Comments are to be postmarked by November 2, 2015
Re: EIS No. 20150281
Naval Facilities Engineering Command Northwest
Attention: Ms. Kimberly Kler - NWTT EIS/OEIS Project Manager
1101 Tautog Circle, Suite 203
Silverdale, WA 98315-1101

My main concern, here is focused on human health effects of the pulsed electromagnetic fields that the Navy plans to use for electronic warfare training and testing in the Olympic peninsula of Washington State. I am concerned about wildlife and plant effects, and these will be briefly discussed in this document as well. Let me say a few words about my professional qualifications. I received by BA degree in Physics at Johns Hopkins University and PhD degree from Caltech, two of the top institutions in the world. These two degrees allow me to assess both the physics of electromagnetic field (EMF) effects and also the biological mechanisms by which such EMFs can impact the cells of our bodies. Neither of these issues are discussed in this "Final EIS" but both of these are essential for assessing any such environmental impact on either humans or other organisms. I am currently Professor Emeritus of Biochemistry and Basic Medical Sciences, at Washington State University, living in Portland. I have published, over the past 2 ½ years 5 professional papers on how EMFs impact the cells of our bodies and have given 28 professional talks (two given after the paper below was written), in 10 countries, in part or in whole on this topic, and also have 4 youtube videos of my talks (3 of the latter were to lay audiences). Each of these papers considers how a large range of health impacts are produced by low-level, non-thermal exposures to microwave and, in some cases, lower frequency EMFs. My first paper on this topic, published in 2013 (ref. 30 in paper below), was honored to be placed on the Global Medical Discovery site as one of the top medical papers of 2013. It should be clear from the previous three sentences, that there has been a tremendous interest in this research. The entire text of my most recent paper on these subjects is copied below, because of its clear and unequivocal relevance to the many deficiencies in the "Final EIS."

There is a long, well accepted literature in the scientific community of non-thermal health effects of various sorts on humans and various animal species. A key review on this was published by the U.S. Office of Naval Research in 1971 in a document (citation 1 in paper copied below), which listed over 100 health effects of non-thermal exposures to low intensity microwave frequency EMFs and provided roughly 2000 citations documenting these non-thermal health effects. In contrast to that, the U.S. Navy, today provides in this "Final EIS," not a single citation to justify its claim that we don't need to worry about such health effects. Since 1971, there have been well over 8000 additional studies on non-thermal health effects. It follows that the U.S. Navy today is not only over 2000 times less knowledgeable than was the U.S, Navy 44 years ago, but is also over 10,000 time less knowledgeable than it should be on these important issues. There are many other reviews discussed in my paper copied below documenting non-thermal health effects, including two other U.S. Government reports, one published in 1981 and another published in 1994. The current U.S. and international EMF safety guidelines and standards are entirely based on only considering heating effects, a major defect which has been protested by many different groups of scientists over the years, as documented in my paper copied below. I will discuss below how these low-intensity EMFs produce health impacts through non-thermal effects, but before that, let us look at how the "Final EIS" considers these issues.

The abstract of the EIS states that "public health and safety" is addressed in this document. In the Summary of Environmental Effects also states that "public health and safety" is considered. The Navy makes it clear in several places in the EIS that they only consider EMF effects under "in-air energy", in other words that they only are considering thermal effects. In section 3.13 of the EIS, there are three very short sections which may be relevant here, which I am quoting in total. P. 3.13-1 stated that "The United States Department of the Navy (Navy) considered all potential stressors, and the following have been

analyzed for public health and safety" listing second "In-Air Energy." They further state under Preferred Alternative 1 that "Because of the Navy's standard operating procedures, impacts on public health and safety would be unlikely." There is no information provided on what those standard operating procedures might be or on what if any scientific basis there may be to conclude that impacts on public health and safety would be unlikely." Furthermore there is no scientific basis provided for another statement on this same page "however, the United States (U.S.) Department of the Navy's (Navy's) safety measures that protect adults from potential impacts also protects children. Therefore the Proposed Action would not proportionately expose children to environmental health or safety risks." Again, no scientific or any other basis for this conclusion is provided.

On p. 3.13-19 there is a section of "In-Air Energy" which may be relevant, stating that "In-air energy stressors include sources of electromagnetic energy and lasers. As described in Section 3.0.5.3.2.1 (Electromagnetic), emission of electromagnetic energy by magnetic influence mine neutralization systems occur only in training activity in Inland Waters." Apparently, they pulled this wording from an EIS on mine neutralization and the writer did not even bother to change the wording, let alone the substance to deal with the fact that this is an electronic warfare issue, not a mine neutralization issue.

However the last quote sends us to Section 3.0.5.3.2.1 which has in it a section entitled "Airborne Electromagnetic Energy" which states "Sources of airborne electromagnetic energy include aircraft on shipboard radar and communications equipment and aircraft jamming systems. All of these systems are operated within Federal Communication Commission-approved frequency ranges designed to eliminate interference issues with common electronic systems used by the public. These systems are also operated at power levels, altitudes and distances from people and animals to ensure that energy received is well below levels that could disrupt behavior or cause injury." It is not clear here whether they are referring to the electronic warfare that is the central issue with this EIS, or not. But what is clear in the last quoted statement, is that they are assuming here that only energy received (in other words heating effects) need be considered – something that the Navy knew to be false 44 years ago.

This is the sum total that is provided in the EIS that relates in any way to human health effects of the electromagnetic fields to be used for electronic warfare testing and training. It is all based on an almost magical belief that the Navy procedures will protect us from health effects while providing not one iota of information on what those procedures are nor why we should believe that they protect us from health and safety effects. It is all based on the claim that only heating effects need be considered something that over 10,000 published studies plus vast scientific opinion literature shows to be false. It is based, therefore, on a stunning ignorance of the scientific literature, such that it is impossible to find anything in these parts of the EIS that give us any confidence whatsoever in their claims.

How Do Non-Thermal EMF Exposures Produce Biological Effects? (Note this is copied from paper below)

The above discussed studies, clearly show that there has been a consensus in the scientific literature from the early 1970s up to the present time on the existence of widespread non-thermal EMF health effects but it has been unclear what mechanism(s) generated these health effects. There were various suggestions about how these might be generated but no confirmation that those suggested mechanisms were correct. The author stumbled onto the mechanism in 2012 and published on it in mid-2013. This 2013 paper [30] was honored by being placed on the Global Medical Discovery web site as one of the most important medical papers of 2013. At this writing, it has been cited 42 times (Note: it is up to 51 already a few weeks later) according to the Google Scholar database, with 18 of those citations during the first half of 2015. So clearly it is having a substantial and rapidly increasing impact on the scientific literature. I have given 26 professional talks, in part or in whole on EMF effects in 10 different countries over the last 2 1/4 years. So it is clear that there has been a tremendous amount of interest in this.

What the 2013 study showed [30], was that in 24 different studies (and there are now 2 more that can now be added [2]), effects of low-intensity EMFs, both microwave frequency and lower frequency EMFs could be blocked by calcium channel blockers, drugs that block what are called voltage-gated calcium channels (VGCCs). There were a total of 5 different types of calcium channel blocker drugs used in these studies, with each type acting on a different site on the VGCCs and each thought to be highly specific for blocking VGCCs. What these studies tell us is that these EMFs act to produce non-thermal effects by activating the VGCCs. Where several effects were studied, when one of them was blocked or greatly lowered, each other effects studied was also blocked or greatly lowered. This tells us that

the role of VGCC activation is quite wide – many effects go through that mechanism, possibly even all non-thermal effects in mammals. There are a number of other types of evidence confirming this mechanism of action of microwave frequency EMFs [2,24,30]. It is now apparent [24] that these EMFs act directly on the voltage sensor of the VGCCs, the part of the VGCC protein that detects electrical changes and can open the channel in response to electrical changes.

The voltage sensor (and this is shown on pp. 102-104 in [24]) is predicted, because of its structure and its location in the plasma membrane of the cell, to be extraordinarily sensitive to activation by these EMFs, about 7.2 million times more sensitive than are single charged groups elsewhere in the cell. What this means is that arguments that EMFs produced by particular devices are too weak to produce biological effects [31], are immediately highly suspect because the actual target, the voltage sensor of the VGCCs is extremely sensitive to these EMFs. (Specifically it means that highest allowable exposures under current safety standards may be something like 7.2 million times too high.)

How, then can the stimulation of the VGCC mechanism lead to health impacts? When the VGCCs are activated, they open up a channel and leads to large increases in intracellular calcium ([Ca2+]i) and it is the excessive intracellular calcium that leads to most if not all of the biological effects. Calcium signaling is very important to the cell, with some effects of it being produced through increases in nitric oxide (NO) as seen in Fig. 1 and Ref 2.

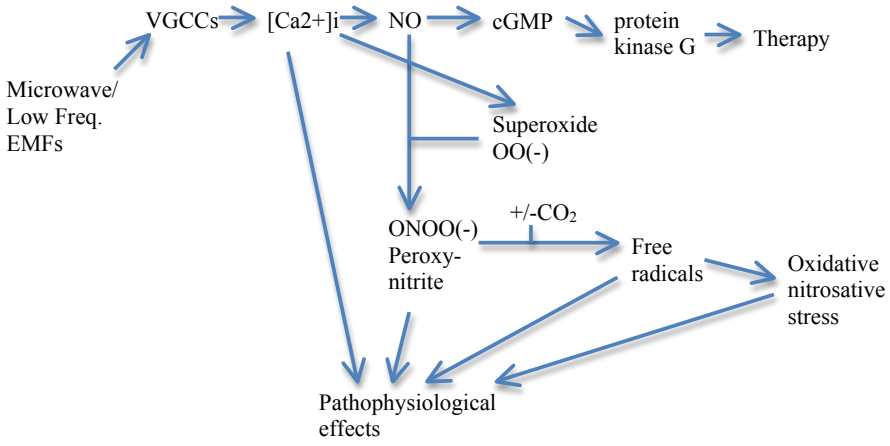

Figure 1. EMFs Act via Downstream Effects of VGCC Activation to Produce Pathophysiological and Therapeutic Effects. Taken from Ref. [24] with permission.

There are non-thermal therapeutic effects produced by these EMFs where they are at the appropriate level and where they are focused on the proper tissue; Such therapeutic effects are produced by the NO signaling pathway across the top of the Figure. However NO can also react with superoxide (which is also elevated by excessive Ca2+]i) to form peroxynitrite, ONOO(-), a potent oxidant. Peroxynitrite can break down to produce reactive free radicals and cause oxidative stress, with all of these acting to produce pathophysiological (that is disease causing) effects (Fig.1). Excess calcium signaling by elevated [Ca2+]i can also contribute to pathophysiological effects.

A number of repeatedly reported effects of effects of microwave EMF exposures can be generated by these mechanisms, as shown in Ref. [24].

Table 1. Apparent Mechanisms of Action for Microwave Exposures Producing Diverse Biological Effects (See Fig. 1)

Reported Biologic Response	**Apparent Mechanism(s)**
Oxidative stress	Peroxynitrite & consequent free radical formation
Single strand breaks in cellular DNA	Free radical attack on DNA
Double strand breaks in cellular DNA	Same as above
Cancer	Single and double strand breaks, 8-nitroguanine and other pro-mutagenic changes in cellular DNA; produced by elevated NO, peroxynitrite

Breakdown of blood-brain barrier	Peroxynitrite activation of matrix metalloproteinases (MMPs) leading to proteolysis of tight junction proteins
Male and female infertility	Induction of double strand DNA breaks; Other oxidative stress mechanisms; [Ca2+]i mitochondrial effects causing apoptosis; in males, breakdown of blood-testis barrier
Therapeutic effects	Increases in [Ca2+]i and NO/NO signaling
Depression; diverse neuropsychiatric symptoms	VGCC activation of neurotransmitter release; other effects?; possible role of excess epinephrine/norepinephrine
Melatonin depletion; sleep disruption	VGCCs, elevated [Ca2+]i leading to disruption of circadian rhythm entrainment as well as melatonin synthesis; elevated [Ca2+]i may also lead to elevated night time levels of norepinephrine
Cataract formation	VGCC activation and [Ca2+]i elevation; calcium signaling and also peroxynitrite/oxidative stress
Tachycardia, arrhythmia, sometimes leading to sudden cardiac death	Very high VGCC activities found in cardiac (sinoatrial node) pacemaker cells; excessive VGCC activity and [Ca2+]i levels produces these electrical changes in the heart

Taken from ref [24] with permission.

A large number of these repeatedly reported effects of such EMF exposures can be caused by various downstream effects of VGCC activation as shown in Fig. 1. This suggests that both Fig. 1 and also Table 1 may explain many of the effects produced by non-thermal exposures to microwave frequency EMFs. These apparent mechanisms of action provide further support that most if not all effects of microwave and lower frequency EMFs are likely to be produced via downstream effects of VGCC activation.

It can be seen from the above, that each of the things we most value as individuals and as a species, our health, our brain function, the integrity of our genomes and our ability to produce healthy offspring are attacked by these EMFs. And these are not only health effects that have been reported to occur, rather they are simply the most extensively documented one. All such reported effects need be considered when considering the issue of safety.

<u>What About Wildlife and Plants in the National Forest, National Park and in the Pacific Ocean? And Anything about Farm Animals?</u>

Certainly, mammals of various sorts are likely to be affected by these EMFs much like humans. But the VGCCs occur universally or almost universally among animals including invertebrates and protozoa. Somewhat surprisingly, plants also have calcium channels in their plasma membranes that are activated by EMF exposures. Although they differ from the animal channels in important ways, they have a very similar voltage sensor to that found on the animal voltage sensor and these appear to be the main target in plants of these EMFs (see, for example Plant, Cell and Enviroment 2007; 30:834-844). It follows from this that there are likely to be major effects on plants in both the National Forest and National Park if the Navy gets its way. There are publications suggesting that migrating birds, amphibia and bees are apparently particularly sensitive to such EMF exposures. Migrating birds have apparently an additional target of EMFs, small magnetic particles which help the birds migrate in accordance with the earth's magnetic field so it is likely that the Navy's claims that birds are not likely to be affected is probably bogus. In humans, one of the common neuropsychiatric consequences of EMF exposures (see ref 2 in paper copied below) is what is called dysesthesia, disruption of sensory function including visual, acoustic and olfactory function. So birds, including eagles which depend on an extremely keen visual perception, may well be visually affected by the Navy EMFs, quite possibly putting the Navy in violation of the Bald and Golden Eagle Protection Act (discussed on p. 3.0-2 or the EIS). There has been published evidence from Balmori's laboratory, showing the amphibia are very sensitive to these EMFs and it has been suggested that the widespread effects of artificial EMFs may contribute to the world wide, unexplained amphibian decline. In any case, it would be a mistake to assume no effects Navy's electronic warfare EMFs on amphibian populations without experimental studies testing whether this is true or not. This brings us to another point. <u>In this entire EIS, the Navy has produced not a single study of biological impacts of the EMFs it plans to unleash on the people, animals and plants of the Olympic peninsula. Their entire argument for safety is based on a theory that only thermal effects need be considered, a theory that the Navy itself knew to be bogus 44 years ago and is still widely known in the scientific community to be bogus. This alone should be more than sufficient to throw out this entire EIS!</u>

There have been published studies showing that bees are very sensitive to electromagnetic fields, suggesting that EMFs are an important contributing factor to colony collapse (along with pesticides). Bees are, of course, important for plant reproduction in the National Forest and Park and there are bees kept for agricultural purposes on the Olympic peninsula, as well. Dairy cattle (which are raised of course, in the Olympic Peninsula) are known to be sensitive to EMF exposure in two ways: EMFs produce a major decline in milk production and, furthermore, pregnant cattle grazing near cell phone towers often produce calves with cataracts, another major effect. The fact that calves get

cataracts but their mothers do not suggest that young growing tissues may be more sensitive to EMFs, an inference also supported by the finding that childhood leukemias (in humans) are much more commonly produced by EMF exposures than are adult leukemias. These two types of observations suggest that the quick conclusion that the Navy makes that we need not have special concerns about childhood exposures is likely to be bogus as well – this is certainly still another example where the Navy makes a quick convenient (at least for the Navy) conclusion based entirely on wishful thinking (or the lack thinking).

Let me make a couple of comments about fish. Sharks are known to have an extremely sensitive detection of very weak electrical fields in, of course a seawater environment. The detector for this electrical sense is made up of T-type VGCCs, the VGCCs that are the most sensitive to electrical changes. The anatomy of the electrical detector in sharks acts to greatly amplify the electrical forces on these VGCCs, an amplification that may also act for EMF effects on the electrical sensor that the shark uses to locate prey. It follows from this that sharks may be unusually sensitive to EMF exposures and this may be still another effect that the Navy blithely dismisses in the EIS. Finally, it is known, of course that salmon have an extremely sensitive olfactory system which allows them to "smell" their way back to their home streams for spawning. It follows from this that the dysesthesia produced by EMF exposures may cause salmon exposed to EMFs to be very sensitive to such exposures as well, possibly causing them to be unable to find their home streams for spawning. Let me say, I do not claim to be an expert on the animals or plants in the Olympic peninsula and these observations are simply common sense observations derived from my knowledge of biological effects of EMFs. There may be dozens, perhaps even hundreds of additional such effects that I don't know about and perhaps no one knows about, but all of which have been blithely dismissed by the Navy.

In summary, then, regarding human, animal or plant effects of the EMFs it plans to use for electronic warfare:

1. The Navy today is at least 2000 times less knowledgeable than the Navy was 44 years ago in 1971; the Navy today is also at least 10,000 times less knowledgeable today than it should be.
2. The Navy provides not a single experimental study on biological effects of the EMFs it plans to use in the Olympic Peninsula. It provides, therefore not an iota of biological evidence to support any of its claims.
3. It provides not even a single citation to the scientific literature to support its claims.
4. The Navy claims are based entirely on the position that only thermal effects need be considered, a position that the Navy knew to be false 44 years ago and a position contradicted by many thousands of published scientific studies. That position is also contradicted by widespread scientific opinion expressed continuously over the past 44 years.
5. Low-intensity microwave frequency EMFs have been shown to produce the following effects in humans and other mammals via non-thermal mechanisms: Oxidative stress; genotoxicity including single and double strand breaks in cellular DNA as well as 8-hydroxyguanine residues in cellular DNA; these are thought, in turn to cause cancer when they occur in the somatic cells of the body; these are thought to also cause germ line mutations when they occur in germ cells, producing in turn deleterious mutations in future generations; male and female infertility; massive damage to the nervous system which in the brain produce widespread neuropsychiatric effects – such widespread neuropsychiatric effects were known to the Navy as shown in its 1971 report; breakdown of the blood brain barrier; cardiac effects including tachycardia and also bradycardia associated with arrhythmias and arrhythmias are known to often lead to sudden cardiac death – such cardiac effects were already known to the Navy as shown by its 1971 report; melatonin depletion and insomnia. The Navy provides not one iota of evidence to show that each of these effects will not be caused by the electronic warfare EMFs in the civilian population of the Olympic Peninsula. It is also of great concern that similar effects may well occur in the pilots of the F18 planes involved.
6. It can be seen from 5 above, that low intensity EMFs attack each of the 4 things we most value as individuals and as a species: Our health, our brain function, the integrity of our genomes and our ability to produce healthy offspring. The EIS provides not one iota of evidence that these 4 things will not be produced in civilians of the Olympic Peninsula and in the F18 pilots by the electronic warfare EMFs.
7. Each of the biological effects listed in 5 and 6 above, can be produced by what are called "downstream effects" of VGCC activation, the predominant mechanism of action of low-intensity EMFs in the cells of our bodies. None of this is considered in the EIS.
8. The voltage sensor of the VGCCs appears to be extraordinarily sensitive to low intensity EMFs based on its physical structure and position in the plasma membrane of our cells. These physical properties, based simply on physics, predict that the forces placed on the voltage sensor by EMFs are about 7.2 million times higher than the forces places on single charged groups found elsewhere in the cell. This argues, therefore, that the acceptable levels of exposure of safety standards/guidelines based only on thermal effects, are about 7.2 million time too high and that much lower levels of exposure can cause major biological effects. This entire area of science is completely ignored by the EIS.
9. The biological effects produced in 7 and 8 above are important and widespread in many animals and also in plants. Certain species, including birds (especially migrating birds and eagles), amphibia, bees, sharks and salmon may be particularly susceptible. It seems likely that still additional especially susceptible species may

be discovered as such studies progress further. There is, therefore, ample reason for great concern about the animals and plants in and around the Olympic Peninsula.

In summary, each of the 9 major flaws in the part of the EIS on biological effects of EMFs are individually sufficient, in my view, to reject the entire EIS and being fatally flawed.

Martin L. Pall
Professor Emeritus of Biochemistry and Basic Medical Sciences
Washington State University

International Journal of Innovative Research in Engineering & Management (IJIREM) ISSN: 2350-0557, Volume-2, Issue -5, September 2015;71-76

How to Approach the Challenge of Minimizing Non-Thermal Health Effects of Microwave Radiation from Electrical Devices

Martin L. Pall, PhD,
Professor Emeritus of Biochemistry and Basic Medical Sciences,
Washington State University

ABSTRACT

Dozens of reviews and thousands of primary literature studies have shown the existence of many different non-thermal health effects of microwave and lower frequency electromagnetic fields (EMFs); however current safety guidelines and standards only recognize thermal effects. This leaves both individuals and companies unprotected, particularly with the very large increases in microwave frequency exposures that are occurring over time. It has recently been shown that many, perhaps even all non-thermal health effects are produced by activation of voltage-gated calcium channels (VGCCs) in the plasma membranes of cells, with EMFs activating these channels, producing large increases in intracellular calcium levels [Ca2+]i. The voltage sensor controlling the VGCCs is thought to be extremely sensitive to activation by weak EMFs. Diverse health effects are thought to be produced by downstream effects of increased [Ca2+]i produced by VGCC activation. It is difficult if not impossible to currently predict the biological effects of different EMFs because pulsation patterns, frequencies and EMF polarization each have strong influences on biological effects; there are also windows of exposure producing maximum biological effects within the exposure window. While decreasing exposures on the order of 100 to 1000-fold will no doubt be useful, we also need to have genuine biological measures of damage to allow optimization of both the type of EMF exposures as well as intensities. Biological optimization should be done by studying cells in culture that have high densities of various types of VGCCs, measuring such effects as increases in [Ca2+]i and increases in nitric oxide (NO) production following EMF exposures. Such cell culture-based assessment of biological damage should allow progressive improvement of wireless communication devices and various other electronic devices by choosing designs that lower biological responses.

Keywords

Microwave frequency EMFs, calcium signaling, nitric oxide, peroxynitrite, oxidative stress

1. There Is a Widespread Literature on Non-Thermal Effects Being Produced by Low-Intensity Microwave/RF Exposures

The earliest major report of widespread non-thermal effects of microwave frequency radiation exposures was the 1971 Naval Medical Research Institute (NMRI) Research Report [1] which listed 40 apparent neuropsychiatric changes produced by non-thermal microwave frequency exposures, including 5 central/peripheral nervous system (NS) changes, 9 central NS effects, 4 autonomic system effects, 17 psychological disorders, 4 behavioral changes and 2 misc. effects [1,2]. It also listed cardiac effects including ECG changes and cardiac necrosis as well as both hypotension and hypertension, and also 8 different endocrine effects. Changes affecting fertility included tubular degeneration in the testis, decreased spermatogenesis, altered sex ratio, altered menstrual activity, altered fetal development and decreased lactation. Many other non-thermal changes were also listed for a total of over 100 non-thermal effects. This NMRI report also provided a supplementary document listing over 2300 citations documenting these and other effects of microwave exposures in humans and in animals, with approximately 2000 of these documenting apparent non-thermal effects.

Tolgskaya and Gordon [3] published a long and detailed review of effects of microwave and lower frequency EMFs on experimental animals, mostly rodents. They report that non-thermal exposures impact many tissues, with the nervous system being the most sensitive organ in the body, based on histological studies, followed by the heart and the testis. They also report effects of non-thermal exposures on liver, kidney, endocrine and many other organs. The nervous system effects are very extensive and are discussed in Reference [2,3] and more modern studies reporting extensive effects of such non-thermal EMF exposures on the brain are also cited in [2]. There are also many modern studies showing effects of non-thermal exposures on fertility in animals.

The Raines 1981 National Aeronautics and Space Administration (NASA) report [4] reviewed an extensive literature based on occupational exposures to non-thermal microwave EMFs. Based on multiple studies, Raines [4] reports 19 neuropsychiatric effects to be associated with occupational microwave/radiofrequency EMFs, as well as cardiac effects, endocrine including neuroendocrine effects and several other effects.

The Bolen 1994 report put out by the Rome Laboratory of the U.S. Air Force [5], acknowledged the role of non-thermal effects of microwave EMFs on humans. This report states in the Conclusion section that "Experimental evidence has shown that exposure to low intensity radiation can have a profound effect on biological processes. The nonthermal effects of RF/MW radiation exposure are becoming important measures of biological interaction of EM fields." Clearly Bolen [5] rejects the claim that only thermal effects occur. So we can see from these four reviews (1,3-5), that there was already a well accepted literature on non-thermal effects of microwave frequency EMFs back in the 1970's through the mid-1990's but it is still the case that U.S. and international safety guidelines and standards are based solely on thermal effects.

22 additional scientific published reviews have each reviewed various types of non-thermal microwave effects in humans and/or experimental animals in various contexts [2,6-26], as have 26 studies in a recently published book [27]. It can be seen from this that there is a widely held consensus in much of the scientific community that various non-thermal effects of microwave EMFs are well documented.

2. Safety Guidelines and Standards Are Based Only On Thermal Effects

Nevertheless, U.S., ICNIRP and almost all other safety guidelines/standards for microwave/lower frequency EMFs have been based solely on thermal (heating) effects, not on non-thermal effects. These have, therefore left both the general public and also companies designing devices emitting electromagnetic fields unprotected by genuine scientifically-based standards. It is the central focus of this paper as to how such companies should respond to this situation.

There have been many scientific statements that have expressed great concern about the inadequacy of these safety guidelines/standards because of their failure to include what in the views of many scientists, are well established non-thermal effects. For example, Havas in a 2013 paper [6] lists 14 statements of this type, written between 2002 and 2012 by various groups of international scientists, each expressing concern about non-thermal effects and the inadequacy of safety guidelines and standards. In addition, recently, there was a petition from various scientists, arguing that the World Health Organization should reclassify microwave EMFs as a Class 1 human carcinogen; 53 scientists signed a petition that the 2014 Canadian Report (discussed further below) had inadequate protection standards for human health; and 206 international scientists signed a statement sent to the United Nations Secretary General and to member states, stating that international safety guidelines and standards are inadequate to protect human health.

3. Four Important Factors Which Make the Biological Activity of EMFs Unpredictable in Terms of Intensity and Unpredictable in General

Many have assumed that it is possible to predict the effects of such EMFs based simply on EMF exposure intensities but such assumptions are clearly false. Empirical observations have shown that four types of factors greatly influence biological responses to microwave EMFs , with all four reviewed by Belyaev [28] and 3 of the 4 each reviewed elsewhere [24,25].

1. One of these is that pulsed fields are *in most cases* more biologically active than non-pulsed fields. The literature on comparing pulsed fields with non-pulsed fields goes back to the 1960's [3] and continues right up to the present [24-26,28,29]. One example of pulsation effects is from studies of therapeutic effects of non-thermal microwave frequency EMFs [26], when they are of the right type and intensity and focused on the right tissue. Such therapy was standardized using pulsed microwave fields back in the mid-1970s because these pulse fields were more active, a standardization that continues to the present day [26]. There are some 4000 studies of pulsed microwave therapy which make up the largest literature on non-thermal biological effects. Unfortunately we don't have enough detailed knowledge of these pulsation effects to be able to predict how biologically active EMFs with different patterns of pulsation will be. With very complex pulsed fields like those from smart meters or smart phones, prediction becomes still more difficult. Panagopoulos et al [29] have argued that complex pulsation patterns are consistently more biologically active than are simpler patterns. There is some evidence that very low frequency pulsations (10 Hz or less) may lower biological responses, which if confirmed may be useful for lowering biological effects of electronic devices. Because all wireless communication devices communicate via pulsations, pulsation effects may be inherent factors with such devices.
2. There are non-linearities in dose response curves and specifically there are specific intensity windows of exposure which produce greater biological effects than exposures of either **higher** or **lower** intensity [24,28,29]. In one experiment, an effect seen within a window was studied and it was found that increasing intensity to even to 150 times higher intensity of exposure lead to lower biological responses than was found in the window. Clearly these intensity windows also create important uncertainties in trying to predict biological effects of EMF exposures.
3. It has also been shown that different frequencies have different biological effects [28]. While this is a simpler issue, than either pulsations or the window effects, it may well add substantial complexity in combination with each of these other two factors.
4. Perhaps most importantly, artificial EMFs are polarized and can be linearly or circularly polarized. However most naturally occurring EMFs are non-polarized or only weakly polarized. Polarized fields can produce much stronger forces on charged groups, which, as discussed below, are likely to have central roles in producing non-thermal biological effects [28,29]. One of the other effects discussed by Belyaev [28] is that circularly polarized fields can be either right handed or left handed and that the handedness of specific fields have extremely large effects on the biological responses, such that fields that are identical in intensity and frequency and differ only in their handedness of circular polarization can have almost completely different biological effects.

All of these things – the effects of pulsations, of window effects, of frequencies and of linear and circular polarization argue compellingly that we cannot predict biological effects based simply on the intensity of EMFs and certainly not on heating effects of EMFs. An attractive approach to measuring biological effects empirically is discussed below.

4. How Do Non-Thermal EMF Exposures Produce Biological Effects?

The above discussed studies, clearly show that there has been a consensus in the scientific literature from the early 1970s up to the present time on the existence of widespread non-thermal EMF health effects but it has been unclear what mechanism(s) generated these health effects. There were various suggestions about how these might be generated but no confirmation that those suggested mechanisms were correct. The author stumbled onto the mechanism in 2012 and published on it in mid-2013. This 2013 paper [30] was honored by being placed on the Global Medical Discovery web site as one of the most important medical papers of 2013. At this writing, it has been cited 42 times according to the Google Scholar database, with 18 of those citations during the first half of 2015. So clearly it is having a substantial and rapidly increasing impact on the scientific literature. I have given 26 professional talks, in part or in whole on EMF effects in 10 different countries over the last 2 1/4 years. So it is clear that there has been a tremendous amount of interest in this.

What the 2013 study showed [30], was that in 24 different studies (and there are now 2 more that can now be added [2]), effects of low-intensity EMFs, both microwave frequency and lower frequency EMFs could be blocked by calcium channel blockers, drugs that block what are called voltage-gated calcium channels (VGCCs). There were a total of 5 different types of calcium channel blocker drugs used in these studies, with each type acting on a different site on the VGCCs and each thought to be highly specific for blocking VGCCs. What these studies tell us is that these EMFs act to produce non-thermal effects by activating the VGCCs. Where several effects were

studied, when one of them was blocked or greatly lowered, each other effect studied was also blocked or greatly lowered. This tells us that the role of VGCC activation is quite wide – many effects go through that mechanism, possibly even all non-thermal effects in mammals. There are a number of other types of evidence confirming this mechanism of action of microwave frequency EMFs [2,24,30]. It is now apparent [24] that these EMFs act directly on the voltage sensor of the VGCCs, the part of the VGCC protein that detects electrical changes and can open the channel in response to electrical changes.

The voltage sensor (and this is shown on pp. 102-104 in [24]) is predicted, because of its structure and its location in the plasma membrane of the cell, to be extraordinarily sensitive to activation by these EMFs, about 7.2 million times more sensitive than are single charged groups elsewhere in the cell. What this means is that arguments that EMFs produced by particular devices are too weak to produce biological effects [31], are immediately highly suspect because the actual target, the voltage sensor of the VGCCs is extremely sensitive to these EMFs.

How, then can the stimulation of the VGCC mechanism lead to health impacts? When the VGCCs are activated, they open up a channel and leads to large increases in intracellular calcium ([Ca2+]i) and it is the excessive intracellular calcium that leads to most if not all of the biological effects. Calcium signaling is very important to the cell, with some effects of it being produced through increases in nitric oxide (NO) as seen in Fig. 1 and Ref 2.

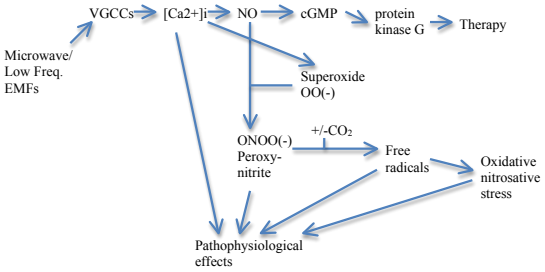

Figure 1. EMFs Act via Downstream Effects of VGCC Activation to Produce Pathophysiological and Therapeutic Effects. Taken from Ref. [24] with permission.

There are non-thermal therapeutic effects produced by these EMFs where they are at the appropriate level and where they are focused on the proper tissue; Such therapeutic effects are produced by the NO signaling pathway across the top of the Figure. However NO can also react with superoxide (which is also elevated by excessive Ca2+]i) to form peroxynitrite, ONOO(-), a potent oxidant. Peroxynitrite can break down to produce reactive free radicals and cause oxidative stress, with all of these acting to produce pathophysiological (that is disease causing) effects (Fig.1). Excess calcium signaling by elevated [Ca2+]i can also contribute to pathophysiological effects.

A number of repeatedly reported effects of effects of microwave EMF exposures can be generated by these mechanisms, as shown in Ref. [24].

Table 1. Apparent Mechanisms of Action for Microwave Exposures Producing Diverse Biological Effects (See Fig. 1)

Reported Biologic Response	**Apparent Mechanism(s)**
Oxidative stress	Peroxynitrite & consequent free radical formation
Single strand breaks in cellular DNA	Free radical attack on DNA
Double strand breaks in cellular DNA	Same as above
Cancer	Single and double strand breaks, 8-nitroguanine and other pro-mutagenic changes in cellular DNA; produced by elevated NO, peroxynitrite
Breakdown of blood-brain barrier	Peroxynitrite activation of matrix metalloproteinases (MMPs) leading to proteolysis of tight junction proteins
Male and female infertility	Induction of double strand DNA breaks; Other oxidative stress mechanisms; [Ca2+]i mitochondrial effects causing apoptosis; in males, breakdown of blood-testis barrier
Therapeutic effects	Increases in [Ca2+]i and NO/NO signaling
Depression; diverse neuropsychiatric symptoms	VGCC activation of neurotransmitter release; other effects?; possible role of excess epinephrine/norepinephrine
Melatonin depletion; sleep disruption	VGCCs, elevated [Ca2+]i leading to disruption of circadian rhythm entrainment as well as melatonin synthesis; elevated [Ca2+]i may also lead to elevated night time levels of norepinephrine
Cataract formation	VGCC activation and [Ca2+]i elevation; calcium signaling and also peroxynitrite/oxidative stress
Tachycardia, arrhythmia, sometimes leading to sudden cardiac death	Very high VGCC activities found in cardiac (sinoatrial node) pacemaker cells; excessive VGCC activity and [Ca2+]i levels produces these electrical changes in the heart

Taken from ref [24] with permission.

A large number of these repeatedly reported effects of such EMF exposures can be caused by various downstream effects of VGCC activation as shown in Fig. 1. This suggests that both Fig. 1 and also Table 1 may explain many of the effects produced by non-thermal exposures to microwave frequency EMFs. These apparent mechanisms of action provide further support that most if not all effects of microwave and lower frequency EMFs are likely to be produced via downstream effects of VGCC activation.

In contrast to this, when the author examined the evidence supporting a strictly thermal mode of action of these microwave frequency EMFs in the 2014 Canadian Report [32], that evidence was found to be deeply flawed [24].

5. Biologically-Based EMF Safety Standards – Why Industry Needs to Look at These and How They May Be Useful

Hardell and Sage [34], the Scientific Panel on Electromagnetic Health Risks [17] and the author [24] have called for biologically-based EMF safety standards, standards that are based on genuine biologically relevant responses to low-level microwave and other EMFs. The best approach to doing so, in the author's view, as discussed earlier [24] involves looking at biological responses of VGCC-containing cells in culture (using methods outlined below). The initial focus here is on how such responses should be useful in quantifying biological effects of electronic devices that produce EMFs.

The goal here is both to use such cell culture studies to quantify biological effects of various EMFs, with regard to effects of frequency, intensity, pulsation pattern and polarization. A wide variety of electronic devices can be tested, so as to improve designs by lowering biological effects. These would include various types of broadcasting devices including antennae, all types of wireless communication devices and also many other electronic devices that inadvertently broadcast EMFs and/or dirty electricity. Smaller devices such as cell phones, cordless phones, cordless phone bases, smart meters, Wi-Fi fields and computers/tablets generating Wi-Fi signals but also many other devices. Panagopoulos et al [25] have recently argued that complex pulsation patterns such as produced by smart phones and smart meters produce higher biological activity. A wide variety of factors should be investigated for improved safety, including improved antenna design, use of frequencies producing lowered biological effects, use of shielding materials and changes in polarization and pulsation patterns. Improved sensitivity of receivers can allow lowered intensities to be used.

In dirty electricity, transients produced by various devices, produce transients in electrical power wiring such that the wiring acts as an antenna, producing in turn, human exposure to EMFs. All digital technology has the potential to produce such dirty electricity, but digital technology involving high current flows may be the major challenge, such as broadcasting antennas, digital power supplies and inverters. It may be important to investigate the use of filters to lower such transients in electrical wiring. It is not uncommon for electronic devices to purposefully introduce signals onto electrical power wiring, such that the wiring is used as a communication conduit. Clearly such purposeful use of power wiring needs to be investigated for biological effects. Filters and other technologies should be investigated to see if these lower biological responses. Even static magnetic fields can activate VGCCs [30], possibly because rapid movement of the VGCCs due to movement of plasma membranes in which they are located. The effects, therefore of many types of EMFs can be assessed biologically through testing of such biological responses.

How then should cells in culture be used to monitor biological effects of various EMFs? Studies would use cell lines with such high VGCC levels, such as neuroblastoma cell lines, glioblastoma/glioma hybrid cell lines or perhaps cell lines derived from endocrine cells with relatively high VGCC levels. Among these cell lines should be the neuroblastoma cell lines previously studied by Dutta et al (discussed in [24]) and shown to produce changes in calcium fluxes in response to very low level EMF exposures. PC12 cells, a commonly used chromaffin cell line may also be useful. In addition, it may useful to use cardiac pacemaker cells which have very high activities of VGCCs and can be derived from stem cells [24]. Because the growth conditions of cells may influence their responsiveness, such conditions must be standardized. Standardization should include growth of cells in a Faraday cage such as to prevent, to the extent possible, previous exposures to EMFs.

Two approaches should be used to measure responses of such cells to EMF exposure: Cells in culture could be monitored for nitric oxide (NO) production using an NO electrode in the gas phase over the culture, using methods similar to those used by Pilla [33]. NO synthesis is stimulated by [Ca2+]i elevation because there are two NO synthase enzymes that are each calcium-dependent and therefore increase in activity with increasing [Ca2+]i. Continuous measurements from an NO electrode can be recorded and easily quantified, allowing accumulation of very large amounts of data in very short time periods in response to various EMFs. Therefore, issues such as reproducibility should be quickly resolved.

Another approach to such studies involves using calcium-sensitive fluorescent probes that concentrate into the cytoplasm of cells, allowing assessments of

[Ca]i levels with a fluorescence microscope or of multiple cells using a fluorometer. Alternatively, transgenic cell lines containing green fluorescent protein (GFP) can be used, where GFP functions as the calcium-sensitive fluorescent probe. This may allow one of obtain information of different types than described in the previous paragraph. One can get information on heterogeneity of responses at the cellular level and also how raised [Ca]i levels may propagate over time from one part of the cell to another. However a limitation to this approach may occur if the fields generated by the microscope perturb the [Ca2+]i levels and cannot be well shielded using a small Faraday cage that does not cage exposures that are to be studied. So these two approaches are distinct from one another and whether they will complement each other as they develop is uncertain. It is my view that both of these should be investigated if only to explore their strong points and weak points, but that the NO electrode approach may be a very good place to start because it has already been used to assess EMF effects [33] and because it allows easy quantification. These two types of approaches should allow comparison of different wireless communications devices for their relative biological effects, possibly permitting easy improvements in design. There is some evidence that some pulsation patterns may lower biological effects and this type of effect might be studied as well.

From the standpoint of industry and engineering of electronic devices, the four factors we discussed above, that each influence biological responses each need to be considered: the roles of pulsations, window effects, frequency and polarization. Each of these can be viewed as a challenge, but also as an opportunity. The opportunities come because by manipulating these factors, it may well be possible to develop devices with much lower biological effects than are produced by current devices. A smart company that gets the information early and uses it effectively may well have a marketing advantage over its competitors.

6. Conclusions

Non-thermal effects of EMF exposures have been extensively documented for over 40 years. However only recently has the mechanism of action of such non-thermal effects been demonstrated. These act via EMF activation of VGCCs, producing increases in intracellular calcium [Ca2+]i. This allows the development of techniques using cells in culture with high densities of multiple types of VGCCs, to assess different devices that emit microwave frequency EMFs by measuring either increases in [Ca2+]i or increases in nitric oxide (NO) produced as a consequence of increased [Ca2+]i. It is the author's view that smart companies should use these cell culture techniques to greatly improve the safety of such devices.

REFERENCES

[1] Naval Medical Research Institute Research Report, June 1971. Bibliography of Reported Biological Phenomena ("Effects") and Clinical Manifestations Attributed to Microwave and Radio-Frequency Radiation. Report No. 2 Revised.

[2] Pall, M. L. 2015. Microwave frequency electromagnetic fields (EMFs) produce widespread neuropsychiatric effects including depression. *J. Chem. Neuroanat.* 2015 Aug 20. pii: S0891-0618(15)00059-9.doi: 10.1016/j.jchemneu.2015.08.001. [Epub ahead of print] Review.

[3] Tolgskaya, M. S., Gordon, Z. V. 1973. *Pathological Effects of Radio Waves*, Translated from Russian by B Haigh. Consultants Bureau, New York/London, 146 pages.

[4] Raines, J. K. 1981. Electromagnetic Field Interactions with the Human Body: Observed Effects and Theories. Greenbelt, Maryland: National Aeronautics and Space Administration 1981; 116 p.

[5] Bolen, S. M. 1994 Radiofrequency/Microwave Radiation Biological Effects and safety standards: a review. AD-A282 886, Rome Laboratory, U.S. Air Force Material Command, Griffiss Air Force Base, New York.

[6] Havas, M. 2013. Radiation from wireless technology affects the blood, the heart, and the autonomic nervous system. *Rev. Environ. Health.* 28(Nov 2013), 75-84.

[8] Adams, J. A., Galloway, T. S., Mondal, D., Esteves, S. C. 2014 Effect of mobile telephones on sperm quality: A systematic review and meta-analysis. *Environment. Int.* 70, 106-112.

[9] Adey, WR. 1993 Biological effects of electromagnetic fields. J Cell Biochem 51:410-416.

[10] Adey W. R. 1981 Tissue interactions with nonionizing electromagnetic fields. *Physiol. Rev.* 61, 435-514.

[11] Dumanskij, J. D., and Shandala, M. G., 1974. The biologic action and hygienic significance of electromagnetic fields of super-high and ultrahigh frequencies in densely populated areas. *Effects and Health Hazards of Microwave Radiation, Proceedings of an International Symposium*, Warsaw, 15-18 Oct. 1973, P. Czerski et al., eds.

[12] Dwyer, M. J., Leeper, D. B. 1978 A Current Literature Report on the Carcinogenic Properties of Ionizing and Nonionizing Radiation. *DHEW Publication (NIOSH)* 78-134, March 1978.

[13] Frey, A. H. 1998. Headaches from cellular telephones: are they real and what are the implications? *Environ. Health Perspect.* 106, 101-103.

[14] Khurana, V. G., Hardell, L., Everaert, J., Bortkiewicz, A., Carlberg, M., Ahonen, M. 2010. Epidemiological evidence for a health risk from mobile phone base stations. *Int. J. Occup. Environ. Health* 16, 263-267.

[15] Lai, H. 1997. Neurological effects of radiofrequency electromagnetic radiation relating to wireless communication technology. Paper presented

at the *IBC-UK Conference: "Mobile Phones – Is There a Health Risk?"* www.papcruzin.com/radiofrequency/henry_lai1.htm
[16] Lerner, E. J. 1980. RF radiation: Biological effects. *IEEE Spectrum* 17(Dec 1980), 51-59.
[17] Fragopoulou A, Grigoriev Y, Johansson O, Margaritis LH, Morgan L, Richter E, Sage C. 2010. Scientific panel on electromagnetic field health risks: consensus points, recommendations, and rationales. *Rev. Environ. Health* 25, 307-317.
[18] Levitt, B. B., Lai, H. 2010. Biological effects from exposure to electromagnetic radiation emitted by cell towers base stations and other antenna arrays. *Environ. Rev.* 18, 369-395.
[19] Murbach, M., Neufeld, E., Christopoulou, M., Achermann, P., Kuster, N. 2014. Modeling of EEG electrode artifacts and thermal ripples in human radiofrequency exposure studies. *Bioelectromagnetics* 35, 273-283.
[20] Walleczek, J. 1992. Electromagnetic field effects on cells of the immune system: the role of calcium signaling. *FASEB J.* 6, 3177-3185.
[21] Yakymenko, I., Sidorik, E., Kyrylenko, S., Chekhun, V. 2011. Long-term exposure to microwave radiation provokes cancer growth: evidences from radars and mobile communication systems. *Exp. Oncol.* 33(2), 62-70.
[22] Herbert, M. R., Sage, C. 2013 Autism and EMF? Plausibility of a pathophysiological link – Part I. *Pathophysiology* 20, 191-209.
[23] Herbert, M. R., Sage, C. 2013. Autism and EMF? Plausibility of a pathophysiological link part II. *Pathophysiology* 20, 211-234.
[24] Pall, M. L. 2015. Scientific evidence contradicts findings and assumptions of Canadian Safety Panel 6: microwaves act through voltage-gated calcium channel activation to induce biological impacts at non-thermal levels, supporting a paradigm shift for microwave/lower frequency electromagnetic field action. *Rev. Environ. Health* 3, 99-116.
[25] Panagopoulos, D. J., Johansson, O., Carlo, G. L. 2015. Real versus simulated mobile phone exposures in experimental studies. *BioMed. Res. Int.* 2015, article ID 607053, 8 pages.
[26] Pilla, A. A. 2013 Nonthermal electromagnetic fields: from first messenger to therapeutic applications. *Electromagn. Biol. Med.* 32, 123-136.
[27] Markov, M. S., Ed. 2015. *Electromagnetic Fields in Biology and Medicine*. CRC Press, Taylor and Francis Group, Boca Raton, FL.
[28] Belyaev, I. 2015. Biophysical mechanisms for nonthermal microwave effects. In: *Electromagnetic Fields in Biology and Medicine*, Marko S. Markov, ed, CRC Press, New York, pp 49-67.
[29] Panagopoulos, D. J., Johansson, O., Carlo, G. L. 2013. Evaluation of specific absorption rate as a dosimetric quantity for electromagnetic fields bioeffects. *PloS ONE* 8(6): e62663. doi:10:1371
[30] Pall, M. L. 2013. Electromagnetic fields act via activation of voltage-gated calcium channels to produce beneficial or adverse effects. *J. Cell. Mol. Med.* 17,958-965.
[31] Sheppard, A. R., Swicord, M. L., Balzano, Q. 2008. Quantitative evaluations of mechanisms of radiofrequency interactions with biological molecules and processes. *Health Phys.* 95, 365-396.
[32] Canadian Royal Society Expert Panel Report on Radiofrequency Fields. 2014. https://rsc-src.ca/sites/default/files/pdf/SC6_Report_Formatted_1.pdf (accessed July 14, 2014).
[33] Pilla, A. A. 2012. Electromagnetic fields instantaneously modulate nitric oxide signaling in challenged biological systems. *Biochem. Biophys. Res. Commun.* 426, 330-333.
[34] Hardell, L., Sage, C. 2008. Biological effects from electromagnetic field exposure and public exposure standards. *Biomed. Pharmacother.* 62, 104-109.