Appendix 2
Activity profiles for genetic and related tests

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Methods

The x-axis of the activity profile represents the bioassays in phylogenetic sequence by endpoint, and the values on the y-axis represent the logarithmically transformed lowest effective doses (LED) and highest ineffective doses (HID) tested. The term 'dose', as used in this report, does not take into consideration length of treatment or exposure and may therefore be considered synonymous with concentration. In practice, the concentrations used in all the in-vitro tests were converted to μg/ml, and those for in-vivo tests were expressed as mg/kg bw. Because dose units are plotted on a log scale, differences in molecular weights of compounds do not, in most cases, greatly influence comparisons of their activity profiles. Conventions for dose conversions are given below.

Profile-line height (the magnitude of each bar) is a function of the LED or HID, which is associated with the characteristics of each individual test system — such as population size, cell-cycle kinetics and metabolic competence. Thus, the detection limit of each test system is different, and, across a given activity profile, responses will vary substantially. No attempt is made to adjust or relate responses in one test system to those of another.

Line heights are derived as follows: for negative test results, the highest dose tested without appreciable toxicity is defined as the HID. If there was evidence of extreme toxicity, the next highest dose is used. A single dose tested with a negative result is considered to be equivalent to the HID. Similarly, for positive results, the LED is recorded. If the original data were analysed statistically by the author, the dose recorded is that at which the response was significant ($p < 0.05$). If the available data were not analysed statistically, the dose required to produce an effect is estimated as follows: when a dose-related positive response is observed with two or more doses, the lower of the doses is taken as the LED; a single dose resulting in a positive response is considered to be equivalent to the LED.

In order to accommodate both the wide range of doses encountered and positive and negative responses on a continuous scale, doses are transformed logarithmically, so that effective (LED) and ineffective (HID) doses are represented by positive and negative numbers, respectively. The response, or logarithmic dose unit (LDU_{ij}), for a given test system i and chemical j is represented by the expressions

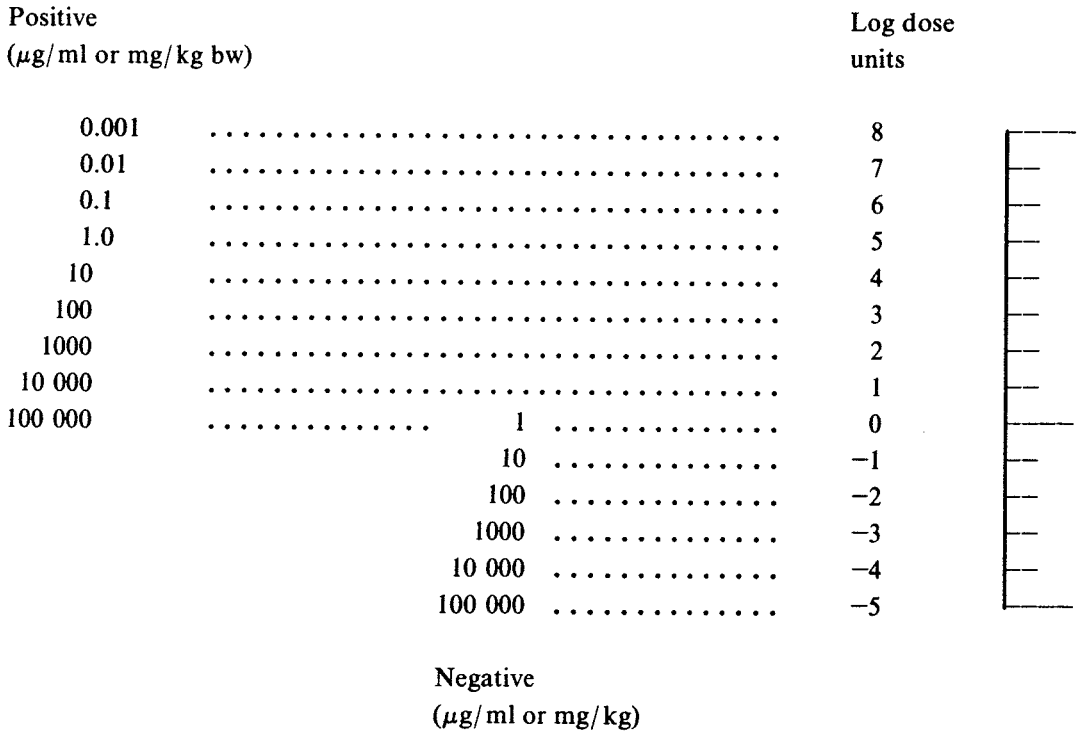
$$LDU_{ij} = -\log_{10}(\text{dose}), \text{ for HID values; } LDU \leqslant 0$$

and (1)

$$LDU_{ij} = -\log_{10}(\text{dose} \times 10^{-5}), \text{ for LED values; } LDU \geqslant 0.$$

These simple relationships define a dose range of 0 to −5 logarithmic units for ineffective doses (1−100 000 μg/ml or mg/kg bw) and 0 to +8 logarithmic units for effective doses (100 000−0.001 μg/ml or mg/kg bw). A scale illustrating the LDU values is shown in Figure 1. Negative responses at doses less than 1 μg/ml (mg/kg bw) are set equal to 1. Effectively, an LED value ≥100 000 or an HID value ≤1 produces an LDU = 0; no quantitative information is gained from such extreme values. The dotted lines at the levels of log dose units 1 and −1 define a 'zone of uncertainty' in which positive results are reported at such high doses (between 10 000 and 100 000 μg/ml or mg/kg bw) or negative results are reported at such low dose levels (1 to 10 μg/ml or mg/kg bw) as to call into question the adequacy of the test.

Fig. 1. Scale of log dose units used on the y-axis of activity profiles



LED and HID are expressed as μg/ml or mg/kg bw.

In practice, an activity profile is computer generated. A data entry programme is used to store abstracted data from published reports. A sequential file (in ASCII) is created for each compound, and a record within that file consists of the name and Chemical Abstracts Service number of the compound, a three-letter code for the test system (see below), the qualitative test result (with and without an exogenous metabolic system), dose (LED or HID), citation number and additional source information. An abbreviated citation for each publication is stored in a segment of a record accessing both the test data file and the citation file. During processing of the data file, an average of the logarithmic values of the data

subset is calculated, and the length of the profile line represents this average value. All dose values are plotted for each profile line, regardless of whether results are positive or negative. Results obtained in the absence of an exogenous metabolic system are indicated by a bar (—), and results obtained in the presence of an exogenous metabolic system are indicated by an upward-directed arrow (↑). When all results for a given assay are either positive or negative, the mean of the LDU values is plotted as a solid line; when conflicting data are reported for the same assay (i.e., both positive and negative results), the majority data are shown by a solid line and the minority data by a dashed line (drawn to the extreme conflicting response). In the few cases in which the numbers of positive and negative results are equal, the solid line is drawn in the positive direction and the maximal negative response is indicated with a dashed line.

Profile lines are identified by three-letter code words representing the commonly used tests. Code words for most of the test systems in current use in genetic toxicology were defined for the US Environmental Protection Agency's GENE-TOX Program (Waters, 1979; Waters & Auletta, 1981). For this publication, codes were redefined in a manner that should facilitate inclusion of additional tests in the future. If a test system is not defined precisely, a general code is used that best defines the category of the test. Naming conventions are described below.

Dose conversions for activity profiles

Doses are converted to μg/ml for in-vitro tests and to mg/kg bw per day for in-vivo experiments.

1. In-vitro test systems
   (*a*) Weight/volume converts directly to μg/ml.
   (*b*) Molar (M) concentration × molecular weight = mg/ml = 10^3 μg/ml; mM concentration × molecular weight = μg/ml.
   (*c*) Soluble solids expressed as % concentration are assumed to be in units of mass per volume (i.e., 1% = 0.01 g/ml = 10 000 μg/ml; also, 1 ppm = 1 μg/ml).
   (*d*) Liquids and gases expressed as % concentration are assumed to be given in units of volume per volume. Liquids are converted to weight per volume using the density (D) of the solution (D = g/ml). If the bulk of the solution is water, then D = 1.0 g/ml. Gases are converted from volume to mass using the ideal gas law, PV = nRT. For exposure at 20-37°C at standard atmospheric pressure, 1% (v/v) = 0.4 μg/ml × molecular weight of the gas. Also, 1 ppm (v/v) = 4×10^{-5} μg/ml × molecular weight.
   (*e*) For microbial plate tests, concentrations reported as weight/plate are divided by top agar volume (if volume is not given, a 2-ml top agar is assumed). For spot tests, in which concentrations are reported as weight or weight/disc, a 1-ml volume is used as a rough approximation.

(*f*) Conversion of asbestos concentrations given in $\mu g/cm^2$ are based on the area (A) of the dish and the volume of medium per dish; i.e., for a 100-mm dish: $A = \pi R^2 = \pi \times (5\ cm)^2 = 78.5\ cm^2$. If the volume of medium is 10 ml, then 78.5 cm^2 = 10 ml and 1 cm^2 = 0.13 ml.

2. In-vitro systems using in-vivo activation

   For the body fluid-urine (BF–) test, the concentration used is the dose (in mg/kg bw) of the compound administered to test animals or patients.

3. In-vivo test systems

   (*a*) Doses are converted to mg/kg bw per day of exposure, assuming 100% absorption. Standard values are used for each sex and species of rodent, including body weight and average intake per day, as reported by Gold *et al.* (1984). For example, in a test using male mice fed 50 ppm of the agent in the diet, the standard food intake per day is 12% of body weight, and the conversion is dose = 50 ppm × 12% = 6 mg/kg bw per day.

   Standard values used for humans are: weight — males, 70 kg; females, 55 kg; surface area, 1.7 m^2; inhalation rate, 20 l/min for light work, 30 l/min for mild exercise.

   (*b*) When reported, the dose at the target site is used. For example, doses given in studies of lymphocytes of humans exposed *in vivo* are the measured blood concentrations in μg/ml.

Codes for test systems

For specific nonmammalian test systems, the first two letters of the three-symbol code word define the test organism (e.g., SA– for *Salmonella typhimurium*, EC– for *Escherichia coli*). In most cases, the first two letters accurately represent the scientific name of the organism. If the species is not known, the convention used is –S–. The third symbol may be used to define the tester strain (e.g., SA8 for *S. typhimurium* TA1538, ECW for *E. coli* WP2*uvrA*). When strain designation is not indicated, the third letter is used to define the specific genetic endpoint under investigation (e.g., ––D for differential toxicity, ––F for forward mutation, ––G for gene conversion or genetic crossing-over, ––N for aneuploidy, ––R for reverse mutation, ––U for unscheduled DNA synthesis). The third letter may also be used to define the general endpoint under investigation when a more complete definition is not possible or relevant (e.g., ––M for mutation, ––C for chromosomal aberration).

For mammalian test systems, the first letter of the three-letter code word defines the genetic endpoint under investigation: A–– for aneuploidy, B–– for binding, C–– for chromosomal aberration, D–– for DNA strand breaks, G–– for gene mutation, I–– for inhibition of intercellular communication, M–– for micronucleus formation, R–– for DNA repair, S–– for sister chromatid exchange, T–– for cell transformation and U–– for unscheduled DNA synthesis.

For animal (i.e., nonhuman) test systems *in vitro*, when the cell type is not specified, the code letters –IA are used. For such assays *in vivo*, when the animal species is not specified, the code letters –VA are used. Commonly used animal species are identified by the third

letter (e.g., ––C for Chinese hamster, ––M for mouse, ––R for rat, ––S for Syrian hamster).

For test systems using human cells *in vitro*, when the cell type is not specified, the code letters –IH are used. For assays on humans *in vivo*, when the cell type is not specified, the code letters –VH are used. Otherwise, the second letter specifies the cell type under investigation (e.g., –BH for bone marrow, –LH for lymphocytes).

Some other specific coding conventions used for mammalian systems are as follows: BF– for body fluids, HM– for host-mediated, ––L for leucocytes or lymphocytes *in vitro* (–AL, animals; –HL, humans), –L– for leucocytes *in vivo* (–LA, animals; –LH, humans), ––T for transformed cells.

Note that these are examples of major conventions used to define the assay code words. The alphabetized listing of codes must be examined to confirm a specific code word. As might be expected from the limitation to three symbols, some codes do not fit the naming conventions precisely. In a few cases, test systems are defined by first-letter code words, for example: MST, mouse spot test; SLP, mouse specific locus test, postspermatogonia; SLO, mouse specific locus test, other stages; DLM, dominant lethal test in mice; DLR, dominant lethal test in rats; MHT, mouse heritable translocation test.

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TABLE 1. ALPHABETICAL LIST OF TEST SYSTEM CODE WORDS

Endpoint	*Code*	*Definition*
C	ACC	*Allium cepa*, chromosomal aberrations
A	AIA	Aneuploidy, animal cells *in vitro*
A	AIH	Aneuploidy, human cells *in vitro*
G	ANF	*Aspergillus nidulans*, forward mutation
R	ANG	*Aspergillus nidulans*, genetic crossing-over
A	ANN	*Aspergillus nidulans*, aneuploidy
G	ANR	*Aspergillus nidulans*, reverse mutation
G	ASM	*Arabidopsis* species, mutation
A	AVA	Aneuploidy, animal cells *in vivo*
A	AVH	Aneuploidy, human cells *in vivo*
F	BFA	Body fluids from animals, microbial mutagenicity
F	BFH	Body fluids from humans, microbial mutagenicity
D	BHD	Binding (covalent) to DNA, human cells *in vivo*
D	BHP	Binding (covalent) to RNA or protein, human cells *in vivo*
D	BID	Binding (covalent) to DNA *in vitro*
D	BIP	Binding (covalent) to RNA or protein *in vitro*
G	BPF	Bacteriophage, forward mutation
G	BPR	Bacteriophage, reverse mutation
D	BRD	Other DNA repair-deficient bacteria, differential toxicity
D	BSD	*Bacillus subtilis rec* strains, differential toxicity
G	BSM	*Bacillus subtilis*, multigene test
D	BVD	Binding (covalent) to DNA, animal cells *in vivo*
D	BVP	Binding (covalent) to RNA or protein, animal cells *in vivo*
C	CBA	Chromosomal aberrations, animal bone-marrow cells *in vivo*
C	CBH	Chromosomal aberrations, human bone-marrow cells *in vivo*
C	CCC	Chromosomal aberrations, spermatocytes treated *in vivo*, spermatocytes observed
C	CGC	Chromosomal aberrations, spermatogonia treated *in vivo*, spermatocytes observed
C	CGG	Chromosomal aberrations, spermatogonia treated *in vivo*, spermatogonia observed
C	CHF	Chromosomal aberrations, human fibroblasts *in vitro*
C	CHL	Chromosomal aberrations, human lymphocytes *in vitro*
C	CHT	Chromosomal aberrations, transformed human cells *in vitro*
C	CIA	Chromosomal aberrations, other animal cells *in vitro*
C	CIC	Chromosomal aberrations, Chinese hamster cells *in vitro*
C	CIH	Chromosomal aberrations, other human cells *in vitro*
C	CIM	Chromosomal aberrations, mouse cells *in vitro*
C	CIR	Chromosomal aberrations, rat cells *in vitro*
C	CIS	Chromosomal aberrations, Syrian hamster cells *in vitro*
C	CIT	Chromosomal aberrations, transformed animal cells *in vitro*
C	CLA	Chromosomal aberrations, animal leucocytes *in vivo*
C	CLH	Chromosomal aberrations, human lymphocytes *in vivo*
C	COE	Chromosomal aberrations, oocytes or embryos treated *in vivo*
C	CVA	Chromosomal aberrations, other animal cells *in vivo*
C	CVH	Chromosomal aberrations, other human cells *in vivo*
D	DIA	DNA strand breaks, cross-links or related damage, animal cells *in vitro*
D	DIH	DNA strand breaks, cross-links or related damage, human cells *in vitro*
C	DLM	Dominant lethal test, mice
C	DLR	Dominant lethal test, rats
C	DMC	*Drosophila melanogaster*, chromosomal aberrations
R	DMG	*Drosophila melanogaster*, genetic crossing-over or recombination
C	DMH	*Drosophila melanogaster*, heritable translocation test
C	DML	*Drosophila melanogaster*, dominant lethal test
G	DMM	*Drosophila melanogaster*, somatic mutation (and recombination)
A	DMN	*Drosophila melanogaster*, aneuploidy
G	DMX	*Drosophila melanogaster*, sex-linked recessive lethal mutations
D	DVA	DNA strand breaks, cross-links or related damage, animal cells *in vivo*
D	DVH	DNA strand breaks, cross-links or related damage, human cells *in vivo*
G	EC2	*Escherichia coli* WP2, reverse mutation
D	ECB	*Escherichia coli* (or *E. coli* DNA), strand breaks, cross-links or related damage; DNA repair
D	ECD	*Escherichia coli pol* A/W3110-P3478 differential toxicity (spot test)
G	ECF	*Escherichia coli* exclusive of strain K12, forward mutation
G	ECK	*Escherichia coli* K12, forward or reverse mutation
D	ECL	*Escherichia coli pol* A/W3110-P3478, differential toxicity (liquid suspension test)
G	ECR	*Escherichia coli* (other miscellaneous strains), reverse mutation
G	ECW	*Escherichia coli* WP2 *uvr*A, reverse mutation
D	ERD	*Escherichia coli rec* strains, differential toxicity
G	G51	Gene mutation, mouse lymphoma L5178Y cells *in vitro*, all other loci

Table 1 (contd)

Endpoint	*Code*	*Definition*
G	G9O	Gene mutation, Chinese hamster lung V79 cells, ouabain resistance
G	GCL	Gene mutation, Chinese hamster lung cells exclusive of V79 *in vitro*
G	GCO	Gene mutation, Chinese hamster ovary cells *in vitro*
G	G9H	Gene mutation, Chinese hamster lung V79 cells, *hprt* locus
G	GIA	Gene mutation, other animal cells *in vitro*
G	GIH	Gene mutation, human cells *in vitro*
G	GML	Gene mutation, mouse lymphoma cells exclusive of L5178Y *in vitro*
G	G5T	Gene mutation, mouse lymphoma L5178Y cells *in vitro*, TK locus
G	GVA	Gene mutation, animal cells *in vivo*
H	HMA	Host-mediated assay, animal cells in animal hosts
H	HMH	Host-mediated assay, human cells in animal hosts
H	HMM	Host-mediated assay, microbial cells in animal hosts
C	HSC	*Hordeum* species, chromosomal aberrations
G	HSM	*Hordeum* species, mutation
I	ICH	Inhibition of intercellular communication, human cells *in vitro*
I	ICR	Inhibition of intercellular communication, animal cells *in vitro*
G	KPF	*Klebsiella pneumonia*, forward mutation
G	MAF	*Micrococcus aureus*, forward mutation
C	MHT	Mouse heritable translocation test
M	MIA	Micronucleus test, animal cells *in vitro*
M	MIH	Micronucleus test, human cells *in vitro*
G	MST	Mouse spot test
M	MVA	Micronucleus test, other animals *in vivo*
M	MVC	Micronucleus test, hamsters *in vivo*
M	MVH	Micronucleus test, human cells *in vivo*
M	MVM	Micronucleus test, mice *in vivo*
M	MVR	Micronucleus test, rats *in vivo*
G	NCF	*Neurospora crassa*, forward mutation
A	NCN	*Neurospora crassa*, aneuploidy
G	NCR	*Neurospora crassa*, reverse mutation
C	PLC	Plants (other), chromosomal aberrations
M	PLI	Plants (other), micronuclei
G	PLM	Plants (other), mutation
S	PLS	Plants (other), sister chromatid exchanges
D	PLU	Plants, unscheduled DNA synthesis
D	PRB	Prophage induction, SOS repair test or DNA strand breaks, cross-links or related damage
C	PSC	*Paramecium* species, chromosomal aberrations
G	PSM	*Paramecium* species, mutation
D	RIA	DNA repair exclusive of unscheduled DNA synthesis, animal cells *in vitro*
D	RIH	DNA repair exclusive of unscheduled DNA synthesis, human cells *in vitro*
D	RVA	DNA repair exclusive of unscheduled DNA synthesis, animal cells *in vivo*
G	SA0	*Salmonella typhimurium* TA100, reverse mutation
G	SA2	*Salmonella typhimurium* TA102, reverse mutation
G	SA3	*Salmonella typhimurium* TA1530, reverse mutation
G	SA4	*Salmonella typhimurium* TA104, reverse mutation
G	SA5	*Salmonella typhimurium* TA1535, reverse mutation
G	SA7	*Salmonella typhimurium* TA1537, reverse mutation
G	SA8	*Salmonella typhimurium* TA1538, reverse mutation
G	SA9	*Salmonella typhimurium* TA98, reverse mutation
D	SAD	*Salmonella typhimurium*, DNA repair-deficient strains, differential toxicity
G	SAF	*Salmonella typhimurium*, forward mutation
G	SAS	*Salmonella typhimurium* (other miscellaneous strains), reverse mutation
G	SCF	*Saccharomyces cerevisiae*, forward mutation
R	SCG	*Saccharomyces cerevisiae*, gene conversion
R	SCH	*Saccharomyces cerevisiae*, homozygosis by mitotic recombination or gene conversion
A	SCN	*Saccharomyces cerevisiae*, aneuploidy
G	SCR	*Saccharomyces cerevisiae*, reverse mutation
G	SGR	*Streptomyces griseoflavus*, reverse mutation
S	SHF	Sister chromatid exchange, human fibroblasts *in vitro*
S	SHL	Sister chromatid exchange, human lymphocytes *in vitro*
S	SHT	Sister chromatid exchange, transformed human cells *in vitro*
S	SIA	Sister chromatid exchange, other animal cells *in vitro*
S	SIC	Sister chromatid exchange, Chinese hamster cells *in vitro*
S	SIH	Sister chromatid exchange, other human cells *in vitro*
S	SIM	Sister chromatid exchange, mouse cells *in vitro*
S	SIR	Sister chromatid exchange, rat cells *in vitro*
S	SIS	Sister chromatid exchange, Syrian hamster cells *in vitro*
S	SIT	Sister chromatid exchange, transformed animal cells *in vitro*
S	SLH	Sister chromatid exchange, human lymphocytes *in vivo*
G	SLO	Mouse specific locus test, other stages
G	SLP	Mouse specific locus test, postspermatogonia
P	SPF	Sperm morphology, F1 mice
P	SPH	Sperm morphology, humans *in vivo*
P	SPM	Sperm morphology, mice
P	SPR	Sperm morphology, rats
D	SSB	*Saccharomyces* species, DNA strand breaks, cross-links or related damage
D	SSD	*Saccharomyces* species, DNA repair-deficient strains, differential toxicity
G	STF	*Streptomyces coelicolor*, forward mutation
G	STR	*Streptomyces coelicolor*, reverse mutation

Table 1 (contd)

Endpoint	*Code*	*Definition*
S	SVA	Sister chromatid exchange, animal cells *in vivo*
S	SVH	Sister chromatid exchange, other human cells *in vivo*
D	SZD	*Schizosaccharomyces pombe*, DNA repair-deficient strains, differential toxicity
G	SZF	*Schizosaccharomyces pombe*, forward mutation
R	SZG	*Schizosaccharomyces pombe*, gene conversion
G	SZR	*Schizosaccharomyces pombe*, reverse mutation
T	TBM	Cell transformation, BALB/c 3T3 mouse cells
T	TCL	Cell transformation, other established cell lines
T	TCM	Cell transformation, C3H 10T1/2 mouse cells
T	TCS	Cell transformation, Syrian hamster embryo cells, clonal assay
T	TEV	Cell transformation, other viral enhancement systems
T	TFS	Cell transformation, Syrian hamster embryo cells, focus assay
T	TIH	Cell transformation, human cells *in vitro*
T	TPM	Cell transformation, mouse prostate cells
T	T7R	Cell transformation, SA7/rat cells
T	TRR	Cell transformation, RLV/Fischer rat embryo cells
T	T7S	Cell transformation, SA7/Syrian hamster embryo cells
C	TSC	*Tradescantia* species, chromosomal aberrations
M	TSI	*Tradescantia* species, micronuclei
G	TSM	*Tradescantia* species, mutation
T	TVI	Cell transformation, treated *in vivo*, scored *in vitro*
D	UBH	Unscheduled DNA synthesis, human bone-marrow cells *in vivo*
D	UHF	Unscheduled DNA synthesis, human fibroblasts *in vitro*
D	UHL	Unscheduled DNA synthesis, human lymphocytes *in vitro*
D	UHT	Unscheduled DNA synthesis, transformed human cells *in vitro*
D	UIA	Unscheduled DNA synthesis, other animal cells *in vitro*
D	UIH	Unscheduled DNA synthesis, other human cells *in vitro*
D	UPR	Unscheduled DNA synthesis, rat hepatocytes *in vivo*
D	URP	Unscheduled DNA synthesis, rat primary hepatocytes
D	UVA	Unscheduled DNA synthesis, other animal cells *in vivo*
D	UVC	Unscheduled DNA synthesis, hamster cells *in vivo*
D	UVH	Unscheduled DNA synthesis, other human cells *in vivo*
D	UVM	Unscheduled DNA synthesis, mouse cells *in vivo*
D	UVR	Unscheduled DNA synthesis, other rat cells *in vivo*
C	VFC	*Vicia faba*, chromosomal aberrations
S	VFS	*Vicia faba*, sister chromatid exchange

ETHANOL[a]

Test code	End point	Test system	Results No act	Act	Dose (LED or HID)	Reference
PRB	D	Prophage induction/SOS repair test/DNA strand breaks, cross-links, etc.	–	0	55000.0000	Kvelland (1983)
ERD	D	Escherichia coli rec strains, differential toxicity	(+)	(+)	25000.0000	De Flora et al. (1984a)
BRD	D	Other DNA repair-deficient bacteria, differential toxicity	–	0	79000.0000	Braun et al. (1982)
SA0	G	Salmonella typhimurium TA100, reverse mutation	–	–	6130.0000	Cotruvo et al. (1977)
SA0	G	Salmonella typhimurium TA100, reverse mutation	–	–	5000.0000	McCann et al. (1975)
SA0	G	Salmonella typhimurium TA100, reverse mutation	–	–	0.0000	Blevins & Shelton (1983)
SA0	G	Salmonella typhimurium TA100, reverse mutation	–	0	0.0000	De Flora et al. (1984a)
SA2	G	Salmonella typhimurium TA102, reverse mutation	(+)	(+)	80000.0000	De Flora et al. (1984b)
SA5	G	Salmonella typhimurium TA1535, reverse mutation	–	–	0.0000	Blevins & Shelton (1983)
SA5	G	Salmonella typhimurium TA1535, reverse mutation	–	–	39500.0000	Blevins & Taylor (1982)
SA5	G	Salmonella typhimurium TA1535, reverse mutation	–	–	6130.0000	Cotruvo et al. (1977)
SA5	G	Salmonella typhimurium TA1535, reverse mutation	–	0	0.0000	De Flora et al. (1984a)
SA7	G	Salmonella typhimurium TA1537, reverse mutation	–	–	0.0000	Blevins & Shelton (1983)
SA7	G	Salmonella typhimurium TA1537, reverse mutation	–	–	39500.0000	Blevins & Taylor (1982)
SA7	G	Salmonella typhimurium TA1537, reverse mutation	–	–	6130.0000	Cotruvo et al. (1977)
SA7	G	Salmonella typhimurium TA1537, reverse mutation	–	0	0.0000	De Flora et al. (1984a)
SA8	G	Salmonella typhimurium TA1538, reverse mutation	–	–	0.0000	Blevins & Shelton (1983)
SA8	G	Salmonella typhimurium TA1538, reverse mutation	–	–	39500.0000	Blevins & Taylor (1982)
SA8	G	Salmonella typhimurium TA1538, reverse mutation	–	–	6130.0000	Cotruvo et al. (1977)
SA8	G	Salmonella typhimurium TA1538, reverse mutation	–	0	0.0000	De Flora et al. (1984a)
SA9	G	Salmonella typhimurium TA98, reverse mutation	–	–	0.0000	Blevins & Shelton (1983)
SA9	G	Salmonella typhimurium TA98, reverse mutation	0	–	29625.0000	Arimoto et al. (1982)
SA9	G	Salmonella typhimurium TA98, reverse mutation	–	–	39500.0000	Blevins & Taylor (1982)
SA9	G	Salmonella typhimurium TA98, reverse mutation	–	–	6130.0000	Cotruvo et al. (1977)
SA9	G	Salmonella typhimurium TA98, reverse mutation	–	0	0.0000	De Flora et al. (1984a)
SAS	G	Salmonella typhimurium (miscellaneous strains), reverse mutation	–	–	6130.0000	Cotruvo et al. (1977)
SCG	R	Saccharomyces cerevisiae, gene mutation	–	0	39450.0000	Barale et al. (1983)
ANG	R	Aspergillus nidulans, genetic crossing-over	+	0	39500.0000	Harsanyi et al. (1977)
SCF	G	Saccharomyces cerevisiae, forward mutation	+	0	150000.0000	Bandas & Zakharov (1980)
SCF	G	Saccharomyces cerevisiae, forward mutation	+	0	15780.0000	Hamada et al. (1985)
SCF	G	Saccharomyces cerevisiae, forward mutation	(+)	0	39250.0000	Cabeça-Silva et al. (1982)
ANF	G	Aspergillus nidulans, forward mutation	–	0	61320.0000	Gualandi & Bellincampi (1981)
ANN	A	Aspergillus nidulans, aneuploidy	+	0	31560.0000	Käfer (1984)
ANN	A	Aspergillus nidulans, aneuploidy	+	0	47000.0000	Morpurgo et al. (1979)
ANN	A	Aspergillus nidulans, aneuploidy	+	0	55230.0000	Gualandi & Bellincampi (1981)
ANN	A	Aspergillus nidulans, aneuploidy	+	0	39500.0000	Harsanyi et al. (1977)
VFS	S	Vicia faba, sister chromatid exchanges	+	0	9200.0000	Schubert et al. (1979)
PLS	S	Plants (other), sister chromatid exchanges	+	0	782.0000	Cortés et al. (1986)
TSI	M	Tradescantia species, micronuclei	+	0	98625.0000	Ma et al. (1984)
PLI	M	Plants (other), micronuclei	–	0	7820.0000	Cortés et al. (1986)
VFC	C	Vicia faba, chromosomal aberrations	+	0	2300.0000	Rieger & Michaelis (1960)
VFC	C	Vicia faba, chromosomal aberrations	+	0	9200.0000	Schubert et al. (1979)
VFC	C	Vicia faba, chromosomal aberrations	+	0	0.0000	Rieger & Michaelis (1970)

ETHANOL (contd)

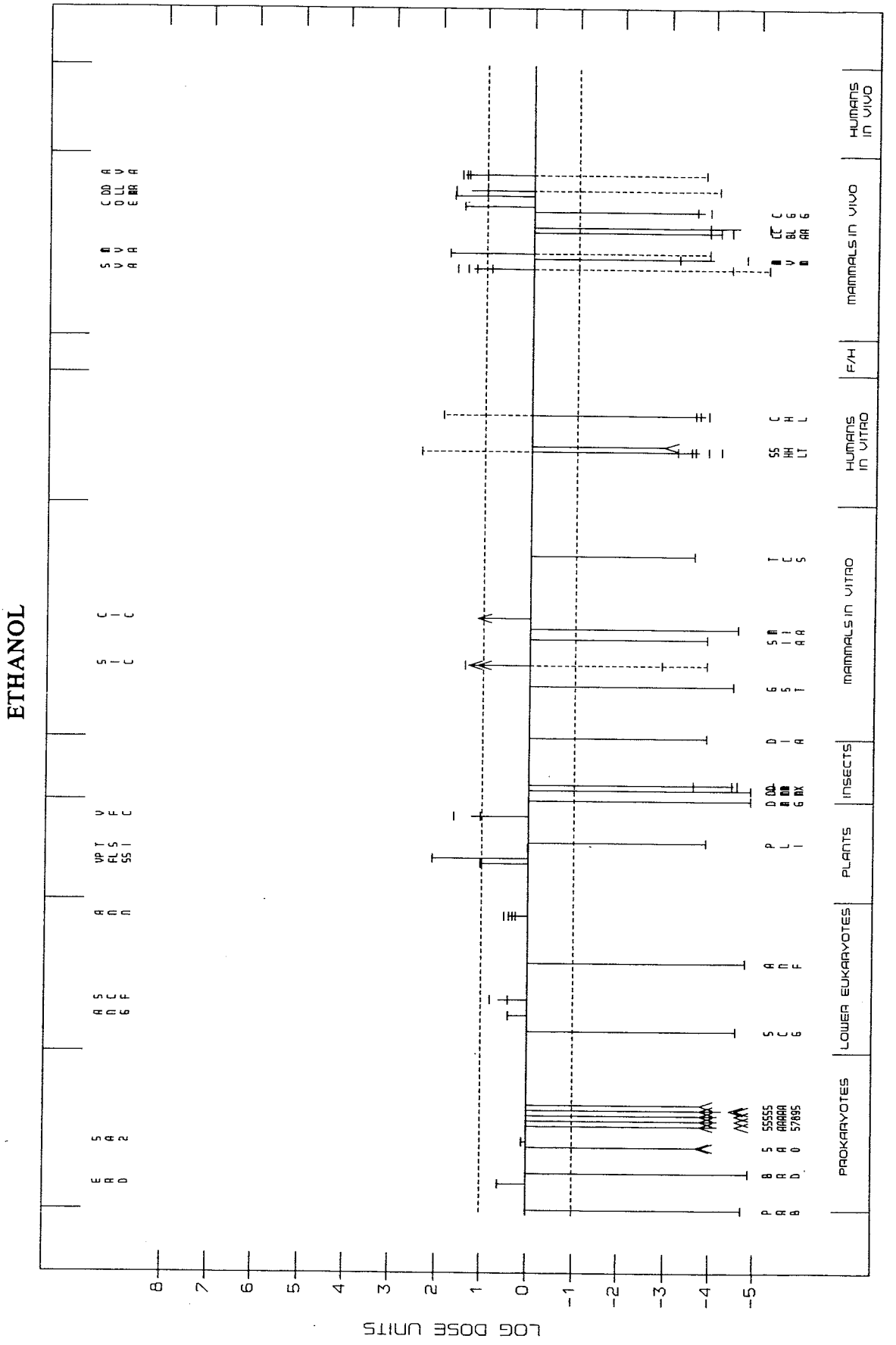
Test code	End point	Test system	Results No act	Act	Dose (LED or HID)	Reference
VFC	C	Vicia faba, chromosomal aberrations	+	0	9200.0000	Rieger et al. (1985)
DMG	R	Drosophila melanogaster, genetic crossing-over or recombination	–	0	78900.0000	Graf et al. (1984)
DMM	G	Drosophila melanogaster, somatic mutation (and recombination)	–	0	78900.0000	Graf et al. (1984)
DMX	G	Drosophila melanogaster, sex-linked recessive lethal mutations	–	0	39450.0000	Vogel & Chandler (1974)
DMX	G	Drosophila melanogaster, sex-linked recessive lethal mutations	–	0	237600.0000	Woodruff et al. (1984)
DMX	G	Drosophila melanogaster, sex-linked recessive lethal mutations	–	0	30000.0000	Creus et al. (1983)
DMX	G	Drosophila melanogaster, sex-linked recessive lethal mutations	–	0	3925.0000	Vogel et al. (1983)
DIA	D	DNA strand breaks, cross-links, etc., animal cells in vitro	–	0	7900.0000	Sina et al. (1983)
G5T	G	Gene mutation, mouse lymphoma L5178Y cells in vitro, TK locus	–	0	31878.0000	Amacher et al. (1980)
SIC	S	Sister chromatid exchange, Chinese hamster cells in vitro	+	+[b]	3900.0000	De Raat et al. (1983)
SIC	S	Sister chromatid exchange, Chinese hamster cells in vitro	–	+	7360.0000	Darroudi & Natarajan (1987)
SIC	S	Sister chromatid exchange, Chinese hamster cells in vitro	–	+	4600.0000	Takehisa & Kanaya (1983)
SIC	S	Sister chromatid exchange, Chinese hamster cells in vitro	–	0	790.0000	Obe & Ristow (1977)
SIA	S	Sister chromatid exchange, other animal cells in vitro	–	0	7900.0000	Schwartz et al. (1982)
MIA	M	Micronucleus test, animal cells in vitro	–	0	7900.0000	Garcia Heras et al. (1982)
CIC	C	Chromosomal aberrations, Chinese hamster cells in vitro	–	0[b]	39450.0000	Lasne et al. (1984)
TCM	T	Cell transformation, C3H 10T1/2 mouse cells	–	+[b]	7360.0000	Darroudi & Natarajan (1987)
TCS	T	Cell transformation, Syrian hamster embryo cells, clonal assay	(+)	0	0.0000	Abernethy et al. (1982)
SHL	S	Sister chromatid exchange, human lymphocytes in vitro	–	0	3950.0000	Bokkenheuser et al. (1983)
SHL	S	Sister chromatid exchange, human lymphocytes in vitro	+	0	395.0000	Alvarez et al. (1980a)
SHL	S	Sister chromatid exchange, human lymphocytes in vitro	–	0	15780.0000	Jansson (1982)
SHL	S	Sister chromatid exchange, human lymphocytes in vitro	–	0	3950.0000	Obe et al. (1977)
SHL	S	Sister chromatid exchange, human lymphocytes in vitro	–	0	3950.0000	Véghelyi & Osztovics (1978)
SHL	S	Sister chromatid exchange, human lymphocytes in vitro	–	0	1578.0000	Athanasiou & Bartsocas (1980)
SHL	S	Sister chromatid exchange, human lymphocytes in vitro	–	0	3200.0000	Hill & Wolff (1983)
SHT	S	Sister chromatid exchange, transformed human cells in vitro	–	0	7900.0000	Königstein et al. (1984)
SHT	S	Sister chromatid exchange, transformed human cells in vitro	–	–	790.0000	Sobti et al. (1982)
CHL	C	Chromosomal aberrations, human lymphocytes in vitro	–	–	790.0000	Sobti et al. (1983)
CHL	C	Chromosomal aberrations, human lymphocytes in vitro	–	0	5000.0000	Cadotte et al. (1973)
CHL	C	Chromosomal aberrations, human lymphocytes in vitro	+	0	1160.0000	Badr et al. (1977)
CHL	C	Chromosomal aberrations, human lymphocytes in vitro	–	0	3950.0000	Obe et al. (1977)
CHL	C	Chromosomal aberrations, human lymphocytes in vitro	–	0	7900.0000	Königstein et al. (1984)
CHL	C	Chromosomal aberrations, human lymphocytes in vitro	–	0	7900.0000	Banduhn & Obe (1985)
SVA	S	Sister chromatid exchange, animal cells in vivo	–	0	7900.0000	Kuwano & Kajii (1987)
SVA	S	Sister chromatid exchange, animal cells in vivo	+	0	6000.0000	Alvarez et al. (1980b)
SVA	S	Sister chromatid exchange, animal cells in vivo	–	0	157000.0000	Korte & Obe (1981)
SVA	S	Sister chromatid exchange, animal cells in vivo	+	0	3850.0000	Tates et al. (1980)
SVA	S	Sister chromatid exchange, animal cells in vivo	+	0	2250.0000	Czajka et al. (1980)
SVA	S	Sister chromatid exchange, animal cells in vivo	+	0	13000.0000	Obe et al. (1979)
SVA	S	Sister chromatid exchange, animal cells in vivo	–	0	25000.0000	Korte et al. (1981)
MVM	M	Micronucleus test, mice in vivo	–	0	0.0000	Nayak & Buttar (1986)
MVM	M	Micronucleus test, mice in vivo	–	0	53000.0000	Chaubey et al. (1977)
			–	0	1580.0000	Watanabe et al. (1982)

ETHANOL (contd)

Test code	End point	Test system	Results No act	Act	Dose (LED or HID)	Reference
MVR	M	Micronucleus test, rats in vivo	+	0	1500.0000	Baraona et al. (1981b)
MVR	M	Micronucleus test, rats in vivo	-	0	7700.0000	Tates et al. (1980)
CBA	C	Chromosomal aberrations, animal bone-marrow cells in vivo	-	0	25000.0000	Korte et al. (1981)
CBA	C	Chromosomal aberrations, animal bone-marrow cells in vivo	-	0	13833.0000	Korte et al. (1979)
CBA	C	Chromosomal aberrations, animal bone-marrow cells in vivo	-	0	7700.0000	Tates et al. (1980)
CLA	C	Chromosomal aberrations, animal leucocytes in vivo	-	0	157000.0000	Korte & Obe (1981)
CLA	C	Chromosomal aberrations, animal leucocytes in vivo	-	0	7700.0000	Tates et al. (1980)
CGG	C	Chromosomal aberrations, spermatogonia treated in vivo	-	0	7880.0000	Halkka & Eriksson (1977)
CGG	C	Chromosomal aberrations, spermatogonia treated in vivo	-	0	3906.0000	Kohila et al. (1976)
COE	C	Chromosomal aberrations, oocytes or embryos treated in vivo	+	0	3140.0000	Kozachuk & Barilyak (1982)
COE	C	Chromosomal aberrations, oocytes or embryos treated in vivo	-	0	0.0000	Barilyak & Kozachuk (1983)
DLM	C	Dominant lethal test, mice	?	0	1580.0000	James & Smith (1982)
DLM	C	Dominant lethal test, mice	+	0	1900.0000	Badr & Badr (1975)
DLR	C	Dominant lethal test, rats	+	0	1970.0000	Mankes et al. (1982)
DLR	C	Dominant lethal test, rats	+	0	10000.0000	Klassen & Persaud (1976)
DLR	C	Dominant lethal test, rats	-	0	12835.0000	Chauhan et al. (1980)
AVA	A	Aneuploidy, animal cells in vivo	+	0	2800.0000	Kaufman & Bain (1984a)
AVA	A	Aneuploidy, animal cells in vivo	+	0	2800.0000	Kaufman & Bain (1984b)
AVA	A	Aneuploidy, animal cells in vivo	+	0	3950.0000	Kaufman (1983)
AVA	A	Aneuploidy, animal cells in vivo	+	0	3490.0000	Hunt (1987)
AVA	A	Aneuploidy, animal cells in vivo	-	0	6250.0000	Daniel & Roane (1987)

[a]The genetic activity profile was prepared in collaboration with the Genetic Toxicology Division of the US Environmental Protection Agency, who also determined the doses used. Only results from experimental systems are given.

[b]Plant activation system


ETHANOL
LOG DOSE UNITS
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PROKARYOTES
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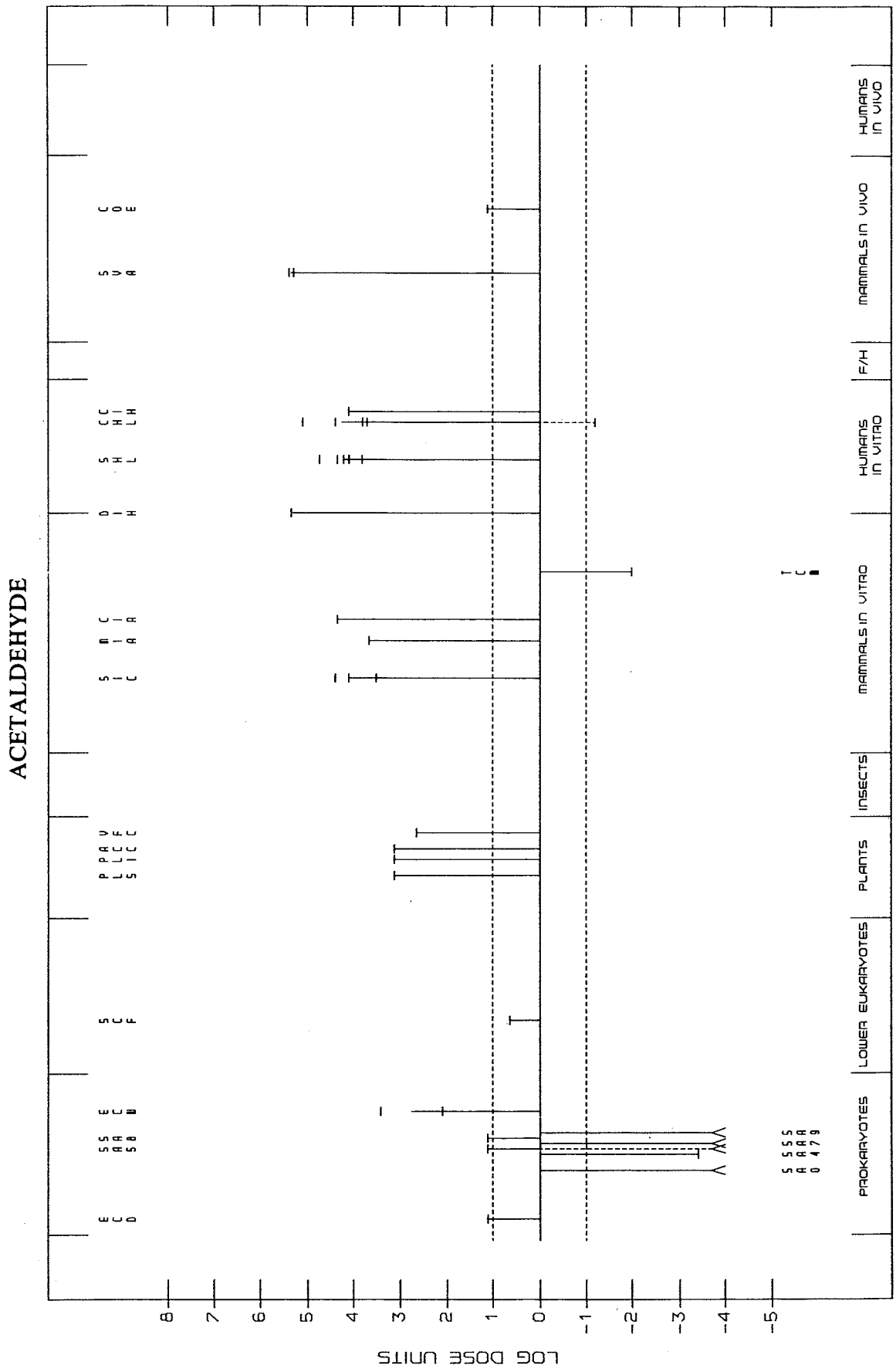
INSECTS
MAMMALS IN VITRO
HUMANS IN VITRO
F/H
MAMMALS IN VIVO
HUMANS IN VIVO

ACETALDEHYDE[a]

Test code	End point	Test system	Results No act	Act	Dose (LED or HID)	Reference
ERD	D	Escherichia coli rec strains, differential toxicity (spot test)	(+)	0	7800.0000	Rosenkranz (1977)
SA0	G	Salmonella typhimurium TA100, reverse mutation	-	-	5000.0000	Mortelmans et al. (1986)
SA4	G	Salmonella typhimurium TA104, reverse mutation	-	0	2515.0000	Marnett et al. (1985)
SA5	G	Salmonella typhimurium TA1535, reverse mutation	(+)	0	7800.0000	Rosenkranz (1977)
SA5	G	Salmonella typhimurium TA1535, reverse mutation	-	-	5000.0000	Mortelmans et al. (1986)
SA7	G	Salmonella typhimurium TA1537, reverse mutation	-	-	5000.0000	Mortelmans et al. (1986)
SA8	G	Salmonella typhimurium TA1538, reverse mutation	(+)	0	7800.0000	Rosenkranz (1977)
SA9	G	Salmonella typhimurium TA98, reverse mutation	-	-	5000.0000	Mortelmans et al. (1986)
ECW	G	Escherichia coli WP2 uvrA, reverse mutation	+	0	39.0000	Véghelyi et al. (1978)
ECW	G	Escherichia coli WP2 uvrA, reverse mutation	+	0	780.0000	Igali & Gaszo (1980)
SCF	G	Saccharomyces cerevisiae, forward mutation	(+)	0	23400.0000	Bandas (1982)
PLS	S	Plants (other), sister chromatid exchanges	+	0	75.0000	Cortés et al. (1986)
PLI	M	Plants (other), micronuclei	+	0	75.0000	Cortés et al. (1986)
ACC	C	Allium cepa, chromosomal aberrations	+	0	75.0000	Cortés et al. (1986)
VFC	C	Vicia faba, chromosomal aberrations	+	0	220.0000	Rieger & Michaelis (1960)
SIC	S	Sister chromatid exchange, Chinese hamster cells in vitro	+	0	3.9000	Obe & Beek (1979)
SIC	S	Sister chromatid exchange, Chinese hamster cells in vitro	+	0	31.2000	Obe & Ristow (1977)
SIC	S	Sister chromatid exchange, Chinese hamster cells in vitro	+	0	4.0000	Obe et al. (1978)
SIA	S	Sister chromatid exchange, other animal cells in vitro	+	+	7.8000	De Raat et al. (1983)
MIA	M	Micronucleus test, animal cells in vitro	+	0	22.0000	Bird et al. (1982)
CIR	C	Chromosomal aberrations, rat cells in vitro	+	0	4.4000	Bird et al. (1982)
TCM	T	Cell transformation, C3H 10T1/2 mouse cells	-	0	100.0000	Abernethy et al. (1982)
DIH	D	DNA strand breaks, cross-links, etc., human cells in vitro	+	0	0.4400	Lambert et al. (1985)
SHL	S	Sister chromatid exchange, human lymphocytes in vitro	+	0	6.0000	Jansson (1982)
SHL	S	Sister chromatid exchange, human lymphocytes in vitro	+	0	8.0000	Böhlke et al. (1983)
SHL	S	Sister chromatid exchange, human lymphocytes in vitro	+	0	7.8000	Ristow & Obe (1978)
SHL	S	Sister chromatid exchange, human lymphocytes in vitro	+	0	1.8000	Véghelyi et al. (1978)
SHL	S	Sister chromatid exchange, human lymphocytes in vitro	+	0	15.6000	Obe et al. (1978)
SHL	S	Sister chromatid exchange, human lymphocytes in vitro	+	0	4.4000	He & Lambert (1985)
CHL	C	Chromosomal aberrations, human lymphocytes in vitro	+	0	20.0000	Badr & Hussain (1977)
CHL	C	Chromosomal aberrations, human lymphocytes in vitro	+	0	16.0000	Böhlke et al. (1983)
CHL	C	Chromosomal aberrations, human lymphocytes in vitro	+	0	4.0000	Obe et al. (1985)
CHL	C	Chromosomal aberrations, human lymphocytes in vitro	-	0	15.6000	Obe et al. (1979)
CHL	C	Chromosomal aberrations, human lymphocytes in vitro	(+)	0	0.7800	Obe et al. (1978)
CIH	C	Chromosomal aberrations, other human cells in vitro	+	0	7.8000	Obe et al. (1979)
SVA	S	Sister chromatid exchange, animal cells in vivo	+	0	0.4000	Obe et al. (1979)
SVA	S	Sister chromatid exchange, animal cells in vivo	+	0	0.5000	Korte & Obe (1981)
COE	C	Chromosomal aberrations, oocytes or embryos treated in vivo	+	0	7800.0000	Barilyak & Kozachuk (1983)
BID	D	Binding (covalent) to DNA in vitro	+	0	44100.0000	Ristow & Obe (1978)

From IARC (1987b)


ACETALDEHYDE
LOG DOSE UNITS
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HUMANS IN VITRO
F/H
MAMMALS IN VIVO
HUMANS IN VIVO