APPENDIX 2

ACTIVITY PROFILES FOR GENETIC AND RELATED EFFECTS

Methods

The x-axis of the activity profile (Waters *et al.*, 1987, 1988) 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.

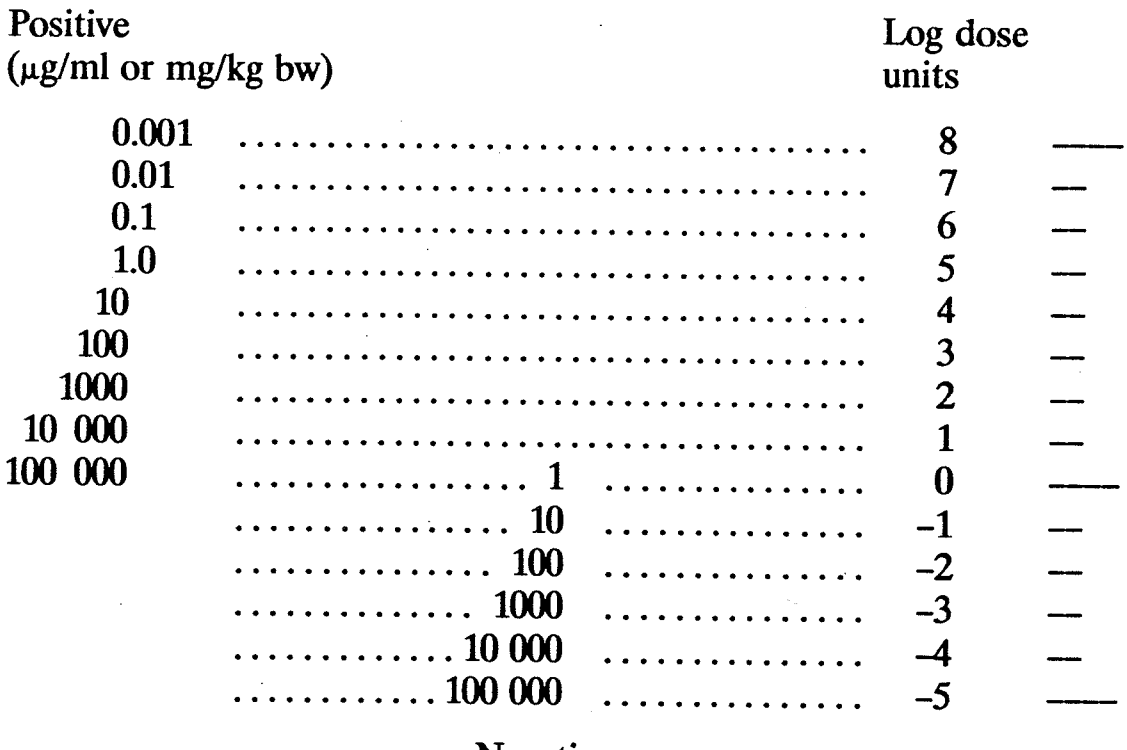
In order to accommodate both the wide range of doses encountered and positive and negative responses on a continuous scale, doses are transformed

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

$$LDU_{ij} = -\log_{10}(\text{dose}), \text{ for HID values; } LDU \leq 0$$
and
$$LDU_{ij} = -\log_{10}(\text{dose} \times 10^{-5}), \text{ for LED values; } LDU \geq 0. \quad (1)$$

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 IARC Monographs Supplement 6, Volume 44 and subsequent volumes, including this publication, codes were redefined in a manner that should facilitate inclusion of additional tests. 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.

Data listings are presented with each activity profile and include endpoint and test codes, a short test code definition, results [either with (M) or without (NM) an exogenous activation system], the associated LED or HID value and a short citation. Test codes are organized phylogenetically and by endpoint from left to right across each activity profile and from top to bottom of the corresponding data listing. Endpoints are defined as follows: A, aneuploidy; C, chromosomal aberrations; D, DNA damage; F, assays of body fluids; G, gene mutation; H, host-mediated assays; I, inhibition of intercellular communication; M, micronuclei; P, sperm morphology; R, mitotic recombination or gene conversion; S, sister chromatid exchange; and T, cell transformation.

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). 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) In microbial plate tests, it is usual for the doses to be reported as weight/plate, whereas concentrations are required to enter data on the activity profile chart. While remaining cognisant of the errors involved in the process, it is assumed that a 2-ml volume of top agar is delivered to each plate and that the test substance remains in solution within it; concentrations are derived from the reported weight/plate values by dividing by this arbitrary volume. For spot tests, a 1-ml volume is used in the calculation.

   (f) Conversion of particulate concentrations given in μg/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).* 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., non-human) 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.

The genetic activity profiles and listings that follow were prepared in collaboration with Environmental Health Research and Testing Inc. (EHRT) under contract to the US Environmental Protection Agency; EHRT also determined the doses used. The references cited in each genetic activity profile listing can be found in the list of references in the appropriate monograph.

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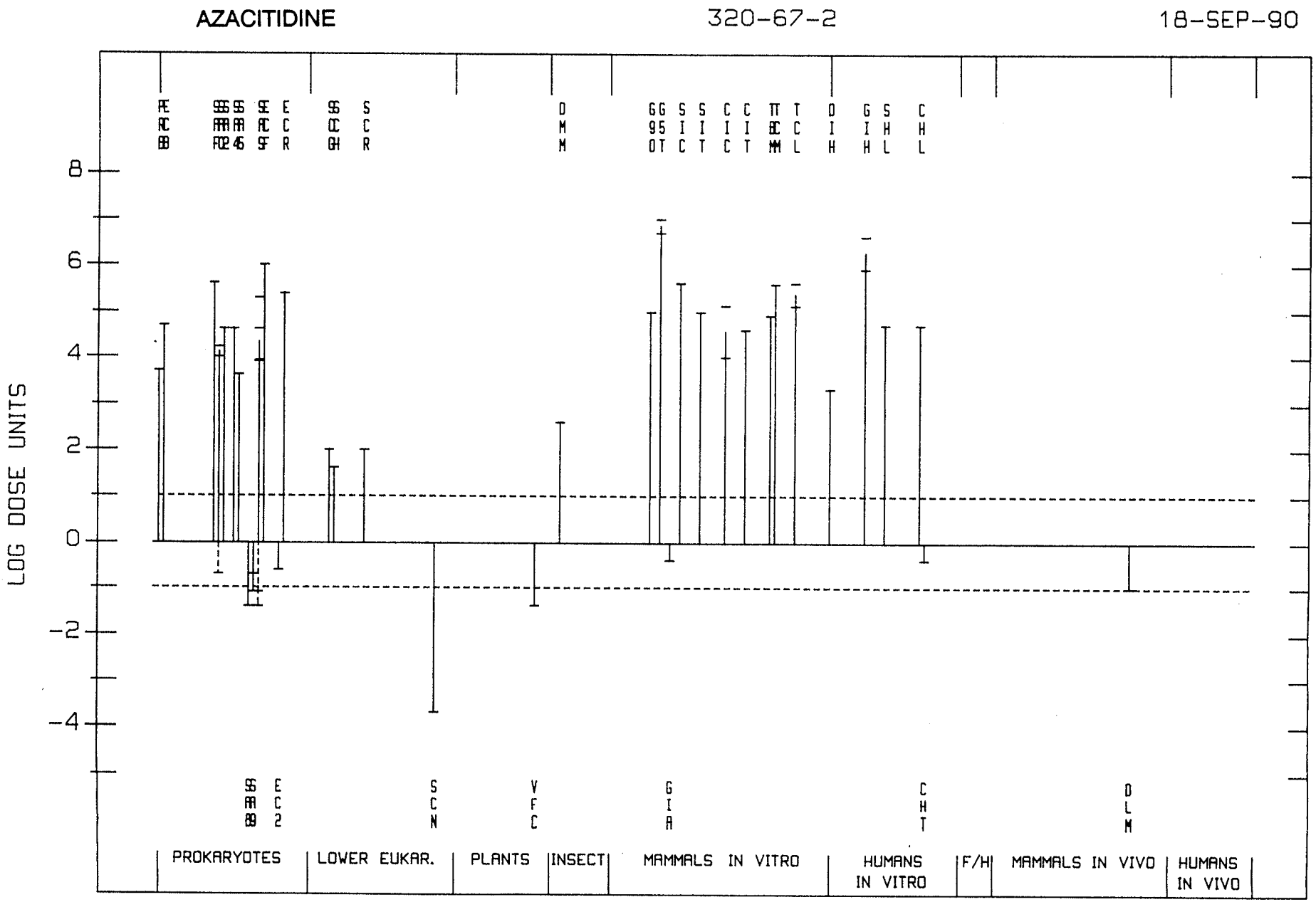
AZACITIDINE

Test system	Result		Dose LED/HID	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
RNA virus, mutation	+	0	5 μg/ml	Halle (1968)
PRB, Prophage induction	+	0	20 μg/ml	Barbe et al. (1986)
ECB, Escherichia coli, DNA damage (dcm+/recA56)	+	0	2.0 μg/ml	Bhagwat & Roberts (1987)
SA0, Salmonella typhimurium TM677, forward mutation	+	0	0.24 μg/ml	Call et al. (1986)
SA0, Salmonella typhimurium TA100, reverse mutation	+	0	10 μg/ml	Marquardt & Marquardt (1977)
SA0, Salmonella typhimurium TA100, reverse mutation	–	0	5 μg/ml	Podger (1983)
SA0, Salmonella typhimurium TA100, reverse mutation	+	0	6 μg/ml	Schmuck et al. (1986)
SA2, Salmonella typhimurium TA102, reverse mutation	+	0	2.4 μg/ml	Schmuck et al. (1986)
SA4, Salmonella typhimurium TA104, reverse mutation	+	0	2.4 μg/ml	Schmuck et al. (1986)
SA5, Salmonella typhimurium TA1535, reverse mutation	+	0	24 μg/ml	Schmuck et al. (1986)
SA8, Salmonella typhimurium TA1538, reverse mutation	–	0	25 μg/ml	Schmuck et al. (1986)
SA9, Salmonella typhimurium TA98, reverse mutation	–	0	5 μg/ml	Podger (1983)
SA9, Salmonella typhimurium TA98, reverse mutation	–	0	25 μg/ml	Schmuck et al. (1986)
SA9, Salmonella typhimurium TA98, reverse mutation	–	0	12.5 μg/ml	Levin & Ames (1986)
SAS, Salmonella typhimurium miscellaneous strains, reverse mutation	+	0	0.5 μg/ml	Podger (1983)
SAS, Salmonella typhimurium TA2638, reverse mutation	+	0	2.4 μg/ml	Schmuck et al. (1986)
SAS, Salmonella typhimurium TA92, reverse mutation	+	0	12 μg/ml	Schmuck et al. (1986)
SAS, Salmonella typhimurium TA2640, reverse mutation	–	0	25 μg/ml	Schmuck et al. (1986)
SAS, Salmonella typhimurium TA96, TA97, hisG428, hisG46, hisG1775, reverse mutation	–	0	12.5 μg/ml	Levin & Ames (1986)
SAS, Salmonella typhimurium TA2661, reverse mutation	+	0	12.5 μg/ml	Levin & Ames (1986)
SAS, Salmonella typhimurium TA4006, reverse mutation	+	0	12.5 μg/ml	Levin & Ames (1986)
EC2, Escherichia coli WP2, reverse mutation	–	0	4 μg/ml	Fucik et al. (1965)
ECF, Escherichia coli exclusive of strain K12, forward mutation	+	0	0.1 μg/ml	Lal et al. (1988)
ECR, Escherichia coli other miscellaneous strains, reverse mutation	+	0	0.4 μg/ml	Fucik et al. (1965)
SCH, Saccharomyces cerevisiae, mitotic recombination	+	0	2500 μg/ml	Zimmermann & Scheel (1984)
SCG, Saccharomyces cerevisiae, mitotic gene conversion	+	0	1000 μg/ml	Zimmermann & Scheel (1984)
SCR, Saccharomyces cerevisiae, reverse mutation	+	0	1000 μg/ml	Zimmermann & Scheel (1984)
SCN, Saccharomyces cerevisiae, aneuploidy	–	0	5000 μg/ml	Zimmermann & Scheel (1984)
VFC, Vicia faba, chromosomal aberrations	–	0	24 μg/ml	Fucik et al. (1970)
DMM, Drosophila melanogaster, wing-spot assay (somatic mutation and recombination)	+	0	244 μg/ml	Katz (1985)
G9H, Gene mutation, Chinese hamster lung V79 cells, hprt locus	–	0	0.7 μg/ml	Landolph & Jones (1982)

AZACITIDINE (contd)

Test system	Result		Dose LED/HID	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
G9O, Gene mutation, Chinese hamster lung V79 cells, ouabain resistance	+	0	1 μg/ml	Marquart & Marquart (1977)
G9O, Gene mutation, Chinese hamster lung V79 cells, ouabain resistance	–	0	0.7 μg/ml	Landolph & Jones (1982)
G5T, Gene mutation, mouse lymphoma L5178Y cells in vitro, tk locus	+	–	0.02 μg/ml	Amacher & Turner (1987)
G5T, Gene mutation, mouse lymphoma L5178Y cells in vitro, tk locus	+	0	0.01 μg/ml	McGregor et al. (1989)
GIA, Gene mutation, mouse C3H/10 T1/2 cells, ouabain resistance	–	0	2.4 μg/ml	Landolph & Jones (1982)
GIA, Gene mutation, BHK cells, hprt locus	–	0	2.4 μg/ml	Bouck et al. (1984)
GIA, Gene mutation, BHK cells, ouabain resistance	–	0	2.4 μg/ml	Bouck et al. (1984)
GIA, Gene mutation, primary rat tracheal epithelial cells, ouabain resistance/hprt locus	–	0	1 μg/ml	Walker & Nettesheim (1986)
GIA, Gene mutation, mouse lymphoma L5178Y cells in vitro, hprt locus	–	0	0.33 μg/ml	McGregor et al. (1989)
SIT, Sister chromatid exchange, hamster cells in vitro	+	0	1.00 μg/ml	Banerjee & Benedict (1979)
SIC, Sister chromatid exchange, hamster cells in vitro	+	0	0.24 μg/ml	Hori (1983)
CIC, Chromosomal aberrations, Chinese hamster Don cells in vitro	+	0	10 μg/ml	Karon & Benedict (1972)
CIC, Chromosomal aberrations, Chinese hamster embryo fibroblasts (CHEF/18) in vitro	+	0	0.73 μg/ml	Harrison et al. (1983)
CIT, Chromosomal aberrations, hamster cells in vitro	(+)	0	2.5 μg/ml	Benedict et al. (1977)
TBM, Cell transformation, BALB/c 3T3 mouse cells	+	0	1.2 μg/ml	Yasutake et al. (1987)
TCM, Cell transformation, C3H 10T1/2 mouse cells	+	0	0.25 μg/ml	Benedict et al. (1977)
TCL, Cell transformation, Chinese hamster embryo fibroblasts (CHEF/18)	+	0	0.73 μg/ml	Harrison et al. (1983)
TCL, Cell transformation, primary rat tracheal epithelial cells	+	0	0.24 μg/ml	Walker & Nettesheim (1986)
DIH, DNA strand breaks, HeLa cells	+	0	48 μg/ml	Snyder & Lachmann (1989)
GIH, Gene mutation, human cells in vitro, hprt locus	+	0	0.12 μg/ml	Call et al. (1986)
GIH, Gene mutation, human cells in vitro, tk locus	+	0	0.024 μg/ml	Call et al. (1986)
SHL, Sister chromatid exchange, human lymphocytes in vitro	+	0	1.95 μg/ml	Lavia et al. (1985)
CHL, Chromosomal aberrations, human lymphocytes in vitro	+	0	1.95 μg/ml	Lavia et al. (1985)
CHT, Chromosomal aberrations, transformed human cells in vitro	–	0	2.4 μg/ml	Call et al. (1986)
DLM, Dominant lethal test, mice	–	0	10 mg/kg x 1, i.p.	Epstein et al. (1972)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6
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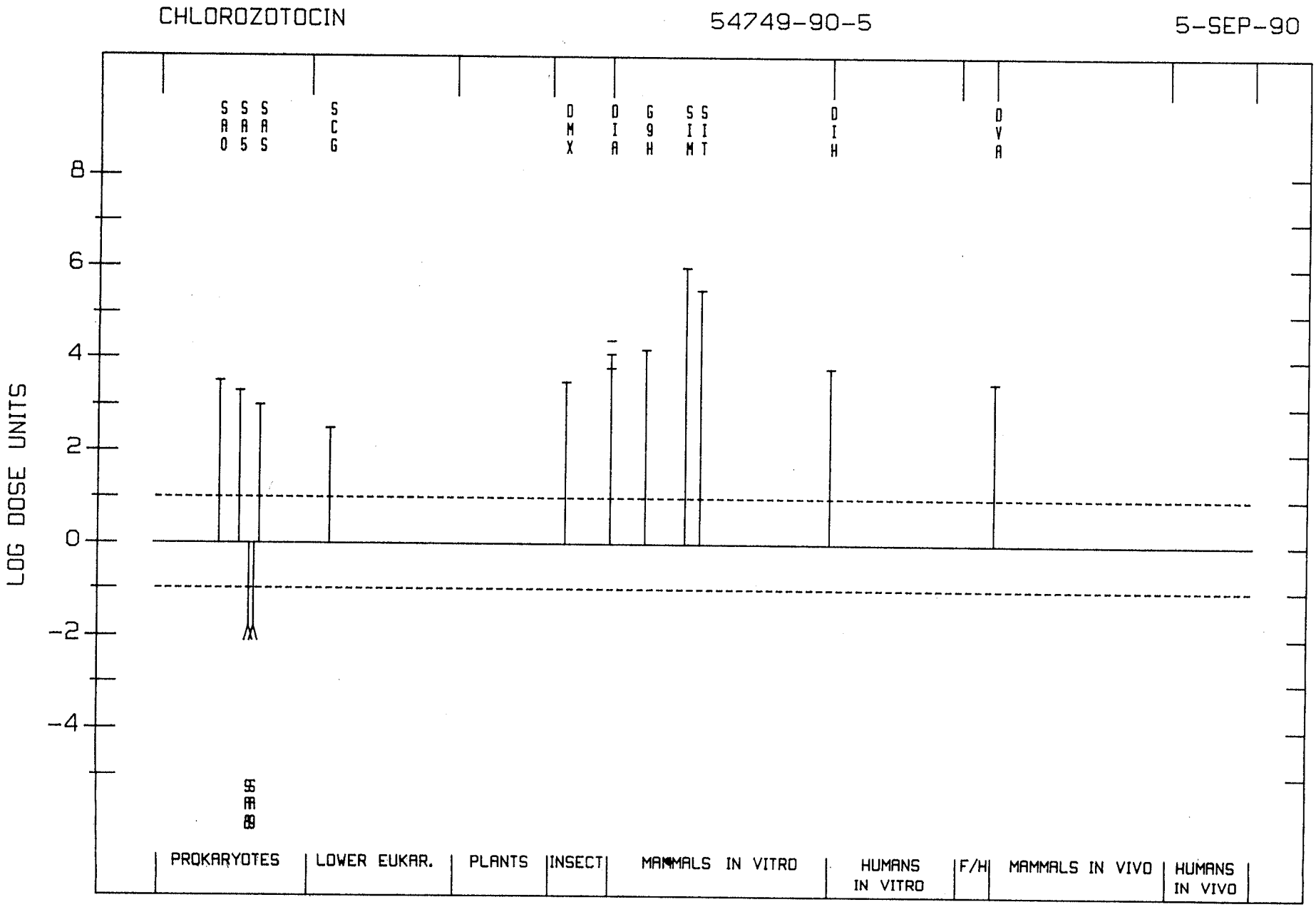
PROKARYOTES
LOWER EUKAR.
PLANTS
INSECT
MAMMALS IN VITRO
HUMANS IN VITRO
F/H
MAMMALS IN VIVO
HUMANS IN VIVO

CHLOROZOTOCIN

Test system	Result		Dose LED/HID	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
PRB, Strand breaks in PM2-CCC DNA	+	0	1570 µg/ml	Lown & McLaughlin (1979)
PRB, Plasmid pBR 322 DNA strand breaks	+	0	2857 µg/ml	Vadi & Reed (1983)
Plasmid pBR 322 DNA alkylation	+	0	2857 µg/ml	Vadi & Reed (1983)
PRB, Plasmid pBR 322 DNA interstrand cross-links	+	0	2857 µg/ml	Vadi & Reed (1983)
DNA cross-links, calf thymus	+	0	1570 µg/ml	Alexander et al. (1986)
SA0, Salmonella typhimurium TA100, reverse mutation	+	+	31 µg/ml	Franza et al. (1980)
SA5, Salmonella typhimurium TA1535, reverse mutation	+	+	0	Franza et al. (1980)
SA5, Salmonella typhimurium TA1535, reverse mutation	+	+	50 µg/ml	Suling et al. (1983)
SA8, Salmonella typhimurium TA1538, reverse mutation	–	–	62 µg/ml	Franza et al. (1980)
SA9, Salmonella typhimurium TA98, reverse mutation	–	–	62 µg/ml	Franza et al. (1980)
SA5, Salmonella typhimurium hisG46, reverse mutation	+	0	100 µg/ml	Zimmer & Bhuyan (1976)
SCG, Saccharomyces cerevisiae, gene conversion	+	0	314 µg/ml	Siebert & Eisenbrand (1977)
DMX, Drosophila melanogaster, sex-linked recessive lethal mutation	+	0	31.4 µg/ml	Kortselius (1978)
DIA, DNA cross-links and strand breaks, mouse leukaemia L1210 cells	+	0	7.85 µg/ml	Ewig & Kohn (1977)
DIA, DNA strand breaks, Chinese hamster V79 cells	+	0	4 µg/ml	Erickson et al. (1978)
DIA, DNA strand breaks, mouse leukaemia L1210 cells	+	0	15.7 µg/ml	Alexander et al. (1986)
G9H, Gene mutation, Chinese hamster lung V79 cells, hprt locus	+	0	6.28 µg/ml	Bradley et al. (1980)
SIM, Sister chromatid exchange, mouse leukaemia L1210 cells	+	0	0.1 µg/ml	Siddiqui et al. (1988)
SIT, Sister chromatid exchange, 9L rat brain tumour cells	+	0	0.3 µg/ml	Tofilon et al. (1983)
DIH, DNA cross-links, human cells in vitro	+	0	15.7 µg/ml	Erickson et al. (1980)
DVA, DNA interstrand cross-links, strand breaks, rat bone-marrow cells in vivo	+	0	31.4 mg/kg x 1, i.p.	Bedford & Eisenbrand (1984)
BVD, DNA binding in vitro	+	0	24 µg/ml	Panasci et al. (1979)
BVD, DNA binding in vitro	+	0	24 µg/ml	Ahlgren et al. (1982)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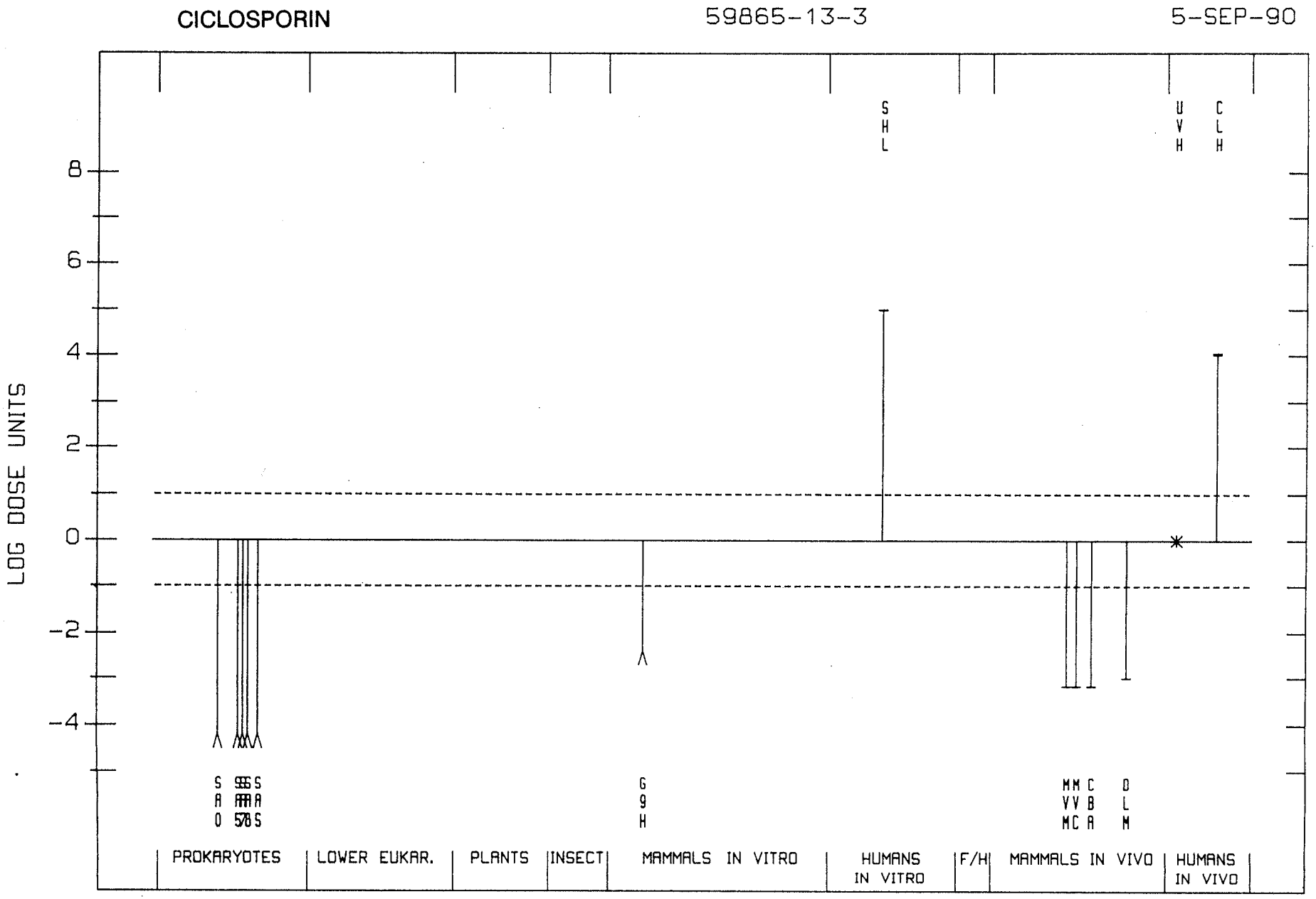
SA5
SAS
SCG
DMX
DIA
G9H
SIM
SIT
DIH
DVA
SA8
PROKARYOTES
LOWER EUKAR.
PLANTS
INSECT
MAMMALS IN VITRO
HUMANS IN VITRO
F/H
MAMMALS IN VIVO
HUMANS IN VIVO

CICLOSPORIN

Test system	Result		Dose LED/HID	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
SA0, Salmonella typhimurium TA100, reverse mutation	–	–	15000 µg/ml	Matter et al. (1982)
SA5, Salmonella typhimurium TA1535, reverse mutation	–	–	15000 µg/ml	Matter et al. (1982)
SA7, Salmonella typhimurium TA1537, reverse mutation	–	–	15000 µg/ml	Matter et al. (1982)
SA8, Salmonella typhimurium TA1538, reverse mutation	–	–	15000 µg/ml	Matter et al. (1982)
SAS, Salmonella typhimurium miscellaneous strains, reverse mutation	–	–	15000 µg/ml	Matter et al. (1982)
G9H, Gene mutation, Chinese hamster lung V79 cells, hprt locus	–	–	250 µg/ml	Zwanenburg et al. (1988)
SHL, Sister chromatid exchange, human lymphocytes in vitro	(+)	0	1 µg/ml	Yuzawa et al. (1986)
SHL, Sister chromatid exchange, human lymphocytes in vitro	(+)	0	1 µg/ml	Yuzawa et al. (1987)
UVM, Unscheduled DNA synthesis, mouse cells in vivo	–	0	0	Matter et al. (1982)
MVM, Micronucleus test, mice in vivo	–	0	1500 mg/kg x 1, p.o.	Matter et al. (1982)
MVC, Micronucleus test, hamsters in vivo	–	0	1500 mg/kg x 1, p.o.	Matter et al. (1982)
CBA, Chromosomal aberrations, animal bone-marrow cells in vivo	–	0	1500 mg/kg x 1, p.o.	Matter et al. (1982)
DLM, Dominant lethal test, mice	–	0	1000 mg/kg x 1, p.o.	Matter et al. (1982)
UVH, Unscheduled DNA synthesis, human lymphocytes in vivo	+	0	0	Petitjean et al. (1986)
CLH, Chromosomal aberrations, human lymphocytes in vivo	(+)	0	9.5 mg/kg[a]	Fukuda et al. (1987)
CLH, Chromosomal aberrations, human lymphocytes in vivo	(+)		9 mg/kg[b]	Fukuda et al. (1988)

[a] Tapering to 5–6 mg/kg per day; prednisolone was also given at 10 mg/person per day.
[b] Tapering to 4 mg/kg per day after one year; prednisolone was also given at 50 mg/person/day and tapering to 10 mg/person per day.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6
4
2
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-2
-4
PROKARYOTES
LOWER EUKAR.
PLANTS
INSECT
MAMMALS IN VITRO
HUMANS IN VITRO
F/H
MAMMALS IN VIVO
HUMANS IN VIVO

THIOTEPA

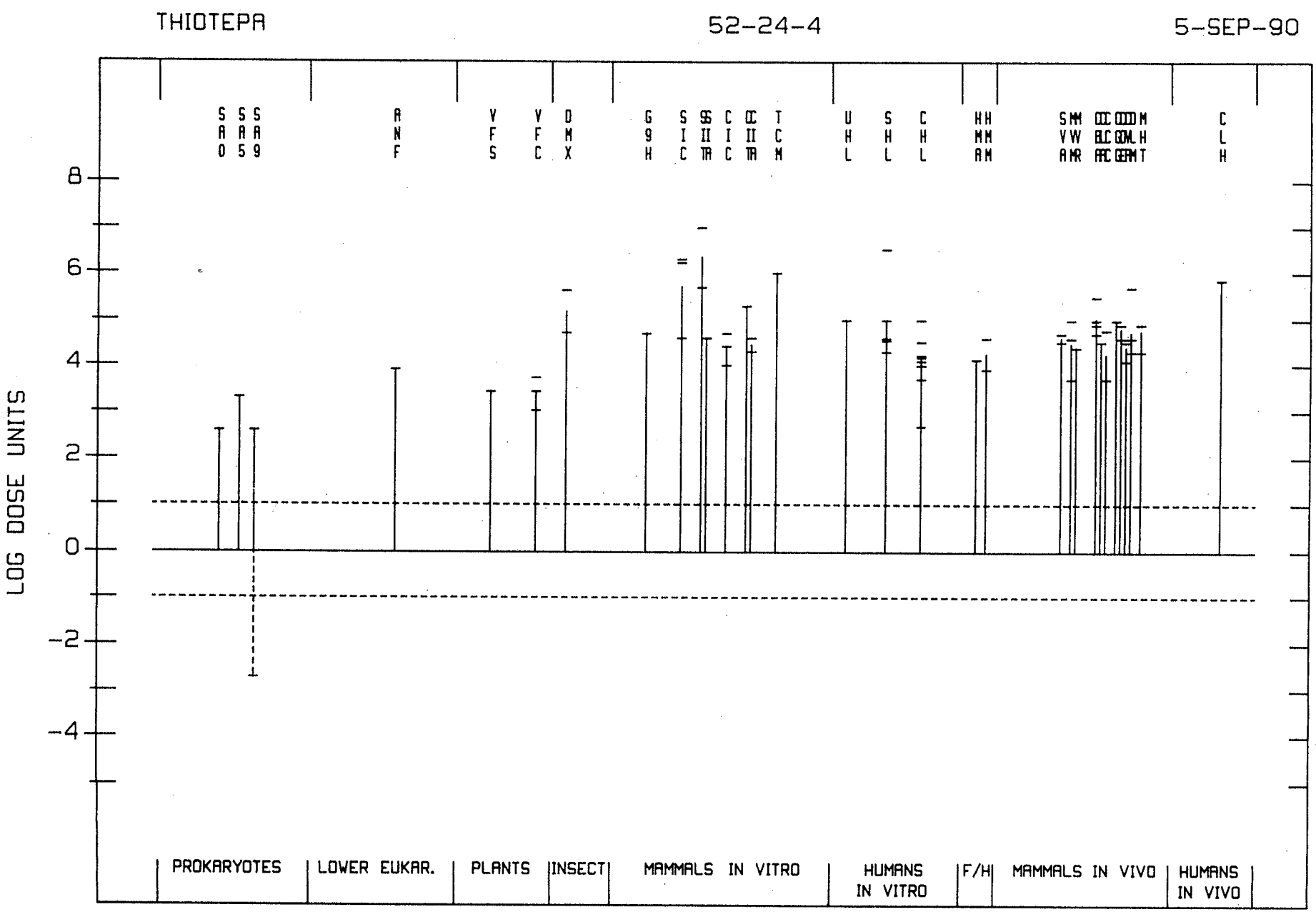
Test system	Result		Dose LED/HID	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
SA0, Salmonella typhimurium TA100, reverse mutation	+	0	250 µg/ml	Pak et al. (1979)
SA5, Salmonella typhimurium TA1535, reverse mutation	+	0	50 µg/ml	Benedict et al. (1977a)
SA9, Salmonella typhimurium TA98, reverse mutation	+	0	250 µg/ml	Bruce & Heddle (1979)
SA9, Salmonella typhimurium TA98, reverse mutation	–	0	500 µg/ml	Pak et al. (1979)
ANF, Aspergillus nidulans, forward mutation	+	0	12.5 µg/ml	Bignami et al. (1982)
VFS, Vicia faba, sister chromatid exchange	+	0	37.8 µg/ml	Kihlman (1975)
VFC, Vicia faba, chromosomal aberrations	+	0	37.8 µg/ml	Kihlman (1975)
VFC, Vicia faba, chromosomal aberrations	+	0	95 µg/ml	Sturelid & Kihlman (1975)
VFC, Vicia faba, chromosomal aberrations	+	0	19 µg/ml	Popa et al. (1976)
DMX, Drosophila melanogaster, sex-linked recessive lethal mutations	+	0	0.23 µg/ml	Lüers & Röhrborn (1965)
DMX, Drosophila melanogaster, sex-linked recessive lethal mutations	+	0	1.9 µg/ml	Fahmy & Fahmy (1970)
G9H, Gene mutation, Chinese hamster V79 lung cells, hprt locus	+	0	2 µg/ml	Paschin & Kozachenko (1982)
SIC, Sister chromatid exchange, Chinese hamster cells in vitro	+	0	2.5 µg/ml	Chebotarev & Selezneva (1979)
SIC, Sister chromatid exchange, Chinese hamster cells in vitro	+	0	0.05 µg/ml	Chebotarev et al. (1980)
SIC, Sister chromatid exchange, Chinese hamster cells in vitro	+	0	0.06 µg/ml	Selezneva et al. (1982)
SIT, Sister chromatid exchange, mouse cells in vitro	+	0	0.2 µg/ml	Andersen (1983)
SIT, Sister chromatid exchange, cloned hamster cells in vitro	+	0	0.01 µg/ml	Banerjee & Benedict (1979)
SIA, Sister chromatid exchange, rhesus monkey cells in vitro	+	0	2.5 µg/ml	Kuzin et al. (1987)
CIC, Chromosomal aberrations, Chinese hamster cells in vitro	+	0	2 µg/ml	Sturelid (1976)
CIC, Chromosomal aberrations, Chinese hamster cells in vitro	+	0	10 µg/ml	Maier & Schmid (1976)
CIC, Chromosomal aberrations, Chinese hamster cells in vitro	+	0	3.78 µg/ml	Sturelid & Kihlman (1975)
CIT, Chromosomal aberrations, cloned hamster cells in vitro	+	0	0.5 µg/ml	Benedict et al. (1977b)
CIA, Chromosomal aberrations, rabbit cells in vitro	+	0	5 µg/ml	Bochkov et al. (1982)
CIA, Chromosomal aberrations, rhesus monkey cells in vitro	+	0	2.5 µg/ml	Kuzin et al. (1987)
TCM, Cell transformation, C3H 10T1/2 mouse cells	+	0	0.1 µg/ml	Benedict et al. (1977a)
UHL, Unscheduled DNA synthesis, human lymphocytes in vitro	+	0	1 µg/ml	Titenko (1983)
SHL, Sister chromatid exchange, human lymphocytes in vitro	+	0	2.5 µg/ml	Littlefield et al. (1979)
SHL, Sister chromatid exchange, human lymphocytes in vitro	+	0	0.03 µg/ml	Mourelatos (1979)
SHL, Sister chromatid exchange, human lymphocytes in vitro	+	0	5 µg/ml	Chebotarev & Listopad (1980)
SHL, Sister chromatid exchange, human lymphocytes in vitro	+	0	1 µg/ml	Listopad & Chebotarev (1982)
SHL, Sister chromatid exchange, human lymphocytes in vitro	+	0	2.8 µg/ml	Shcheglova & Chebotarev (1983a)
CHL, Chromosomal aberrations, human lymphocytes in vitro	+	0	3 µg/ml	Hampel et al. (1966)
CHL, Chromosomal aberrations, human lymphocytes in vitro	+	0	1 µg/ml	Bochkov & Kuleshov (1972)
CHL, Chromosomal aberrations, human lymphocytes in vitro	+	0	10 µg/ml	Bochkov et al. (1972)

THIOTEPA (contd)

Test system	Result		Dose LED/HID	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
CHL, Chromosomal aberrations, human lymphocytes in vitro	+	0	8 μg/ml	Chebotarev (1974)
CHL, Chromosomal aberrations, human lymphocytes in vitro	+	0	20 μg/ml	Kirichenko (1974)
CHL, Chromosomal aberrations, human lymphocytes in vitro	+	0	10 μg/ml	Kirichenko & Chebotarev (1976)
CHL, Chromosomal aberrations, human lymphocytes in vitro	+	0	6 μg/ml	Yakovenko & Nazarenko (1977)
CHL, Chromosomal aberrations, human lymphocytes in vitro	+	0	6 μg/ml	Bochkov et al. (1979)
CHL, Chromosomal aberrations, human lymphocytes in vitro	+	0	200 μg/ml	Wolff & Arutyunyan (1979)
CHL, Chromosomal aberrations, human lymphocytes in vitro	+	0	10 μg/ml	Yakovenko & Kagramanyan (1982)
CHL, Chromosomal aberrations, human lymphocytes in vitro	+	0	6.6 μg/ml	Shcheglova & Chebotarev (1983a)
HMA, Host-mediated assay, mouse leukaemia L5187Y cells in mice	+	0	7.5 mg/kg x 1, s.c.	Lee (1973)
HMM, Host-mediated assay, Salmonella typhimurium in mice	+	0	12.4 mg/kg x 3, i.p.	Arni et al. (1977)
HMM, Host-mediated assay, Salmonella typhimurium in mice	+	0	2.5 mg/kg x 2, p.o.	Devi & Reddy (1980)
SVA, Sister chromatid exchange, mouse bone-marrow cells in vivo	+	0	2 mg/kg x 1, i.p.	Shcheglova & Chebotarev (1983b)
SVA, Sister chromatid exchange, rhesus monkey lymphocytes in vivo	+	0	3 mg/kg x 1, i.v.	Kuzin et al. (1987)
MVM, Micronucleus test, mice in vivo	+	0	1 mg/kg x 2, i.p.	Maier & Schmid (1976)
MVM, Micronucleus test, mice in vivo	+	0	20 mg/kg x 1, i.p.	Ioan et al. (1977)
MVM, Micronucleus test, mice in vivo	+	0	2.5 mg/kg x 5, i.p.	Bruce & Heddle (1979)
MVM, Micronucleus test, mice in vivo	+	0	2.5 mg/kg x 1, i.p.	Leonard et al. (1979)
MVR, Micronucleus test, rat in vivo	+	0	4 mg/kg x 1, i.p.	Setnikar et al. (1976)
CBA, Chromosomal aberrations, mouse bone-marrow cells in vivo	+	0	0.32 mg/kg x 1, i.p.	Malashenko & Surkova (1974b)
CBA, Chromosomal aberrations, mouse bone-marrow cells in vivo	+	0	2 mg/kg x 1, i.p.	Malashenko & Surkova (1975)
CBA, Chromosomal aberrations, mouse bone-marrow cells in vivo	+	0	1.25 mg/kg x 1, i.p.	Leonard et al. (1979)
CBA, Chromosomal aberrations, mouse bone-marrow cells in vivo	+	0	1 mg/kg x 1, i.p.	Shcheglova & Chebotarev (1983b)
CCC, Chromosomal aberrations, mouse spermatocytes in vivo	+	0	1.66 mg/kg x 2, p.o.	Devi & Reddy (1980)
CCC, Chromosomal aberrations, mouse spermatocytes in vivo	+	0	20 mg/kg x 1, i.p.	Meistrich et al. (1982)
CGG, Chromosomal aberrations, mouse spermatogonia in vivo	+	0	1 mg/kg x 1, i.p.	Malashenko & Beskova (1988)
CVA, Chromosomal aberrations, mouse liver cells in vivo	+	0	8 mg/kg x 1, i.p.	Korogodina & Lil'p (1978)
COE, Chromosomal aberrations, preimplantation mouse embryos in vivo	+	0	1.25 mg/kg x 1, i.p.	Malashenko et al. (1978)
CVA, Chromosomal aberrations, embryonal mouse liver in vivo	+	0	2.5 mg/kg x 1, i.p.	Korogodina et al. (1979)
COE, Chromosomal aberrations, preimplantation mouse embryos in vivo	+	0	1.25 mg/kg x 1, i.p.	Semenov & Malashenko (1979)
COE, Chromosomal aberrations, embryonal mouse liver in vivo	+	0	2.5 mg/kg x 1, i.p.	Korogodina & S'yakste (1981)
CLA, Chromosomal aberrations, rabbit lymphocytes in vivo	+	0	3 mg/kg x 1, i.v.	Bochkov et al. (1982)
CVA, Chromosomal aberrations, rhesus monkey lymphocytes in vivo	+	0	3 mg/kg x 1, i.v.	Kuzin et al. (1987)
DLM, Dominant lethal test, mice	+	0	5 mg/kg x 1, i.p.	Machemer & Hess (1971)
DLM, Dominant lethal test, mice	+	0	5 mg/kg x 1, i.p.	Epstein et al. (1972)

THIOTEPA (contd)

Test system	Result		Dose LED/HID	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
DLM, Dominant lethal test, mice	+	0	0.2 mg/kg x 10, i.p.	Sram (1976)
DLM, Dominant lethal test, mice	+	0	1.25 µg/kg x 1, i.p.	Malashenko et al. (1978)
DLM, Dominant lethal test, mice	+	0	2.5 mg/kg x 1, i.p.	Semenov & Malashenko (1981)
MHT, Mouse heritable translocation test	+	0	5 mg/kg x 1, i.p.	Malashenko & Surkova (1974a)
MHT, Mouse heritable translocation test	+	0	1.25 mg/kg x 1, i.p.	Semenov & Malashenko (1977)
MHT, Mouse heritable translocation test	+	0	1.25 mg/kg x 1, i.p.	Malashenko et al. (1978)
MHT, Mouse heritable translocation test	+	0	1.25 mg/kg x 1, i.p.	Malashenko & Goetz (1981)
CLH, Chromosomal aberrations, human lymphocytes in vivo	+	0	0.14 mg/kg x 4 – x 10, i.m.	Selezneva & Korman (1973)
SPM, Sperm morphology, mice in vivo	+	0	2.5 mg/kg x 5, i.v.	Bruce & Heddle (1979)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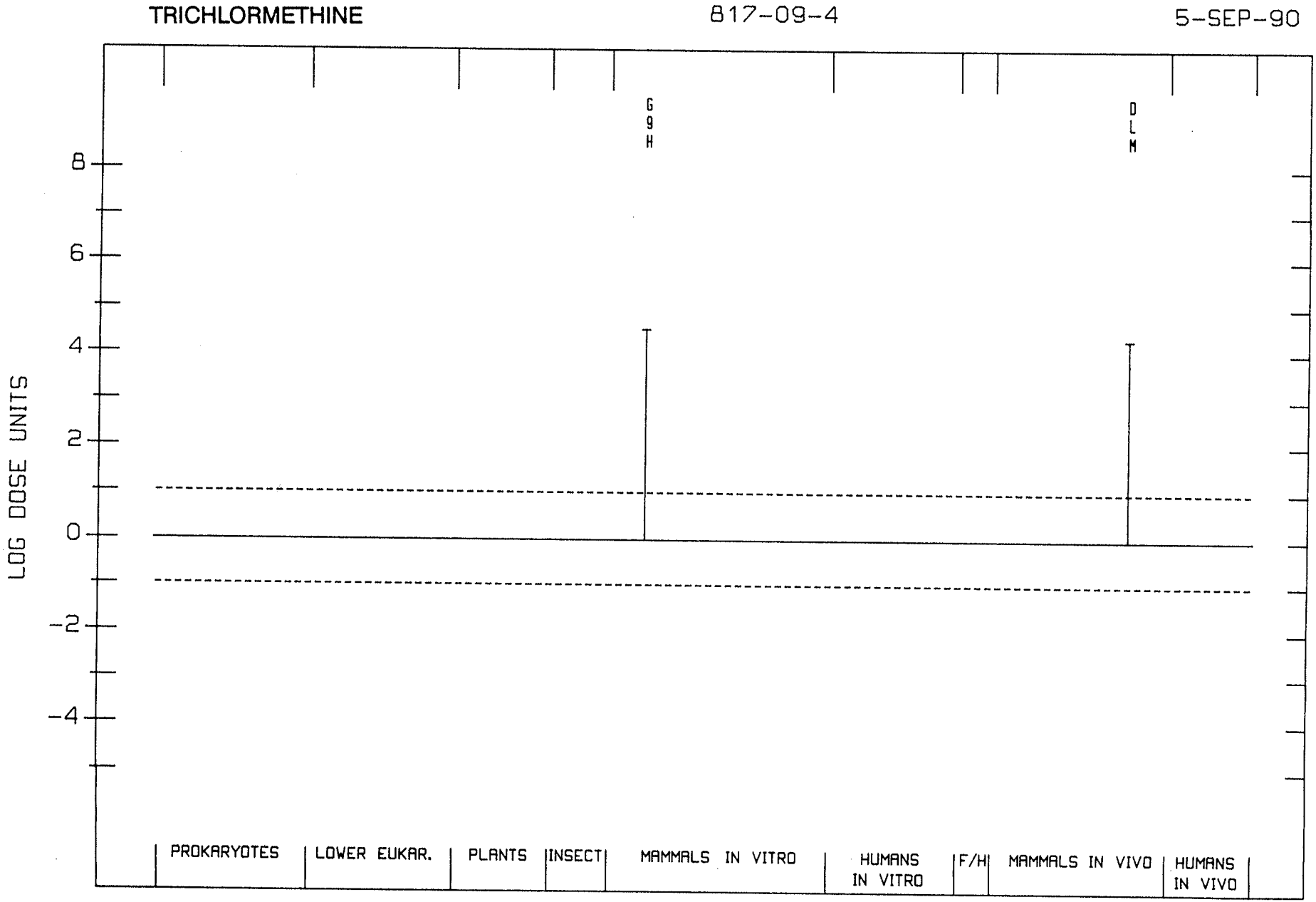
-4
PROKARYOTES
LOWER EUKAR.
PLANTS
INSECT
MAMMALS IN VITRO
HUMANS IN VITRO
F/H
MAMMALS IN VIVO
HUMANS IN VIVO

TRICHLORMETHINE

Test system	Result		Dose LED/HID	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
C9H, Gene mutation, Chinese hamster lung V79 cells, hprt locus	+	0	3 µg/ml	Slamenova et al. (1983)
CIT, Chromosomal aberrations, Walker 256 cells	+	0	1 mg/kg x 4 - x 10, i.p.	Boyland et al. (1948)
CIT, Chromosomal aberrations, Walker 256 cells	+	0	0	Koller (1969)
DLM, Dominant lethal test, mice	+	0	5 mg/kg x 1, i.p.	Sykora & Gandalovicova (1978)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5-SEP-90
LOG DOSE UNITS
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-2
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G
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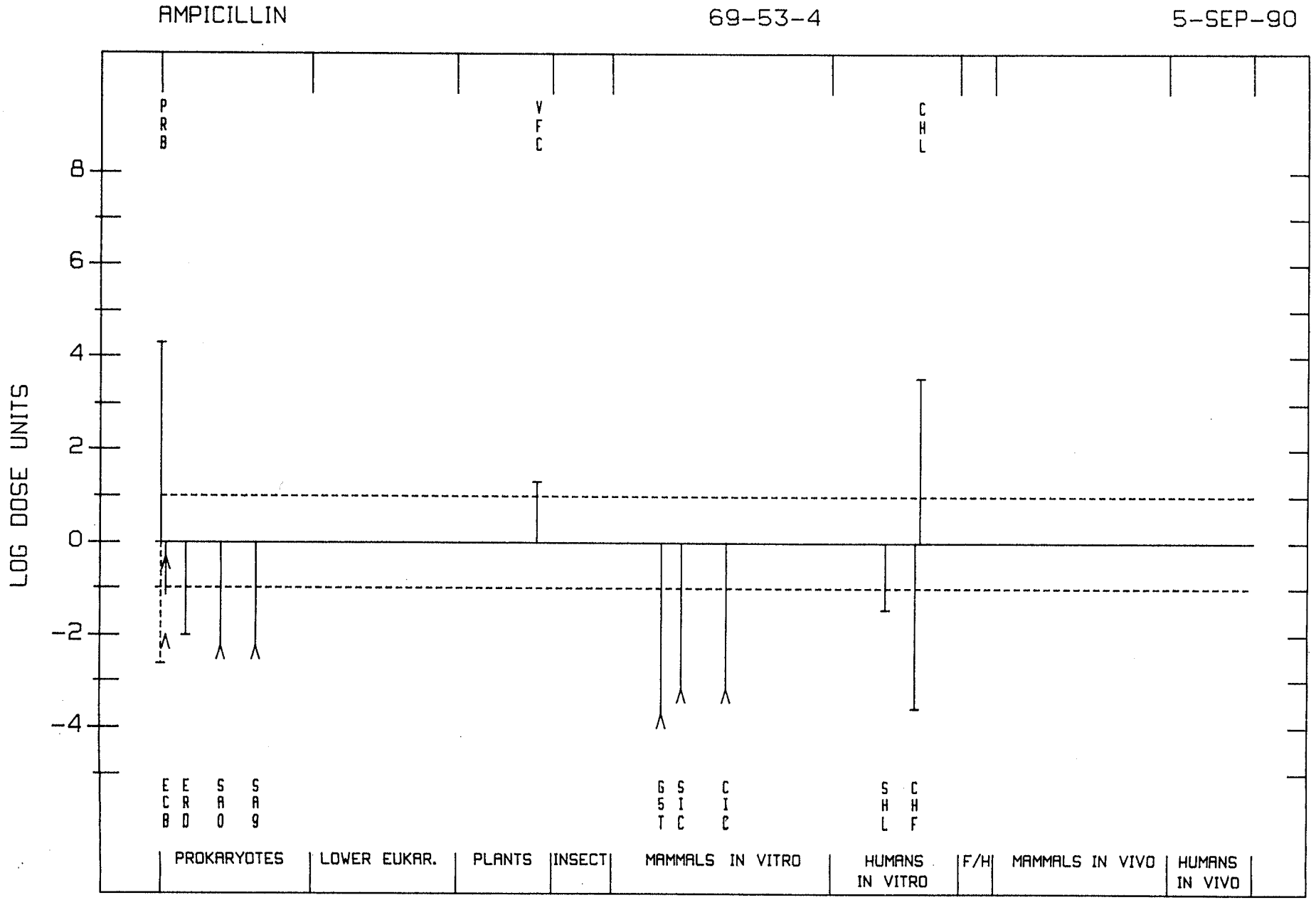
H
D
L
M
PROKARYOTES
LOWER EUKAR.
PLANTS
INSECT
MAMMALS IN VITRO
HUMANS IN VITRO
F/H
MAMMALS IN VIVO
HUMANS IN VIVO

AMPICILLIN

Test system	Result		Dose LED/HID	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
PRB, Staphylococcus aureus, prophage induction	+	0	5 µg/ml	Manthey et al. (1975)
PRB, Escherichia coli PQ37, SOS induction	–	0	417 µg/ml	Venier et al. (1989)
ERD, Escherichia coli, DNA repair	–	0	100 µg/ml	Green & Tweats (1981)
ECB, Escherichia coli, DNA repair	0	–	100 µg/ml	Tweats et al. (1981)
ECB, Escherichia coli, DNA repair	–	–	2 µg/ml	De Flora et al. (1984)
SA0, Salmonella typhimurium TA100, reverse mutation	–	0	0.00	De Flora et al. (1984)
SA0, Salmonella typhimurium TA100, reverse mutation	–	–	167 µg/ml	Mortelmans et al. (1986)
SA5, Salmonella typhimurium TA1535, reverse mutation	–	0	0.00	De Flora et al. (1984)
SA5, Salmonella typhimurium TA1535, reverse mutation	–	–	1 µg/ml	Mortelmans et al. (1986)
SA7, Salmonella typhimurium TA1537, reverse mutation	–	0	0.00	De Flora et al. (1984)
SA7, Salmonella typhimurium TA1537, reverse mutation	–	–	1 µg/ml	Mortelmans et al. (1986)
SA8, Salmonella typhimurium TA1538, reverse mutation	–	0	0.00	De Flora et al. (1984)
SA9, Salmonella typhimurium TA98, reverse mutation	–	0	0.00	De Flora et al. (1984)
SA9, Salmonella typhimurium TA98, reverse mutation	–	–	167 µg/ml	Mortelmans et al. (1986)
SA5, Salmonella typhimurium TA97, reverse mutation	–	0	0.00	De Flora et al. (1984)
VFC, Vicia faba, aberrant cell division	+	0	5000 µg/ml	Prasad (1977)
G5T, Gene mutation, mouse lymphoma L5178Y cells, TK locus	–	–	5000 µg/ml	National Toxicology Program (1987)
SIC, Sister chromatid exchange, Chinese hamster cells in vitro	–	–	1500 µg/ml	National Toxicology Program (1987)
CIC, Chromosomal aberrations, Chinese hamster cells in vitro	–	–	1500 µg/ml	National Toxicology Program (1987)
SHL, Sister chromatid exchange, human lymphocytes in vitro	–	0	28 µg/ml	Jaju et al. (1984)
CHF, Chromosomal aberrations, human fibroblasts in vitro	–	0	4000 µg/ml	Byarugaba et al. (1975)
CHL, Chromosomal aberrations, human lymphocytes in vitro	+	0	28 µg/ml	Jaju et al. (1984)


AMPICILLIN
69-53-4
5-SEP-90
LOG DOSE UNITS
8
6
4
2
0
-2
-4
PRB
VFC
CHL
ECB
ERD
SAO
SA9
GST
SIC
CIC
SHL
CHF
PROKARYOTES
LOWER EUKAR.
PLANTS
INSECT
MAMMALS IN VITRO
HUMANS IN VITRO
F/H
MAMMALS IN VIVO
HUMANS IN VIVO

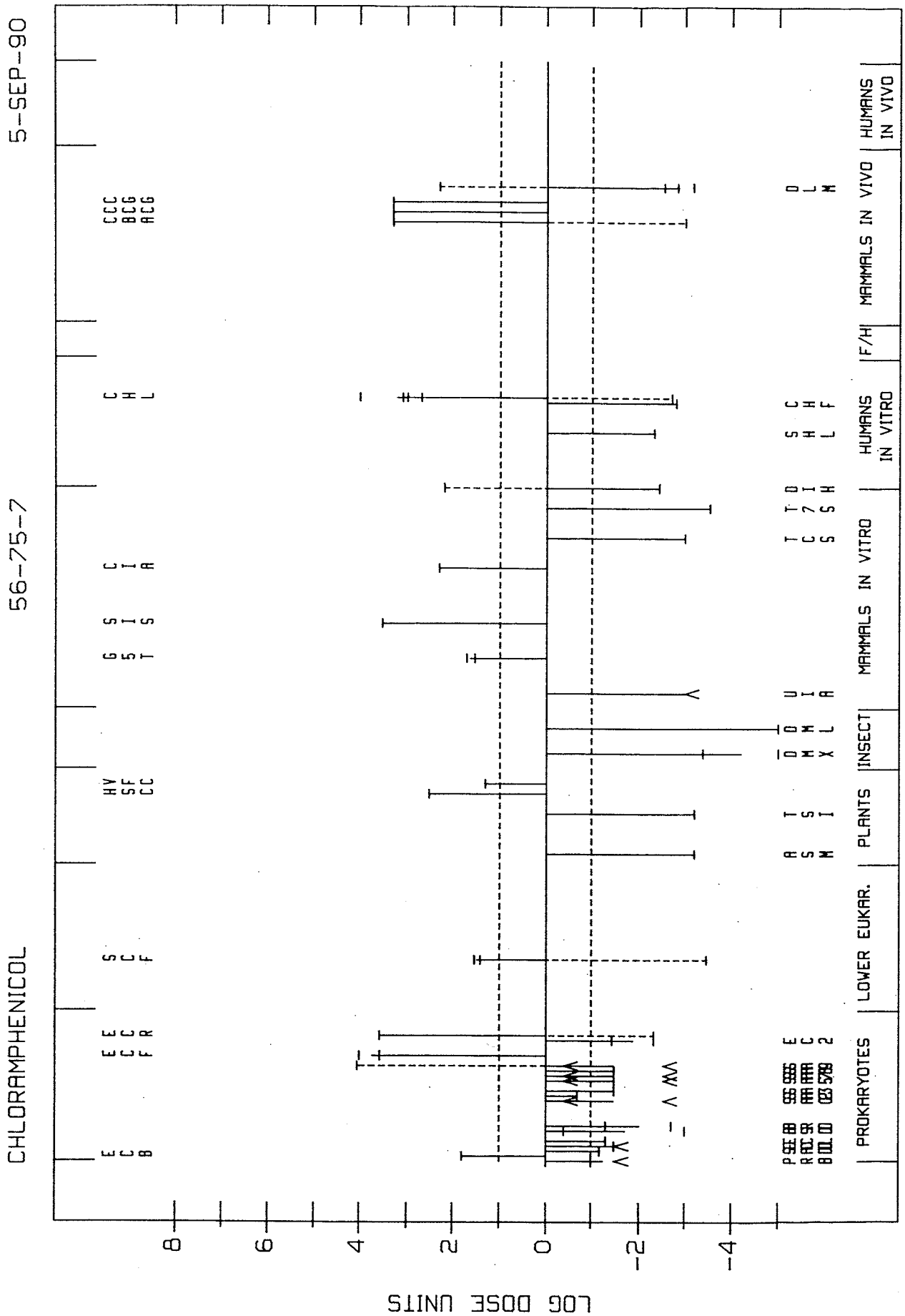
Test system	Result		Dose LED/HID	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
PRB, Prophage induction, SOS repair test, DNA strand breaks	–	0	10 µg/ml	Manthey et al. (1975)
PRB, Escherichia coli, DNA damage	–	–	30 µg/ml	Mamber et al. (1986)
Salmonella typhimurium, DNA breaks	±	0	0	Jackson et al. (1977)
ECB, Escherichia coli, DNA breaks	+	0	1615 µg/ml	Jackson et al. (1977)
SAD, Salmonella typhimurium, differential toxicity	–	0	15 µg/ml	Russell et al. (1980)
SAD, Salmonella typhimurium, differential toxicity	–	0	5 µg/ml	Nader et al. (1981)
ECD, Escherichia coli pol A, differential toxicity (spot test)	–	–	30 µg/ml	Longnecker et al. (1974)
ECD, Escherichia coli pol A, differential toxicity (spot test)	–	0	30 µg/ml	Nestmann et al. (1979)
ECD, Escherichia coli pol A, differential toxicity (spot test)	–	0	30 µg/ml	Boyle & Simpson (1980)
ECD, Escherichia coli pol A, differential toxicity (spot test)	–	–	30 µg/ml	Leifer et al. (1981)
ECL, Escherichia coli pol A, differential toxicity (liquid)	–	0	20 µg/ml	Leifer et al. (1981)
ECD, Escherichia coli, differential toxicity	–	0	30 µg/ml	Slater et al. (1971)
ECD, Escherichia coli, differential toxicity	–	0	0	Venturini & Monti-Bragadin (1978)
ERD, Escherichia coli, differential toxicity	+	0	0	Suter & Jaeger (1982)
ERD, Escherichia coli rec, differential toxicity	–	0	0.6 µg/ml	Shimizu & Rosenberg (1973)
BSD, Bacillus subtilis, differential toxicity	–	0	1000 µg/ml	Kada et al. (1972)
BSD, Bacillus subtilis, differential toxicity	–	0	2.5 µg/ml	Sekizawa & Shibamoto (1982)
BSD, Bacillus subtilis, differential toxicity	–	0	0	Suter & Jaeger (1982)
BRD, Bacteria (other), differential toxicity	–	0	500 µg/ml	Adler et al. (1976)
BRD, Bacteria (other), differential toxicity	–	0	20 µg/ml	Leifer et al. (1981)
SA0, Salmonella typhimurium TA100, reverse mutation	–	0	0	Jackson et al. (1977)
SA0, Salmonella typhimurium TA100, reverse mutation	0	–	2.5 µg/ml	McCann et al. (1975)
SA0, Salmonella typhimurium TA100, reverse mutation	–	–	333 µg/ml	Mortelmans et al. (1986)
SA3, Salmonella typhimurium TA1530, reverse mutation	–	0	30 µg/ml	Brem et al. (1974)
SA2, Salmonella typhimurium TA102, reverse mutation	–	0	5 µg/ml	Albertini & Gocke (1988)
SA5, Salmonella typhimurium TA1535, reverse mutation	–	0	30 µg/ml	Brem et al. (1974)
SA5, Salmonella typhimurium TA1535, reverse mutation	0	–	2.5 µg/ml	McCann et al. (1975)
SA5, Salmonella typhimurium TA1535, reverse mutation	–	0	0	Jackson et al. (1977)
SA5, Salmonella typhimurium TA1535, reverse mutation	–	–	333 µg/ml	Mortelmans et al. (1986)
SA7, Salmonella typhimurium TA1537, reverse mutation	0	–	2.5 µg/ml	McCann et al. (1975)
SA7, Salmonella typhimurium TA1537, reverse mutation	–	–	333 µg/ml	Mortelmans et al. (1986)
SA8, Salmonella typhimurium TA1538, reverse mutation	–	0	30 µg/ml	Brem et al. (1974)
SA9, Salmonella typhimurium TA98, reverse mutation	0	–	2.5 µg/ml	McCann et al. (1975)
SA9, Salmonella typhimurium TA98, reverse mutation	(+)	(+)	9 µg/ml	Mitchell et al. (1980)

CHLORAMPHENICOL (contd)

Test system	Result		Dose LED/HID	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
SA9, Salmonella typhimurium TA98, reverse mutation	–	–	333 µg/ml	Mortelmans et al. (1986)
SA9, Salmonella typhimurium TA98, reverse mutation	–	0	0	Jackson et al. (1977)
ECF, Escherichia coli, forward mutation	+	+	10 µg/ml	Mitchell et al. (1980)
ECF, Escherichia coli WP2, forward mutation	+	0	27 µg/ml	Mitchell & Gilbert (1985)
ECF, Escherichia coli CM891, forward mutation	(+)	0	27 µg/ml	Mitchell & Gilbert (1985)
EC2, Escherichia coli WP2, reverse mutation	–	0	200 µg/ml	Hemmerly & Demerec (1955)
EC2, Escherichia coli WP2, reverse mutation	–	0	27 µg/ml	Mitchell & Gilbert (1985)
ECR, Escherichia coli CM891, reverse mutation	–	0	200 µg/ml	Hemmerly & Demerec (1955)
ECR, Escherichia coli CM891, reverse mutation	+	0	27 µg/ml	Mitchell & Gilbert (1985)
SCF, Saccharomyces cerevisiae D1121, petite mutations	(+)	0	4000 µg/ml	Weislogel & Butow (1970)
SCF, Saccharomyces cerevisiae D35 and 44, petite mutations	(–)	0	3000 µg/ml	Carnevali et al. (1971)
SCF, Saccharomyces cerevisiae, petite mutations	(+)	0	3000 µg/ml	Williamson et al. (1971)
ASM, Arabidopsis species, mutation	–	0	1620 µg/ml	Muller (1965)
TSI, Tradescantia paludosa, micronuclei	–	0	1615 µg/ml	Ma et al. (1984)
HSC, Hordeum species, chromosomal aberrations	+	0	300 µg/ml	Yoshida et al. (1972)
VFC, Vicia faba, chromosomal aberrations	+	0	5000 µg/ml	Prasad (1977)
DMX, Drosophila melanogaster, sex-linked recessive lethal mutation	–	0	2500 µg/ml	Clark (1963)
DMX, Drosophila melanogaster, sex-linked recessive lethal mutation	–	0	100000 µg/ml	Nasrat et al. (1977)
DML, Drosophila melanogaster, dominant lethal test	–	0	100000 µg/ml	Nasrat et al. (1977)
UIA, Unscheduled DNA synthesis, Syrian hamster cells in vitro	–	–	1000 µg/ml	Suzuki (1987)
G5T, Gene mutation, mouse lymphoma L5178Y cells, TK locus	+	+	3000 µg/ml	Mitchell et al. (1988)
G5T, Gene mutation, mouse lymphoma L5178Y cells, TK locus	+	+	2000 µg/ml	Myhr & Caspary (1988)
SIS, Sister chromatid exchange, Syrian hamster cells in vitro	+	0	30 µg/ml	Suzuki (1987)
CIA, Chromosomal aberrations, other animal cells in vitro	+	0	500 µg/ml	Quéinnec et al. (1975)
TCS, Cell transformation, Syrian hamster embryo cells	–	0	1000 µg/ml	Suzuki (1987)
T7S, Cell transformation, SA7/Syrian hamster embryo cells	(–)	0	3490 µg/ml	Hatch et al. (1986)
DIH, DNA strand breaks, human lymphocytes in vitro	(+)	0	646 µg/ml	Yunis et al. (1987)
DIH, DNA strand breaks, human lymphocytes in vitro	–	0	258 µg/ml	Isildar et al. (1988)
DIH, DNA strand breaks, human lymphoblastoid cells in vitro	–	0	258 µg/ml	Isildar et al. (1988)
DIH, DNA strand breaks, human bone-marrow cells in vitro	–	0	258 µg/ml	Isildar et al. (1988)
SHL, Sister chromatid exchange, human lymphocytes in vitro	–	0	200 µg/ml	Pant et al. (1976)
CHF, Chromosomal aberrations, human fibroblasts in vitro	–	0	625 µg/ml	Byarugara et al. (1975)
CHL, Chromosomal aberrations, human lymphocytes in vitro	+	0	10 µg/ml	Mitus & Coleman (1970)
CHL, Chromosomal aberrations, human lymphocytes in vitro	–	0	500 µg/ml	Jensen (1972)

CHLORAMPHENICOL (contd)

Test system	Result		Dose LED/HID	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
CHL, Chromosomal aberrations, human lymphocytes in vitro	+	0	100 µg/ml	Sasaki & Tonomura (1973)
CHL, Chromosomal aberrations, human lymphocytes in vitro	+	0	80 µg/ml	Goh (1979)
CHL, Chromosomal aberrations, human lymphocytes in vitro	+	0	200 µg/ml	Pant et al. (1976)
CBA, Chromosomal aberrations, animal bone-marrow cells in vivo	–	0	1000 mg/kg x 3, i.m.	Jensen (1972)
CBA, Chromosomal aberrations, animal bone-marrow cells in vivo	(+)	0	50 mg/kg x 1, i.m.	Manna & Bardhan (1973)
CBA, Chromosomal aberrations, animal bone-marrow cells in vivo	(+)	0	50 mg/kg x 1, i.m.	Manna & Bardhan (1977)
CGG, Chromosomal aberrations, Swiss mouse meiotic cells in vivo	(+)	0	50 mg/kg x 1, i.m.	Roy & Manna (1981)
CCC, Chromosomal aberrations, Swiss mouse meiotic cells in vivo	(+)	0	50 mg/kg x 1, i.m.	Roy & Manna (1981)
DLM, Dominant lethal test, mice	–	0	333 mg/kg x 1, i.p.	Epstein & Shafner (1968)
DLM, Dominant lethal test (101KC3H)F1 mice	–	0	1500 mg/kg x 1, i.p.	Ehling (1971)
DLM, Dominant lethal test, mice	–	0	666 mg/kg x 1, i.p.	Epstein et al. (1972)
DLM, Dominant lethal test, mice	+	0	500 mg/kg x 1, i.p.	Sram (1972)


CHLORAMPHENICOL
56-75-7
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PROKARYOTES
LOWER EUKAR.
PLANTS
INSECT
MAMMALS IN VITRO
HUMANS IN VITRO
F/H
MAMMALS IN VIVO
HUMANS IN VIVO

NITROFURAL (NITROFURAZONE)

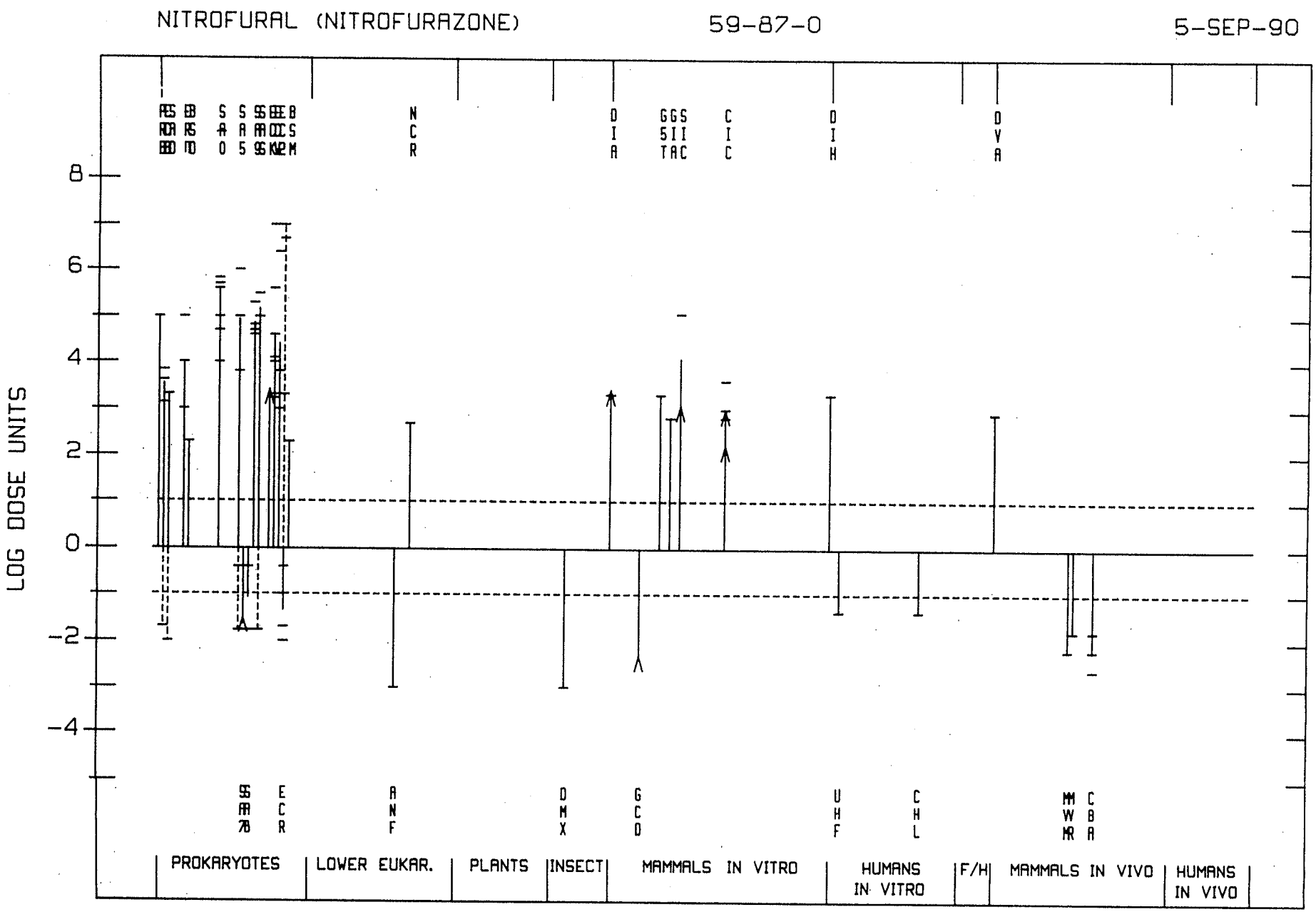
Test system	Result		Dose LED/HID	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
PRB, *Escherichia coli* T44(1), prophage induction	+	0	1.0 µg/ml	McCalla & Voutsinos (1974)
ECB, *Escherichia coli* B/R, DNA strand breaks	+	0	25 µg/ml	McCalla et al. (1971)
ECB, *Escherichia coli* c1256, DNA strand breaks	+	0	75 µg/ml	Tu & McCalla (1975)
ECB, *Escherichia coli* WP2A, DNA strand breaks	+	0	15 µg/ml	Wentzell & McCalla (1980)
ECB, *Escherichia coli* nfr-207, DNA strand breaks	–	0	50 µg/ml	McCalla et al. (1971)
SAD, *Salmonella typhimurium* TA1975, DNA strand breaks	+	0	50 µg/ml	McCalla et al. (1975)
SAD, *Salmonella typhimurium* TA1975, differential toxicity	–	0	100 µg/ml	Yahagi et al. (1974)
ERD, *Escherichia coli* WP100, differential toxicity	+	0	10 µg/ml	Haveland-Smith et al. (1979)
ERD, *Escherichia coli* WP67, differential toxicity	?	0	10 µg/ml	Haveland-Smith et al. (1979)
ERD, *Escherichia coli*, differential toxicity	+	0	100 µg/ml	Yahagi et al. (1974)
ERD, *Escherichia coli*, differential toxicity	+	0	1 µg/ml	Ebringer & Bencova (1980)
BSD, *Bacillus subtilis* HLL3g vs HJ-15, differential toxicity	+	0	500 µg/ml	Tanooka (1977)
BSM, *Bacillus subtilis* TKJ5211, mutation	+	0	500 µg/ml	Tanooka (1977)
SA0, *Salmonella typhimurium* TA100, fluctuation test	+	0	0.0001 µg/ml	Green et al. (1977)
SA0, *Salmonella typhimurium* TA100, reverse mutation	+	+	0.15 µg/ml	National Toxicology Program (1988)
SA0, *Salmonella typhimurium* TA100, reverse mutation	+	0	0.25 µg/ml	Goodman et al. (1977)
SA0, *Salmonella typhimurium* TA100, reverse mutation (spot test)	+	0	1 µg/ml	Yahagi et al. (1976)
SA0, *Salmonella typhimurium* TA100, reverse mutation	+	0	0.198 µg/ml	Chin et al. (1978)
SA0, *Salmonella typhimurium* TA100, reverse mutation	+	0	1.98 µg/ml	Rosin & Stich (1978)
SA0, *Salmonella typhimurium* TA100, reverse mutation	+	0	2 µg/ml	Bruce & Heddle (1979)
SA0, *Salmonella typhimurium* TA100, reverse mutation	+	0	10 µg/ml	Ebringer & Bencova (1980)
SA5, *Salmonella typhimurium* TA1535, fluctuation test	+	0	0.1 µg/ml	Green et al. (1977)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	(+)	+	16 µg/ml	National Toxicology Program (1988)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	–	0	2.5 µg/ml	McCalla et al. (1975)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	–	0	59.4 µg/ml	Yahagi et al. (1974)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	(+)	0	1 µg/ml	Yahagi et al. (1976)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	–	–	33 µg/ml	National Toxicology Program (1988)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	–	0	59.4 µg/ml	Yahagi et al. (1974)
SA8, *Salmonella typhimurium* TA1538, reverse mutation	–	0	2.5 µg/ml	McCalla et al. (1975)
SA8, *Salmonella typhimurium* TA1538, reverse mutation	–	0	59.4 µg/ml	Yahagi et al. (1974)
SA9, *Salmonella typhimurium* TA98, reverse mutation	+	+	2.5 µg/ml	Ni et al. (1987)
SA9, *Salmonella typhimurium* TA98, reverse mutation	+	+	1.5 µg/ml	National Toxicology Program (1988)
SA9, *Salmonella typhimurium* TA98, reverse mutation	+	0	0.5 µg/ml	Goodman et al. (1977)
SA9, *Salmonella typhimurium* TA98, reverse mutation	+	0	2 µg/ml	Bruce & Heddle (1979)

NITROFURAL (NITROFURAZONE) (contd)

Test system	Result		Dose LED/HID	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
SAS, Salmonella typhimurium TA98NR, reverse mutation	+	+	1 μg/ml	Ni et al. (1987)
SAS, Salmonella typhimurium TA98/1,8-DNP6, reverse mutation	+	+	1 μg/ml	Ni et al. (1987)
SAS, Salmonella typhimurium TA1536, reverse mutation	–	0	59.4 μg/ml	Yahagi et al. (1974)
SAS, Salmonella typhimurium TA97, reverse mutation (fluct. test)	+	0	0.32 μg/ml	Obaseiki-Ebor & Akerele (1986)
ECF, Escherichia coli 343/113/R-9, forward mutation	–	+	40 μg/ml	Baars et al. (1980)
ECW, Escherichia coli WP2uvrA, reverse mutation (spot test)	+	0	50 μg/ml	McCalla & Voutsinos (1974)
ECW, Escherichia coli WP2uvrA, reverse mutation	+	0	8 μg/ml	McCalla & Voutsinos (1974)
ECW, Escherichia coli WP2uvrA, reverse mutation (fluctuation test)	+	0	0.01 μg/ml	Green et al. (1977)
ECW, Escherichia coli WP2uvrA, reverse mutation	+	0	0.25 μg/ml	Haveland-Smith et al. (1979)
ECW, Escherichia coli WP2uvrA, reverse mutation	+	0	2.5 μg/ml	McCalla et al. (1975)
ECW, Escherichia coli WP2uvrA, reverse mutation	+	0	59.4 μg/ml	Yahagi et al. (1974)
ECW, Escherichia coli WP2uvrA, reverse mutation	+	0	10 μg/ml	Lu et al. (1979)
EC2, Escherichia coli WP2, reverse mutation (spot test)	(+)	0	100 μg/ml	McCalla & Voutsinos (1974)
EC2, Escherichia coli WP2, reverse mutation	+	0	16 μg/ml	McCalla & Voutsinos (1974)
EC2, Escherichia coli WP2, reverse mutation (fluctuation test)	(+)	0	0.04 μg/ml	Obaseiki-Ebor & Akerele (1986)
ECR, Escherichia coli nfr 343, reverse mutation	–	0	10 μg/ml	McCalla & Voutsinos (1974)
ECR, Escherichia coli nfr 343, reverse mutation	–	0	2.5 μg/ml	McCalla et al. (1975)
ECR, Escherichia coli nfr 345, reverse mutation	–	0	10 μg/ml	McCalla & Voutsinos (1974)
ECR, Escherichia coli CM561, reverse mutation	–	0	100 μg/ml	McCalla & Voutsinos (1974)
ECR, Escherichia coli CM571, reverse mutation	–	0	100 μg/ml	McCalla & Voutsinos (1974)
ECR, Escherichia coli CM611, reverse mutation	–	0	50 μg/ml	McCalla & Voutsinos (1974)
ECR, Escherichia coli S, Lac, reverse mutation	+	0	50 μg/ml	Zampieri & Greenberg (1964)
ECR, Escherichia coli CM611, reverse mutation (fluctuation test)	+	0	0.01 μg/ml	Green et al. (1977)
ECR, Escherichia coli EE97, reverse mutation (fluctuation test)	+	0	0.02 μg/ml	Obaseiki-Ebor & Akerele (1986)
ECR, Escherichia coli 343/113/R-9, reverse mutation	–	+	40 μg/ml	Baars et al. (1980)
ANF, Aspergillus nidulans, forward mutation	–	0	1000 μg/ml	Bignami et al. (1982)
NCR, Neurospora crassa, reverse mutation	+	0	198 μg/ml	Ong (1977)
DMX, Drosophila melanogaster, sex-linked recessive lethal mutation	–	0	990 μg/ml	Kramers (1982)
DIA, DNA single strand breaks, mouse L929 cells in vitro	+	0	49.5 μg/ml	Olive & McCalla (1975)
DIA, DNA single strand breaks, hamster BHK-21 cells in vitro	+	0	49.5 μg/ml	Olive & McCalla (1975)
DIA, DNA single strand breaks, mouse L929 cells in vitro	–	+	39.6 μg/ml	Olive (1978)
URP, Unscheduled DNA synthesis, rat primary hepatocytes	–	0	0.011 μg/ml	Mori et al. (1987)
UIA, Unscheduled DNA synthesis, mouse hepatocytes in vitro	–	0	0.011 μg/ml	Mori et al. (1987)
GCO, Gene mutation, Chinese hamster ovary cells in vitro	–	–	200 μg/ml	Anderson & Phillips (1985)
GIA, Gene mutation, Chinese hamster V79 cells, 6-thioguanine res.	+	0	150 μg/ml	Olive (1981)

NITROFURAL (NITROFURAZONE) (contd)

Test system	Result		Dose LED/HID	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
G5T, Gene mutation, mouse lymphoma L5178Y cells, TK locus	+	0	50 µg/ml	National Toxicology Program (1988)
SIC, Sister chromatid exchange, Chinese hamster CHO cells in vitro	+	0	0.83 µg/ml	National Toxicology Program (1988)
SIC, Sister chromatid exchange, Chinese hamster CHO cells in vitro	0	+	83.3 µg/ml	National Toxicology Program (1988)
CIC, Chromosomal aberrations, Chinese hamster lung cells in vitro	+	+	150 µg/ml	Ishidate (1988)
CIC, Chromosomal aberrations, Chinese hamster ovary cells in vitro	+	+	100 µg/ml	Anderson & Phillips (1985)
CIC, Chromosomal aberrations, Chinese hamster ovary cells in vitro	+	0	25 µg/ml	National Toxicology Program (1988)
CIC, Chromosomal aberrations, Chinese hamster ovary cells in vitro	0	–	600 µg/ml	National Toxicology Program (1988)
CIC, Chromosomal aberrations, Chinese hamster CHL cells in vitro	–	+	100 µg/ml	Matsuoka et al. (1979)
DIH, DNA single strand breaks, human KB cells in vitro	+	0	49.5 µg/ml	Olive & McCalla (1975)
UHF, Unscheduled DNA synthesis, normal human fibroblasts in vitro	–	0	23.8 µg/ml	Tonomura & Sasaki (1973)
UHF, Unscheduled DNA synthesis, human XP fibroblasts in vitro	–	0	23.8 µg/ml	Tonomura & Sasaki (1973)
CHL, Chromosomal aberrations, human lymphocytes in vitro	–	0	23.8 µg/ml	Tonomura & Sasaki (1973)
DVA, DNA strand breaks, mouse tissue in vivo	+	0	120 mg/kg x 25, p.o.	Olive (1978)
MVM, Micronucleus test, mice in vivo	–	0	150 mg/kg x 5, i.p.	Bruce & Heddle (1978)
MVR, Micronucleus test, Sprague–Dawley rats in vivo	–	0	60 mg/kg x 1, i.p.	Goodman et al. (1977)
MVR, Micronucleus test, Long-Evans rats in vivo	–	0	60 mg/kg x 1, i.p.	Goodman et al. (1977)
CBA, Chromosomal aberrations, rat bone-marrow cells in vivo	–	0	60 mg/kg x 1, i.p.	Goodman et al. (1977)
CBA, Chromosomal aberrations, rat bone-marrow cells in vivo	–	0	400 mg/kg x 1, p.o.	Anderson & Phillips (1985)
CBA, Chromosomal aberrations, rat bone-marrow cells in vivo	–	0	150 mg/kg x 5, p.o.	Anderson & Phillips (1985)
SPF, Sperm morphology, F1 mice in vivo	–	0	150 mg/kg x 5, i.p.	Bruce & Heddle (1978)


NITROFURAL (NITROFURAZONE)
59-87-0
5-SEP-90
LOG DOSE UNITS
8
6
4
2
0
-2
-4
PROKARYOTES
LOWER EUKAR.
PLANTS
INSECT
MAMMALS IN VITRO
HUMANS IN VITRO
F/H
MAMMALS IN VIVO
HUMANS IN VIVO

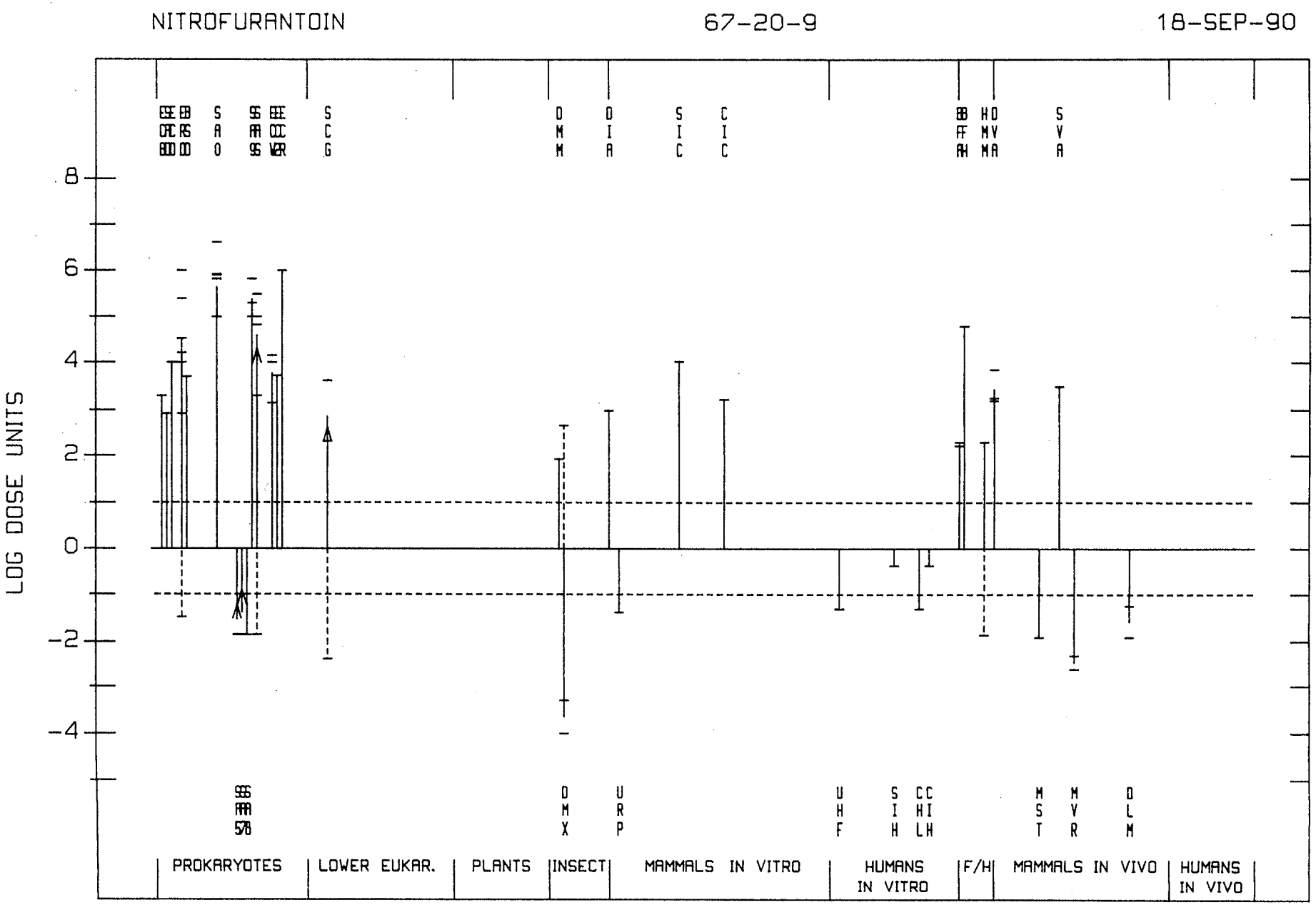
Test system	Result		Dose LED/HID	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
SAD, Salmonella typhimurium, differential toxicity	+	0	119 µg/ml	Yahagi et al. (1974)
ECB, Escherichia coli DNA strand breaks	(+)	0	50 µg/ml	McCalla et al. (1971)
ECD, Escherichia coli W3110 vs p3478 differential toxicity	+	0	10 µg/ml	McCarroll et al. (1981a)
ERD, Escherichia coli WP2 vs WPuvrA, differential toxicity	+	0	10 µg/ml	Ebringer & Bencova (1980)
ERD, Escherichia coli WP2 vs WPuvrA, differential toxicity	+	0	3 µg/ml	McCarroll et al. (1981a)
ERD, Escherichia coli WP2 vs WP67, differential toxicity	–	0	30 µg/ml	McCarroll et al. (1981a)
ERD, Escherichia coli WP2 vs CM611 differential toxicity	+	0	3 µg/ml	McCarroll et al. (1981a)
ERD, Escherichia coli WP2 vs WP100, differential toxicity	+	0	0.1 µg/ml	McCarroll et al. (1981a)
ERD, Escherichia coli WP2 vs WP67, differential toxicity	+	+	6.25 µg/ml	De Flora et al. (1984)
ERD, Escherichia coli WP2 vs CM871, differential toxicity	+	+	0.4 µg/ml	De Flora et al. (1984)
ERD, Escherichia coli, differential toxicity	+	0	119 µg/ml	Yahagi et al. (1974)
ERD, Escherichia coli, differential toxicity	+	0	0	Suter & Jaeger (1982)
BSD, Bacillus subtilis, H-17 vs M-45, differential toxicity	+	0	20 µg/ml	McCarroll et al. (1981b)
BSD, Bacillus subtilis, rec strains, differential toxicity	+	0	0	Suter & Jaeger (1982)
SA0, Salmonella typhimurium TA100, reverse mutation	+	0	0.15 µg/ml	Wang & Lee (1976)
SA0, Salmonella typhimurium TA100, reverse mutation	+	+	0.025 µg/ml	De Flora (1979)
SA0, Salmonella typhimurium TA100, reverse mutation	+	+	0.15 µg/ml	Haworth et al. (1983)
SA0, Salmonella typhimurium TA100, reverse mutation	+	0	0.125 µg/ml	Goodman et al. (1977)
SA0, Salmonella typhimurium TA100, reverse mutation	+	+	1 µg/ml	Rosenkranz & Speck (1976)
SA0, Salmonella typhimurium TA100, reverse mutation	+	0	0.119 µg/ml	Shirai & Wang (1980)
SA0, Salmonella typhimurium TA100, reverse mutation	+	0	1 µg/ml	Yahagi et al. (1974)
SA0, Salmonella typhimurium TA100, reverse mutation	+	0	1 µg/ml	Ebringer & Bencova (1980)
SA5, Salmonella typhimurium TA1535, reverse mutation	–	–	16 µg/ml	Haworth et al. (1983)
SA5, Salmonella typhimurium TA1535, reverse mutation	–	0	71 µg/ml	Yahagi et al. (1974)
SA7, Salmonella typhimurium TA1537, reverse mutation	–	–	8 µg/pl	Haworth et al. (1983)
SA7, Salmonella typhimurium TA1537, reverse mutation	–	0	71 µg/ml	Yahagi et al. (1974)
SA8, Salmonella typhimurium TA1538, reverse mutation	–	0	71 µg/ml	Yahagi et al. (1974)
SA9, Salmonella typhimurium TA98, reverse mutation	+	+	0.15 µg/ml	Haworth et al. (1983)
SA9, Salmonella typhimurium TA98, reverse mutation	+	+	1 µg/ml	Ni et al. (1987)
SA9, Salmonella typhimurium TA98, reverse mutation	+	0	0.5 µg/ml	Goodman et al. (1977)
SA5, Salmonella typhimurium TA100FR1, reverse mutation	+	0	1.5 µg/ml	Wang & Lee (1976)
SA5, Salmonella typhimurium TA98NR, reverse mutation	+	+	50 µg/ml	Ni et al. (1987)
SA5, Salmonella typhimurium TA98/1,8-DNP6, reverse mutation	+	+	1 µg/ml	Ni et al. (1987)

NITROFURANTOIN (contd)

Test system	Result		Dose LED/HID	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
SAS, Salmonella typhimurium TA1536, reverse mutation	–	0	71 μg/ml	Yahagi et al. (1974)
SAS, Salmonella typhimurium TA97, reverse mutation (fluct. test)	+	0	0.32 μg/ml	Obaseiki-Ebor & Akerele (1986)
SAS, Salmonella typhimurium TA100FR1, reverse mutation	–	+	5 μg/ml	Rosenkranz & Speck (1976)
ECW, Escherichia coli WP2 uvrA, reverse mutation	+	0	71 μg/ml	Yahagi et al. (1974)
ECW, Escherichia coli WP2 uvrA, reverse mutation	+	0	10 μg/ml	McCalla & Vouteinos (1974)
ECW, Escherichia coli WP2 uvrA, reverse mutation	+	0	7.14 μg/ml	Lu et al. (1979)
EC2, Escherichia coli WP2, reverse mutation (fluctuation test)	–	0	0.4 μg/ml	Obaseiki-Ebor & Akerele (1986)
EC2, Escherichia coli WP2, reverse mutation	(+)	0	19 μg/ml	McCalla & Vouteinos (1974)
ECR, Escherichia coli EE97, reverse mutation (fluctuation test)	+	0	0.1 μg/ml	Obaseiki-Ebor & Akerele (1986)
SCG, Saccharomyces cerevisiae D4-RDII, mitotic gene conversion	+	0	23.8 μg/ml	Siebert et al. (1979)
SCG, Saccharomyces cerevisiae D4-RDII, mitotic gene conversion	0	+	238 μg/ml	Siebert et al. (1979)
SCG, Saccharomyces cerevisiae D7, mitotic gene conversion	+	0	476 μg/ml	Callen (1981)
ANG, Aspergillus nidulans, crossing over	+	0	0	Bignami et al. (1974)
SCG, Saccharomyces cerevisiae D4, reverse mutation/gene conversion	–	0	238 μg/ml	Setnikar et al. (1976)
DMX, Drosophila melanogaster, sex-linked recessive lethal mutation	(+)	0	214 μg/ml	Kramers (1982)
DMX, Drosophila melanogaster, sex-linked recessive lethal mutation	–	0	2000 μg/ml (food)	Zimmering et al. (1985)
DMX, Drosophila melanogaster, sex-linked recessive lethal mutation	–	0	10000 μg/ml (injection)	Zimmering et al. (1985)
DMM, Drosophila melanogaster, somatic mutation	+	0	1190 μg/ml	Graf et al. (1989)
DIA, DNA single strand breaks, mouse L cells in vitro	+	0	102 μg/ml	Olive & McCalla (1977)
URP, Unscheduled DNA synthesis, rat primary hepatocytes	–	0	23.8 μg/ml	Williams et al. (1989)
SIC, Sister chromatid exchange, Chinese hamster CHO cells in vitro	+	0	9.5 μg/ml	Shirai & Wang (1980)
CIC, Chromosomal aberrations, Chinese hamster lung cells in vitro	+	0	60 μg/ml	Ishidate (1988)
UHF, Unscheduled DNA synthesis, human fibroblasts in vitro	–	0	20 μg/ml	Tonomura & Sasaki (1973)
UHF, Unscheduled DNA synthesis, human XP fibroblasts in vitro	–	0	20 μg/ml	Tonomura & Sasaki (1973)
SIH, Sister chromatid exchange, human HE2144 cells in vitro	–	0	2.38 μg/ml	Sasaki et al. (1980)
CHL, Chromosomal aberrations, human lymphocytes in vitro	–	0	20 μg/ml	Tonomura & Sasaki (1973)
CIH, Chromosomal aberrations, human HE2144 cells in vitro	–	0	2.38 μg/ml	Sasaki et al. (1980)
BFA, Salmonella typhimurium TA100, reverse mutation (rat urine)	+	0	600 mg/kg x 4, p.o.	Wang & Lee (1976)
BFA, Salmonella typhimurium TA100FR1, reverse mutation (rat urine)	(+)	0	600 mg/kg x 4, p.o.	Wang & Lee (1976)
BFA, Saccharomyces cerevisiae D4-RDII, mitotic gene conversion	+	0	500 mg/kg x 1, p.o.	Siebert et al. (1979)
BFH, Salmonella typhimurium TA100, reverse mutation (human urine)	+	0	1.6 mg/kg x 1, p.o.	Wang et al. (1977)
BFH, Salmonella typhimurium TA100FR1, reverse mutation (human urine)	(+)	0	1.6 mg/kg x 1, p.o.	Wang et al. (1977)
HMM, Saccharomyces cerevisiae D4, reverse mutation/gene conversion	–	0	71 mg/kg x 1, p.o.	Setnikar et al. (1976)
HMM, Saccharomyces cerevisiae D4-RDII, mitotic gene conversion	–	0	500 mg/kg x 1, p.o. 6 h	Siebert et al. (1979)

NITROFURANTOIN (contd)

Test system	Result		Dose LED/HID	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
HMM, Saccharomyces cerevisiae D4-RDII, mitotic gene conversion	+	0	500 mg/kg x 1, p.o. 8h	Siebert et al. (1979)
DVA, DNA damage, Sprague-Dawley rats in vivo	+	0	56 mg/kg x 1, i.p.	Russo et al. (1982)
DVA, DNA damage, Sprague-Dawley rats in vivo	+	0	14 mg/kg x 1, i.p.	Parodi et al. (1983)
DVA, DNA damage, mouse bone-marrow cells in vivo	+	0	64 mg/kg x 1, i.p.	Parodi et al. (1983)
MST, Mouse spot test	-	0	80 mg/kg x 1, i.p.	Gocke et al. (1983)
SVA, Sister chromatid exchange, mouse bone-marrow cells in vivo	+	0	32 mg/kg x 1, i.p.	Parodi et al. (1983)
MVR, Micronucleus test, Sprague-Dawley rats in vivo	-	0	400 mg/kg x 1, p.o.	Setnikar et al. (1976)
MVR, Micronucleus test, Sprague-Dawley rats in vivo	-	0	200 mg/kg x 1, i.p.	Goodman et al. (1977)
CCC, Chromosomal aberrations, male NMRI mice meiotic cells	?	0	40 mg/kg x 2, i.p.	Fonatsch (1977)
DLM, Dominant lethal test, ICR/Ha Swiss mice	-	0	80 mg/kg x 1, i.p.	Epstein et al. (1972)
DLM, Dominant lethal test, NMRI mice	-	0	17.5 mg/kg x 1, p.o.	Setnikar et al. (1976)


NITROFURANTOIN
67-20-9
18-SEP-90
LOG DOSE UNITS
8
6
4
2
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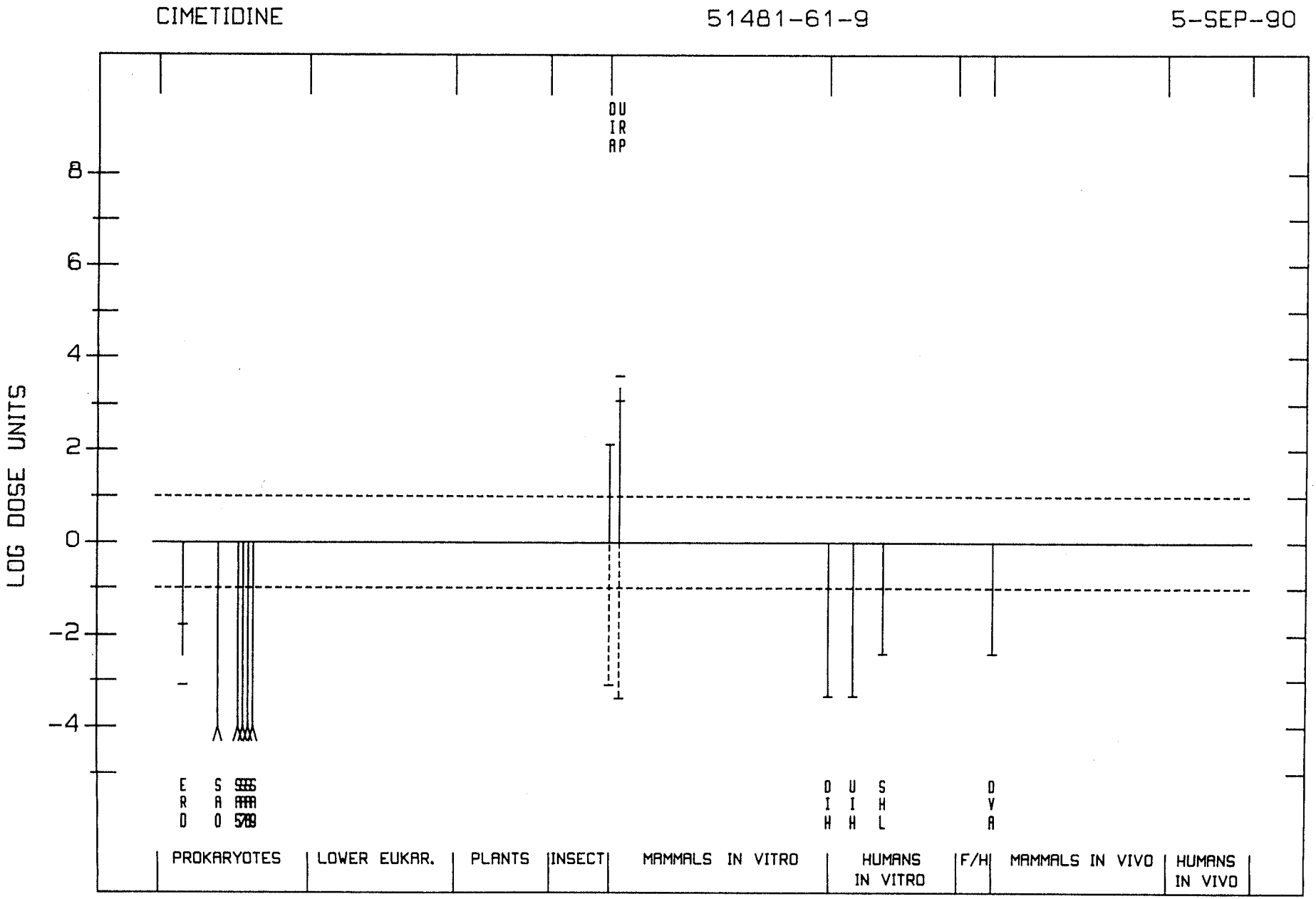
-2
-4
PROKARYOTES
LOWER EUKAR.
PLANTS
INSECT
MAMMALS IN VITRO
HUMANS IN VITRO
F/H
MAMMALS IN VIVO
HUMANS IN VIVO

CIMETIDINE

Test system	Result		Dose LED/HID	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
ERD, Escherichia coli, differential toxicity	–	0	60 µg/ml	Pool et al. (1979
ERD, Escherichia coli, differential toxicity	–	0	1250 µg/ml	De Flora (1981)
SA0, Salmonella typhimurium TA100, reverse mutation	–	–	10000 µg/ml	De Flora & Picciotto (1980)
SA5, Salmonella typhimurium TA1535, reverse mutation	–	–	10000 µg/ml	De Flora & Picciotto (1980)
SA7, Salmonella typhimurium TA1537, reverse mutation	–	–	10000 µg/ml	De Flora & Picciotto (1980)
SA8, Salmonella typhimurium TA1538, reverse mutation	–	–	10000 µg/ml	De Flora & Picciotto (1980)
SA9, Salmonella typhimurium TA98, reverse mutation	–	–	10000 µg/ml	De Flora & Picciotto (1980)
DIA, DNA strand breaks, transformed mouse epithelial cells in vitro	–	0	1260 µg/ml	Schwarz et al. (1980)
DIA, DNA damage, rat hepatocytes in vitro	+	0	756 µg/ml[a]	Martelli et al. (1983)
URP, Unscheduled DNA synthesis, rat primary hepatocytes	+	0	83 µg/ml[a]	Martelli et al. (1983)
URP, Unscheduled DNA synthesis, rat primary hepatocytes	–	0	2520 µg/ml	Lefevre & Ashby (1985)
URP, Unscheduled DNA synthesis, rat primary hepatocytes	+	0	25.2 µg/ml[a]	Lefevre & Ashby (1985)
DIH, DNA damage, human hepatocytes in vitro	–	0	2268 µg/ml[a]	Martelli et al. (1986)
UIH, Unscheduled DNA synthesis, human hepatocytes in vitro	–	0	2268 µg/ml[a]	Martelli et al. (1986)
SHL, Sister chromatid exchange, human lymphocytes in vitro	–	0	252 µg/ml	Inoue et al. (1985)
DVA, DNA damage, rat liver cells in vivo	–	0	250 mg/kg x1 – x20 p.o.[b]	Brambilla et al. (1982)
DVA, DNA damage, rat gastric mucosa in vivo	–	0	250 mg/kg x 1 p.o.[b]	Pino & Robbiano (1983)

[a] Cimetidine hydrochloride
[b] With $NaNO_2$, 80 mg/kg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51481-61-9
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SH
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DV
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PROKARYOTES
LOWER EUKAR.
PLANTS
INSECT
MAMMALS IN VITRO
HUMANS IN VITRO
F/H
MAMMALS IN VIVO
HUMANS IN VIVO

N-NITROSOCIMETIDINE/CIMETIDINE PLUS NITRITE

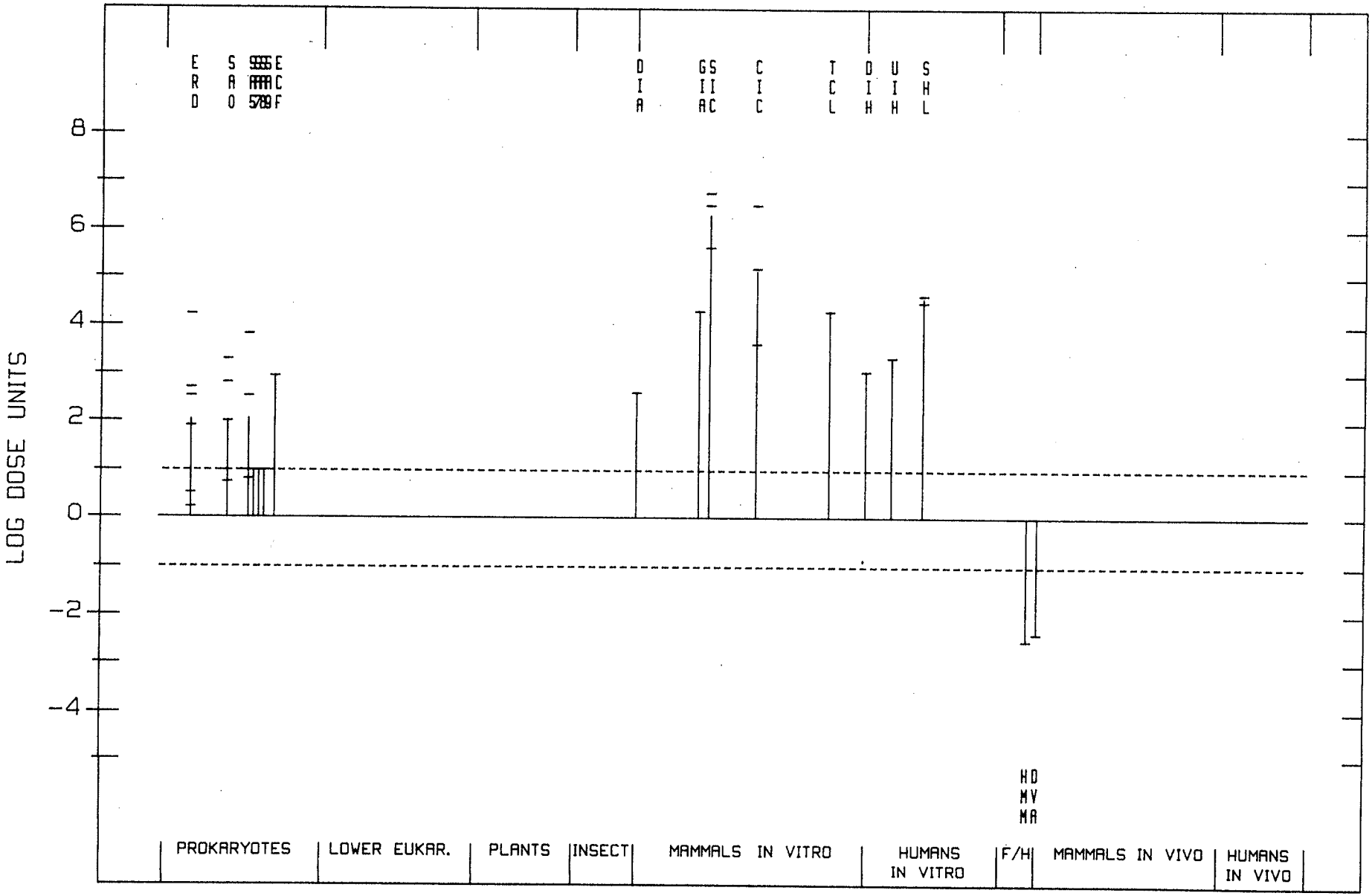
Test system	Result		Dose LED/HID	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
ERD, Escherichia coli, differential toxicity	+	0	6 µg/ml	Pool et al. (1979)
ERD, Escherichia coli, differential toxicity	+	0	1250 µg/ml[a]	De Flora (1981)
ERD, Escherichia coli, differential toxicity	+	0	60000 µg/ml[b]	Ichinotsubo et al. (1981)
ERD, Escherichia coli, differential toxicity	+	0	200 µg/ml[c]	Ichinotsubo et al. (1981)
ERD, Escherichia coli (WP2 trp–) strains, differential toxicity	+	0	30000 µg/ml[b]	Ichinotsubo et al. (1981)
ERD, Escherichia coli (WP2 trp–) strains, differential toxicity	+	0	300 µg/ml[c]	Ichinotsubo et al. (1981)
ECF, Escherichia coli, forward mutation	+	0	112 µg/ml	Alldrick et al. (1984)
SA0, Salmonella typhimurium TA100, reverse mutation	+	0	155 µg/ml[d]	De Flora & Picciotto (1980)
SA0, Salmonella typhimurium TA100, reverse mutation	+	+	10000 µg/ml[d]	De Flora & Picciotto (1980)
SA0, Salmonella typhimurium TA100, reverse mutation	+	+	50 µg/ml	De Flora (1981)
SA0, Salmonella typhimurium TA100, reverse mutation	+	0	17500 µg/ml[b]	Ichinotsubo et al. (1981)
SA0, Salmonella typhimurium TA100, reverse mutation	+	0	1000 µg/ml[c]	Ichinotsubo et al. (1981)
SA5, Salmonella typhimurium TA1535, reverse mutation	+	0	15 µg/ml	Pool et al. (1979)
SA5, Salmonella typhimurium TA1535, reverse mutation	+	+	10000 µg/ml[d]	De Flora & Picciotto (1980)
SA5, Salmonella typhimurium TA1535, reverse mutation	+	0	15000 µg/ml[b]	Ichinotsubo et al. (1981)
SA5, Salmonella typhimurium TA1535, reverse mutation	+	0	300 µg/ml[c]	Ichinotsubo et al. (1981)
SA7, Salmonella typhimurium TA1537, reverse mutation	+	+	10000 µg/ml[d]	De Flora & Picciotto (1980)
SA8, Salmonella typhimurium TA1538, reverse mutation	+	+	10000 µg/ml[d]	De Flora & Picciotto (1980)
SA9, Salmonella typhimurium TA98, reverse mutation	+	+	10000 µg/ml[d]	De Flora & Picciotto (1980)
DIA, DNA damage, transformed mouse epithelial cells	+	0	252 µg/ml	Schwarz et al. (1980)
GIA, Gene mutation, BHK-21/C113 hamster cells in vitro	+	0	5 µg/ml	Barrows et al. (1982)
SIC, Sister chromatid exchange, Chinese hamster CHO cells in vitro	+	0	0.03 µg/ml[b]	Athanasiou & Kyrtopoulos (1981)
SIC, Sister chromatid exchange, Chinese hamster CHO cells in vitro	+	0	0.23 µg/ml[b]	Ichinotsubo et al. (1981)
SIC, Sister chromatid exchange, Chinese hamster CHO cells in vitro	+	0	0.017 µg/ml[c]	Ichinotsubo et al. (1981)
CIC, Chromosomal aberrations, Chinese hamster CHO cells in vitro	+	0	0.03 µg/ml	Athanasiou & Kyrtopoulos (1981)
CIC, Chromosomal aberrations, Chinese hamster CHO cells in vitro	+	0	23.18 µg/ml[b]	Ichinotsubo et al. (1981)
CIC, Chromosomal aberrations, Chinese hamster CHO cells in vitro	+	0	0.65 µg/ml[c]	Ichinotsubo et al. (1981)
TCL, Cell transformation, BHK-21/C113 hamster cells	+	0	5 µg/ml	Barrows et al. (1982)]
DIH, DNA damage, human lymphoblastoid cell line in vitro	+	0	88 µg/ml	Henderson et al. (1981)
UIH, Unscheduled DNA synthesis, human leukocytes in vitro	+	0	45 µg/ml	Henderson et al. (1981)
UIH, Unscheduled DNA synthesis, human lymphoblasts in vitro	+	0	45 µg/ml	Henderson et al. (1981)
SHL, Sister chromatid exchange, human lymphocytes in vitro	+	0	3.28 µg/ml	Inoue et al. (1985)
SHL, Sister chromatid exchange, human lymphocytes in vitro	+	0	2.37 µg/ml	Inoue et al. (1985)
HMM, Host-mediated assay, Salmonella typhimurium in mice	–	0	350 mg/kg[e]	Baumeister (1982)

N-NITROSOCIMETIDINE/CIMETIDINE PLUS NITRITE (contd)

Test system	Result		Dose LED/HID	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
DVA, DNA damage, rat liver cells in vivo	-	0	250 mg/kg[f] x1 - x20 p.o.	Brambilla et al. (1982)
DVA, DNA damage, rat gastric mucosa in vivo	-	0	250 mg/kg[f] x 1 p.o.	Pino & Robbiano (1983)

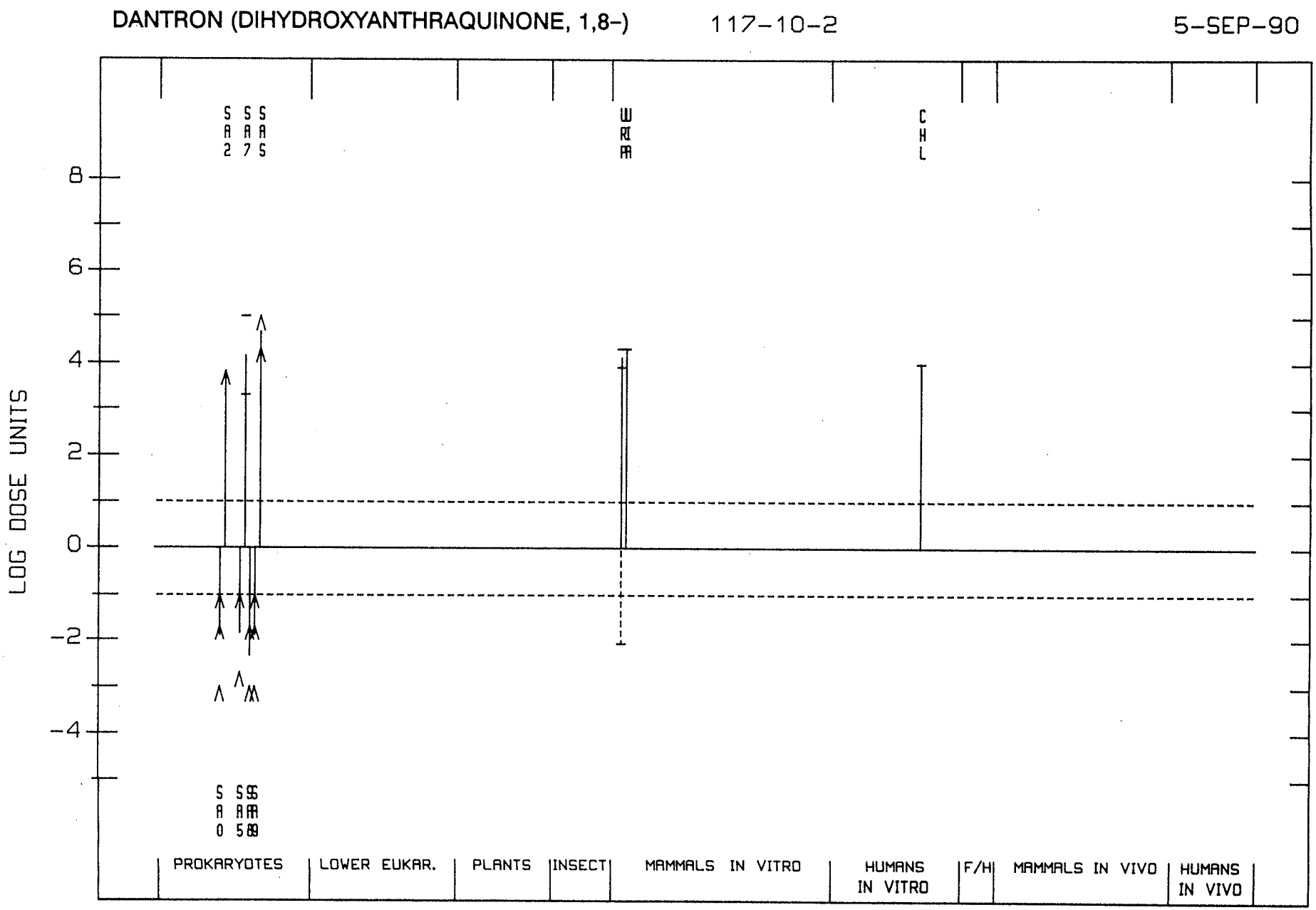
[a] With 2.5 mg $NaNO_2$, pH 3, 1 h
[b] Mononitrosocimetidine
[c] Dinitrosocimetidine
[d] With 5 mg $NaNO_2$, human gastric juice, pH 1.37, 1 h, 37°C
[e] With 60/120 mg/kg $NaNO_2$
[f] With 80 mg/kg $NaNO_2$

N-NITROSOCIMETIDINE 73785-40-7 5-SEP-90



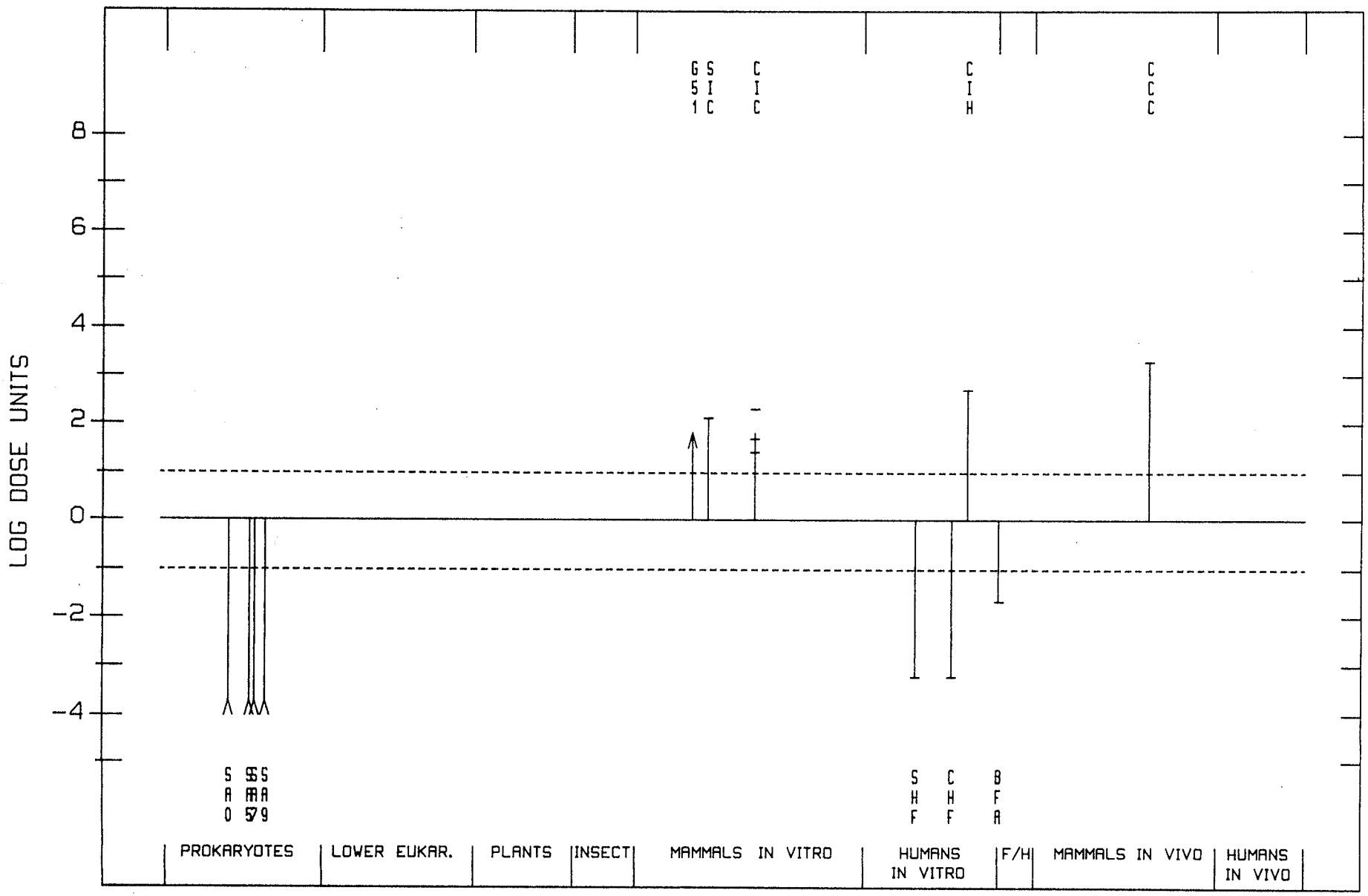
DANTRON (1,8-DIHYDROXYANTHRAQUINONE)

Test system	Result		Dose LED/HID	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
SA0, Mutation, Salmonella typhimurium TA100	–	–	1000 µg/ml	Brown & Brown (1976)
SA0, Mutation, Salmonella typhimurium TA100	–	–	10 µg/ml	Liberman et al. (1982)
SA0, Mutation, Salmonella typhimurium TA100	–	–	50 µg/ml	Tikkanen et al. (1983)
SA2, Mutation, Salmonella typhimurium TA102	–	+	15 µg/ml	Levin et al. (1984)
SA5, Mutation, Salmonella typhimurium TA1535	–	–	500 µg/ml	Brown & Brown (1976)
SA5, Mutation, Salmonella typhimurium TA1535	–	–	10 µg/ml	Liberman et al. (1982)
SA7, Mutation, Salmonella typhimurium TA1537	+	+	50 µg/ml	Brown & Brown (1976)
SA7, Mutation, Salmonella typhimurium TA1537	+	+	1 µg/ml	Liberman et al. (1982)
SA8, Mutation, Salmonella typhimurium TA1538	–	–	1000 µg/ml	Brown & Brown (1976)
SA8, Mutation, Salmonella typhimurium TA1538	–	–	50 µg/ml	Liberman et al. (1982)
SA9, Mutation, Salmonella typhimurium TA98	–	–	1000 µg/ml	Brown & Brown (1976)
SA9, Mutation, Salmonella typhimurium TA98	–	–	10 µg/ml	Liberman et al. (1982)
SA9, Mutation, Salmonella typhimurium TA98	–	–	50 µg/ml	Tikkanen et al. (1983)
SAS, Mutation, Salmonella typhimurium TA104	0	+	4.8 µg/ml	Chesis et al. (1984)
SAS, Mutation, Salmonella typhimurium TA2637	–	+	1 µg/ml	Tikkanen et al. (1983)
SCR, Saccharomyces cerevisiae, forward mutation	+	0	0	Zetterberg & Swanbeck (1971)
URP, Unscheduled DNA synthesis, rat primary hepatocytes	–	0	120 µg/ml	Probst et al. (1981)
URP, Unscheduled DNA synthesis, rat primary hepatocytes	+	0	4.8 µg/ml	Mori et al. (1984)
URP, Unscheduled DNA synthesis, rat primary hepatocytes	+	0	12 µg/ml	Kawai et al. (1986)
UIA, Unscheduled DNA synthesis, mouse hepatocytes	+	0	4.8 µg/ml	Mori et al. (1984)
CHL, Chromosomal aberrations, human lymphocytes in vitro	+	0	10 µg/ml	Carballo et al. (1981)
ICR, Inhibition of intercellular communication, animal cells in vitro	–	0	3 µg/ml	Zeilmaker & Yamasaki (1986)
ICR, Inhibition of intercellular communication, animal cells in vitro	–	0	2.4 µg/ml	Si et al. (1988)


DANTRON (DIHYDROXYANTHRAQUINONE, 1,8-)
117-10-2
5-SEP-90
LOG DOSE UNITS
8
6
4
2
0
-2
-4
SA2
SA7
SA5
WRA
CHL
SA0
SA5
SA8
PROKARYOTES
LOWER EUKAR.
PLANTS
INSECT
MAMMALS IN VITRO
HUMANS IN VITRO
F/H
MAMMALS IN VIVO
HUMANS IN VIVO

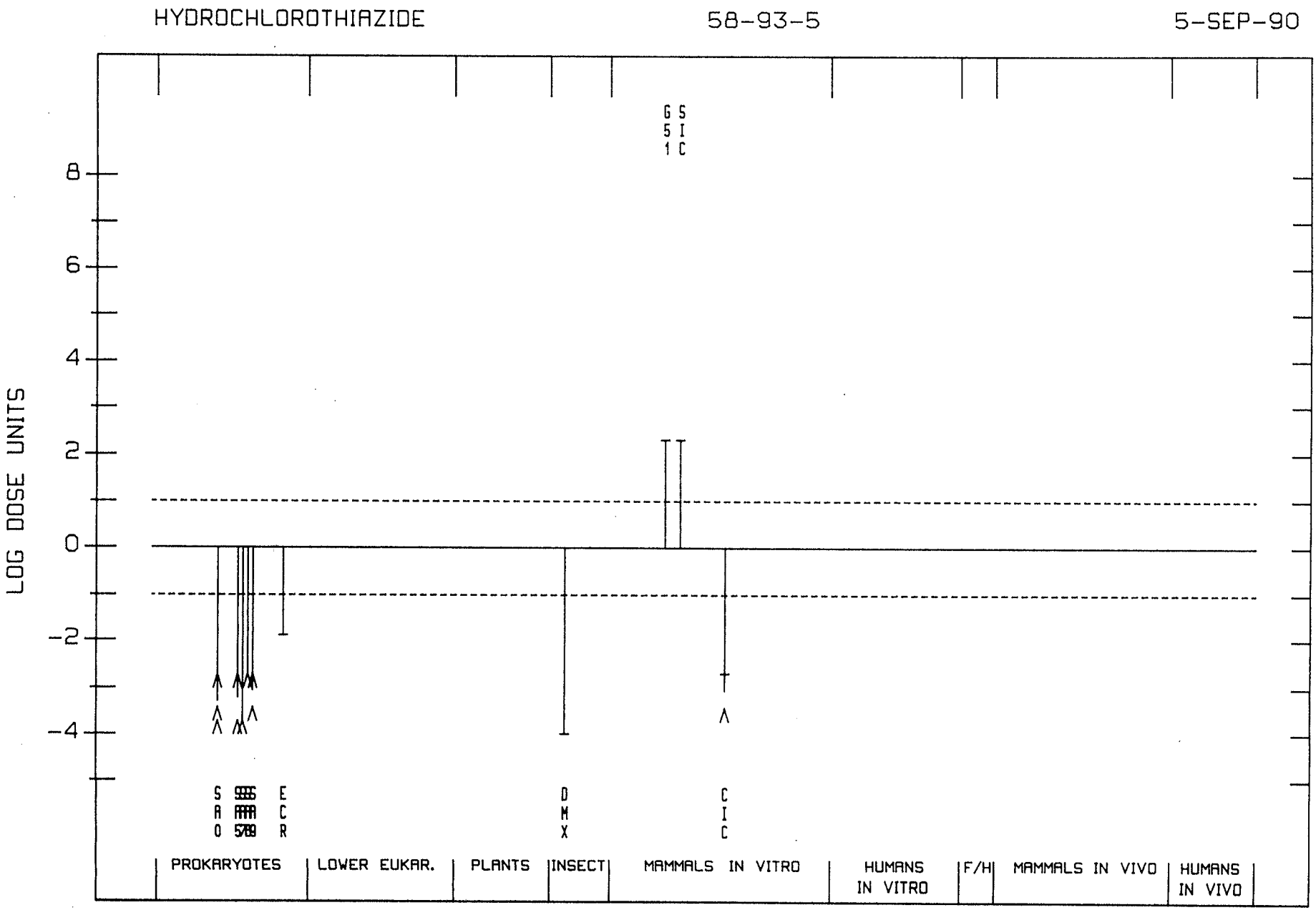
FUROSEMIDE

Test system	Result		Dose LED/HID	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
SA0, Salmonella typhimurium TA100, reverse mutation	–	–	5000 µg/ml	National Toxicology Program (1989)
SA5, Salmonella typhimurium TA1535, reverse mutation	–	–	5000 µg/ml	National Toxicology Program (1989)
SA7, Salmonella typhimurium TA1537, reverse mutation	–	–	5000 µg/ml	National Toxicology Program (1989)
SA9, Salmonella typhimurium TA98, reverse mutation	–	–	5000 µg/ml	National Toxicology Program (1989)
G51 Gene mutation mouse lymphoma L 5178Y cells	–	(+)	1500 µg/ml	National Toxicology Program (1989)
SIC Sister chromatid exchange, Chinese hamster ovary cells	(+)	(+)	750 µg/ml	National Toxicology Program (1989)
CIC, Chromosomal aberrations, Chinese hamster lung cells in vitro	(+)	0	2000 µg/ml	Ishidate (1988)
CIC, Chromosomal aberrations, Chinese hamster lung cells in vitro	(+)	–	500 µg/ml	Matsuoka et al. (1979)
CIC, Chromosomal aberrations, Chinese hamster ovary cells	(+)	(+)	3750 µg/ml	National Toxicology Program (1989)
SHF, Sister chromatid exchange, human fibroblasts in vitro	–	0	1654 µg/ml	Sasaki et al. (1980)
CHF, Chromosomal aberrations, human fibroblasts in vitro	–	0	1654 µg/ml	Sasaki et al. (1980)
CIH, Chromosomal aberrations, human leukocytes in vitro	+	0	200 µg/ml	Jameela et al. (1979)
CCC, Chromosomal aberrations, C3H/He mouse germ cells in vivo	+	0	50 mg/kg x 1, i.p.	Subramanyam & Jameela (1977)
BFA, Saccharomyces cerevisiae D4-RDII, gene conversion mouse urine	–	0	45 mg/kg x 1, i.p.	Marquardt & Siebert (1971)


FUROSEMIDE
54-31-9
18-SEP-90
LOG DOSE UNITS
8
6
4
2
0
-2
-4
G S C
5 I C
1 C I
C
I
H
C
C
C
S S S
A R A
0 5 9
S C B
H H F
F F A
PROKARYOTES
LOWER EUKAR.
PLANTS
INSECT
MAMMALS IN VITRO
HUMANS IN VITRO
F/H
MAMMALS IN VIVO
HUMANS IN VIVO

HYDROCHLOROTHIAZIDE

Test system	Result		Dose LED/HID	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
ECR, Escherichia coli Hs30R, reverse mutation	-	0	77.5 µg/ml	Fujita (1985)
SA0, Salmonella typhimurium TA100, reverse mutation	-	-	5000 µg/ml	Mortelmans et al. (1986)
SA0, Salmonella typhimurium TA100, reverse mutation	-	-	2500 µg/ml	Waskell (1978)
SA0, Salmonella typhimurium TA100, reverse mutation	-	-	500 µg/ml	Andrews et al. (1984)
SA5, Salmonella typhimurium TA1535, reverse mutation	-	-	5000 µg/ml	Mortelmans et al. (1986)
SA5, Salmonella typhimurium TA1535, reverse mutation	-	-	500 µg/ml	Andrews et al. (1984)
SA7, Salmonella typhimurium TA1537, reverse mutation	-	-	5000 µg/ml	Mortelmans et al. (1986)
SA8, Salmonella typhimurium TA1538, reverse mutation	-	-	500 µg/ml	Andrews et al. (1984)
SA9, Salmonella typhimurium TA98, reverse mutation	?	-	5000 µg/ml	Mortelmans et al. (1986)
SA9, Salmonella typhimurium TA98, reverse mutation	-	-	2500 µg/ml	Waskell (1978)
SA9, Salmonella typhimurium TA98, reverse mutation	-	-	500 µg/ml	Andrews et al. (1984)
ANG, Aspergillus nidulans, non-disjunction and mitotic crossing-over	+	0	0.00	Bignami et al. (1974)
DMX, Drosophila melanogaster, sex-linked recessive lethal mutation	-	0	10000 µg/ml	Valencia et al. (1985)
G51, Gene mutation, mouse lymphoma L5178Y cells	+	0	500 µg/ml	National Toxicology Program (1989)
SIC, Sister chromatid exchange, Chinese hamster ovary cells in vitro	+	+	500 µg/ml	Galloway et al. (1987)
CIC, Chromosomal aberrations, Chinese hamster ovary cells in vitro	-	-	2600 µg/ml	National Toxicology Program (1989)
CIC, Chromosomal aberrations, Chinese hamster lung cell	-	0	500 µg/ml	Ishidate (1988)

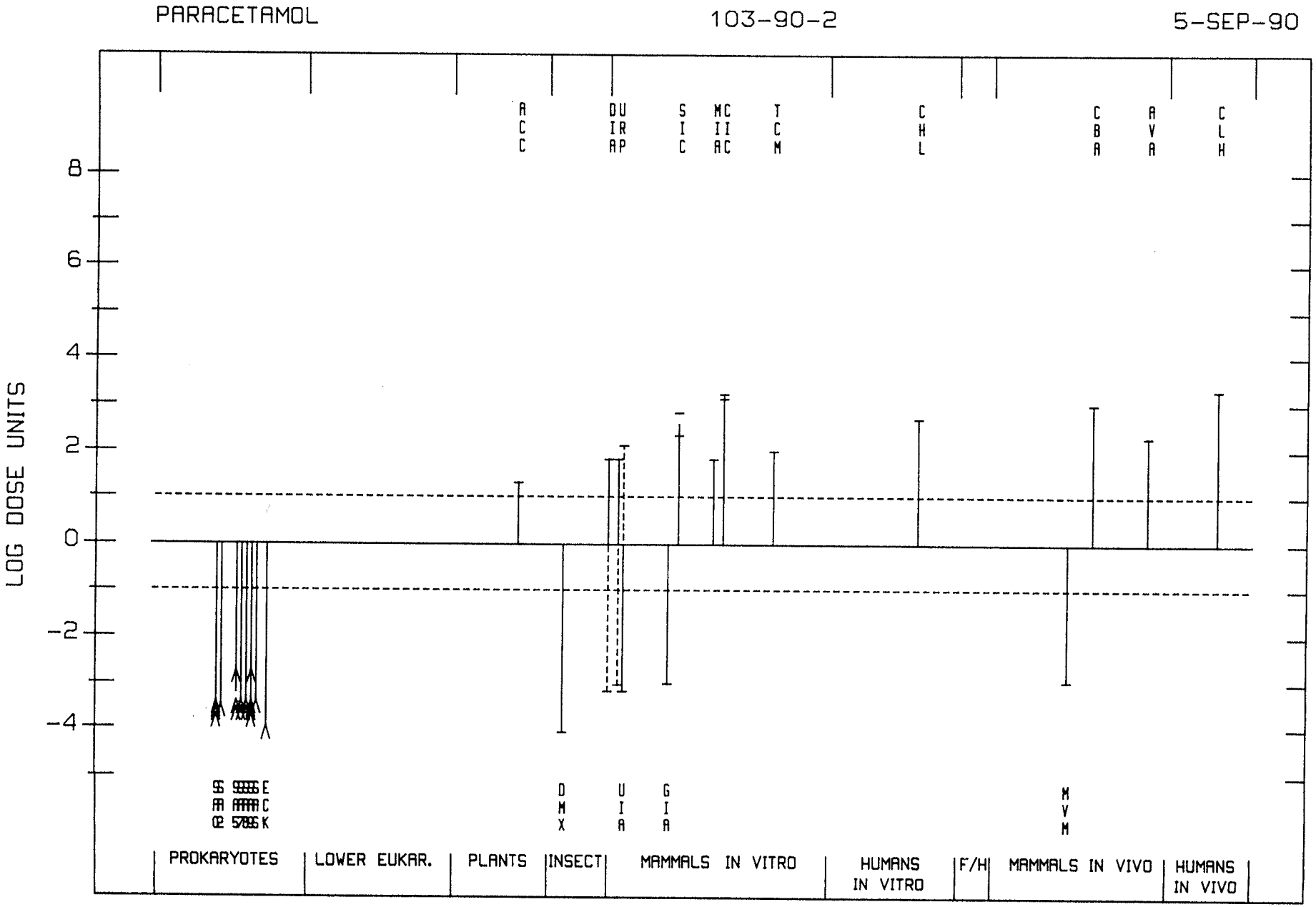

HYDROCHLOROTHIAZIDE
58-93-5
5-SEP-90
LOG DOSE UNITS
8
6
4
2
0
-2
-4
G S
5 I
1 C
S
A
O
E
C
R
D
M
X
C
I
C
PROKARYOTES
LOWER EUKAR.
PLANTS
INSECT
MAMMALS IN VITRO
HUMANS IN VITRO
F/H
MAMMALS IN VIVO
HUMANS IN VIVO

PARACETAMOL

Test system	Result		Dose LED/HID	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
SA0, Salmonella typhimurium TA100, reverse mutation	–	–	3576 µg/ml	King et al. (1979)
SA0, Salmonella typhimurium TA100, reverse mutation	–	–	0	Wirth et al. (1980)
SA0, Salmonella typhimurium TA100, reverse mutation	0	–	3020	Dybing et al. (1984)
SA0, Salmonella typhimurium TA100, reverse mutation	–	–	2500 µg/ml	Oldham et al. (1986)
SA0, Salmonella typhimurium TA100, reverse mutation	–	–	5000 µg/ml	Jasiewicz & Richardson (1987)
SA2, Salmonella typhimurium TA102, reverse mutation	0	–	3020 µg/ml	Dybing et al. (1984)
SA5, Salmonella typhimurium TA1535, reverse mutation	–	–	3576 µg/ml	King et al. (1979)
SA5, Salmonella typhimurium TA1535, reverse mutation	–	–	2500 µg/ml	Oldham et al. (1986)
SA5, Salmonella typhimurium TA1535, reverse mutation	–	–	500 µg/ml	Jasiewicz & Richardson (1987)
SA7, Salmonella typhimurium TA1537, reverse mutation	–	–	3576 µg/ml	King et al. (1979)
SA7, Salmonella typhimurium TA1537, reverse mutation	–	–	2500 µg/ml	Oldham et al. (1986)
SA7, Salmonella typhimurium TA1537, reverse mutation	–	–	2500 µg/ml	Jasiewicz & Richardson (1987)
SA8, Salmonella typhimurium TA1538, reverse mutation	–	–	3576 µg/ml	King et al. (1979)
SA8, Salmonella typhimurium TA1538, reverse mutation	–	–	2500 µg/ml	Oldham et al. (1986)
SA8, Salmonella typhimurium TA1538, reverse mutation	–	–	2500 µg/ml	Jasiewicz & Richardson (1987)
SA9, Salmonella typhimurium TA98, reverse mutation	–	–	3576 µg/ml	King et al. (1979)
SA9, Salmonella typhimurium TA98, reverse mutation	–	–	500 µg/ml	Wirth et al. (1980)
SA9, Salmonella typhimurium TA98, reverse mutation	0	–	3020 µg/ml	Dybing et al. (1984)
SA9, Salmonella typhimurium TA98, reverse mutation	–	–	2500 µg/ml	Oldham et al. (1986)
SA9, Salmonella typhimurium TA98, reverse mutation	–	–	5000 µg/ml	Jasiewicz & Richardson (1987)
SA5, Salmonella typhimurium TA97, reverse mutation	–	–	2500 µg/ml	Jasiewicz & Richardson (1987)
ECK, Escherichia coli K12/343/113, mutation	–	–	8940 µg/ml	King et al. (1979)
ACC, Allium cepa root cells, chromosomal aberrations	+	0	5000 µg/ml	Reddy & Subramanyam (1981)
DMX, Drosophila melanogaster, sex-linked recessive lethal mutation	–	0	11920 µg/ml	King et al. (1979)
DIA, DNA damage, Reuber hepatoma cells in vitro	–	0	1510 µg/ml	Dybing et al. (1984)
DIA, DNA damage, Chinese hamster V79 cells in vitro	(+)	0	1510 µg/ml	Hongslo et al. (1988)
URP, Unscheduled DNA synthesis, rat hepatocytes in vitro	–	0	1057 µg/ml	Milam & Byard (1985)
URP, Unscheduled DNA synthesis, rat hepatocytes in vitro	(+)	0	1510 µg/ml	Holme & Soderlund (1986)
UIA, Unscheduled DNA synthesis, mouse hepatocytes in vitro	+	0	755 µg/ml	Dybing et al. (1984)
UIA, Unscheduled DNA synthesis, mouse hepatocytes in vitro	+	0	755 µg/ml	Holme & Soderlund (1986)
UIA, Unscheduled DNA synthesis, hamster hepatocytes in vitro	–	0	1510 µg/ml	Holme & Soderlund (1986)
UIA, Unscheduled DNA synthesis, guinea-pig hepatocytes in vitro	–	0	1510 µg/ml	Holme & Soderlund (1986)
UIA, Unscheduled DNA synthesis, Chinese hamster V79 cells in vitro	–	0	1510 µg/ml	Hongslo et al. (1988)
GIA, Gene mutation, mouse C3H 10T1/2 clone 8 cells in vitro	–	0	1000 µg/ml	Patierno et al. (1989)

PARACETAMOL (contd)

Test system	Result		Dose LED/HID	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
SIC, Sister chromatid exchange, Chinese hamster V79 cells in vitro	+	+	453 µg/ml	Hongslo et al. (1988)
SIC, Sister chromatid exchange, Chinese hamster V79 cells in vitro	+	0	151 µg/ml	Holme et al. (1988)
MIA, Micronucleus test, rat kidney cells in vitro	+	0	1510 µg/ml	Dunn et al. (1987)
CIC, Chromosomal aberrations, Chinese hamster lung cells in vitro	(+)	0	60 µg/ml	Ishidate et al. (1978)
CIC, Chromosomal aberrations, Chinese hamster Don-6 cells in vitro	+	0	75 µg/ml	Sasaki et al. (1980)
TCM, Cell transformation, C3H 10T1/2 clone 8 cells in vitro	(+)	+	1000 µg/ml	Patierno et al. (1989)
CHL, Chromosomal aberrations, human lymphocytes in vitro	+	0	200 µg/ml	Watanabe (1982)
MVM, Micronucleus test, NMRI mice in vivo	–	0	894 mg/kg x 2, i.p.	King et al. (1979)
CBA, Chromosomal aberrations, Swiss mice bone-marrow cells in vivo	(+)	0	100 mg/kg x 3, p.o.	Reddy (1984)
CCC, Chromosomal aberrations, male Swiss mice germ cells in vivo	?	0	100 mg/kg x 3, p.o.	Reddy & Subramanyam (1985)
AVA, Aneuploidy, rat embryos in vivo	+	0	500 mg/kg x 25, p.o.	Tsuruzaki et al. (1982)
CLH, Chromosomal aberrations, human lymphocytes in vivo	+	0	50 mg/kg x 1, p.o.	Kocisova et al. (1988)


PARACETAMOL
103-90-2
5-SEP-90
LOG DOSE UNITS
8
6
4
2
0
-2
-4
ACC
DUR AP
SIC
MC II AC
TCM
CHL
CBA
AVA
CLH
DMX
UIA
GIA
MVM
PROKARYOTES
LOWER EUKAR.
PLANTS
INSECT
MAMMALS IN VITRO
HUMANS IN VITRO
F/H
MAMMALS IN VIVO
HUMANS IN VIVO