Table 2. Tests of magnetic fields in carcinogenesis bioassays.

Rodent strain	Initiator/(promoter)	EMF exposure[a]	Comments on quality criteria	Results reported by author	Reference
			Tests aimed primarily at detecting initiators		
F344/N rats and $B6C3F_1$ mice (male and female, 100 per sex group)		60-Hz, 2 µT, 0.2 mT, or 1 mT (18.5 hr/d, 7 d/wk for 106 wk); or 60-Hz, 1 mT (intermittent: 1 hr on/1 hr off, 18.5 hr/d, 7 d/wk, 106 wk)	GLP; independent audits of pathology data, specimens, and tables	Equivocal evidence of carcinogenic activity[b] in male rats based on increased incidence of thyroid gland C-cell neoplasms in male rats exposed to 2 µT and 0.2 mT MFs ($p < 0.01$)	(*11–13*)
F344/DuCrj rats (male and female, 48 per sex group)		50-Hz, 0.5 mT, 5 mT 22.6 hr/d for 2 yr	Histopathologic analysis limited to tissues exhibiting macroscopic signs of disease	Negative. A statistically significant ($p < 0.05$) increase in fibroma of the subcutis in male rats was considered not biologically significant when compared to historical controls	(*16*)
F344 rats (female, 50 per group)		60-Hz, 2 µT, 20 µT, 200 µT, or 2 mT (20 hr/d, 2 yr beginning 2 d before birth)	Independent analyses to monitor animal health, and Q/A audits of the exposure systems and pathology data and diagnoses; both the exposure and the histopathologic analyses were conducted under blinded conditions	Negative	(*14*)
C57Bl/6 mice (females, 380 per MF-exposed group)		60-Hz, 1.41 mT, circularly polarized, 18.5 hr/d. Exposure began at 4 wk and ended at natural death (~ 29 mo)	GLP; internal and external peer reviews of the histopathologic diagnoses; the exposure and histopathologic analyses were conducted under blinded conditions	Negative for lymphoid cell neoplasms	(*15*)
CFW mice (male and female). Numbers of animals exposed to the MF = 3 (1st gen.); 44 (2nd gen.); 92 (3rd gen.)		60-Hz, 25 mT (23 hr/d)	Unusual experimental design; limited information provided on some critical aspects of the experimental protocol and pathologic analysis	Positive. Statistically significant increase in lymphoma incidence in third-gen. animals exposed to the MF compared to unexposed controls	(*17*)
			Tests aimed primarily at detecting agents that affect postinitiation stages of carcinogenesis		
Rat mammary gland					
Outbred rats (females, ~ 40–50 per group)	MNU (50 mg/kg, i.v., 1×/wk for 3 wk)	50-Hz, ~ 20 µT ac or dc; 3 hr/d for 15 mo; MF exposure began 2 d after the first injection	Insufficient information on the design of the exposure system and the rat strain employed	Positive. Increased incidence of adenocarcinoma in animals exposed (under 24-hr light conditions) to MNU and ac fields compared to rats exposed to MNU alone ($p < 0.05$); decreased latency in rats exposed (under 12 hr light/12 hr dark) to MNU and ac fields compared to rats exposed to MNU alone ($p < 0.05$); and decreased latency in rats exposed (under 24-hr light condition) to MNU and dc fields compared to rats exposed to MNU alone ($p < 0.05$)	(*29*)
Sprague-Dawley rats (females, 99 per group)	DMBA (5 mg/rat, i.g., 1×/wk for 4 wk)	50-Hz, 100 µT, 24 hr/d, 7 d/wk for 91 d	No histopathologic analysis; all phases of the study conducted under blinded conditions; exposure parameters validated by independent audit; exposure system patterned on an NTP-recommended protocol	Positive. Increased incidence of palpable mammary tumors in rats exposed to the MF compared to sham-exposed animals. At necropsy, increased incidence of macroscopically visible tumors (83% vs 62% at 91 d, $p < 0.05$)	(*32*)
Sprague-Dawley rats (females, 99 per group)	DMBA (10 mg/rat, i.g., 1×)	50-Hz, 100 µT, 24 hr/d, 7 d/wk for 27 wk	All phases of the study conducted under blinded conditions; exposure parameters independently validated at regular intervals	Positive. Increased incidence of palpable mammary tumors in MF-exposed rats compared to sham-exposed controls at wk 13, 14, 15, 17, and 18 ($p < 0.05$). At necropsy, increased incidence of macroscopically visible histologically verified tumors ($p < 0.05$)	(*38*)
Sprague-Dawley rats (females, 99 per group)	DMBA (5 mg/rat, i.g., 1×/wk for 4 wk)	50-Hz, 10 µT, 24 hr/d, 7 d/wk for 91 d	Partial histopathologic analysis; exposure and biochemical measurements conducted under blinded conditions.	Negative	(*31*)
Sprague-Dawley rats (females, 60 per group)	DMBA (7 mg/rat, i.g., 1×)	50-Hz, 0.25 and 0.5 mT, 15 sec on/15 sec off, 19–21 hr/ d for 21 wk beginning 1 wk followiing DMBA	Use of a rat substrain with a high propensity to develop mammary tumors spontaneously; no vehicle control group; malignant status of tumors not confirmed histologically	Negative	(*30*)

(*Continued*)

Table 2. *Continued.*

Rodent strain	Initiator/(promoter)	EMF exposure[a]	Comments on quality criteria	Results reported by author	Reference
Sprague-Dawley rats (females, 100 per group)	DMBA (5 mg/rat, i.g., 1×/wk for 4 wk)	50-Hz, 0.1 mT or 0.5 mT; or 60-Hz, 0.1 mT for 18.5 hr/d, 7 d/wk for 13 wk	GLP; magnetic field characterizations independently verified; pathology slides, data records, and tables verified by independent evaluation and reviewed, under blinded conditions, by the NTP Pathology Working Group; complete study audit by an independent Q/A contractor	Negative, but high control incidences of mammary tumors precluded a determination of possible magnetic field effects	(*33,34*)
Sprague-Dawley rats (females, 100 per group)	DMBA (2 mg/rat, i.g., 1×/wk for 4 wk)	50-Hz, 0.1 mT or 0.5 mTfor 18.5 hr/d, 7 d/wk for 13 wk		Negative	(*33,34*)
Sprague-Dawley rats (females, 100 per group)	DMBA (10 mg/rat, i.g., 1×)	50-Hz, 0.1 mT or 0.5 mT; or 60-Hz, 0.1 mT for 18.5 hr/d, 7 d/wk for 26 wk		Negative	(*33,35*)
Mouse skin—promotion					
SENCAR mice (females, 56 per group; nontumor biomarkers for tumor promotion were examined in an additional 24 mice per group)	DMBA (10 nmol/mouse, topical)	60-Hz, 2 mT, 6 hr/d, 5 d/wk for 23 wk	GLP	Negative for skin tumors and nontumor biomarkers	(*54,55*)
Mouse skin—co-promotion					
SENCAR mice (females, 56 per group; nontumor biomarkers for tumor promotion were examined in an additional 24 mice per group)	DMBA (10 nmol/mouse, topical, 2 wk prior to TPA); +/– TPA (1.04, 2, or 4.2 µg/wk)	60-Hz, 2 mT, 6 hr/d, 5 d/wk for 23 wk	GLP	Negative for skin tumors and nontumor biomarkers	(*52,54,55*)
SENCAR mice (sex unspecified, 47–48 per group)	DMBA (10 nmol)/mouse, topical/(PMA, 0.3 µg/mouse/wk for 23 wk beginning 1 wk following DMBA)	60-Hz, 2 mT, 6 hr/d, 6 d/wk for 23 wk		Negative.	(*53*)
K2 mice (female transgenics over-expressing ODC and their nontransgenic littermates, 21–22 per group)	UV (200 J/m^2, 3×/wk) for 10.5 mo	50-Hz, continuous: 0.1 mT; intermittent: 1.3, 13, and 130 µT, each applied in succession for 20 min followed by a 2 hr pause. Both conditions applied 24 hr/d for 10.5 mo except for UV exposure time and cage and room cleaning (2 hr/wk)	Inadequate detail in data presentation	Positive. Statistically significant ($p < 0.015$) increase in rate of onset of macroscopically detectable tumors in both transgenic mice exposed to UV and MFs compared to UV controls	(*56*)
SENCAR mice (number per group not reported)	DMBA (10 nmol/mouse, topical)/(TPA (0.25 mg)/mouse, 2×/wk)[c]	60-Hz, continuous: 0.2 mT and 2 mT; intermittent (30 min on/30 min off): 2 mT. Both conditions applied 7 hr/d, 7 d/wk for 43 wk	Insufficient information provided for analysis	Positive. 0.2 mT, continuous: 20% increase in tumor incidence at 43 wk; 22% increase in total tumors/papillomas and tumors/papillomas per animal at 43 wk. 2 mT, intermittent: small increase in tumors/papillomas per animal between 10–20 wk. Authors do not indicate whether results were statistically significant	(*57*)
Mouse lymphoma					
C57Bl/6 mice (females, 190–380 per group)	Ionizing radiation (cobalt 60): 3.0 Gy, 4.0 Gy, or 5.1 Gy, delivered as fractionated doses at 4 weekly intervals beginning at 4 wk	60-Hz, 1.41 mT, circularly polarized, 18.5 hr/d. Exposure began at 4 wk and ended at 29 mo	GLP; internal and external peer reviews of the histopathologic diagnoses; exposure and histopathologic analyses conducted under blinded conditions	Negative for a variety of lymphoid/leukemia neoplasms.	(*15*)

(*Continued*)

Table 2. *Continued.*

Rodent strain	Initiator/(promoter)	EMF exposure[a]	Comments on quality criteria	Results reported by author	Reference
Swiss-Webster mice (male and female, 75-89 per sex group)	DMBA (35 µg/ mouse, 1×, s.c. at birth)	50-Hz, 1 mT (3 hr/d, 6 d/wk for 16 wk beginning at 14 d of age	Incomplete data presentation	Statistically significant ($p < 0.01$) increase in metastatic infiltration by lymphoma cells into liver in the MF-exposed group compared to sham-exposed controls. No statistically significant differences between MF-exposed and sham-exposed groups in thymic lymphoma incidence at 32 wk	(*84*)
Rat leukemia transplant					
F344 Fischer rats (males, 126/group)	LGL leukemia cells (2.2×10^7/rat, i.p.) injected on the first d of MF exposure	60-Hz, 1 mT, 20 hr/d, 7 d/wk for 18 wk	GLP; progress of experiments periodically reviewed by an independent auditor; positive control group receiving 5 Gy whole body irradiation included	Negative. Disease parameters (body weight, splenomegaly) monitored for 18 wk. Hematologic, morphologic, and and histopathologic parameters monitored for 10–11 wk by repeated bleeding (18 animals per group) and serial sacrifice (108 animals per group)	(*80–82*)
F344 Fischer rats (males, 18/group)	LGL leukemia cells (2.2×10^7 or 2.2×10^6 cells/rat, i.p.) injected on the first d of MF exposure	60-Hz, 1 mT, continuous or intermittent (3 min on/off), 20 hr/d, 7 d/wk for 22 wk	GLP; characteristics of magnetic field exposure validated by the National Institute of Standards and Technology	In the group exposed to intermittent fields, enhancement of the onset of leukemia in the group injected with 2.2×10^7 cells only ($p < 0.01$). Hematologic parameters monitored for 14 wk wk (2.2×10^7 injected cell groups) or 16 wk (2.2×10^6 injected cell groups)	(*79*)
Lymphoma/leukemia-prone mouse strains—transgenic systems					
TSG-*p53* mice (hemizygous for the *p53* null-allele) (males and females, 30/sex group)		60-Hz, 1 mT, 18.5 hr/d for 23 wk	GLP	Negative	(*77*)
Eµ-*pim*-1 mice (males and females, 30/sex group)	ENU (25 mg/kg, 1×, i.p.) one d prior to MF exposure	60-Hz, 2 µT, 200 µT, 1 mT (continuous, 18.5 hr/d for 23 wk); or 60-Hz, 1 mT (intermittent, 1hr on/1 hr off, 18.5 hr/d for 23 wk)		Negative. Lymphoma incidence in males exposed to 1 mT continuous fields significantly reduced ($p < 0.05$) compared to controls	(*77*)
Eµ-*pim*-1 mice (females, ~ 100/ group)		50-Hz, 1 µT, 100 µT, or 1 mT (continuous, 20 hr/d) up to 18 mo; and 50-Hz, 1 mT (pulsed, 15 min on/off)	Necropsies performed only on animals exhibiting clinical signs of disease; incomplete analysis due to autolysis or other causes; exposure and pathology conducted under blinded conditions; histopathology independently evaluated; positive control (ENU) included	Negative. Statistically significant increase in a lethal nontumor end point: a transgene-dependent renal glomerular disease in 1 mT (continuous) MF-exposed group compared to sham-exposed controls	(*83*)
Lymphoma/leukemia-prone mouse strains—leukemia-prone mice					
AKR mice		12-Hz, 6 µT; or 460-Hz, pulsed. Both exposures for 30 min, 2×/wk for 5 generations	Incomplete characterization of exposure and other aspects of study protocol; high spontaneous incidence of leukemia in control	Negative for leukemia	(*85*)
Rat brain					
F344/N (females, 50/group)	ENU (5 mg/kg i.v. on d 18 of gestation)	60-Hz, 2 µT, 20 µT, 200 µT, or 2 mT for 16 mo beginning 48 hr after ENU treatment	GLP; variability in tumor indidence among control groups; exposure, clinical observations, and pathologic evaluations conducted under blinded conditions; exposure system and pathology evaluations validated by independent audit; pathology slides reviewed under blinded conditions; positive control (TPA) included	Negative	(*133*)
C57Bl/6 mice (females, 190-380 per group)	Ionizing radiation (cobalt 60): 3.0 Gy, 4.0 Gy, or 5.1 Gy, delivered as fractionated doses at 4 weekly intervals beginning at 4 wk	60-Hz, 1.41 mT, circularly polarized, 18 hr/d. Exposure began at 4 wk and ended at 29 mo	GLP; internal and external peer reviews of the histopathologic diagnoses; exposure and histopathologic analyses conducted under blinded conditions	Negative	Babbitt et al. (see discussion of the RAPID Working Group (*3*)

Abbreviations: d, day; ENU, *N*-ethyl-*N*-nitrosourea; gen., generation; J, joule; mo, month; PMA, phorbol 12-myristate 13-acetate; TPA, 12-*O*-tetradecanoylphorbol-13-acetate wk, weeks; yr, year; ~, approximately. [a]ac fields are sinusoidal unless otherwise noted. [b]An evidence category used by the NTP. Equivocal evidence of carcinogenic activity is demonstrated by studies that are interpreted as showing a marginal increase of neoplasms that may be exposure related (*11*). [c]This very high dose of TPA is most likely a typographical error in Byus et al. (*57*).