Report prepared for

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On the Investigated Cancer Cluster in the Literature Building at UCSD

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EXECUTIVE SUMMARY

A cancer cluster has been reported in the Literature Building. Cases were reported through the Department of Literature, based mainly on self-reports. Dr. Cedric Garland investigated this apparent cancer cluster and determined that there were about 4-5 times more cases than expected based on the incidence in the California general population. After considering some other exposures, Dr. Garland focused on (electromagnetic fields) EMF as a culprit, particularly on the fields generated by the centrally-located elevator.

The Field Management Services (FMS) undertook an Extremely Low Frequency (ELF) magnetic field survey of areas adjacent to electrical facilities which support operation of hydraulic elevators in the Literature Building. While some peak values of 44 and 96 mG were recorded, all measurements in the areas which people occupy were very low. As expected, fields decay rapidly within 4 to 6 feet of the peak value and become less than 1-2 mG throughout most areas of the building.

Electric and magnetic fields are present in the environment as an inevitable consequence of the use of electricity by society. They induce currents in the body which, at high levels, can cause nerve stimulation. The field levels required to produce these effects are, however, rarely experienced in the environment. In the Literature Building in particular, present day measurements indicate very low average fields.

Magnetic fields are classified by the International Agency for Research on Cancer (IARC) and the World Health Organization (WHO) as "possibly carcinogenic to humans" based on studies of childhood leukemia and the lack of support from toxicologic studies. The evidence for magnetic fields causing any diseases other than childhood leukemia is much weaker than that relating to childhood leukemia. For breast cancer, which has been investigated in several large EMF studies, the epidemiologic evidence, particularly when based on well-designed studies, does not support an association. This, coupled with low fields currently measured in the building, argues against EMF (and the elevator) as a causative agent of the apparent cluster.

Cancers can and do occur by chance alone and differentiating between those that have occurred by chance and those that might have a common cause is often difficult. The most productive studies of clusters have been those of extremely rare diseases or of diseases with markedly changed patterns. In addition, these studies have often involved high-level and relatively well-defined exposures. However, these circumstances or cluster characteristics are fairly uncommon. Most cluster investigations involve a great deal of uncertainty and, complicating matters, must be performed in a politically-charged environment. This uncertainty is often the result of small numbers, poorly identified study populations and vague definitions of exposure and disease. Furthermore, these types of investigations are extremely susceptible to bias and, therefore, statistical inference is quite difficult (Kheifets, 1993). Except for the disease definition, the apparent Literature Building cluster exhibits all of the problems identified. Nevertheless, based on the currently available data there appears to be an increase in risk of breast cancer among women in literature building. Since Dr. Garland's report one new case has been diagnosed for a total of ten cases of breast cancer reported in women who worked in the Literature Building from 1991to the present. One of the cases was diagnosed shortly after moving into the building in 1991 and three of the cases were diagnosed after they left employment.

When incomplete data do not allow us to dismiss an increased risk completely, such as the case here, a next step to gather and study more complete data might be warranted. Only a comprehensive epidemiologic study can evaluate the true risk in the Literature Building. In addition, such a study can include information on other risk factors for breast cancer, comprehensive measurements of magnetic fields and investigation of other exposures. Such a database will also form a basis for future surveillance should that be needed. No matter what is done, the study would be limited by small numbers. Cluster investigations rarely identify the cause of the cluster. Nevertheless, the study would be able to decrease uncertainty and mitigate some biases, and include further measurements to address the concerns of the occupants. Based on EMF measurements conducted in the building, I believe that shielding is not warranted.

I. INTRODUCTION

Given the ubiquitous nature of extremely low frequency (ELF) electromagnetic fields (EMF), there is concern regarding their potential to adversely affect health. Numerous health effects have been studied in relation to EMF exposure: cancer, reproductive disorders, as well as neurodegenerative and cardiovascular diseases. Cancer, especially childhood cancer, has received the most attention.

EMF are imperceptible, ubiquitous, have multiple sources, and can vary greatly over time and short distances (Bracken et al., 1993). In the absence of a biological mechanism, exposure assessment of EMF has varied over the years. Epidemiologic studies in the last decade have employed improved exposure assessment methods. Most of the epidemiologic studies use the time-weighted average (TWA) measurement to characterize exposure. Furthermore, with technological advances and increased study sample size, higher exposures, i.e. > 4 mG, are being explored. Although epidemiologic evidence is not conclusive, it is generally agreed that the possibility of a causal association between EMF and adverse health outcomes cannot be excluded and that epidemiologic studies of childhood leukemia provide the strongest evidence of an association.

Epidemiologic evidence is a major contributor to the understanding of the potential effects of EMF on health. The International Agency for Research on Cancer (IARC) classified EMF as a "possible human carcinogen", or a Group 2B carcinogen; (IARC, 2002) this classification was mostly based on consistent epidemiological evidence of an association between exposure to these fields and childhood leukemia and laboratory studies in animals and cells, which were not supportive of exposure to EMF causing cancer. Although 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. Other epidemiological studies have looked at a wide range of other health effects in relation to magnetic and electric fields, sometimes finding associations and sometimes not, but without the same consistency as exists for childhood leukaemia and magnetic fields. For breast cancer in particular, the research began with a biological hypothesis, namely that EMF and light at night can affect breast cancer through suppression of melatonin. While some early studies appear to have been supportive of the hypothesis, more rigorous epidemiologic studies that followed showed no effect, thus major scientific bodies who recently reviewed the literature conclude that EMF fields are not involved in the development of breast cancer.

In this report, I begin with what is known about breast cancer. I also provide details on exposure to EMF that occurs in both occupational and residential settings. Then I review the state of science for EMF and breast cancer, including briefly *in vitro* and toxicologic data, followed by a more detailed presentation of epidemiologic studies of EMF and both male and female breast cancer. The review portion is concluded with conclusions of major reviews and policies adopted worldwide.

The second portion of the report examines previous reports provided to me: Dr. Garland's report on the apparent cancer cluster in the UCSC Literature Building and the Field Management Services (FMS) measurement report.

The final section of this report focuses on possible ways forward, such as measurement programs, a potential epidemiologic study, and precautionary measures. This report is longer and more detailed than initially expected to give management and staff as much information as possible to help interpret the results and to decide what action might be taken.

II. EMF and BREAST CANCER REVIEW

1. Breast Cancer Rates and Risks

Breast cancer is the most commonly occurring malignancy in women in the U.S. One in eight women will develop breast cancer over her lifetime (see National Cancer Institute: http://www.cancer.gov/cancertopics/factsheet/Detection/probability-breast-cancer and breastcancer.org). A considerable body of epidemiologic research has identified numerous factors that affect the risk of developing breast cancer in females. The disease occurs most frequently among whites, women of upper social class, women without children or with few children, and those who had their first child at a late age. Other risk factors include early age of menarche (menses), late age of menopause, obesity for postmenopausal women, proliferative fibrocystic disease, and a first degree relative with breast cancer, especially if it was diagnosed at a young age. Considerably less is known about male breast cancer, but indications are that genetic and environmental factors including obesity, familial history, and endocrine factors play a causative role. Occupational studies indicate elevated rates of breast cancer among men in such jobs as newspaper printing, soap and perfume manufacturing, and health care.

Breast cancer incidence rates are highest in North America and northern Europe and lowest in Asia and Africa. Until recently, the search for possible explanations of this pattern had focused on the differences in dietary and reproductive patterns of women in societies with different degrees of industrialization. However, the role of diet in the etiology of breast cancer remains uncertain and reproductive risk factors apparently account for only a fraction of the excess disease reported in modernized societies.

It has been proposed that one factor contributing to the greater occurrence of breast cancer in industrialized compared to non-industrialized societies is the use of electric power and higher exposures to light at night or to magnetic fields. Stevens (1987) hypothesized that EMF and light at night can affect breast cancer through suppression of melatonin. In 2007 IARC classified “shift-work that involves circadian disruption” as "probably carcinogenic to humans" (Group 2A), on the basis of "limited evidence in humans for the carcinogenicity of shift-work that involves night work", and "sufficient evidence in experimental animals for the carcinogenicity of light during the daily dark period (biological night)".

The time-delay, between the putative exposures and the diagnosis of clinical cancer, is called the "incubation period" or the "latency period." Breast cancer has latency between 10-40 years and is likely to vary among individuals and for exposures.

2. Sources and Environmental Levels

Extremely low frequency electro-magnetic fields (ELF EMF) are associated with all aspects of the production, transmission, and use of electricity. The fields are imperceptible to humans and are ubiquitously present in modern societies. Fields exist wherever electricity is used, following well established laws of physics; it is not possible to use or to transmit electricity without producing EMFs.

At power frequencies (60 Hz in the US) the two fields, electric and magnetic, are essentially separate entities. Electric fields are produced by voltages and are independent of the current; magnetic fields depend on current and are independent of voltage. Both decrease with increased distance from the source. In practical electrical circuits, where there has to be a "go" and "return", both fields also depend on the physical separation of the component conductors. A key difference is that electric fields are perturbed by conducting objects; in particular, the electric field produced by a source outside a home is largely screened inside the home by the building structure. Magnetic fields are perturbed very little by normal building materials or by human beings.

Typical residential exposure levels are under 10 V/m. In the immediate vicinity of electric appliances, exposure levels can reach as high as several hundreds of V/m, whereas exposure levels immediately under high-tension power lines can reach several kilovolts per meter (kV/m) i.e. several thousand V/m.

Typical residential exposure levels are around 1 mG. In the immediate vicinity of electric appliances that are in use, magnetic fields could be as high as several thousands of mG but are usually only of short duration. Average magnetic field exposures in the workplace have been found to be higher in electrical occupations which include power and telephone line workers, electricians, and electrical engineers, among others, than in other occupations such as office workers. Exposures range from 4–6 mG for electricians and electrical engineers to approximately 10 mG for power line workers, and above 30 mG for welders, railway engine drivers and textile workers.

Power-frequency magnetic fields are usually substantially smaller than the earth's static field and can therefore be regarded as a ripple superimposed on top of it. For any biological effect that depended on the total field, the result, averaged over times longer than a single cycle, would, to first order, be due just to the earth's field; the alternating field could have at most only a second-order effect. But any biological effect that depended specifically on the alternating component would, of course, not be affected by the earth's field.

2.1 Sources of exposure

The commonest source of magnetic field in homes, present wherever there is an electricity supply, is the low-voltage distribution wiring carrying electricity to the home. Sometimes the field is dominated by currents in the wiring within the home. Most countries wire their distribution systems in a way that results in the "go" and "return" currents in each circuit not being exactly equal; there is an out-of-balance current, and it is principally these out-of-balance currents, usually called "net" or "ground" currents, that produce the field. This "background" field is present over the whole volume of every home and does not greatly depend on whether the distribution wiring is overhead or underground.

In addition to the background field, there are localized areas of higher magnetic field produced by domestic electrical appliances when they are operating, usually falling to background levels within a meter or so of the appliance. The field from domestic appliances is experienced only when quite close to them, and in most cases, exposure is therefore of short duration. Therefore, although appliances usually provide the highest instantaneous exposure of an individual to power-frequency fields over the course of a day, time-average exposure from them is limited, being estimated variously as 50% or less of total time-average exposure. However, mobile phones (which produce ELF as well as radio-frequency fields) and computers are increasingly used for long periods close to the body and may now contribute more to time-average exposure.

Magnetic fields are also produced by high-voltage transmission lines. Fields from such lines typically fall to background levels within 100 m or less. Only a small fraction of homes are this close to such lines, but for homes which are, the high-voltage power line becomes the principal source of the magnetic field inside the home.

Electric fields from sources outside the home are less significant inside the home because of screening by the building materials. Therefore, electric fields in homes come mainly from internal sources, such as house wiring and appliances, and tend to be more variable over the area of the home than magnetic fields.

For adults at work in certain occupations, exposure can be significant, but many do not encounter major sources of exposure outside the home. In office buildings, computers and copy machines are common sources of magnetic fields. Power distribution facilities and large motors used to drive building air conditioning systems can also contribute significantly to the magnetic field environment. In factories, high magnetic fields are encountered near large electric machines, electrical heating equipment, and other high current-carrying devices.

Average exposures have been found to be higher in “electrical occupations” than in other occupations such as office work (see above). Much less is known about exposures in non-electrical occupations; little data, if any, is available for many jobs and industrial environments. Of note in the few surveys conducted are high exposures among railway engine drivers (about 40 mG) and seamstresses (about 30 mG). The best information on work exposures among the general population is available in a survey conducted by Zaffannela (1993). The survey included 525 workers employed in a variety of occupations. The largest geometric mean (16 mG) for the distributions of the average magnetic fields during work occurred in electrical occupations and in service occupations. Technical, sales, and administrative support positions had a geometric mean of 1.1 mG; managerial and professional specialty occupations, 1 mG. Work exposures were often significantly higher and more variable than other exposures; people spent significantly more time, for example, in fields exceeding 16 mG at work than at home. Nevertheless, average work exposures for the general population are low, with only 4% exposed to magnetic fields above 5 mG.

2.2 Difficulties in exposure assessment

That assessment of exposure is a major weakness of epidemiologic studies of EMF is not surprising, because several factors make assessment of EMF exposure more difficult than assessment of many other environmental exposures. Magnetic fields are variable in time and space and our understanding of the contributions of the multitude of different sources to total exposure is limited. EMF exposure is ubiquitous, but neither detectable nor memorable in most circumstances. The difficulties in exposure assessment are further exacerbated by the retrospective nature of most EMF epidemiologic research, as many diseases have long latency periods. To quantify past exposure that was unnoticed and unmeasured, epidemiologists rely on surrogate measurements or indicators of exposure. The surrogates used to study EMF have included wire codes, occupational job titles, questions regarding appliance use and present day measurements. Further, some studies must rely on information provided by proxy respondents, if the study subject has died or has been incapacitated.

Although occupational exposures are generally much higher than exposures encountered elsewhere, they are usually fleeting. Many of the "highly exposed" workers do not encounter high fields for hours, but rather, for seconds or minutes at a time while working. When we consider EMF exposure integrated over time, the brevity of high exposures in most work places and the large amount of time the individual spends in non-occupational environments combine to wash out the distinctions between the supposedly "highly exposed" occupational groups and the general population. Thus, we often might not have enough separation between high and low-exposure groups to detect an effect of EMF exposure if we rely on time-weighted averages.

Because EMF exposures are complex, numerous parameters have been used to characterize them, including transients, harmonic content, resonance conditions, peak values, as well as average levels. It is not known which of these parameters or what combinations of parameters, if any, are biologically relevant. If there were a known biological mechanism of interaction for carcinogenesis, it might be possible to identify critical parameters of exposure, including the relevant period or timing of exposure. Furthermore, environmental EMF is not detectable by the exposed person, nor is it memorable. Because it is ubiquitous, exposure assessment has to separate the more exposed from the less exposed, a much more difficult task than simply delineating the exposed from the non-exposed. There is also a considerable degree of variability in exposure in both the short- and long- terms, both of which are influenced by the variability in exposure over space, for example occupational versus household exposure.

All of these difficulties with EMF exposure assessment are likely to have led to substantial exposure misclassification, which is likely, in turn, to interfere with detection of an association between exposure and disease (if indeed such an association exists). In particular, if the true association is small or moderate, it will be difficult to detect with this amount of measurement error.

3. EMF and Breast Cancer

3.1 In vitro

The main interest in this area was caused by the claim that exposure to magnetic fields can block the inhibitory effect of melatonin on growth of breast cancer cells. The original work was reported by Liburdy et al. (1993) in a study using a human oestrogen-responsive breast cancer cell line (MCF-7). They found that the proliferation of MCF-7 cells can be slowed by the addition of physiological concentrations of melatonin (1 nM). However, if the cells are simultaneously exposed to a 60 Hz, 12 mG magnetic field, then the effect of melatonin on the rate of proliferation is reduced. The effects are fairly small and can only been seen after 7 days in culture. They suggested that the magnetic field disrupted either the ligand/receptor interaction or the subsequent signaling pathway. The authors found no effect at a magnetic field strength of 2 mG and suggested a threshold between 2 and 12 mG. No effect was seen using field exposure alone. A similar effect of a 60 Hz field was reported by Harland and Liburdy (1997) but using tamoxifen (100 nM) rather than melatonin to bring about the initial inhibition. The effect has been reported in other cell lines, namely a second breast cancer cell line, T47D, (Harland et al., 1998) and a human glioma cell line 5F757 (Afzal et al., 1998). However, the effect seen in the initial study (Liburdy et al., 1993) was small (10–20 % growth over 7 days) and some concern was noted regarding the robustness of the effect. (see AGNIR, 2001b; NIEHS, 1998).

Blackman et al. (2001) set out to replicate these findings, using the MCF-7 cells supplied by Liburdy, but with a modified and improved experimental protocol. Melatonin caused a 17% inhibition of MCF-7 growth which was abolished by exposure to a 60 Hz magnetic field at 12 mG, confirming the results of Liburdy et al (1993). In addition, Tamoxifen caused a 25% inhibition in cell numbers, which was reduced to a 13% inhibition by exposure to a 60 Hz magnetic field at 12 mG. This result confirmed the results reported by Harland and Liburdy (1997), in which a 40% inhibition was reduced to 25% by EMF exposure. A later study by Ishido et al. (2001) exposed MCF-7 cells (supplied by Liburdy) to 0, 12 or 1000 mG at 50 Hz for 7 days. Melatonin at concentrations of 10-9 M or higher, induced inhibition of intracellular cyclic AMP which was blocked by exposure to a 50 Hz field at 1000 mG. Similarly DNA synthesis, which was inhibited by 10-11 M melatonin levels, was partially released by exposure at 12 mG.

However, although the MCF-7 cell line has undoubtedly provided a useful model to investigate effects on isolated breast cancer cells it is only one possible model in cells that have been separated from their natural environment, and therefore its implication for breast cancer in general is limited. The cell line is rather heterogeneous; different sub clones show different growth characteristics (e.g. Luben & Morgan, 1998; Morris et al., 1998) raising the possibility that the effects were specific to individual sub clone phenotypes. The effects of stronger magnetic fields were studied by Leman et al. (2001) in three breast cancer cell lines that were reported to have different metastatic capabilities: MDA-MB-435 cells, which were considered to be highly metastatic, MDA-MB-231 cells which were considered to be weakly metastatic, and MCF-7 cells, which were considered as non-metastatic. Only the weakly and non-metastatic cells responded to melatonin and optimum inhibition was achieved at 1mM concentration of melatonin (a million-fold higher than used in the Liburdy study). Exposure for 1 h to a pulsed field at 3000 mG repeated for 3 days had no effect on growth in either cell line.

The results of volunteer studies, as well as residential and occupational studies, suggests that the neuroendocrine system is not adversely affected by exposure to power-frequency electric and/or magnetic fields. This applies particularly to the circulating levels of specific hormones of the neuroendocrine system, including melatonin, released by the pineal gland, and a number of hormones involved in the control of body metabolism and physiology, released by the pituitary gland. Subtle differences were sometimes observed in the timing of melatonin release or associated with certain characteristics of exposure, but these results were not consistent. It is very difficult to eliminate possible confounding by a variety of environmental and lifestyle factors that might also affect hormone levels. Most laboratory studies of the effects of ELF exposure on night-time melatonin levels in volunteers found no effect when care was taken to control possible confounding.

The effects of ELF exposure on melatonin production or release in isolated pineal glands were variable, although relatively few in vitro studies have been undertaken. The evidence that ELF exposure interferes with the action of melatonin on breast cancer cells in vitro is intriguing and there appears to be some supporting evidence in terms of independent replication using MCF-7 cells. However this system suffers from the disadvantage that the cell lines frequently show genotypic and phenotypic drift in culture that can hinder transferability between laboratories.

3.2 Laboratory animal studies

3.2.1 Mammary Tumors

The induction of mammary tumors in female rats has been used as a standard assay in the investigation of potential carcinogenesis, often using carcinogens such as DMBA as an initiator and promoter in the two-stage initiator/promoter model of carcinogenesis. Four groups of researchers have investigated the effects of ELF magnetic field exposure on the incidence and the development of chemically-induced mammary tumors.

Beniashvili et al. (1991) found an increased incidence and shortened tumor latency with EMF exposure for 3 h per day, but not with 0.5 h per day. The experimental details were, however, presented very briefly, which hinders evaluation of the study. Similar results have been reported in a series of medium-term studies of magnetic field effects on DMBA-induced mammary tumor incidence carried out by Löscher and colleagues (Baum et al., 1995; Löscher et al., 1993; Löscher et al., 1994; Löscher et al., 1997; Löscher & Mevissen, 1995; Mevissen et al., 1993a; Mevissen et al., 1993b; Mevissen et al., 1996b; Mevissen et al., 1996a; Mevissen & Häußler, 1998). These authors reported significant increases by chronic EMF exposure in the incidence of palpable tumors (detected during exposure) and macroscopically visible tumors (detected during post-mortem examination) (Löscher et al., 1993; Mevissen et al., 1996a). They found a linear dose-response relationship over the flux-density range 3–1 0 mG up to 1,000 mG (Löscher & Mevissen, 1995). No significant effect on tumor incidence could be found following a full histopathalogical analysis for exposure at 1,000 mG (Baum et al., 1995; Löscher et al., 1994). Löscher and Mevissen (1995) argued that magnetic field exposure does not alter the incidence of neoplastic mammary lesions but accelerates tumor growth, thus enhancing the number of tumors macroscopically visible when the rats are sacrificed. In addition, Baum et al. (1995) reported that there was a statistically significant increase in the number of rats with mammary gland adenocarcinomas that had been exposed to 1,000 mG. However, the total number of malignant tumors in the exposed group was not significantly increased.

A replicate study at 1,000 mG (Mevissen & Häußler, 1998) reported that the incidence of macroscopically-visible tumors in the sham-exposed group was almost double the incidence in the earlier study. This was carried out at a different time of the year and seasonal influences were reported to occur (Mevissen & Häußler, 1998). A re-analysis of all of these data showed a statistically significant linear correlation between increase in tumor incidence and magnetic flux density (Mevissen & Häußler, 1998). More recently, these authors (Thun-Battersby et al., 1999) reported a significantly increased incidence of mammary tumors following 1,000 mG exposure for 27 weeks following initiation by a single dose of 10 mg DMBA.

In an attempted replication study of the 1,000 mG exposure by Löscher (1994), Anderson et al. (1999) and Boorman et al. (1999a) found no evidence that magnetic field exposure was associated with an earlier onset or an increased multiplicity or incidence of mammary tumors. There were, however, clear differences in the responsiveness to DMBA of the rats used in the replication study (Anderson et al., 1999; Boorman et al., 1999a) compared to those used by Löscher and colleagues and there was a variety of differences in the experimental protocols (Anderson et al., 2000; Löscher, 2001). Ekström et al. (1998) found no effect on DMBA-induced mammary tumor incidence in the same rat strain following prolonged exposure to intermittent power-frequency magnetic fields. There were no statistically significant differences in the number of tumor bearing animals and no differences in the total number of tumors between the different groups. In addition, the rate of tumor appearance was the same in all groups.

In their most recent study (Fedrowitz et al., 2004), the Löscher group tested the hypothesis that the different results are explained by the use of different sub-strains of Sprague Dawley rats. Exposure to a 1,000 mG, 50 Hz magnetic field enhanced mammary tumor development in one sub-strain, but not in another that was obtained from the same breeder. The tumor data were supported by the finding that exposure to an ELF magnetic field increased cell proliferation in the mammary gland of the sensitive sub-strain, but no such effect was seen in the insensitive sub-strain.

Thus three independent large-scale studies of rats provided no evidence of an effect of ELF magnetic fields on the incidence of spontaneous mammary tumors. A substantial number of studies have examined the effects of ELF magnetic fields on chemically-induced mammary tumors in rats. Inconsistent results were obtained that may be due in whole or in part to differences in experimental protocols, such as the use of specific sub-strains.

3.2.2 Melatonin

From the large number of animal studies investigating power-frequency EMF effects on rat pineal and serum melatonin levels, some reported that exposure resulted in night-time suppression of melatonin. The changes in melatonin levels first observed in early studies of electric-field exposures up to 100 kVm-1 could not be replicated. The findings from a series of more recent studies which showed that circularly-polarized magnetic fields suppressed night-time melatonin levels were weakened by inappropriate comparisons between exposed animals and historical controls. The data from other magnetic fields experiments in laboratory rodents, covering intensity levels over three orders of magnitude from a few tens of mG to 5 mT, were equivocal, with some results showing depression of melatonin but others showing no change. In seasonally breeding animals, the evidence for an effect of exposure to power-frequency fields on melatonin levels and melatonin-dependent reproductive status is predominantly negative. No convincing effect on melatonin levels has been seen in a study of non-human primates chronically exposed to power-frequency fields, although a preliminary study using two animals reported melatonin suppression in response to an irregular and intermittent exposure.

3.3 Epidemiology

Epidemiologic investigations addressing the potential link between breast cancer and exposure to magnetic fields include occupational and residential studies that examine breast cancer risk in relation to proximity to electric installations and the use of electric blankets.

3.3.1 Female Breast Cancer

3.3.1.1 Residential Exposures

Several studies of residential exposures examined risk of breast cancer in populations residing near power lines. One of these studies found an association between pre- but not post-menopausal breast cancer and wiring configuration. (Wertheimer et al., 1982) The other two studies (McDowall et al., 1986; Schreiber et al., 1993) did not detect any associations.

Davis et al. (2002) conducted a case-control study in the greater Seattle, Washington area. Exposure to magnetic fields was estimated by both direct measurement and wire-code configuration. Continuous 48-hour measurements of magnetic field in the bedroom of each person's current residence were done using an EMDEX II meter set to record broadband (40–800 Hz) and harmonic (100–800 Hz) magnetic fields at 15-s intervals. Three variables based on broadband magnetic field measurements were constructed by averaging over two nights: (1) mean night-time (10 pm to 5 am) bedroom magnetic field; (2) proportion of night-time bedroom magnetic field measurements $\geq$ 2 mG; and (3) short-term variability in the night-time bedroom magnetic field based on grouping of measurement data into 10-min intervals. The wire-coding scheme of Wertheimer and

Leeper (1979) was used to classify the participant's current residence and all previous residences occupied for at least six consecutive months within the greater Seattle metropolitan area in the 5 and 10 years prior to diagnosis of breast cancer. Wire codes were ordered (1–5) according to their respective in-home night-time mean magnetic field measurements using data from the controls. In addition, a questionnaire provided data on use of electrical appliances in the home. The magnetic field analyses included 744 (of 813) cases and 711 (of 793) controls. None of the metrics of mean night-time magnetic field exposure was associated with breast cancer risk; for the highest quartile (≥ 58%) of the percentage of magnetic field measurements ≥ 2 mG, the adjusted odds ratio was 1.1 (95% CI: 0.7–1.8). For the mean night-time bedroom broadband magnetic field treated as a continuous variable, the adjusted odds ratio per 1 mG was 1.04 (95% CI: 0.97–1.12). No associations were found after stratification by age, menopausal or estrogen receptor status. There was also no association with wire codes either from current configuration or a weighted score for wire codes at residences over the previous 5 or 10 years. For wire codes at home of diagnosis (or reference date for controls), the odds ratio for very high versus very low current configuration was 0.8 (95% CI: 0.5–1.3). Further analysis of this study, published in 2006 confirmed lack of association between breast cancer and magnetic fields.

London et al. (2003) carried out a nested case-control study of residential exposure to magnetic fields among a cohort of African American, Latina and Caucasian residents in Los Angeles County, aged 45–74 at recruitment, selected primarily from the file of licensed drivers. Incident breast cancer cases from 1993 to 1999 were ascertained by linkage to state tumor registries. Wiring configuration codes were derived according to the scheme of Wertheimer and Leeper (1979) in homes occupied at time of diagnosis (or reference date for controls) and over the previous 10 years. Seven-day measurements of magnetic fields in the bedroom were obtained using an EMDEX II meter, to include both broadband (40–800 Hz) and harmonic (100–800 Hz) magnetic fields sampled at 120-s intervals. The primary magnetic field measurement metric was the night-time mean based on questionnaire response for each participant concerning usual times of going to bed, obtained separately for weekdays and weekends. Three variables based on magnetic field measurements (separately for broadband and harmonic fields) over night-time hours for seven days were constructed: (1) mean night-time bedroom magnetic field; (2) proportion of night-time bedroom magnetic field measurements ≥ 4 mG; and (3) short-term variability in the night-time bedroom magnetic field. Wire configuration codes for address at diagnosis (cases) or reference date (controls) were available for 743 (of 751) cases and 699 (of 702) controls, and 7-day measurements of magnetic fields in the bedroom for 347 cases and 286 controls. None of the metrics of mean night-time magnetic field exposure (broadband or harmonic fields) was associated with breast cancer risk; adjusted odds ratios compared with mean night-time bedroom broadband exposure < 1 mG were 1.1 (95% CI: 0.43–2.8) for mean night-time bedroom broadband exposure 2–2,9 mG (11 cases), 2.1 (95% CI: 0.58–7.5) for 3,0–3.9 mG (8 cases), and 1.2 (95% CI: 0.50–3.0) for mean night-time bedroom broadband exposure ≥ 4.0 mG. For mean night-time bedroom broadband magnetic field treated as a continuous variable, adjusted odds ratio per 1 mG was 1.0 (95% CI: 0.94–1.07). No associations were found after stratification by age, menopausal or estrogen receptor status, or other potential effect modifiers. There was also no association with wire codes either from current configuration or a weighted score for wire codes at residences over the previous 10 years; for wire codes at home of diagnosis (reference), adjusted odds ratio for very high versus very low current configuration was 0.76 (95% CI: 0.49–1.18).

Schoenfeld et al. (2003) carried out a case-control study of EMF exposure (EBCLIS) within the Long Island Breast Cancer Study Project (LIBCSP) of women under 75 years at enrollment, identified between August 1996 and June 1997, who had lived in the same Long Island home for at least 15 years. Both spot (front door, bedroom and most lived-in room) and 24-hour measurements (bedroom and most lived-in room) were collected using EMDEX II meters programmed to record both broadband (40–800 Hz) and harmonic (100–800 Hz) magnetic fields sampled at 3-s intervals for the spot measurements and 15-s intervals for the 24-hour measurements. Ground-current magnetic field measurements were also obtained. Wiring maps were obtained and used to classify homes according to the modified method of Wertheimer and Leeper (Wertheimer & Leeper, 1979). Questionnaire data on electrical appliance use was reported in Kabat et al. (2003). None of the exposure metrics was associated with risk of breast cancer. For 24-hour measurements in the bedroom, adjusted odds ratio for highest quartile (≥ 1.72 mG) versus lowest quartile broadband magnetic field was 0.97 (95% CI: 0.69–1.4) and for the mean of the spot measurements it was 1.15 (95% CI: 0.82–1.6) (highest quartile ≥ 1.45 mG). For estimated personal exposure ≥ 2 mG (based on mean 24-hour broadband measurements in bedroom and most lived-in room and test-load coefficient for most lived-in room) compared with < 0.39 mG, adjusted odds ratio was 1.08 (95% CI: 0.77–1.5). For the wire code configuration, adjusted odds ratio for very high current configuration compared with underground/very low current configuration was 0.90 (95% CI: 0.54–1.5).

Kliukiene et al. (2004) carried out a nested case-control study of female breast cancer within a nationwide cohort in Norway. This comprised all women aged 16 or over who on November 1, 1980, or on January 1 of at least one of the years between 1986 and 1996 were living in a residence within a defined corridor near high-voltage power lines (corridor distances ranging from 40 m for 33 kV lines to 300 m for 420 kV lines). The cohort included around 5% of all women in Norway during 1980–1996; cases (n = 1,830) with invasive breast cancer were identified for this period from the national cancer registry. Two controls per case (3,658 in total) were selected randomly from the cohort according to the following criteria: born within 5 years of the case, free of breast cancer and alive at time of diagnosis, and from the same municipality as the case at entry into the cohort. Exposure to magnetic fields from the high-voltage lines was estimated from 1967 based on residential address. Utilizing a computer program (Teslaw) developed at SINTEF Energy, Norway, the estimates accounted for height of the towers, distance between phases, ordering of phases, distance between power line and a house, and mean load on the power line during each year that a study participant lived in the house. Distances of houses from the power lines were checked on maps for the half of the corridor nearest the line. Time-weighted average residential exposure to magnetic fields from the lines was estimated, both from 1967 and for the last 5 years before diagnosis of a case. Occupational exposure was estimated – on a scale from 1 (< 4 h exposure at > 1 mG per week) to 3 (≥ 24 h exposure at > 1 mG per week) – based on a job-exposure matrix from information on job title provided at decennial census, for the period January 1, 1955 (based on 1960 census) until date of diagnosis (assuming working age 18–67 years). A cumulative category of occupational exposure measure was then calculated. For combined residential and occupational exposure (based on 1,296 cases and 2,597 controls with available data), women were considered exposed if time-weighted average residential exposure ≥ 0. 5 mG and occupational exposure > 30 category-years. For residential exposure in most recent 5 years, the odds ratio (all ages) for time-weighted average exposure ≥ 2 mG was 1.6 (95% CI: 1.3–2.0); odds ratio at < 50 years was 1.8 (95% CI: 1.2–2.8) and at ≥ 50 years 1.6 (95% CI: 1.2–2.0). Odds ratios for time-weighted average exposure of 0.5–1.9 mG were similar to those for ≥ 2 mG. For ≥ 2 mG, the odds ratio for the total period (all ages) was 1.4 (95% CI: 1.0–1.8). For women with highest estimated occupational exposure compared with the lowest, odds ratio (all ages) was 1.1 (95% CI: 0.9–1.4). For combined residential and occupational exposure, the odds ratio (all ages) was 1.3 (95% CI: 0.8–2.1) based on 26 cases. There was no statistically significant increase when residential and occupational exposures were considered together, but numbers were small. No measurements of magnetic fields were undertaken for persons included in the study. Occupational data were available for 71% of cases and controls. There was only limited control for confounding: age at birth of first child, education, type of residence.

Thus importantly, four recently completed large and well conducted breast cancer residential studies found no association with exposure to electric or magnetic fields (Davis et al., 2002; London et al., 2003; Schoenfeld et al., 2003).

3.3.1.2 Electric Blankets

Two early case-control studies (Vena et al., 1994; Vena et al., 1991) did not support the hypothesis that the use of electric blankets increases the risk of post- or pre-menopausal breast cancer. Vena et al. (1994) combined these two studies and found elevated risk among women who reported some use of blankets throughout the night (RR 1.5, 95% CI: 1.1-1.9) in the previous 10 years; however, the risk was not the highest among the highest exposure group, that is, those who reported daily use of the blankets in season and continuously throughout the night for 10 years (RR 1.20, 95% CI: 0.8-1.9).

3.3.1.3 Occupational Studies

Few occupational studies of electrical workers included sufficient numbers of females to address the potential association of occupational EMF exposure and development of breast cancer. Albeit based on small numbers, four studies found no elevation in risk of breast cancer among females working in occupations with potential exposure to EMF as compared to low exposure occupations (Guenel et al., 1993; Kelsh & Sahl, 1996; Vagero et al., 1985; Vagero & Olin, 1983).

One large study (Loomis et al., 1994) used computerized mortality files from the National Center for Health Statistics for the years 1985 to 1989. Death certificates included the occupation and industry in which the decedent usually worked, coded according to the 1980 U.S. Census. Excluded were women whose occupation was listed as "homemaker" and those whose death certificate provided no occupational data; these two groups made up more than half of the database. Seven electrical occupations used in previous studies were included, along with seven other occupations presumed to have a large number of female workers and some potential for above-background EMF exposure, such as computer programmers and telephone operators. All other occupations were considered unexposed. Among 27,882 breast cancer cases and 110,949 controls, 68 cases and 199 controls had been employed in traditional electrical occupations. The relative risk for breast cancer among those employed in electrical occupations was 1.4 (95% CI: 1.0-1.8). In a more detailed analysis, the association was the strongest for the managerial/professional class, and for those 45 to 54 years of age. The relative risks for the other occupations with potential exposure were around 1.0 or lower. In a separate analysis of the same data, but with a different approach to exposure grouping, Cantor et al. (1995) did not find an association of female breast cancer and potential workplace exposure to EMF.

Epidemiologic studies based on death certificates alone have many limitations and are considered to be of a preliminary nature. In such studies, the population at risk is unknown. Thus, an apparent increase in the proportion of deaths from breast cancer among electrical workers may be due to an increase in the proportions of deaths from other causes in the control group. The validity of the study results depends upon the accuracy of the occupational information reported on death certificates and the extent to which job titles alone reflect exposure to magnetic fields. Also, the authors could not adjust for many risk factors known to be associated with breast cancer, including reproductive and family histories. Working in male-dominated jobs may have favored nulliparity, delayed childbearing, or other characteristics related to risk of breast cancer. The authors attempted to control for some of these characteristics by adjusting for social class. However, it is not clear how effectively social class was determined, and at best, it can serve only as a partial control for known risk factors of breast cancer.

Although some earlier registry-based studies provided some support for a possible association between EMF exposure and female breast cancer (Kheifets & Matkin, 1999), the most recent very large study, which, importantly, incorporated exposure measurements in female workers, did not find an association (Forssén et al., 2005).

A study of Forssén et al. (2005) included 20,400 cases of female breast cancer (identified through the regional cancer registry) and 116,227 controls from women gainfully employed in Stockholm or Gotland County in Sweden between 1976 and 1999. Exposure assessment was based on information about occupation obtained from the population censuses from 1960 to 1990. Information about magnetic field exposure was obtained from a job-exposure matrix derived from an electromagnetic field measurement programme performed in Stockholm County between March 2001 and October 2002. It included 49 of the most common occupations among women in Stockholm County (around 85% of the gainfully employed women in 1980 census). Measurements were made using an EMDEX Lite personal monitor, carried on a belt for 24 hours; volunteers also completed a diary from which exposures at work could be estimated. Between five and 24 participants were measured in each occupation category. Exposure was estimated as the geometric mean of the time-weighted average. At all ages, compared with reference (< 1 mG), the OR (adjusted for age, socio-economic status and year of diagnosis) was 1.0 (95% CI: 1.0–1.1) (11,369 cases) for 1–1.9 mG; 1.0 (95% CI: 0.9–1.1) (3,243 cases) for 2.0– 2.9 mG; and 1.0 (95% CI: 0.9–1.1) (814 cases) for ≥ 3.0 mG. Adjusted odds ratios were similar (all non-significant) at < 50 and ≥ 50 years, and for estrogen receptor positive and negative cases. Whereas earlier studies reported some positive results, this study was largely negative and was larger, had a better job exposure matrix (based on measurements collected from women), and had more data available for female occupations than the earlier studies.

3.3.2 Male Breast Cancer

3.3.2.1 Occupational Studies

As described earlier, many studies have examined cancer in electrical occupations. As part of that examination, many considered breast cancer as one of the outcomes. Male breast cancer is so rare, and most of the studies are not based on sufficiently large populations, so estimates of risk for male breast cancer often are not included in tables of results unless an excess risk has been observed (Vagero et al., 1985; Vagero & Olin, 1983; Guberan et al., 1989; Milham, 1985; Olin et al., 1985; Pearce et al., 1989; Spinelli et al., 1991; Tornqvist et al., 1986). This makes it difficult to evaluate the potential for the excess risk of male breast cancer. Nevertheless, several reports (Guenel et al., 1993; Demers et al., 1991; Floderus et al., 1994; Matanoski et al., 1993; Tynes & Andersen, 1990) are suggestive of a positive association, while negative results were reported by Loomis (1992) and Camarano, (1984). The large studies of electrical workers (Sahl et al., 1993; Theriault et al., 1994; Savitz & Loomis, 1995) did not identify any excess of male breast cancer.

For male and female breast cancer, the research began with a biological hypothesis confirmed by some early studies. More rigorous epidemiologic studies that followed showed no effect, thus it appears that EMF fields are not involved in the development of breast cancer.

4. Reviews and Evaluations

During the past decade, a number of national and international expert panels, including ones assembled by the U.S. National Institute of Environmental Health Sciences (NIEHS), the International Agency for Research on Cancer (IARC) and the World Health Organization (WHO) have reviewed the evidence on the potential relationship between exposure to ELF EMF and various adverse health outcomes (National Institute of Environmental Health Sciences, 1999; International Agency for Research on Cancer, 2002; World Health Organization, 2007). Evaluations by these expert panels generally agree that short-term, adverse effects do not occur at exposures to magnetic fields below 1000 mG. Current guidelines are based on avoiding the risks to health that result from the interaction of the induced fields and currents with electrically excitable nerve tissue, particularly that of the central nervous system. For general public exposure, the reference levels for power frequency electric and magnetic fields are of the order of 5kV/m and 1000 mG, respectively. These values are well above levels encountered in most environments.

However, based on these intensive reviews, the NIEHS, IARC and WHO classified ELF magnetic (but not electric) fields as a “possible human carcinogen,” or a Group 2B carcinogen. This classification was based both on epidemiologic evidence showing a consistent association between exposure to ELF magnetic fields and childhood leukemia even though laboratory studies in animals and cells do not support an association between exposure to ELF magnetic fields and cancer. The NIEHS assessment (but not the IARC or WHO assessments) concluded that there was also sufficient epidemiologic evidence for an association between adult chronic lymphocytic leukemia and occupational exposure to ELF magnetic fields to warrant a classification as a “possible human carcinogen”.

Below, I summarise conclusions of these International Organizations as they relate to breast cancer:

4.1 Summary and Conclusions from recent International Reviews:

National Institute of Environmental Health Sciences (NIEHS) 1999:

Some evidence exists for an association between brain cancers and exposure to ELF-EMF and between female breast cancers and ELF-EMF exposure; however, the studies evaluating these associations are inconsistent and have limits as to their interpretation, making them inadequate for supporting or refuting an effect.

International Agency for Research on Cancer (IARC) 2002:

- There is *limited evidence* in humans for the carcinogenicity of extremely low-frequency magnetic fields in relation to childhood leukaemia.
- There is *inadequate evidence* in humans for the carcinogenicity of extremely low-frequency magnetic fields in relation to all other cancers.
- There is *inadequate evidence* in humans for the carcinogenicity of static electric or magnetic fields and extremely low-frequency electric fields.

California EMF Program (CADHS) Report 2002:

The reviewers used two distinct sets of guidelines to evaluate the evidence for an association between female breast cancer and EMF:

- Using the traditional guidelines of the International Agency for Research on Cancer (IARC) the DHS Reviewers considered the evidence “Inadequate” (Group 3) to implicate EMFs. This was also the opinion of review panels at IARC and the National Institutes of Environmental Health Sciences (NIEHS).
- Using the guidelines developed by the California EMF program one reviewer was “Close to the Dividing Line between Believing and not Believing” and two were “Prone Not to Believe” that EMFs increase the risk of female breast cancer to any degree.

UK Advisory Group on Non-ionising Radiation (AGNIR) 2006:

A recent review by the Independent concludes that the evidence to date does not support the hypothesis that exposure to power frequency (ELF EMF) affects melatonin levels or the risk of breast cancer.

World Health Organization (WHO) 2006:

"Subsequent to the IARC monograph a number of reports have been published concerning the risk of female breast cancer in adults associated with ELF magnetic field exposure. These studies are larger than the previous ones and less susceptible to bias, and overall are negative. With these studies, the evidence for an association between ELF magnetic field exposure and the risk of female breast cancer is weakened considerably and does not support an association of this kind".

Additionally: "For adult breast cancer more recent studies have convincingly shown no association with exposure to ELF magnetic fields. Therefore further research into this association should be given very low priority".

Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) of European Union. 2007:

Breast cancer caught particular interest because of experimental results suggesting that melatonin synthesis was related to ELF field exposure, and because melatonin might play a role in the development of breast cancer. Several studies also reported an increased breast cancer risk among subjects with elevated ELF exposure. However, more recent large and well-controlled studies have been entirely negative, and the hypothesis of a link between ELF field exposure and breast cancer risk is essentially written off.

Swedish radiation protection authority, SSI (Statens strålskyddsinstitut) Independent Expert Group on Electromagnetic Fields 2008:

The scientific evidence supporting a linkage between exposure to ELF magnetic fields and any of these diseases is weaker than for childhood leukemia, and in some cases (for example, for cardiovascular disease or breast cancer) the evidence is sufficient to give confidence that magnetic fields do not cause the disease.

4.2 Other Reviews:

In addition to these reviews, other scientists have taken positions to both sides of the mainstream. On the one hand, some scientists have viewed the evidence for health effects as considerably stronger than the conventional assessment. With regard to childhood leukemia, they suggest different exposure-response relationships and assert that the attributable fraction of childhood leukemia could thereby be higher, and that this association is sufficiently strong to justify exposure limits. They would also say that the scientific evidence on a number of other, more prevalent diseases is being underestimated. An example would be a **BioInitiative report (2008),** which concludes:

> The constellation of relevant scientific papers providing mutually-reinforcing evidence for an association between power-frequency electromagnetic fields (ELF-EMF) and breast cancer is strongly supported in the scientific literature.
>
> ELF at environmental levels negatively affects the oncostatic effects of both melatonin and tamoxifen on human breast cancer cells. Numerous epidemiological studies over the last two decades have reported increased risk of male and female breast cancer with exposures to residential and occupational levels of ELF. Animal studies have reported increased mammary tumor size and incidence in association with ELF exposure.
>
> There is rather strong evidence from case-control studies that long term, high occupational exposure (> 10 mG or 1.0 μT) to ELF magnetic fields is a risk factor for breast cancer.

On the other hand, there are senior scientists who feel confident enough to declare that the evidence does not justify concern, that there are no effects, or that effects are exceedingly unlikely at exposure levels to which the public is exposed. An example would be the **American Physics Society (1995)** which states:

> The scientific literature and the reports of reviews by other panels show no consistent, significant link between cancer and power line fields. This literature includes epidemiological studies, research on biological systems, and analyses of theoretical interaction mechanisms. No plausible biophysical mechanisms for the systematic initiation or promotion of cancer by these power line fields have been identified. Furthermore, the preponderance of the epidemiological and biophysical/biological research findings have failed to substantiate those studies which have reported specific adverse health effects from exposure to such fields. While it is impossible to

prove that no deleterious health effects occur from exposure to any environmental factor, it is necessary to demonstrate a consistent, significant, and causal relationship before one can conclude that such effects do occur. From this standpoint, the conjectures relating cancer to power line fields have not been scientifically substantiated.

5. Policy and Prevention

As with many other agents, international guidance or exposure limits on occupational and public exposure to EMF is based on avoiding risks to health that are well understood and for which there is good scientific evidence (IARC, 2002). Once that basis is adopted, setting the actual guidance is relatively uncontroversial, but because it addresses effects at much higher levels of exposure (principally experienced occupationally) than the public generally experiences, it is often viewed by the public as not addressing their concerns (CADHS. 2002; Sage, C. et.al. 2008; SAGE, 2007).

The combination of widespread exposures, established biological effects from acute, high-level exposures, and the possibility of leukemia in children from low-level, chronic exposures have made it necessary but difficult to develop consistent public health policies. In view of these uncertainties, WHO concludes that it might be advisable to adopt general no- and low-cost measures to reduce exposure (WHO, 2007).

The conventional scientific view is, however, that even if there is a risk, it would be unlikely to be of major public-health significance. This is because the evidence, as reviewed by, e.g., IARC and WHO, really only implicates one relatively rare disease, childhood leukemia, and the exposures that are implicated are at the top end of the normal range of exposure and are therefore also relatively rare. Estimates are of just a few percent of cases of childhood leukemia being attributable to magnetic fields if there is an effect. (Kheifets et al., 2006; Greenland and Kheifets 2006)

Use of electricity brings enormous benefits to societies and thus the appropriate risk governance includes consideration of a large number of trade-offs, including the potential for risk offset, risk substitution, risk transfer, and risk transformation, as well as benefits and costs.

5.1 Guidelines

Acute effects on the nervous system form the basis of international guidelines. None of the guidelines consider potential long-term effects, such as cancer, to be sufficiently established to serve as a basis for standards. In particular, exposure limits are based on the acute effects on electrically excitable tissues, particularly those in the central nervous system. The ACGIH standard is an older standard that specifies ceiling values for occupational exposures that should not be exceeded. This standard is the one that most industrial hygienists are familiar with. Compliance is only mandatory if the standard has been adopted by a regulatory agency. For magnetic fields, the limit is 1 mT (10,000 mG) for 60 Hz. These limits are five times higher if they are limited to arms and legs and ten times higher if they are limited to hands and feet. The current limits from the International Commission on Non-Ionizing Radiation Protection (ICNIRP) (ICNIRP, 1998) for workers are 10 kV/m and 5,000 mG for 50 Hz and 8.3 kV m-1 and 4,200 mG for 60 Hz. The Institute of Electrical and Electronic Engineers (IEEE) (IEEE, 2002) exposure levels are 20 kV m-1 and 27,100 mG at 60 Hz. The differences in the guidelines, derived independently by the IEEE and the ICNIRP, result from the use of different adverse reaction thresholds, different safety factors, and different transition frequencies, i.e. those frequencies at which the standard function changes slope.

The occupationally exposed population consists of adults who are generally exposed under known conditions and are trained to be aware of potential risks and to take appropriate precautions. By contrast, the general public comprises individuals of all ages and of varying health status, and may include particularly susceptible groups or individuals. Therefore, typically, exposure limits for the general public are lower by a factor of 5 than occupational exposures limits, or exposures in the Controlled Environments, as they are referred to in some guidelines.

There is no EMF regulation in the US, and international guidelines are not enforced. Some states have adopted policies that mainly relate to sitting of new power lines.

5.2 Precautionary Policies

Implementing suitable precautionary procedures to reduce exposure is reasonable and warranted. However, electric power brings obvious health, social and economic benefits, and precautionary approaches should not compromise these benefits. Furthermore, given both the weakness of the evidence for a link between exposure to ELF magnetic fields and childhood leukaemia, and the limited impact on public health if there is a link, the benefits of exposure reduction on health are uncertain. Thus, if precautionary measures are to be implemented, their costs should be very low.

Some Scandinavian countries adopted precautionary approaches, albeit not terribly specific in their requirements, and Australia and California (and some other US states) adopted precautionary policies (then known under the label "prudent avoidance") where modest amounts of money should be spent to reduce exposures where practicable when new power lines are built (Kheifets et al., 2005).

Switzerland, Israel and Italy have incorporated the precautionary principle into their national legislation and established stricter numeric guidelines. The stricter limits mostly apply to new constructions near sensitive areas (where children spend time) with a 2 mG as a *de minimis* level meaning no further reduction necessary beyond this level.

III. UCSD AND RELATED REPORTS

1. Dr. Garland's Report

1.1 Summary

Dr. Garland conducted a first stage cluster investigation in the Literature Building. Cases were reported through the Department of Literature, based mainly on self-reports. At the time of Dr. Garland's report a total of nine cases of breast cancer were known by the Department of Literature in women who worked in the Literature Building during 1991-present. Of these, eight were diagnosed during 2000-2006, and were the principal focus of his investigation. Using this approximate method of estimation, the observed incidence of invasive breast cancer in the Literature Building was about 4-5 times the expected incidence in the California general population.

After considering some other exposures, Dr. Garland focuses on EMF: Some epidemiological and laboratory studies have linked exposure to residential levels of electromagnetic fields, although the literature on this association is mixed.

1.2 Critique

Nota Bene: References cited in the body of Dr. Garland's report do not correspond to the references provided at the end of his report, thus some of the statements were difficult to follow and verify.

1.2.1 Issues related to cluster definition and assessment

Dr. Garland refers to a previous study in Southern California that compared self-reports of cancer with medical records and found that examination of supporting medical records did not generally result in substantial changes from self-reported diagnoses. While this might be the case in general, heightened concern, as is the case in the Literature building, can lead to reporting bias and/or earlier diagnosis. This was, in fact, documented in at least one case in a similar breast cancer cluster in Australia. Additionally, it will be important to ascertain that all of the cases are only primary (original) cancers and not cancers that have spread (metastasized) from another part of the body. This is important because metastatic cancers do not have the same causes as primary cancers. Whether or not these issues are of importance in this case can be only determined with a comprehensive epidemiologic investigation.

A cancer cluster is the occurrence of more than the expected number of cancers within a group of people, a geographic area, or a period of time. Cancer clusters may be suspected when people report that several family members, friends, neighbors or coworkers have been diagnosed with the same or related cancer(s). With their knowledge of diseases, environmental science and statistics, epidemiologists try to distinguish actual cancer excesses from excesses that are due only to chance. Epidemiologists generally suspect that an excessive number of cancer cases is a true cluster, if it involves a large number of cases of a specific type of cancer (rather than several different types), a rare type of cancer (rather than common types), or an increased number of cases of a certain type of cancer in an group that is not usually affected by that type of cancer (from http://www.ccrcal.org/brochure/monitor.pdf).

While this investigation properly focuses on a specific type of cancer (breast cancer), other conditions are not met, i.e. breast cancer is, unfortunately very common, particularly among highly educated women.

Dr. Garland calculated relative risk under various assumptions regarding age and ethnicity of the women working in the Literature Building, and determined that the observed incidence would be statistically significant, regardless of reasonable assumptions. He further calculates the probability that the cluster could have occurred by chance.

Unfortunately, I was unable to obtain details of the data Dr. Garland used in his calculations and, in addition, could not reproduce exactly some of his probability calculations. Key to any calculation would be number of women regularly working in the building by year and their age distribution. Risk substantially varies with age and somewhat by ethnicity.

In addition, it is unclear why the principal focus was on cases diagnosed during 2000-2006. When earlier years 1991-1999 are added to the calculations the risk is reduced substantially.

Inclusion of other socio-demographic and reproductive variables could have added useful detail, but these were not available on all subjects. Again, detailed information on these factors, as well as family history, would only be possible in an epidemiologic study.

While I agree with Dr. Garland that genetics accounts for less than 10-15% of incidence of the disease, his conclusion that genetics was not a major factor in this analysis, since all but two of the cases were unrelated, does not necessarily follow. Family history might or might not be important for these cases, regardless of whether they are related to each other. This, as well, can only be investigated by a comprehensive study.

1.2.2 Issues related to EMF science

While Dr. Garland refers to only few among numerous studies conducted, I agree that the literature is mixed. Nevertheless, the overwhelming conclusions of major reviews (see above for details and exceptions) is that evidence for an association between EMF and increased breast cancer risk is very weak and that better designed studies point to no risk.

Dr. Garland further states that occupational EMF exposures **larger** (emphasis mine –LK) than those generally identified in the Literature Building have been associated with a small to moderate increase in risk of breast cancer in some but not all studies. Here again, the largest (more than 20,000 cases and 100,000 controls) and most relevant study from Sweden (as it is the only one with a large number of measurements for women) is completely negative and does not find any risk even in the highest exposure category.

1.2.3 Issues related to EMF exposure assessment

Key to Dr. Garland's conclusions was a difference of approximately 30 feet between a breast cancer incidence centroid and the population centroid of the Literature Building.

Unfortunately, no one was able to provide me with a copy of these data, and thus I am unable to comment. I do want to note, though, that magnetic fields from an elevator or panels would decrease dramatically at a small distance from the source (within 10 feet), while offices of the cases appear to be 18 to 72 feet away. I have conducted a walk-through of the building, and taken a number of measurements in the building's hallways, near an elevator (running and not), and in the large number of offices. All measurements where people are or were sitting are very low. Moreover, the measurements are dominated by the office equipment used (computers, printers and copy machines) and not by building sources. Spaces near buss bars exhibited (as expected and present in any building) somewhat higher fields, but they are either in the hallway or at the wall of the meeting room and are not of concern.

Dr. Garland also states that, in previous studies, distance from the source of the EMF to the point of human exposure was considerably more closely related to risk of breast cancer than were measurements using the available instrumentation. I am not sure as to the basis of this statement, as no references are given, but I do not believe this to be factual. In fact, as detailed above, I believe that for breast cancer there is no consistent evidence for either distance or measurements. On the other hand, for childhood leukemia, which is the basis of all EMF risk assessments, the evidence is more consistent for measurements (based mostly on average measurements in the child's bedroom) than either for distance or wire codes.

Dr. Garland applies wire code methodology - developed by Wertheimer and Leeper as a proxy of average magnetic field exposure in homes and from overhead power lines - to the mechanical and elevator equipment rooms of the Literature Building. This is highly unusual. In fact, I do not believe this methodology has been ever applied to non-residential dwellings. And, as far as I know, it has never been applied to any other sources. For such an application, substantial measurement and engineering work would have to be done to determine proper classification of various sources (such as a motor), electric supply to the sources (such as bus bars), distance, and other parameters.

Measurements done in the building so far by everyone, including Dr. Garland and myself, indicate very low average fields (the only aspect of fields measured so far).

1.2.4 Issues related to EMF policy

Dr. Garland states that the Swedish Confederation of Professional Employees (TCO) has defined a worker exposure standard of no more than 2.0 milliGauss as the de facto standard for EMF.

In fact, TCO does not issue limits. TCO is a Swedish trade union. They have a standard for VDT's, with which a VDT has to comply in order to get the TCO certificate. The values in the TCO standard were set about as low as was technically possible to achieve at the time. TCO also has a similar standard for mobile phones, but, apparently it is not used by phone manufacturers. In Sweden, it is the Swedish Radiation Safety Authority that sets limits and policies. They currently do not have a 2 mG limit. The Swedish Radiation Safety Authority has adopted EU recommendations (based on ICNIRP guidelines) just as they are, for the entire EMF spectrum (0-300 GHz). (From personal communication Lars Mjönes, Senior Advisor, Swedish Radiation Safety Authority, 2009)

Dr. Garland also refers to the concept of prudent avoidance and the OTA report which suggests that reasonable measures should be taken to minimize human exposure to power-line EMF, pending further research.

I completely agree and fully support the concept of prudent avoidance, better known as the precautionary principle (Kheifets et al., 2001). However, the OTA report was written before much of the research on breast cancer was completed. As stated above, more recent and better studies of breast cancer do not provide evidence of risk. Thus, and according to precautionary principle, money would not be spent based on breast cancer evidence.

Nevertheless, I think several of Dr. Garland's recommendations are reasonable (e.g., providing information to women on Tamoxifen, conversion of rooms 118, 123, 124, 133, and 134 to infrequent use areas, such as for copying (if the occupants concur that such action would be desirable). The main difference is that, I am far from convinced that levels of EMF exposure in the buildings are high or that the elevator is the culprit in the apparent cluster.

2. Field Management Services (FMS) Report

2.1 Summary

The FMS report presents results of an Extremely Low Frequency (ELF) magnetic field survey of areas adjacent to electrical facilities which support operation of hydraulic elevators in a structure known as the "Literature Building – 3000" located on the UCSD Campus in La Jolla, California. On December 22, 2008 an FMS technical representative visited the UCSD site and with the assistance of Richard Moore, Power Testing and Energization, Inc., conducted a detailed magnetic field survey to measure, document, and further characterize ELF magnetic fields present in the areas of interest.

ELF magnetic field measurements were taken using a Dexsil Fieldstar 1000 Gauss meter and a Dexsil Magnum 310 Gauss meter. Short term measurements were taken in occupied areas including hallways, adjacent to the Literature Building's Ground Floor electrical & elevator equipment room, and in occupied areas of the Second Floor electrical room which is immediately above the Ground Floor electrical room.

Measurements were taken with and without the two adjacent hydraulic drive elevators in operation.

While some peak values of 44 and 96 mG were recorded, all measurements in the areas which people occupy are very low. As expected, fields decay rapidly within 4 to 6 feet of the peak value and become less than 1- 2 mG throughout most areas.

2.2 Critique

The measurements taken are very reassuring and are well below any standards anywhere in the world. Recall that there is no standard in the US, that most of the international standards are orders of magnitude above these levels (ICNIRP general public: 833 mG for 60 Hz; IEEE 9,004 mG; Higher for occupational exposures). Even precautionary measures adopted in a few countries are above the levels in the Literature Building (see section below).

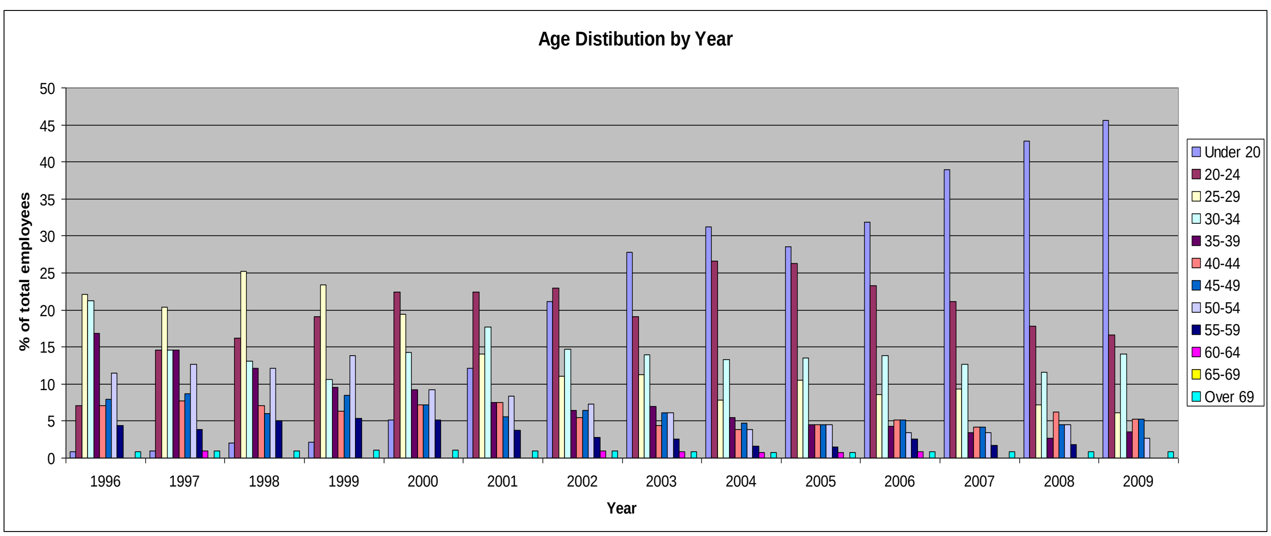
It is unfortunate that these measurements were only made after some of the changes to the electrical system were made. Note however, that measurements made by San Diego Gas and Electric over a year ago and prior to changes similarly indicate low overall levels. Other limitations of the measurements include: the measurements were taken during the time when the building was sparsely occupied, they were limited only to floors 1 and 2, and long-term measurements (e.g. day or week long) were not performed.

Based on this measurement shielding would not be recommended.

IV. STATISTICAL CALCULATIONS

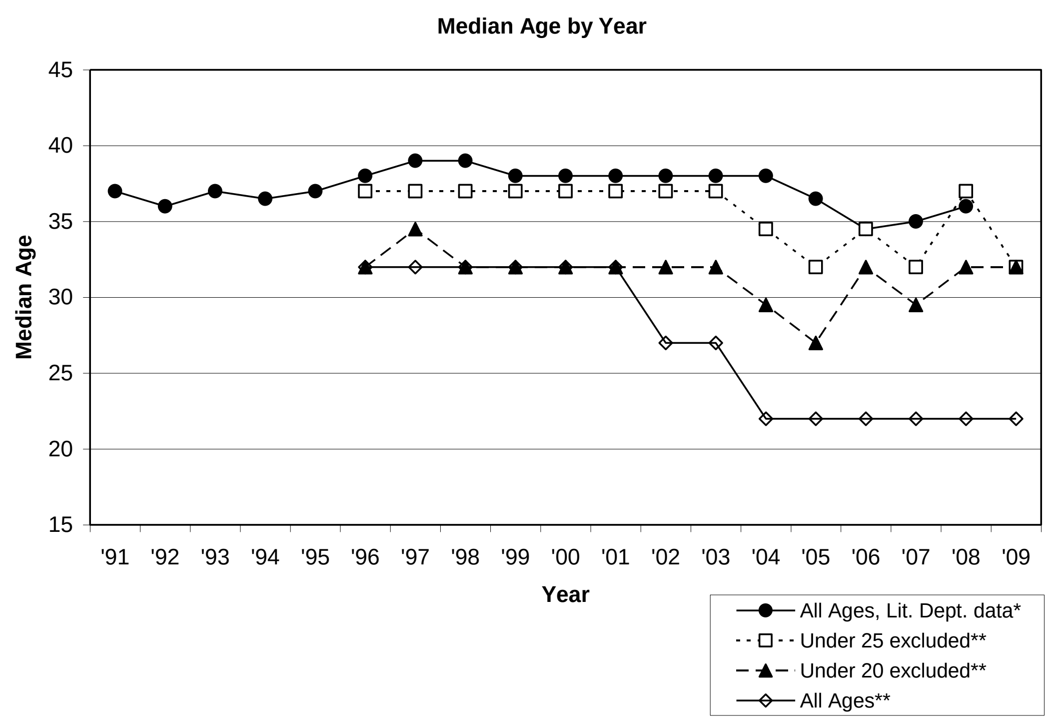
There are three possible sources of error: ascertaining the number of cancers, calculating the expected number of breast cancer cases, and counting the number of person-years at risk. A thorough ascertainment of all cases of breast cancer is only possible in a comprehensive epidemiologic investigation. Such an investigation would confirm that cases are in the scope of the investigation and are confirmed histopathologically. Often in a cluster investigation, some cases that were initially thought to belong to the cluster are subsequently not included for a variety of reasons. On the other hand, linkage to the cancer registry might identify additional cases that were previously missed. For these calculations we have to rely on self-reports.

Calculations of the expected number of breast cancer cases are based on age-specific breast cancer incidence rates in California and San Diego County. Data were obtained by 5-year age groups. Additionally, rates might vary by ethnicity and year. We obtained rates from the California Cancer Registry for the years 1990-2006. These rates are relatively stable and reliable. We used age-specific rates, which is far superior to the calculations based on median age, but require the age distribution of the building population. The age distribution of the Literature Department employees per year was provided by the UCSD personnel office. The data were available for the years 1996-2008, but not for the years 1991-1995.



Most notable is a sharp increase of younger employees (particularly under the age of 20) in the later years. Also somewhat surprising is the small number of employees over the age of 55.

As previous calculations relied on the median age of female employees (with a focus on median age of 45 and consideration of median ages of 40 and 50), below we present median ages based on the data provided to us.



* Median calculation based on data from Literature Department emplyment records (1991-2008).

** Median calculation assumes that 18 is the average age for women under 20 years old, and 72 is the average age for women 70 or older. Calculation based on data from UCSD Personnel Office (1996-2009).

Even when women under 20, who are likely to be undergraduate students, who did not spend a substantial amount of time in the building are excluded, the median age appears to be substantially lower than expected and appears to be in the 30-35 year range.
This data has a number of problems. First, payroll information is linked to a department and not to the building. As the building is mostly occupied by the Department of Literature we had to focus on that department. Small parts of several other departments that have offices in the building could not be included.

Second, payroll records could be summarized by all individuals on the departmental payroll in a given year or as a snapshot in time. Using all individuals on the departmental payroll in a given year and assuming that they have contributed the whole year would overestimate person-years (and thus artificially decrease risk estimates). Thus we can only base our calculations on a snapshot in time (i.e. the number on the payroll as of January 1st of each year). This assumes, for each year, that the number of months counted for employees who left employment before the end of the year is on average the same as the number of months not counted for the employees who started work after the first of the year.

Towards the end of the investigation, the Literature department provided us with additional data, which were considered more reliable and were used in the calculations presented in the tables. Nevertheless, these data too are incomplete, particularly as they relate to employees in the building who worked for different departments and to teaching assistants that spend substantial amount of time in other locations. For these groups we made the following best guesses based on the data provided to us.

Estimation of total person-years was based on the following assumptions:

1. We assume 45 teaching assistants per year, for each of 1991-1999 years and 60 teaching assistants per year for each of 2000-2008, that they were 75% female, each spend 25% time in Literature Building, 70% Caucasian, half age 25-29, half age 30-34;
2. For the Warren Provost Office we assume 20 women per year average age is 44 during 1990-1999 (and 47 for later years) and 70% Caucasian;
3. For additional small programs on the 2nd floor, we assume 3 females per year, average age is 40, 70% Caucasian;
4. For the Ethnic Studies Department, we assume 7 women for years 1990-1994; average age is 44, 70% Caucasian;
5. For the Dean of Arts and Humanities, we assume 4 women for 5 years, average age is 44 (and 47 for later years), 70% Caucasian.

We also assumed that the age distribution and person-years during the 2007-2008 academic years were the same as that of 2006-2007, and the age calculations assumed birthdays occurred at the beginning of each academic year.

In some of the calculations we excluded 3 cases that retired or left the Literature building prior to diagnosis of breast cancer as complete follow-up of retirees (and thus their person-years) were not available. In some of the calculations we assumed that the data provided to us is a reasonable approximation of the complete follow-up. We also excluded one case diagnosed in 1991. The building was first occupied by the Literature Department in 1991, and therefore this case had insufficient latency to be included in analysis. Total person-years for each woman were reduced by 1 year to help account for this and for minimal latency.

Calculation of the age-specific population at risk among the female staff of the building was most problematic. The workforce in the building was not constant over the occupancy of the building, thus the population at risk should be calculated in terms of "person-years at risk" (PYAR). However, information needed for such calculation and to account for retirees can only be assembled in a comprehensive epidemiologic study. Thus, we had to rely on an approximation.

Table 1 summarizes observed and expected cases by decade and age group.

Table 1. Observed and Expected Cases by Decade and by Age Group

			All Races					Adjusted for Race	
Age	Observed cases	Total Person-Years	Annual Population Rate (per 100,000 population)[d]	Expected cases [(#pop*rate)/100000]	Obs/Exp (95% CI) (All ages)	Obs/Exp (95% CI) (Excluding Under 20)	Obs/Exp (95% CI) (Excluding Under 25)	Expected cases [(#pop*rate)/100000]	Obs/Exp (95% CI) (All ages)
1991-1999									
Under 20	0	0	0.0	0.000	0.00			0.000	0.00
20-24	0	3	0.0	0.000	0.00	0.00		0.000	0.00
25-29	0	55	8.5	0.005	0.00	0.00	0.00	0.005	0.00
30-34	0	113	24.9	0.028	0.00	0.00	0.00	0.029	0.00
35-39	0	170	57.9	0.098	0.00	0.00	0.00	0.099	0.00
40-44	0	145	118.0	0.171	0.00	0.00	0.00	0.173	0.00
45-49	0	168	185.6	0.311	0.00	0.00	0.00	0.311	0.00
50-54	0	92	244.8	0.226	0.00	0.00	0.00	0.223	0.00
55-59	2	42	322.5	0.135	14.84	14.84	14.84	0.138	14.54
60-64	0	6	389.3	0.021	0.00	0.00	0.00	0.024	0.00
65-69	0	0	444.6	0.000	0.00	0.00	0.00	0.000	0.00
Over 69	0	0	2009.3	0.000	0.00	0.00	0.00	0.000	0.00
Total[a]	**1**	**591**		**0.745**	**1.34 (0.03-7.48)**	**1.34**	**1.34**	**0.74**	**1.34 (0.03-7.48)**
Total[b]	1	677		0.859	1.16 (0.03-6.49)	1.16	1.16	0.861	1.16 (0.03-6.47)
Total[c]	2	793		0.995	2.01 (0.24-7.26)	2.01	2.01	1.00	2.00 (0.24-7.22)
2000-2008									
Under 20	0	0	0.0	0.000	0.00			0.000	0.00
20-24	0	2	0.0	0.000	0.00	0.00		0.000	0.00
25-29	0	61	7.2	0.004	0.00	0.00	0.00	0.005	0.00
30-34	1	138	26.8	0.037	27.00	27.00	27.00	0.037	26.88
35-39	0	156	58.6	0.091	0.00	0.00	0.00	0.094	0.00
40-44	1	213	125.7	0.268	3.73	3.73	3.73	0.269	3.72
45-49	0	167	196.2	0.327	0.00	0.00	0.00	0.332	0.00
50-54	0	146	250.4	0.365	0.00	0.00	0.00	0.370	0.00
55-59	1	98	316.9	0.310	3.23	3.23	3.23	0.311	3.22
60-64	4	72	371.2	0.267	14.97	14.97	14.97	0.276	14.49
65-69	1	31	424.9	0.130	7.72	7.72	7.72	0.143	7.00
Over 69	0	8	1746.2	0.140	0.00	0.00	0.00	0.127	0.00
Total[a]	5	656		1.158	4.32 (1.40-10.08)	4.32	4.32	1.169	4.28 (1.39-9.98)
Total[b]	8	1011		1.871	4.28 (1.85-8.43)	4.28	4.28	1.904	4.20 (1.81-8.28)
Total[c]	8	1091		1.939	4.13 (1.78-8.13)	4.13	4.13	1.963	4.08 (1.76-8.03)
Overall									
Total[a]	**6**	**1247**		**1.903**	**3.15 (1.16-6.86)**	**3.15**	**3.15**	**1.91**	**3.14 (1.15-6.82)**
Total[b]	9	1688		2.730	3.30 (1.51-6.26)	3.30	3.30	2.765	3.26 (1.49-6.18)
Total[c]	10	1884		2.934	3.41 (1.63-6.27)	3.41	3.41	2.964	3.37 (1.62-6.20)

a. Excluding 3 cases that retired prior to diagnosis of breast cancer and one case diagnosed in 1991. Person-years for each employee reduced by one year to account for latency.

b. Excluding one case diagnosed in 1991. Person-years for each employee reduced by one year to account for latency. Person-years for all employees counted until 2008, until death, or until diagnosis. Cases who retired prior to diagnosis have been included in this analysis.

c. Including all cases. Person-years for all employees counted until 2008, until death, or until diagnosis.

d. Age-specific annual rates of breast cancer for 2000-2008 based on CA Cancer Registry rates from 2000-2006; Rates for 1991-1999 based on CA Cancer Registry rates from 1990-1999.

When interpreting these data assumptions, caveats and data limitations described above should be kept in mind. The standardized incidence ratio (SIR) was calculated as SIR = O / E. Values of SIR greater than 1 indicate an increased risk of breast cancer among the female staff compared to the San Diego County rates.

For the 1991-1999 time period the observed and expected numbers are not materially different due to very small number of cases. For the 2000-2008 period the SIR for 5 observed cases was 4.3 [95% confidence interval: 1.4-10.1]. For the overall time period the SIR for 6 observed cases was 3.2 [95% confidence interval: 1.2 -6.9]. The results did not change much when retirees are included.

We performed several sensitivity analyses to see whether results were dependant on some of the assumptions. The results did not change when younger age groups (both <20 and <25) were excluded or when race was taken into account. Similar results were obtained when California-wide rates (rather than San Diego) were used (data not shown). Including the additional case that was diagnosed in 1991 (and adjusting PY appropriately) did not materially change results.

Use of payroll data lead to much higher estimates, but was considered unreliable by the personnel of the Literature Department.

We performed additional calculations based on projected risk of breast cancer in the next 10 years (from BreastCancer.Org).

Estimates in Table 2 are similar to those obtained in Table 1.

Table 2. Observed and Expected Cases by Decade and by Age Group Using 10-year Risk

Age	Observed cases	Average # in Population Per Year	10-year Population Risk[d]	Expected cases	Obs/Exp
1991-1999					
20-29	0	6	0.0005	0.003	
30-39	0	31	0.0043	0.135	
40-49	0	35	0.0140	0.486	
50-59	2	15	0.0260	0.387	
60+	0	1	0.0370	0.023	
Total[a]	1	66		0.774	1.29 (0.03-7.20)
Total[b]	1	75		0.893	1.12 (0.03-6.24)
Total[c]	2	88		1.035	1.93 (0.23-6.98)
2000-2008					
20-29	0	7	0.0005	0.004	
30-39	1	33	0.0043	0.140	
40-49	1	42	0.0140	0.591	
50-59	1	27	0.0260	0.703	
60+	5	12	0.0370	0.454	
Total[a]	5	73		1.096	4.56 (1.48-10.64)
Total[b]	8	112		1.834	4.36 (1.88-8.59)
Total[c]	8	121		1.892	4.23 (1.83-8.33)
Overall					
Total[a]	**6**	**139**		**1.871**	**3.21 (1.18-6.98)**
Total[b]	9	188		2.727	3.30 (1.51-6.27)
Total[c]	10	209		2.927	3.42 (1.64-6.28)

a. Excluding 3 cases that retired prior to diagnosis of breast cancer and one case diagnosed in 1991. Person-years for each employee reduced by one year to account for latency.

b. Excluding one case diagnosed in 1991. Person-years for each employee reduced by one year to account for latency. Person-years for all employees counted until 2008, until death, or until diagnosis. Cases who retired prior to diagnosis have been included in this analysis.

c. Including all cases. Person-years for all employees counted until 2008, until death, or until diagnosis.

d. Age-specific annual rates of breast cancer for 2000-2008 based on CA Cancer Registry rates from 2000-2006; Rates for 1991-1999 based on CA Cancer Registry rates from 1990-1999.

Overall, these results suggest that the incidence of breast cancer among female staff in the literature building may be about 3-3.5 times higher than what could be expected based on the age-specific breast cancer incidence rates of San Diego County. The excess is mostly in the later time period.

1. Comparisons with other calculations

Our results differ from calculations by Dr. Garland due to several reasons. First we were made aware of an additional case. Secondly, he based the calculations on an assumption that building occupancy has been a steady 130 women. The data we were given indicate that the number of female occupants is lower and has varied from year to year. Thirdly, we were able to use more precise information such as decade-specific San Diego County rates by ethnicity. Fourth, information on the actual yearly age distribution for the Literature Department allowed us to use age-specific rates, which is far superior to the assumption that rates for the median age apply to the whole population. Fifth, the age distribution provided to us by the university indicates that the group is substantially younger than based on the data provided by the Literature Department.

2. Difficulties with statistical inference

Often a first step in cluster evaluation is a calculation of the probability that the increase is due to chance alone. However, even when an increase appears to be unusual interpretation is difficult. This difficulty is known as a **Texas sharpshooter fallacy.** The name comes from a story about a Texan who fires several shots at the side of a barn, then paints a target centered on the hits and claims to be a sharpshooter.

In this context the issue is the definition of a cluster in time and space and the existence of implicit multiple comparisons. Time and space here can be reasonably assumed to be the building which has been occupied from 1991-present. A selective focus on only a period 2000-2006 or only first 2 floors (selected because that is where most cases are) would be an example of such a fallacy.

The calculation of "occurrence by chance alone" is even more difficult. "When a cluster is reported from one community, it implies that comparisons have taken place in many similar communities about which we do not hear because no clusters were found" (Armon et. al., 1991). Inference is difficult, as such clusters can and do occur by chance alone and some of the crucial information is not currently available.

V. A WAY FORWARD

This report is written with an openness to new scientific ideas and to lay perspectives whilst retaining scientific integrity and insisting on a valid scientific basis for policy. I have tried to avoid prejudice and bias in both reviews of the evidence and in suggesting further research. I also believe it is important to face up to the implications of an absence of evidence and to appreciate both the nature and validity of the social dimensions of risk. I further believe that stakeholder engagement in the decision making process is crucial. Present best advice about the conduct of cancer cluster investigations suggests that epidemiological investigations should be done only when these conditions are met (Thun et. al. 2004):

1. The observed number of cases of a specific type of cancer significantly exceeds the number expected;
2. Either the type of cancer or the age at onset is highly unusual;
3. The population at risk can be defined; and
4. Prolonged exposures to known or suspected carcinogens at levels that exceed environmental limits can be documented.

At least under some of the assumptions 1 and 3 are satisfied. Breast cancer is one of the most common cancers, thus condition 2 is probably not satisfied. However, we do not know if subtypes of cancer or age of onset are unusual. Also, the 4th requirement, that prolonged exposures to known or suspected carcinogens at levels that exceed environmental limits can be documented, does not appear to be satisfied.

To evaluate with more certainty whether there is an excess risk of breast cancer (and other cancers) in the Literature Building, and to evaluate whether EMF exposure is related to the risk of cancer in this population, one can conduct a cohort study. A cohort study has an additional advantage of being able to evaluate several outcomes. In this study, we can collect information on the total female workforce from 1991 to present to allow for an accurate estimate of person-years of employment of female staff members during this period. Further, such a study would allow for a more complete case ascertainment, including linkage to the California Cancer Registry and collection of proper pathology information. Additionally, those who retired or left employment can be traced and thus included in the analysis. Information on women and their possible exposures can be collected in face-to-face interviews and supplemented by measurements of various exposures. Of interest would be body max index, education and socio-economic status, family and reproductive history (menarche, menopause, child bearing, use of contraceptives, breast feeding, hormone replacement) and behavior (including smoking, drinking, and exercise). Work history including length of employment and time spent in the building, shift work, and exposures to EMF, RF, ionizing radiation and chemicals (benzene, organic solvents and polycyclic aromatic hydrocarbons) should also be investigated.

A desire to include higher frequencies and momentary surges (expressed by Dr. Garland and some of the building occupants) substantially increases the complexity of the study. Here we would have to deal with complex, non-portable, and at times, poorly tested instrumentation. Furthermore, we would not have a good comparison benchmark for these measurements. If one was to undertake this, I would recommend inclusion of another, similar building in the study.

No matter what is done, the study would be limited by small numbers. Cluster investigations rarely identify the cause of the cluster. Nevertheless, the study would be able to decrease uncertainty and minimize some biases.

VI. CONCLUSION

In a time of enhanced health awareness on the part of the public, researchers and public health authorities must respond to the concomitant increased demand to investigate health event aggregates.

The most productive studies of clusters have been those of extremely rare diseases or of diseases with markedly changed patterns. In addition, these studies have often involved high-level and relatively well-defined exposures. Unfortunately, these circumstances or cluster characteristics are fairly uncommon. Most cluster investigations involve a great deal of uncertainty and, complicating matters, must be performed in a politically-charged environment. This uncertainty is the result of small numbers, poorly identified study populations and vague definitions of exposure and disease. Furthermore, these types of investigations are extremely susceptible to bias and, therefore, statistical inference is quite difficult (Kheifets, 1993). Except for the disease definition, this cluster exhibits all of the problems identified.

Electric and magnetic fields are present in the environment as an inevitable consequence of the use of electricity by society. They induce currents in the body which, at high levels, can cause nerve stimulation. The field levels required to produce these effects are however, rarely experienced in the environment. In the Literature Building in particular, current measurements indicate very low average fields.

Magnetic fields are classified by IARC and WHO as “possibly carcinogenic to humans”: the key effect being childhood leukemia. The evidence in favor of this classification is almost entirely epidemiological. Weighing against causation are the absence of robust experimental evidence of carcinogenicity despite thousands of experiments, the absence of a plausible biophysical mechanism, and the likelihood that some degree of bias is present in at least some of the epidemiological studies. Weighing in favor of causation are the consistency of the epidemiological studies and the failure to find alternative explanations.

The evidence for magnetic fields causing any diseases other than childhood leukemia is significantly weaker than that relating to childhood leukemia. For breast cancer, which has been investigated in several large EMF studies, the epidemiologic evidence does not support an association. This, coupled with low fields currently measured in the building, argues against EMF as a causative agent of the apparent cluster.

Precautionary measures adopted in a few countries are above the levels in the Literature Building. Note that precautionary levels generally refer to average levels, and to new construction in sensitive areas (often where children spend a substantial amount of time, because precautionary advice is mostly based on the childhood leukemia data).

Thus, current levels in the Literature Building are in line with precaution. However, only a comprehensive epidemiologic study can evaluate the true risk in the Literature Building. Such a study can include information on other risk factors for breast cancer and comprehensive measurements of magnetic fields. Such a study would represent a next step in a cluster investigation, where initial, necessarily rough calculations indicate an increased risk. Furthermore, such a study can serve as surveillance. No matter what is done, the study would be limited by small numbers. Cluster investigations rarely identify the cause of the cluster. Nevertheless, the study would be able to decrease uncertainty and mitigate some biases.

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GLOSSARY

Cohort study
A cohort study is a type of epidemiologic study where a group of individuals are followed over time to assess the occurrence of a given disease or condition. Enrollment into the study is based on exposure characteristics or membership in a group.

Confidence interval (CI)
An interval calculated from data when making inferences about an unknown parameter. In hypothetical repetitions of the study, the interval will include the parameter in question on a specified percentage of occasions (eg 95% for a 95% confidence interval).

Latency
Latency is the period of subclinical disease following exposure that ends with the onset of disease.

Odds ratio
The ratio of the odds of disease occurrence in a group with exposure to a factor to that in an unexposed group; within each group, the odds are the ratio of the numbers of diseased add non-diseased individuals.

Population at risk
The term "population at risk" defines the denominator for the calculation of rates of incidences and prevalence. It alludes to the number of persons potentially capable of experiencing the outcome of interest. The number or persons who actually experience the event make up the numerator of the rate. As rates incorporate an element of time, the denominator is often expressed in person-years rather than as the population at risk.