporting 'lowest effects levels' two or three orders of magnitude lower than in 2006, down from the microwatt/cm2 range to the nanowatt/cm2 range.

SAR Studies (Sperm Studies and Ovarian Damage with Cell Phone Radiation Exposures)

Studies on male fertility (adverse effects on sperm, on the testes size and morphology, etc) coming from cell phone-in-the-pocket-on-stand-by-mode and wireless laptop studies provide us with a flood of new data showing very low-intensity effects to guide precautionary actions and to educate the public about potential risks to health, fertility and reproduction.

*The RF Color Charts in this Report are a guide to reported biological effects and those RFR levels reported to cause them.

Sperm and fertility studies with 'effects levels' in the 9 microwatt/kg to 80 milliwatt/kg range are Kumar et al (2012) (male infertility) and Aitken et al (2005) (sperm DNA damage). Sperm studies with 'effect levels' in the 90 to 900 milliwatt/kg range are De Iuliis et al (2009) (human sperm cell damage), Salama et al (2008) (decrease in sperm mobility and concentration), Panagopoulous et al (2012) (ovarian damage) and Kesari et al (2012) (sperm damage). Studies from 1 W/kg to 1.8 W/kg that report sperm or reproductive damage are Gul et al (2009) (toxic effect on ovaries), Agarwal et al (2008) (sperm damage), Agarwal et al (2009) (sperm damage) and Yan et al (2007) (deformed sperm cells, disabled for swimming).

The WI-FI laptop study by Atasoy et al (2012) reports that exposures to laptops estimated at 0.091 W/kg increase DNA damage and reduce DNA repair in damaged sperm, and "*raise questions about safety of radiofrequency exposure from WI-FI internet access dvices for growing organisms of reproductive age, with a potential effect on fertility and integrity of germ lines*."

Altered fetal development in mice exposed to RFR at SARs of 0.3 to 60 milliwatt/kg is reported to result in consequent adverse effects on learning and behavior (Aldad et al, 2012). Fragopoulou et al (2009) reported changes at 600 to 900 milliwatts/kg in mouse embryos.

General Approach to Delineating a Precautionary Action Level

As a methodology, is not necessary or wise to use an averaging approach among studies. The technique itself is too vulnerable to weighting problems by the older studies that did not test for effects at the lowest range of exposures to RFR (or did not have the power to assess effects). Averaging also is insensitive in giving proper visibility to important NEW results at the very low-intensity (nanowatt, picowatt and femtowatt/cm2 range). Even when they are averaged together, these studies contribute vanishingly small influence when averaged together with studies of much higher power density to determine a scientific benchmark for harm.

One limitation of the sperm studies using base station-level RFR exposures is that good estimates of exposure are available if sperm are tested outside the body (in petri dishes), but that does not reflect the more realistic situation of sperm exposed in humans themselves (using or carrying a mobile phone near the testes) where exposure estimates are more difficult to determine. So, it is useful and informative to observe the combined results of both in-vivo and ex-vivo studies as a guide. For base station studies on human populations, the quality of exposure assessments is variable, and in some cases inadequate. Further, very few base station studies are conducted so that test subjects do not know if/when they are subjected to elevated RFR (blinded studies), so that some bias may influence results. People often report more ill effects because they are aware of the exposure (from a nearby base station, for example). These variations in quality across the studies, however, do not offset their usefulness in the aggregate for delineating what the lowest observable effect exposures are, and helping to guide decision-making for public health and precautionary actions.

A further concern is that time-averaging of RFR to give a single numeric recommendation for a precautionary action guideline does not address the critical difference between peak power levels (RFR spikes that occur intermittently) and measurements that hide how high peak power spikes are by dilution. Biological responses can last over seconds of time, or have even longer effects on proteins and enzymes, while the RFR pulses may be in microseconds or milliseconds in duration. It is entirely possible that what causes bioeffects is the high, intermittent RFR spikes that the body perceives and responds to as one continuous, high-power assault. For example, the DECT phone peak power is about 100 times larger than what RFR is measured with time-averaging. A person near a cell tower that produces an RFR measurement of 0.1 microwatts/cm2 is probably getting RFR power density spikes of eight times higher, if one could measure the spikes individually. None of the studies profiled in this section deal with peak power pulses and biological response times that are longer than the 'intermission' between RFR spikes. Thus, precautionary action levels should err on the side of being conservative.

The planning of base stations, and other site evaluations needs to have a scientific benchmark below which effects have not (not yet) been characterized, published or vetted. Then, a reasonable safety buffer should be added - remembering that the design life of such facilities may be 30-50 years long. This is standard procedure for environmental planning constraints.

Health Agencies Should Act Now

Health agencies and regulatory agencies that set public safety standards for ELF-EMF and RFR should act now to adopt new, biologically-relevant safety limits that key to the lowest scientific benchmarks for harm coming from the recent studies, plus a lower safety margin. Existing public safety limits are too high by several orders of magnitude, if prevention of bioeffects and resulting adverse health effects are to be minimized or eliminated. Most safety standards are a thousand times or more too high for healthy populations, and even less effective in protecting sensitive subpopulations.

New, biologically-based public exposure standards are critically needed now and should key to scientific benchmarks for harm, plus a safety margin below that level.

Standard of Evidence for Judging the Science

The standard of evidence for judging the scientific evidence should be based on good public health principles rather than demanding scientific certainty before actions are taken.

Sensitive Populations Require Special Protections

Safety standards for sensitive populations will need to be set at lower levels than for healthy adult populations to protect the developing fetus, the infant and young child, school-age children, the elderly, those with pre-existing chronic diseases, and those with

developed electrical sensitivity (EHS). Men of child-bearing age should not wear wireless devices on their body in order to protect the integrity of sperm DNA. Sperm should be considered a 'sensitive population'. Scientific benchmarks for lowest effect levels should be identified, and applied with additional safety margin reductions to safeguard populations against excessively high exposure to chronic ELF-EMF and RFR.

Protect Children Against Chronic Exposure to Wireless Devices

Strong precautionary action and clear public health warnings are universally warranted for use of cordless and cell phones to help prevent a global epidemic of brain tumors. This is especially important for children, adolescents and young adults, while new safety standards are established and implemented. Children should not use wireless devices except in the case of emergencies, or be exposed on an involuntary and chronic basis to wireless in their living, sleeping or learning environments.

Common Sense Precautionary Measurees are Warranted Now

Common sense measures to limit both ELF-EMF and RFR in the fetus and newborn infant are needed, especially with respect to avoidable exposures like baby monitors in the crib and baby isolettes (incubators) in hospitals that can be modified; and where education of the pregnant mother with respect to laptop computers, mobile phones and other sources of ELF-EMF and RFR are easily instituted.

Wireless laptops and other wireless devices should be strongly discouraged in schools for children of all ages, and wireless systems already installed should be replaced with wired (cable) alternatives. While without question it is important for children to have access to the internet, wired computer laboratories will have no elevated exposure to RFR. What might be lost in flexibility of moving rooms arounds will be more than gained by reducing exposure to RFR if wired connections, rather than wireless, are used. Pregnant women should be strongly cautioned not to use wireless devices during pregnancy. If a school already has wireless facilities, classrooms without wireless should

be made available to students, teachers and staff during the transition if sensitivities to EMF are reported by the individual. Special education classroom teaching environments should offer wired teaching environments (not wireless), nor should they be exposed to off-site wireless radiofrequency radiation from other sources that elevate interior levels for children.

Special Protections for the Integrity of the Genome and Reproduction

Reducing life-long health risks should begin in the earliest stages of embryonic and fetal development. Development pace is accelerated for the infant and very young child compared to adults, and is not complete in young people (as far as brain and nervous system maturation) until the early 20's. Windows of critical development mean that risk factors once laid down in the cells, or in epigenetic changes in the genome may have grave and life-long consequences for health or illness for every individual, and furthermore these genetic and epigenetic changes may be passed to the next generation. All relevant environmental conditions, including biologically active exposures to EMF and RFR that can degrade the human genome, and impair normal health and development of all species including humans - should be given weight in defining and implementing strong precautionary actions now to protect public health. The consequence of ignoring clear evidence of large-scale health risks to global populations, when the risk factors are largely avoidable or preventable is too high a risk to take.

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SECTION 25

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SECTION 26

Glossary of Terms and Abbreviations

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Absorption. In radio wave propagation, attenuation of a radio wave due to dissipation of its energy, i.e., conversion of its energy into another form, such as heat.

Athermal effect. Any effect of electromagnetic energy on a body that is not a heat-related effect.

Blood–brain barrier. A functional concept developed to explain why many substances that are transported by blood readily enter other tissues but do not enter the brain; the "barrier" functions as if it were a continuous membrane lining the vasculature of the brain. These brain capillary endothelial cells form a nearly continuous barrier to entry of substances into the brain from the vasculature.

Conductance. The reciprocal of resistance. Expressed in siemens (S).

Conductivity: A property of materials that determines the magnitude of the electric current density when an electric field is impressed on the material.

Continuous wave. A wave whose successive oscillations are identical under steady-state conditions.

Current density. A vector of which the integral over a given surface is equal to the current flowing through the surface; the mean density in a linear conductor is equal to the current divided by the cross-sectional area of the conductor. Expressed in ampere per square metre (A $m^{!2}$).

Depth of penetration. For a plane wave electromagnetic field (EMF), incident on the boundary of a good conductor, depth of penetration of the wave is the depth at which the field strength of the wave has been reduced to 1/e, or to approximately 37% of its original value.

Dielectric properties: In the context of this document the properties of materials conductivity and permeability.

Dosimetry. Measurement, or determination by calculation, of internal electric field strength or induced current density, of the specific energy absorption, or specific energy absorption rate distribution, in humans or animals exposed to electromagnetic fields.

Electric field strength. The force (**E**) on a stationary unit positive charge at a point in an electric field; measured in volt per metre (V $m^{!1}$).

Electrosensitivity (Electrohypersensitivity): A working definition of EHS from Bergqvist et al. (1997) is "a phenomenon where individuals experience adverse health effects while using or being in the vicinity of devices emanating electric, magnetic or electromagnetic fields (EMFs)".

Electromagnetic energy. The energy stored in an electromagnetic field. Expressed in joule (J).

Electric field strength (E): The magnitude of a field vector at a point that represents the force (F) on a charge (q). E is defined as E = F/q and is expressed in units of Volt per meter (V/m).

Electromagnetic field: Electromagnetic phenomena expressed in vector functions of space and time.

Electromagnetic radiation: The propagation of energy in the form of electromagnetic waves through space.

EMF. Electric, magnetic, and electromagnetic fields.

Exposure: Exposure occurs wherever a person is subjected to electric, magnetic or electromagnetic fields or contact currents other than those originating from physiological processes in the body.

Extra low frequency (ELF): Extra low frequency fields include, in this document, electromagnetic fields from 1 to 300 Hz. Alternately, **ELF-** Extremely low frequency where the European convention is extremely low frequncy, US is extra-low frequency.

Frequency modulation (FM): Frequency Modulation is a type of modulation representing information as variations in the frequency of a carrier wave. FM is often used at VHF frequencies (30 to 300 MHz) for broadcasting music and speech.

Far field. The region where the distance from a radiating antenna exceeds the wavelength of the radiated EMF; in the far-field, field components (**E** and **H**) and the direction of propagation are mutually perpendicular, and the shape of the field pattern is independent of the distance from the source at which it is taken.

Frequency. The number of sinusoidal cycles completed by electromagnetic waves in 1 second; usually expressed in hertz (Hz).

Impedance, wave. The ratio of the complex number (vector) representing the transverse electric field at a point to that representing the transverse magnetic field at that point. Expressed in ohm (S).

Magnetic flux density (B): The magnitude of a field vector at a point that results in a force (F) on a charge (q) moving with the velocity (v). The force F is defined by F = q*(v x B) and is expressed in units of Tesla (T).

Magnetic field strength (H): The magnitude of a field vector that is equal to the magnetic flux density (B) divided by the permeability (μ) of the medium. H is defined as H = B/μ and is expressed in units of Ampere per metre (A/m).

Magnetic permeability. The scalar or vector quantity which, when multiplied by the magnetic field strength, yields magnetic flux density; expressed in henry per metre ($H\ m^{-1}$). *Note:* For isotropic media, magnetic permeability is a scalar; for anisotropic media, it is a tensor quantity.

Microwaves: Microwaves are defined in the frame of this expertise as electromagnetic waves with wavelengths of approximately 30 cm (1 GHz) to 1 mm (300 GHz).

Milligauss (mG): A milligauss is a measure of ELF intensity and is abbreviated mG. This is used to describe electromagnetic fields from appliances, power lines, interior electrical wiring.

Milliwatt (mW): A unit of power equal to 10^{-3}.

Microwatt (uW): A unit of power equal to 10^{-6}

Microwatts per centimeter squared (µW/cm2)

Radiofrequency radiation in terms of power density is measured in microwatts per centimeter squared and abbreviated (µW/cm2). It is used when talking about emissions from wireless facilities, and when describing ambient RF in the environment. The amount of allowable RF near a cell tower is 1000 µW/cm2 for some cell phone frequencies, for example.

Nanowatt (nW): A unit of power equal to 10^{-9} Watt.

Non – thermal effects (or athermal effects): An effect which can only be explained in terms of mechanisms other than increased molecular motion (i.e. heating), or occurs at absorbed power levels so low, that a thermal mechanism seems unlikely, or displays so unexpected a dependence upon some experimental variable that it is difficult to see how heating could be the cause.

Near field. The region where the distance from a radiating antenna is less than the wavelength of the radiated EMF. *Note:* The magnetic field strength (multiplied by the impedance of space) and the electric field strength are unequal and, at distances less than one-tenth of a wavelength from an antenna, vary inversely as the square or cube of the distance if the antenna is small compared with this distance. Near field exposures are unreliable for estimation of exposures by calculation. The can zero out or be additive and nearly infinite, thus creating problems for exposure assessment.

Non-ionizing electromagnetic radiation (NIER). Includes all radiations and fields of the electromagnetic spectrum that do not normally have sufficient energy to produce ionization in matter; characterized by energy per photon less than about 12 eV, wavelengths greater than 100 nm, and frequencies lower than 3×10^{15} Hz.

Occupational exposure. All exposure to EMF experienced by individuals in the course of performing their work. Safety limits are five times higher for allowable occupational exposures than for general public exposures in the US.

Permeability (µ): A property of materials that indicates how much polarisation occurs when an electric field is applied.

Permittivity. A constant defining the influence of an isotropic medium on the forces of attraction or repulsion between electrified bodies, and expressed in farad per metre ($F\ m^{!1}$); *relative permittivity* is the permittivity of a material or medium divided by the permittivity of vacuum.

Public Exposure. All exposure to EMF experienced by the general public excluding exposure during medical procedures and occupational work environments. Public exposure limits in the US are five times lower than for occupational exposures, where informed consent by employees is required.

Power Density. The power as measured in free space (ambient) as opposed to measured by SAR or specific absorption rate (within tissues or the body). The unit of measurement can be watts per square meter, milliwatts per square meter or microwatts per centimeter squared. Radiofrequency (RF). Any frequency at which electromagnetic radiation is useful for telecommunications, or broadcasting for radio and television. Frequency range is usually defined as 300 Hz (300 hertz) to 300 GHz (300 gigahertz).

Radiofrequency (RF): The frequencies between 100 kHz and 300 GHz of the electromagnetic spectrum.

Reasonance. The change in amplitude occurring as the frequency of the wave approaches or coincides with a natural frequency of the medium; whole body absorption of electromagnetic waves presents its highest value, i.e., the reasonance. for frequencies (in MHz or megahertz) corresponding to approximately 114/L where L is the height of the individual in meters. Reasonance can also be applicable to organs, tissues, or other body parts.

Specific Absorption Rate (SAR is measured in watts per kilogram or W/Kg)
SAR stands for specific absorption rate. It is a calculation of how much RF energy is absorbed into the body, for example when a cell phone or cordless phone is pressed to the head. SAR is expressed in watts per kilogram of tissue (W/Kg). The amount of allowable energy into 1 gram of brain tissue from a cell phone is 1.6 W/Kg in the US. For whole body exposure, the exposure is 0.8 W/Kg averaged over 30 minutes for the general public. International standards in most countries are similar, but not exactly the same.

Static electric field: Static fields produced by fixed potential differences.

Static magnetic fields: Static fields established by permanent magnets and by steady currents.

VDU: Video display units for computers, videos, TV and some measurement devices using cathode ray tubes

WI-FI: Stands for wireless fidelity. WI-FI systems create zones of wireless RF that allow access to wireless internet for computers, internet phone access and other wireless services. Access points that provide WI-FI to access Land Area Networks (LANs) can be installed on streets (for city-wide coverage) or indoors in buildings, Restaurants, hotels, coffee shops, airports, malls and other commercial enterprises are widely installing WI-FI. The range of typical WI-FI systems is about 300 feet.

WI-MAX: Stands for "Wireless interoperability for Microwave Access" and is a telecommunications technology aimed at providing wireless data over long distances. Like WI-FI, WI-MAX systems are designed to provide wireless access but over much broader geographic areas, with some systems transmitting signal up to 10 miles. Higher levels of RF are produced at the wireless transmission facilities than for WI-FI.s

Section 20 LIST OF ABBREVIATIONS

µT	microtesla
µW	microwatt
AC	Alternating current
ALS	Amyotrophic Lateral Sclerosis
AM	Amplitude modulation
B	Magnetic flux density
BBB	Blood-Brain-Barrier
CENELEC	European Committee for Electrotechnical Standardization
CI	Confidence Interval
CNS	Central Nervous System
CW	Continuous wave
DC	Direct current
DECT	Digital Enhanced Cordless Telephone
DMBA	7,12-dimethylbenz[a]anthracene
DNA	Deoxyribonucleic acid
EEG	Electroencephalogram
EHS	Electromagnetic hypersensitivity
ELF	Extra low frequency (also ELF-EMF)
EMF	Electromagnetic field
FM	Frequency Modulation
GSM	Global System for Mobile Communication
H	Magnetic field strength
HSP	Heat-shock proteins (stress proteins)
Hz	Frequency in Hertz
IARC	International Agency for Research on Cancer
IL	Interleukin
kg	Kilogram
kHz	Kilohertz
kV	Kilovolt
MF	Magnetic Field (sometimes MF-ELF)
MHz	Megahertz
ms	Milliseconds
mT	Millitesla
mG	Milligauss
mW	Milliwatt
nT	Nanotesla

nW Nanowatt

NRPB National Radiation Protection Board (HPA)

OR Odds Ratio (measure of increased risk of disease)

REFLEX European Research Program for Radiofrequency Hazards

RF Radiofrequency Radiation (also written as RFR or RF-EMF)

SCENIHR Scientific Committee on Emerging and Newly Identified Health Risks

TNO Nederlandse Onderzoek (Netherlands Organisation Applied Scientific Research

UMTS Universal Mobile Telephony System **UNEP** United Nations Environmental

VDT Video display terminal (VDU – for computers, videos, TV, that use cathode ray tubes).

Wi-Fi Short for wireless fidelity – wireless internet access - works for short- distances for cell phone and laptop computer access without wires.

WLAN Wireless Local Area Network (wireless internet coverage usually up to 300' provided by access points that create elevated radiofrequency radiation for that service zone.

WiMAX Worldwide Interoperability for Microwave Access (wireless service up to 10 miles in comparison to Wi-Fi that may serve 300' area)

WHO World Health Organisation

FCC The Federal Communications Commission (FCC) is an independent United States government agency, created, directed, and empowered by Congressional statute to oversee the regulation of radio and TV broadcasting and wireless technologies. It is not a health agency.

HPA Health Protection Agency (UK) that was formerly the National Radiation Protection Division Board). The Health Protection Agency (HPA) is an independent body that protects the health and well-being of the population. The Agency plays a critical role in protecting people from infectious diseases and in preventing harm when hazards involving chemicals, poisons or radiation occur.

DNA Deoxyribonucleic acid, or DNA is a nucleic acid molecule that contains the genetic instructions used in the development and functioning of all living things.

Melatonin Melatonin is a hormone produced in the brain by the pineal gland, It is a potent anti-oxidant that protects against oxidative damage from free radicals that can cause DNA damage.

Alzheimer's Alzheimer's disease is a progressive brain disorder that gradually destroys a person's memory and ability to learn, reason, make judgments, communicate and carry out daily activities. As Alzheimer's progresses, individuals may also experience changes in personality and behavior, such as anxiety, suspiciousness or agitation, as well as delusions or hallucinations.

RFIAWG Radiofrequency Interagency Working Group (US) composed of members from federal agencies with some interest in radiofrequency radiation issues. This Working Group was made up of representatives from the US government's National Institute for Occupational Safety and Health (NIOSH), the Federal Communications Commission (FCC), Occupational Health and Safety Administration (OSHA), the Environmental Protection Agency (US EPA), the National Telecommunication and Information Administration, and the US Food and Drug Administration (FDA).

ICNIRP International Commission on Non-Ionizing Radiation. It is a body of independent scientific experts consisting of a main Commission of 14 members, 4 Scientific Standing Committees covering Epidemiology, Biology, Dosimetry and Optical Radiation and a number of consulting experts. This expertise is brought to bear on addressing the important issues of possible adverse effects on human health of exposure to non-ionising radiation.

SECTION 27

Appendix 20-A Average Residential Exposures to ELF (Power Frequency Fields)

Prepared for the BioInitiative Working Group

July 2007

What are Ambient ELF and RF Levels?

A nation-wide survey in the United States by Zaffanella et al (1993) collected engineering data on sources and levels of 60 Hz electric power magnetic fields that exist inside residences in the United States.

Approximately 1000 residences were randomly selected for the survey. The goals were to 1) identify all significant sources of magnetic field, 2) estimate for each source the percentage of residences where magnetic fields exceeded specified levels, 3) to determine the relation between magnetic field and sources and 4) to characterize the field varations in time.

The median field was identified as 0.5 mG and the average field was 0.9 mG. Thus, this confirms that average residential magnetic fields based on the 1000-home study is less than 1 mG.

Appliances produce magnetic fields but these diminish rapidly with distance (at $1/R^3$),

Power lines generally produce the largest average residential magnetic field when the entire living space of a residence and a 24-hour period are considered. Power line magnetic field exceeds 1 mG in 17%, exceed 2.5 mG in 9.5% and exceed 5 mG in 0.3% of all the residences surveyed.

Zaffanella (1998) conducted measurements to characterize typical EMF exposure levels in persons living in the United States - a study called the 1000-Person Study. Table A-S.2 shows that about half of all people in the US have EMF exposures at home under 0.75 mG; in bed are 0.48 mg; at school 0.60 mG; at work 0.99 mG; and 0.87 mG is the median EMF exposure for an average 24-hour day.

Table A-S.2

Table S.2 Descriptive Statistics for Different Activity Periods

Parameter	Home not in Bed	In Bed	Work	School	Travel	24-Hour
Number of Valid Data Sets	1011	996	525	139	765	1012
1st Percentile	0.10 mG	0.01 mG	0.14 mG	0.13 mG	0.13 mG	0.18 mG
5th Percentile	0.20 mG	0.08 mG	0.24 mG	0.18 mG	0.29 mG	0.27 mG
10th Percentile	0.27 mG	0.12 mG	0.30 mG	0.29 mG	0.41 mG	0.35 mG
25th Percentile	0.44 mG	0.24 mG	0.60 mG	0.35 mG	0.66 mG	0.51 mG
50th Percentile	0.75 mG	0.48 mG	0.99 mG	0.60 mG	0.98 mG	0.87 mG
75th Percentile	1.39 mG	1.24 mG	1.78 mG	1.01 mG	1.46 mG	1.41 mG
90th Percentile	2.49 mG	2.44 mG	3.32 mG	1.64 mG	2.18 mG	2.38 mG
95th Percentile	3.89 mG	3.63 mG	5.00 mG	1.77 mG	2.73 mG	3.38 mG
99th Percentile	9.50 mG	9.19 mG	13.5 mG	3.55 mG	5.43 mG	6.16 mG
Mean	1.29 mG	1.11 mG	1.73 mG	0.82 mG	1.22 mG	1.25 mG
Standard Deviation	2.54 mG	2.06 mG	3.09 mG	0.70 mG	0.99 mG	1.51 mG
Geometric Mean	0.80 mG	0.52 mG	1.03 mG	0.64 mG	0.96 mG	0.89 mG
Geometric Standard Deviation	2.50	3.52	2.57	2.06	2.03	2.18

In Sweden, Mild et al (1996) report that overall mean residential ELF exposures are 0.4 mG, and in Norway are 0.13 mG.

Average Occupational Exposures to ELF

Average occupational exposures in commercial office buildings are 1-2 mG or less and have been reported fairly consistently across numerous studies of exposure assessment (Table 1). Powerline and electrical workers have higher average occupational exposures from 10 mG to 16.6 mG.

Table A-2: Average Occupational Exposures to ELF

EMF RAPID Program – Questions and Answers, NIEHS, June 2002	
Office buildings (median)	0.6 mG
Support staff	0.5 mG
Professional staff	0.6 mG
Maintenance staff	0.6 mG
Visitors	0.6 mG
EMF RAPID Program Engineering Project #3 Executive Summary, May 1996	
Office building (average)	0.7 mG
Office building (median)	0.4 mG
Electric and Magnetic Field Fundamentals (EPRI Resource Paper, March 1994)	
Typical magnetic fields in offices	1 – 2 mG
Power line workers	10 mG
Occupational EMF Exposure Assessment (EPRI Resource Paper, February 1994)	
Office Worker Comparison Group	1.6 mG
All Occupationally Exposed Utility Workers	16.6 mG
Table 7 – Other Studies Cited	
Bracken Study (1990)	1.0 mG
Deadman Study (1988)	1.6 mG
Bowman Study (1992)	0.9 – 1.8 mG

Limits on Operation of Sensitive Electronic Equipment

Companies that manufacture or use equipment in nanotechnology and biotechnology and found 1.0 mG is generally the limit for proper operation of electron beam devices (mass spectrometers, scanning electron microscopes, lithography, etc) used in these technologies. Ten (10) milligauss (mG) is the EMF limit for normal computers – above 10 mG can introduce "computer jitter" and other problems.

What are Ambient Radiofrequency Radiation/Microwave Levels?

Prior to the rapid development of wireless communications for personal and business usage, RF power density levels were primarily related to AM, FM and television broadcasting signal in both urban and rural areas of the United States. Microwave frequencies used for wireless communications were negligible.

Original extra-planetary sources of microwave radiation were infinitesimally small, on the order of a billionth of a microwatt per centimeter squared (10^{-12} uW/cm^2). Human evolution took place without any appreciable exposure to microwave radiation from background sources. The human body has no evolutionary protection against microwave radiation, as it does for ultraviolet radiation from the sun (Johannson, 2000). Wireless voice and communications have introduced unprecedented levels of public exposure in the last decade.

Mantiply (1997) measured and reported common sources and levels of RF in the environment. He identified areas near cellular base stations on the ground near towers to be from 0.003 to 0.3 μW/cm2. Background level ambient RF exposures in cities and suburbs in the 1990's were generally reported to be below 0.003 μW/cm2.

Hamnerius (2000) reported that ambient RF power density measurements in twelve (12) large cities in Sweden were roughly ten times higher than in the United States for equivalent measurement locations by Mantiply in 1978 (when no cellular phone service existed in the US). He reported a total mean value of 26 measured sites in the study was 0.05 μW/cm2 and the median value was 40 μW/cm2. An office location with a base station nearby at about 300 feet distance tested 150 μW/cm2. A train station with antennas mounted indoors tested at about 3 μW/cm2. Both indoor and outdoor ambient RF power density measurements showed high variability depending on proximity to transmitting antennas.

Sage Associates reported on microwave frequency RF power density levels at outdoor locations both near and far from wireless antenna sites in the United States (Sage, 2000). Within the first 100-300 feet, power density levels have been measured at 0.01 to 3.0 μW/cm2. Elevated RF power density levels from a major wireless antenna site can often be detected at 1000 feet or more. Power density levels away from wireless antenna sites measure between 0.001 μW/cm2 to 0.000001 μW/cm2. Vegetation often reduces signal (and therefore the reach of elevated RF exposures) but dry building materials used to visually screen wireless sites do not appreciably diminish signal transmission. Therefore, many sites that are "out-of-sight" because of stealth design can still produce elevated RF levels in nearby areas where people live, work and go to

school. For purposes of this evaluation, a 10 dB attenuation has been incorporated to take building material shielding effects into account.

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APPENDIX 20-B

STANDARDS OF EVIDENCE FOR DECISIONMAKING DIFFERS AMONG PROFESSIONS

There is a large difference between what constitutes causal evidence for purposes of achieving scientific consensus, what constitutes sufficient evidence for purposes of interim public health policy, and what constitutes "a more likely than not" case. A central confusion in this debate is whether prudent policy and public health decisions necessarily require conclusive scientific evidence first. This is not the case. The state of the science needs to be presented in an understandable and scientifically accurate manner, but prudent public health actions do not and should not require 100% proof of harm. In fact, precautionary and preventative actions are specifically justified at a point in time before scientific proof is established. If the growing weight of evidence is positive (although all studies need not report positive effects) then it may be essential to take preventative actions and implement policies that are protective of public health, safety and welfare rather than wait for absolute certainty. The following discussion is presented to highlight some of the main differences in professional approach and traditional ways of viewing and interpreting scientific evidence. In reality, the basis for taking action (preventative or precautionary action) is a continuum – there are no hard and fast rules. The bar for Public Health Policy may be higher or lower than shown in Figure 2; based on many factors, including how widespread the risk, how dread the disease, the cost of inaction (doing nothing until there is proof, but many may be harmed), etc.

A. Scientific Standard of Evidence

There are several levels of proof for adverse effects of environmental exposures. The most rigorous is a scientific standard, where virtual proof of causation is typically required by scientists to arrive at consensus about an effect. This approach works best in physics and chemistry. In biological systems this is rarely possible.

In this case, the 'scientific standard' refers to the overall evidence that the science community typically requires before rendering opinions on the strength of evidence, and what evidence they believe is necessary to establish a causal link (proof).

Figure 1 shows Standards of Evidence that are routinely employed by various interest groups in the EMF debate (Sage, 1997). It can be used to focus on various accepted standards for evidence that are legitimately used by scientific and professional groups to determine when an action is appropriate. The varying levels of certainty about an outcome will dictate different decision-making among different groups that may all be appropriate given their professional charge. Even though the evidence required to make a scientific determination about causality has a far higher standard than a legal determination on the 'weight of the evidence' or 'preponderance of evidence' (a legal standard), neither negates the correctness of the other in its proper jurisdiction. Scientists typically want all possible evidence (animal, cell and epidemiological studies, with replications) showing a high degree of consistency. This can generally be described as a 95% to

99% degree of certainty before drawing conclusions (it does not refer to the 95% confidence interval in epidemiology, except as a part of the overall proof).

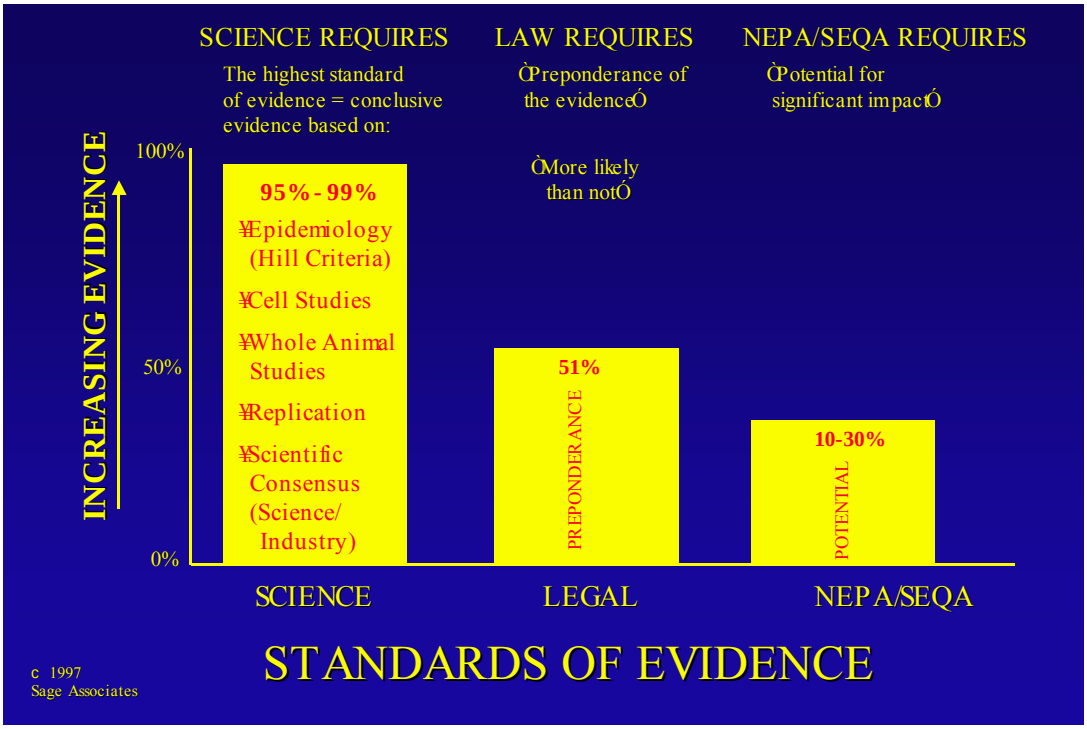

Figure 1 Variable Standards of Evidence (By Profession)

B. Legal Standard of Evidence

The second level of proof is the standard applied in legal proceedings, which is 'more likely than not' or 'preponderance of the evidence' (Figure 1). This is to say if there is a 50%+ likelihood of harm, this is taken as evidence for a relationship (Sage, 1997). At least this level of evidence is reached for the studies of adult cancer and neurodegenerative diseases and 50/60 Hz magnetic field exposures. As with childhood leukemia, while we have documented associations, this does not necessarily indicate causation. Failure to meet either the scientific or the legal standard of proof does not mean that there is no relationship between exposure and disease. In the case of EMF exposure, where everyone is exposed, the societal implications may be huge if there is a real risk whose magnitude has simply just not yet been clarified. Public policies are needed to address this issue of decision-making in the face of this scientific uncertainty.

C. Environmental Protection Standard of Evidence

National and state environmental quality acts (The National Environmental Policy Act) and various state environmental quality acts (SEQA) require that assessments use a standard of "potential for a significant impact on the environment which is a relatively low level of certainty (10% to 30%). The potential for a significant impact requires that mitigation strategies be developed, i.e, require precautionary or preventative actions when only the potential for risk is present (Figure 1).

For example, the potential for risk to humans from building on an active earthquake fault will require a finding of potentially significant impact, and will require mitigative action; even when there is no certainty (no causal evidence) that the fault will rupture and cause damage within the design lifetime of the building. Proof of harm is not a pre-condition for taking action, and the level of certainty is low in comparison to a scientific or legal standard of certainty. Nonetheless, each standard has validity, and will have a different level of evidence required to take action. What decision-makers need to address is what standard of evidence is appropriate now to guide them with respect to EMF exposures that are clearly of environmental and public health concern.

D. Public Health Standard of Evidence

The prudent approach from a public health point of view is to take preventive actions as if causation had been proven, while at the same time to continue to search for mechanisms of action. In the case of childhood leukemia and ELF exposure there is a consistent and statistically significant association in most studies, while for many of the other diseases the results are less consistent although strong associations are found in some studies (Figure 2). This bar graph should be considered illustrative only, since the level of certainty may be higher or lower (above or below 50%) depending on the circumstances of the potential risk, and costs of those risks to society.

Whether magnetic fields actually cause childhood leukemia and the other cancers and neurological diseases documented in this Report; or whether it is some other component in the electromagnetic environment that is responsible for the association is a subject of debate within the scientific community, but from a public health point of view it doesn't matter. The fact that there are unknowns does not negate or override the ultimate public health responsibility, which is to protect the population from exposures which cause disease. Those who make public health decisions, as well as policymakers who rely on them and who approve construction of new schools and homes near power lines, those who provide insurance or financing of new construction, those who must choose siting routes for new electrical facilities all face making decisions with some uncertainty about the potential health risks from EMF exposure. Important social issues must often be decided on the basis of incomplete or uncertain scientific information.

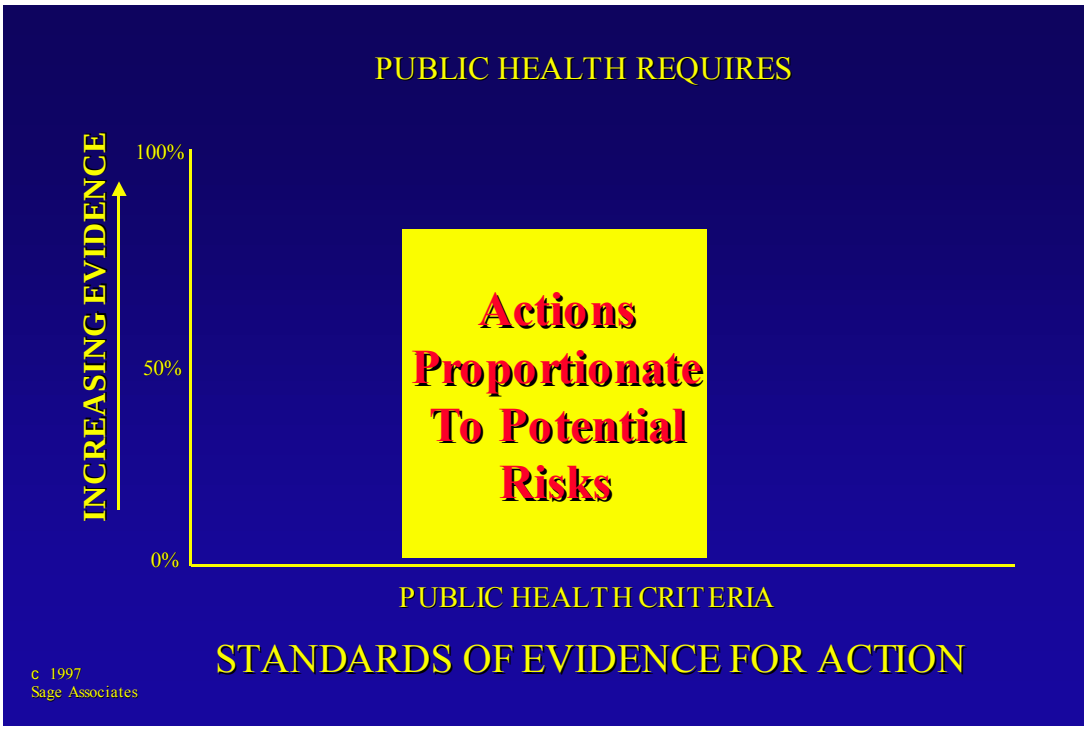

Figure 2 **Public Health Standard of Evidence for Decisions**

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