TOPIC #5: QUALITY ASSURANCE

SYNOPSIS

Prepared by
Fred Dietrich
Electric Research and Management, Inc.
Pittsburgh, PA

Purpose

To summarize the state of knowledge of engineering-related quality-assurance measures for EMF laboratory, epidemiology, and exposure assessment studies.

To provide the NIEHS risk assessment process with criteria for ascertaining quality of engineering in EMF studies.

Summary

Engineering quality assurance in electric- and magnetic-field research is often taken to mean assurance that field conditions are accurately quantified. Over the past 20 years, “quantification” has evolved from simply measuring the rms intensity of the electric or magnetic field to characterizing a variety of field parameters that have been suggested as having a possible role in biological interactions. Moreover, engineering quality assurance has broadened from its focus on field conditions to an assessment of whether other environmental factors—such as heat, vibration, noise, and so on—that correlate with fields might be a factor in laboratory research.

Relevant Concerns

Work conducted to characterize human exposure to electric and magnetic fields or to reproduce relevant field exposures in the laboratory in order to identify potential adverse health impacts is hampered by uncertainty about which aspects of field exposure, if any, are biologically relevant. The inability to obtain unambiguous biological responses in highly exposed human populations (e.g., bare-hand electric transmission-line workers) or highly exposed *in-vivo* or *in-vitro* laboratory model systems prevents evaluation of the relevance of various field parameters. Moreover, the abundance of hypothesized mechanisms by which weak fields might interact with biological systems suggests that simple quantification of field intensity could be an ineffective representation of biologically relevant dose. Valberg (1995) described 18 aspects of magnetic field and related exposures that may be relevant to exposure assessment in humans or characterization of laboratory exposures of *in-vitro* or *in-vivo* subjects:

- Intensity of the magnetic field;
- Timing and duration of each EMF exposure;
- Repetition of exposure periods;
- Circadian time of exposure;
- Frequency of field oscillation;
- Harmonic content;
- Intermittency;
- Turn-on, turn-off transients;
- Coherence in time;
- Circular and linear polarization;
- Relative orientation and magnitude of AC and DC magnetic fields;
- Spatial homogeneity;
- Superimposed electric fields;
- Static (earth's) magnetic field;
- Incidental unplanned EMF exposure;
- Geometry of the cell culture system;
- Size, number, and movement of exposed animals; and
- Accessory non-EMF exposure.

Justification exists for adding more parameters to that list.

Unfortunately, most studies of human exposure focus on rms intensity and possibly some coarse analysis of temporal variability in rms levels. Even in laboratory experiments using controlled exposure conditions, researchers seldom report more than about half of the parameters Valberg identifies as potentially relevant. Unmeasured or unreported characteristics of the field or accessory agents might be important uncontrolled variables.

Instrumentation

A variety of instruments is available to measure ELF electric and magnetic fields. These range from simple survey meters to logging exposure monitors and rather sophisticated instrumentation systems. Minimum specifications (IEEE, 1994a; IEEE, 1994c) and calibration procedures (IEEE, 1994a; IEEE, 1994b; IEEE, 1994c) are well established but sometimes not rigorously followed by the manufacturer and/or user. Credibility of results is enhanced in those studies where the investigators report periodic calibration of their instrumentation over the range of field conditions they seek to measure. Much, but not all, of the available instrumentation performs well when measuring power-frequency fields; however, many instruments are not accurate at other frequencies (EPA, 1992). Hence, the investigator must interpret field measurements in light of the frequency response of the field meter near video display terminals, home electronic equipment, industrial equipment, electrified transportation systems, and other devices that produce other than power-frequency fields.

Instrumentation to characterize transient and "pulsed" fields is not standardized. Wide-bandwidth sensors that respond directly to the magnetic field are scarce. Large pulsed fields have been measured with Hall sensors, but their limited bandwidth raises questions about the accuracy of recorded rise and fall times. Fluxgate sensors offer significant improvement in sensitivity and bandwidth, but have not been used extensively. Many measurements are made with sensing coils that produce an output voltage proportional to the dB/dt of the field. The magnetic-field waveform can be derived from dB/dt (e.g., Lerchl et al., 1990), but not all investigators do so. On some occasions, the magnetic-field derivative waveform is incorrectly reported as the magnetic-field waveform. On other occasions, pulsed or transient field waveforms are not measured. Characteristics of current or voltage waveforms applied to the field-generating device may be reported, with no evidence that the resulting fields actually have similar waveforms. Hence, the quality of engineering data on transient or pulsed field exposures must be evaluated case-by-case.

Laboratory Research

Laboratory research seeking to shed light on the biological effects of ELF electric- or magnetic-field exposure has been hampered by the lack of robust, easily replicable findings. Reported observations tend to be subtle, and require appropriate exposure equipment and procedures to ensure that the observed effects are in fact due to fields and not another factor. Heat, noise, vibration, and corona from the exposure equipment have received varying degrees of attention in different laboratories. Some laboratories have measured temperature, but most dismiss noise, vibration, and corona if they are not detectable by the investigator's ear, touch, or sight. Actual measurements of those agents have been made in few exposure systems. When they have, their interpretation is hampered by lack of information about thresholds at which they pose a concern.

Weaver (Weaver et al., 1997) has discussed the importance of temperature control and suggested that small differences that would have escaped detection in most measurements could be relevant. The use of double-wound coils for magnetic-field production (Kirschvink, 1992) helps mitigate possible temperature effects but does not control for vibration (Jones et al., 1996) as some have claimed. Some exposure equipment physically isolates racks holding exposure subjects of cultures from the field-producing apparatus to minimize vibratory coupling. Vibration is more likely a concern in other systems lacking such isolation, especially those systems with ferromagnetic (e.g., mu-metal) shields supporting the racks holding exposure subjects or material. Because of the uncertain role of exposure to agents auxiliary to the electric or magnetic field, replication in a second laboratory or in a second exposure system is especially critical.

Because electric- and magnetic-field effects may be subtle and possibly sensitive to differences in environmental factors or handling, simultaneous double-blind real and sham exposure is viewed as an important quality-control procedure in those experiments where it is possible. Random or counter-balanced assignment of the active and sham exposure units is required, with blinding for maximum effectiveness. Frequent sham-sham experiments to identify non-field-related differences in outcome between exposure units is another important quality-control action that has probably been underused in most research.

Failures to replicate findings between laboratories can arise for a number of reasons. As discussed above, one engineering-related cause is the involvement of an agent auxiliary to the electric or magnetic field. Another possible cause is the involvement of an uncontrolled and unquantified attribute of the exposure field. Much attention has been drawn to the possible significance of transients and harmonics, but there is little methodical demonstration of their impact. Field intermittency, polarization, and coherence have been suggested as other possibly relevant attributes. Undoubtedly, there are others. Finally, co-exposures to specific static fields, light at specific colors or intensities, etc. may be critical to an experimental outcome. For this reason, careful and complete characterization and documentation of field parameters and co-exposures is an important part of engineering quality in a laboratory experiment.

Examples of unsuccessful replication attempts within or between laboratories are numerous. While those inconsistent outcomes appear to offer opportunities for systematic research to identify parameters accounting for the discordant results, there have been few cooperative efforts to do so. The few attempts that have been undertaken have not identified such a field parameter. Some unilateral efforts have claimed to identify transients, harmonics, polarization, “noise” fields, etc. as factors accounting inconsistent results, but those reports have generally not been verified by similar research in other laboratories.

Some feel that experimental results in this field suggest that "clean 60-Hz fields" have less impact than "real world" fields. If so, that observation would suggest that greater attention to characterizing the full range of "real world" field attributes is indicated. Such characterization is, of course, a difficult task without systematic evidence from the laboratory as to which field attributes are actually important.

Epidemiology Studies

Assessing the magnetic- or electric-field exposure of subjects in retrospective epidemiology studies is by definition problematic because the relevant exposures occurred in the past. Since the actual exposure can not be directly measured, epidemiologists are forced to estimate past exposure based on measurable or observable surrogates, whether they be contemporaneous field levels, wire codes, job categories, residential proximity to electrical facilities, or calculation of one or more components of previous exposure. Regardless of the approach, retrospective exposure assessment is imprecise. Furthermore, the degree of imprecision of various approaches can not be measured, since the parameter of interest itself can not be measured. Speculation about the relative merit of various approaches or of specific approaches in certain studies is the subject of numerous journal articles and was a central issue in the recent EMF RAPID Science Review Symposium on Epidemiological Research Findings (NIEHS, 1998).

Aside from the question of effectiveness of various exposure-assessment methodologies, which has been discussed elsewhere, the engineering quality control in the actual conduct of the major epidemiology studies has been generally good. Engineering quality control has been generally good in major epidemiology studies. Studies with a field-measurement component have usually developed carefully crafted protocols, used quality instruments, and regularly verified the instruments' calibration. Measurement personnel have generally been well trained. Cost, rather than correctable data-quality issues, has limited the scope and duration of the measurements. Studies using observational data (such as wiring configurations for exposure assessment) have usually recorded field observations in detail, using rigorous protocols and appropriate measurement instruments. Many studies have repeated some portion of the observations, using different personnel to gauge the effectiveness of the protocols and observer training. Data management and internal quality-assurance checks have been very good in the larger studies. These features of the epidemiology studies account for the repeatability of exposure-assessment determinations under the protocols of the individual studies (Dovan et al., 1993). The accuracy of exposure assessment in epidemiology studies is limited to a far greater extent by the uncertainty regarding relevant dose metrics, unavoidable time delays between assessment and the relevant exposure time, and practical limitations in measurement scope due to cost rather than to engineering data-quality issues.

Field Measurement Studies

Field measurement studies have ranged from small efforts that are sometimes poorly reported to large systematic studies carried out in accordance with relatively formal protocols. Due to the limited reporting of the smaller efforts, no statements can be made about their overall data quality. The credibility of those small studies must be evaluated case-by-case. Engineering quality control in the larger studies is generally very good and consistent with the intent of the study. However, those studies are very different in purpose. Some (e.g., Zaffanella, 1993) have focused measurement of limited field attributes (such as rms intensity of the magnetic field over a limited frequency range) on large statistical samples of people, sites, and so on. In those studies, appropriate care is generally taken in the selection of unbiased samples. Other studies (e.g., Dietrich et al., 1993) have concentrated detailed characterization of static and ELF field attributes (including transients) but on a necessarily limited sample of sites or sources. In those studies, the focus has been on obtaining quality data on a comprehensive list of field attributes.

Implications for Risk Assessment

The quality of the engineering aspects of electric- and magnetic-field research has improved markedly over the last few decades. Available instrumentation has for some time permitted detailed quantification of human or laboratory subject exposure to fields and related environmental agents with a precision far beyond that required to identify thresholds or dose-response relationships for poorly defined biological endpoints. As engineering quality has improved, exposure characterization has become more extensive, and design and procedural steps have been included to mitigate the unwanted influence of environmental agents correlated with exposure.

While no identifiable date divides studies with poor quality engineering from studies with good quality engineering, the thoroughness of the exposure quantification and the presence of procedural features such as randomized double-blind exposures, the use of positive and negative controls, and the use of sham-sham exposures to identify and mitigate possible sources of systematic error are consistent with high quality.

Independent external quality-control visits and measurements by personnel from NIST, DOE, or elsewhere have also been a part of many studies for the last 20 years and add credibility to those studies. Table 5-1, at the end of this section, identifies laboratories sponsored by governmental or major private funding sources that have received independent quality-control visits from representatives of NIST or the DOE.

Remaining Questions

The capability exists to characterize, completely and precisely, the exposure of humans, laboratory animals or *in-vitro* preparations to electric and magnetic fields. However, past measurements have focused on only a subset of the possibly relevant field parameters. There is no clear answer to the question of how detailed exposure quantification must be in order to be meaningful. If one of the infrequently characterized field parameters has a central role in determining the biological relevance of field exposure, its lack of control could contribute to the difficulty in replicating experiments in different laboratories. On the other hand, comprehensive field characterization is expensive and diverts funds from the critical need to identify and characterize biological responses. This question will probably remain an issue of investigator opinion until a better understanding of electric- or magnetic-field "dose" emerges.

References

Dietrich, F.M., P.N. Papas, W.W. Feero, W.L. Jacobs, and G.A. Steiner (1993), Safety of High Speed Guided Ground Transportation Systems: Magnetic and Electric Field Testing of the Massachusetts Bay Transportation Authority (MBTA) Urban Transit System, Report DOT/FRA/ORD-93/05.I & II, US Department of Transportation, Washington, DC.

Dovan, T., W.T. Kaune, and D.A. Savitz (1993), “Repeatability of Measurements of Residential Magnetic Fields and Wire Codes,” Bioelectromagnetics 14:145-159.

EPA (1992), Laboratory Testing of Commercially Available Power Frequency Magnetic Field Survey Meters, Report 400R-92-010, US Environmental Protection Agency, Washington, DC.

IEEE (1994a), IEEE Recommended Practice for Instrumentation Specifications for Magnetic Flux Density and Electric Field Strength Meters - 10 Hz to 3 kHz, Std 1308-1994, Institute of Electrical and Electronic Engineers, New York, NY.

IEEE (1994b), IEEE Standard Procedure for Measurement of Power Frequency Electric and Magnetic Fields From AC Power Lines, Std 644-1994, Institute of Electrical and Electronic Engineers, New York, NY.

IEEE (1994c), <u>IEEE Standard Test Procedures for the Measurement of Electric and Magnetic Fields From Video Display Terminals (VDTs) From 5 Hz to 400 kHz</u>, Std 1140-1994, Institute of Electrical and Electronic Engineers, New York, NY.

Jones, R.A., J. Walleczek, and W.R. Adey (1996), “Mechanical Vibrations in ‘Double Wound’ Magnetic Field Exposure Coils,” Bioelectromagnetics 17:516-518.

Kirschvink, J.L. (1992) “Uniform Magnetic Fields and Double-Wrapped Coil Systems: Improved Techniques for the Design of Bioelectromagnetic Experiments,” Bioelectromagnetics 13:401-411.

Lerchl, A., K.O. Nonaka, K.-A. Stokkan, and R.J. Reiter (1990), "Marked Rapid Alterations in Nocturnal Pineal Serotonin Metabolism in Mice and Rats Exposed to Weak Intermittent Magnetic Fields," Biochemical and Biophysical Research Communications 169:102-108.

NIEHS (1998), <u>EMF Science Review Symposium Breakout Group Reports for Epidemiological Research Findings</u>. Report of the National Institute of Environmental Health Sciences, Research Triangle Park, NC.

Valberg, P.A. (1995), “Designing EMF Experiments: What is Required to Characterize ‘Exposure’,” Bioelectromagnetics 16:396-401.

Weaver, J.C., G.T. Martin, and T.E. Vaughn (1997) “Molecular Changes Due to Temperature Variations Within Biological Systems are Larger Than Those Expected From Weak EMF Exposures,” presented at the Annual Review of Research on Biological Effects of Electric and Magnetic Fields From the Generation, Delivery, and Use of Electricity, November 9-13, San Diego, CA.

Zaffanella L.E. (1993), <u>Survey of Residential Magnetic Field Sources</u>. Report TR-102759. Electric Power Research Institute. Palo Alto, CA.

Table 5-1: Quality-control site visits and verification measurements of exposure conditions

Facility	Investigator	Sponsor	NIST Visit	*	DOE Visit	*
Argonne National Laboratory	C. Ehret K. Groh	DOE			one or more visits per yr. 1979 - 89	
Argonne National Laboratory	G. Woloschak	NIEHS RAPID			8/9/96	x
Battelle PNL	L. Anderson et al.	DOE EPRI NYSPLP NIEHS	1/12/83 1/28-29/87 10/5-6/88 5/3/90 6/19-20/96 2/24-25/97	 x x x x x	one or more visits per yr. 1979 - 97 10/22/82 10/05/88	 x x
Bowman-Grey Med Ctr.	J. Lymengrover	NYSPLP			8/25/82	
Brookhaven National Laboratory	A. Carsten	NYSPLP	3/28-29/83 4/12/84 1/29/86	 x x	one or more visits per yr. 1983 - 85	
Brown Univ. / Roger Williams Hospital	S. Mehta C. Polk	NIEHS RAPID			10/31/96	x
California Dept. Of Health Services	R. Neutea et al.	CDHS	5/2/89 2/9/91		3/31/89 4/17/91	
California Inst. of Technology	J. Kirschvink	NIEHS RAPID			3/13/96	
Catholic Univ.	T. Litovitz	NIEHS RAPID			2/11/97	x
Colorado State Univ.	J. Reif	NIEHS DOE RAPID			2/15/95 6/26/96	
Columbia Magnetics		DOE	5/9/94	x		
Columbia Univ.	M. Blank	EPRI DOE NIEHS RAPID	2/2/94	x	4/20/93 1/14/97	 x
Columbia Univ.	R. Goodman	DOE EPRI NIEHS RAPID	2/2/94	x	1/30/86 8/20/91 4/20/93 1/15/97	 x
Columbia Univ.	R. Miller T. Hei H. Lieberman	NIEHS RAPID			1/15/97	x
Florida Atlantic Univ.	D. Binninger	NIEHS RAPID			2/28/96	x

Facility	Investigator	Sponsor	NIST Visit	*	DOE Visit	*
Hunter College	A. Henderson	DOE	7/13/88	x	1/30/86	
		EPRI			12/1/89	x
					8/20/91	
					4/13/93	x
					5/12/94	x
Institute for Basic Research - Rockefeller U.	J. Charey W. Bailey	DOE			one or more visits per yr. 1980 - 85	
IIT Research Institute	M. Preech	DOE			6/13/79 9/12/79	
IIT Research Institute	D. McCormick et al.	NIEHS	5/26-27/93	x	9/24/97	x
			9/8-9/94	x		
			9/28-29/95	x		
			11/7-8/96	x		
Institut Armand Frappier (Univ. of Quebec)	R. Mandeville	NIEHS	4/22-23/93	x	10/17/96	x
		RAPID	7/31-8/1/95	x		
		et al.				
Lawrence Berkeley Laboratory	R. Liburdy et al.	DOE			one or more visits per yr. 1986 - 97	x
		NIEHS				
		RAPID				
					7/9/96	x
					8/20/97	
Los Alamos National Laboratory - Sandea	R. Toby	DOE			one or more visits per yr. 1979 - 81	
Louisiana State Univ. Med. School	A. Marino	DOE	7/17/81	x	7/17/81	
		NIEHS			2/27/96	
		RAPID				
Massachusetts Inst. of Technology	J. Weaver	DOE			10/30/96	
Michigan State University	J. Trosko	EPRI	12/5/96	x		
Midwest Research Institute	C. Graham	NYSPLP	11/10/82		one or more visits per yr. 1982 - 97	x
		DOE	3/17-18/83	x		
		EPRI	1/13/94	x		
		NIEHS			6/25/96	x
		RAPID			9/23/97	
New Jersey School of Medicine and Dent.	A. Gona	NYSPLP	5/9/84	x	one or more visits per yr. 1983 - 85	
			4/11/96	x		
New York Dept of Health - Wadsworth	J. Wolpaw	NYSPLP	3/19-20/84	x	one or more visits per yr. 1984 - 86	
	R. Seegal		4/8/86	x		
Oakland University, Henry Ford Hospital	A. Liboff				4/16/87 2/23/88	
Polytechnic Institute of New York	K. Salzinger	NYSPLP	6/27/85	x	7/13/83	
			7/17/85	x	3/20/85	
					7/22/85	

Facility	Investigator	Sponsor	NIST Visit	*	DOE Visit	*
Randomline, Inc.	A. Frey	DOE	11/7/80	x	one or more visits per yr. 1979 - 81	
Rhode Island Hospital	R. Aaron	NIEHS RAPID			10/31/96	x
Roswell Park Cancer Institute	S-W. Hui	NIEHS RAPID			11/1/96	x
Southwest Research Institute	J. Orr	DOE	2/27/97 5/16/84 2/27/85 9/6-7/90	 x x x	one or more visits per yr. 1979 - 91 2/27/85	x
Stanford University	J. Walleczek	DOE			8/15/95 7/8/96	
Stanford Research Institute	S. Miller	NIEHS RAPID			12 /20 /94 7/8/96	x x
State Univ. of New York - Binghamton	D. Murrish	NYSPLP	3/20-21/84 4/8/96	x x	one or more visits per yr. 1984 - 86	
State Univ. of New York - Stony Brook	K. McLeod	EPRI NIEHS RAPID	3/12/93	x		
Tulane Univ.	J. Seto	NYSPLP	7/16/81 3/26/84	x x	11/16/79 7/16/81	
Univ. of California, Berkeley	Kreuger M. Yost	DOE	1/83		one or more visits per yr. 1980 - 84	
Univ. of California, Davis	R. Nuccitelli	NIEHS RAPID			7/10/96	x
Univ. of California, Los Angeles Env. Bio. Lab.		DOE	2/25-26/77	x		
Univ. of California, Los Angeles / VA Med. Ctr.	T. Hahn	EPRI NIEHS RAPID	9/29/93 3/26/84	x x		
Univ. of California, Riverside	R. Luben C. Byus	NIEHS DOE			one or more visits per yr. 1983 - 97 3/11/96 8/18-19/97	x x
Univ. of California, San Diego	D. Kripke	NIEHS RAPID			9/15/97	
Univ. of Colorado	D. Savitz	NYSPLP			one or more visits per yr. 1984 - 86	
Univ. of Connecticut		NYSPLP	7/26/84	x	9/6/83 7/26/84	

Facility	Investigator	Sponsor	NIST Visit	*	DOE Visit	*
Univ. of Kentucky	J. Sisken	EPRI NIEHS RAPID	10/23/91 12/17/92	x x	9/25/97	x
Univ. of Maryland Med. Center, Baltimore	M. Cohen	NYSPLP	8/27/84 7/17/85 5/6/96 12/18/86	x x x x	4/18/83 11/15/83 7/25/84 7/17/85	
Univ. of Maryland, Baltimore	Balcer-Kubiczek G. Harrison	NIEHS RAPID	8/23/95	x	8/28/95	
Univ. of Minnesota	F. Uckun	NIEHS RAPID			10/24/96	x
Univ. of Nevada, Reno	G. Craviso	NIEHS RAPID			9/16/97	x
Univ. of North Carolina	H.B. Peng	NIEHS RAPID			10/2/96	x
Univ. of North Carolina	C. Rinehart	NIEHS RAPID	8/1-2/96	x	10/2/96	x
Univ. of Rochester	S. Michaelson M. Miller S. Stern	DOE EPRI	12/14-15/82 4/6/89 2/22/90 4/4/92	 x x x	one or more visits per yr. 1979 - 90 4/3/90 5/14/92 4/14/94	 x
Univ. of Texas Health Science Ctr.	W. Winters	NYSPLP	5/4-5/83 12/15/83	x x	one or more visits per yr. 1983 - 84	
Univ. of Texas Health Science Ctr.	R. Reiter	EPRI NIEHS RAPID			10/8/86 3/10/89 3/20/90 10/27/93 2/26/96	 x x x
Univ. of Toronto	P. Basu	NYSPLP	10/11/84 5/1/86	x x	one or more visits per yr. 1984 - 85	
Univ. of Utah	G. Livingston	NYSPLP	7/27/83 8/28/85	x x	one or more visits per yr. 1983 - 85	
Univ. of Utah	Grissom	EPRI	4/12/93	x		
Univ. of Washington	A. Guy	DOE			7/30/80 2/18/84	
Univ. of Washington	L. Costa M. Yost	NIEHS RAPID			9/17/97	x
Univ. of Washington	H. Lai	NIEHS RAPID			3/14/96	x

Facility	**Investigator**	**Sponsor**	**NIST Visit**	*****	**DOE Visit**	*****
Univ. of Western Ontario	K-P. Ossenkopp	NYSPLP			7/14/83 4/25/84	
Univ. of Wisconsin, Parkside	E. Goodman R. Gunderson B. Greenbaum	NYSPLP	5/18/83	x	1/27/83 5/18/83 5/4/84	
US Environmental Protection Agency	C. Blackman	DOE			8/26/82 10/18/91 4/19/95 10/3/96	 x x
US Food and Drug Administration (Rockville)	R. Owen	FDA NIEHS	8/22,28/90 9/21/94 8/29/95 3/22,26/96	 x x x		
US Naval Medical Research Center	J. Thomas	NYSPLP	11/17/84	x	7/12/83 1/17/84 7/16/85	
US National Inst. of Env. Health Science	J-S. Hong	NIEHS RAPID			10/2/96	
US National Inst. of Occupational Safety and Health	G. Lotz	NIOSH	4/10-11/96			
Veteran's Administration Hospital - Loma Linda	W. R. Adey et al.	DOE	1/28/80 1/17/83	x	one or more visits per yr. 1979 - 97	

Notes:

* "x" indicates that independent measurements of exposure fields were made during the visit.