APPENDIX 3

GENETIC AND RELATED EFFECTS

Appendix 3A. Test system code words for genetic and related effects

End-point[a]	Code	Definition
		NON-MAMMALIAN SYSTEMS
		Prokaryotic systems
D	PRB	Prophage, induction, SOS repair test, DNA strand breaks, cross-links or related damage
D	ECB	*Escherichia coli* (or *E. coli* DNA), DNA strand breaks, cross-links or related damage; DNA repair
D	SAD	*Salmonella typhimurium*, DNA repair-deficient strains, differential toxicity
D	ECD	*Escherichia coli pol* A/W3110-P3478, differential toxicity (spot test)
D	ECL	*Escherichia coli pol* A/W3110-P3478, differential toxicity (liquid suspension test)
D	ERD	*Escherichia coli rec* strains, differential toxicity
D	BSD	*Bacillus subtilis rec* strains, differential toxicity
D	BRD	Other DNA repair-deficient bacteria, differential toxicity
G	BPF	Bacteriophage, forward mutation
G	BPR	Bacteriophage, reverse mutation
G	SAF	*Salmonella typhimurium*, forward mutation
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
G	SAS	*Salmonella typhimurium* (other miscellaneous strains), reverse mutation
G	ECF	*Escherichia coli* exclusive of strain K12, forward mutation
G	ECK	*Escherichia coli* K12, forward or reverse mutation
G	ECW	*Escherichia coli* WP2 *uvr*A, reverse mutation
G	EC2	*Escherichia coli* WP2, reverse mutation
G	ECR	*Escherichia coli* (other miscellaneous strains), reverse mutation
G	BSM	*Bacillus subtilis*, multigene test
G	KPF	*Klebsiella pneumoniae*, forward mutation
G	MAF	*Micrococcus aureus*, forward mutation

[a] Endpoints are grouped within each phylogenetic category 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; T, cell transformation

Appendix 3A (contd)

End-point[a]	Code	Definition
		NON-MAMMALIAN SYSTEMS (contd)
		Lower eukaryotic systems
D	SSB	*Saccharomyces* species, DNA strand breaks, cross-links or related damage
D	SSD	*Saccharomyces* species, DNA repair-deficient strains, differential toxicity
D	SZD	*Schizosaccharomyces pombe*, DNA repair-deficient strains, differential toxicity
R	SCG	*Saccharomyces cerevisiae*, gene conversion
R	SCH	*Saccharomyces cerevisiae*, homozygosis by mitotic recombination or gene conversion
R	SZG	*Schizosaccharomyces pombe*, gene conversion
R	ANG	*Aspergillus nidulans*, genetic crossing-over
G	SCF	*Saccharomyces cerevisiae*, forward mutation
G	SCR	*Saccharomyces cerevisiae*, reverse mutation
G	SGR	*Streptomyces griseoflavus*, reverse mutation
G	STF	*Streptomyces coelicolor*, forward mutation
G	STR	*Streptomyces coelicolor*, reverse mutation
G	SZF	*Schizosaccharomyces pombe*, forward mutation
G	SZR	*Schizosaccharomyces pombe*, reverse mutation
G	ANF	*Aspergillus nidulans*, forward mutation
G	ANR	*Aspergillus nidulans*, reverse mutation
G	NCF	*Neurospora crassa*, forward mutation
G	NCR	*Neurospora crassa*, reverse mutation
G	PSM	*Paramecium* species, mutation
C	PSC	*Paramecium* species, chromosomal aberrations
A	SCN	*Saccharomyces cerevisiae*, aneuploidy
A	ANN	*Aspergillus nidulans*, aneuploidy
A	NCN	*Neurospora crassa*, aneuploidy
		Plant systems
D	PLU	Plants, unscheduled DNA synthesis
G	ASM	*Arabidopsis* species, mutation
G	HSM	*Hordeum* species, mutation
G	TSM	*Tradescantia* species, mutation
G	PLM	Plants (other), mutation
S	VFS	*Vicia faba*, sister chromatid exchange
S	PLS	Plants (other), sister chromatid exchange
M	TSI	*Tradescantia* species, micronuclei
M	PLI	Plants (other), micronuclei
C	ACC	*Allium cepa*, chromosomal aberrations
C	HSC	*Hordeum* species, chromosomal aberrations
C	TSC	*Tradescantia* species, chromosomal aberrations
C	VFC	*Vicia faba*, chromosomal aberrations
C	PLC	Plants (other), chromosomal aberrations

Appendix 3A (contd)

End-point[a]	Code	Definition
		NON-MAMMALIAN SYSTEMS (contd)
		Insect systems
R	DMG	*Drosophila melanogaster*, genetic crossing-over or recombination
G	DMM	*Drosophila melanogaster*, somatic mutation (and recombination)
G	DMX	*Drosophila melanogaster*, sex-linked recessive lethal mutations
C	DMC	*Drosophila melanogaster*, chromosomal aberrations
C	DMH	*Drosophila melanogaster*, heritable translocation test
C	DML	*Drosophila melanogaster*, dominant lethal test
A	DMN	*Drosophila melanogaster*, aneuploidy
		MAMMALIAN SYSTEMS
		Animal cells in vitro
D	DIA	DNA strand breaks, cross-links or related damage, animal cells *in vitro*
D	RIA	DNA repair exclusive of unscheduled DNA synthesis, animal cells *in vitro*
D	URP	Unscheduled DNA synthesis, rat primary hepatocytes
D	UIA	Unscheduled DNA synthesis, other animal cells *in vitro*
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	G90	Gene mutation, Chinese hamster lung V79 cells, ouabain resistance
G	GML	Gene mutation, mouse lymphoma cells exclusive of L5178Y *in vitro*
G	G5T	Gene mutation, mouse lymphoma L5178Y cells, TK locus
G	G51	Gene mutation, mouse lymphoma L5178Y cells, all other loci
G	GIA	Gene mutation, other animal cells *in vitro*
S	SIC	Sister chromatid exchange, Chinese hamster 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	SIA	Sister chromatid exchange, other animal cells *in vitro*
M	MIA	Micronucleus test, animal cells *in vitro*
C	CIC	Chromosomal aberrations, Chinese hamster 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	CIA	Chromosomal aberrations, other animal cells *in vitro*
A	AIA	Aneuploidy, animal cells *in vitro*
T	TBM	Cell transformation, BALB/c 3T3 mouse cells
T	TCM	Cell transformation, C3H 10T1/2 mouse cells
T	TCS	Cell transformation, Syrian hamster embryo cells, clonal assay
T	TFS	Cell transformation, Syrian hamster embryo cells, focus assay

Appendix 3A (contd)

End-point[a]	Code	Definition
		MAMMALIAN SYSTEMS (contd)
		Animal cells in vitro *(contd)*
T	TPM	Cell transformation, mouse prostate cells
T	TCL	Cell transformation, other established cell lines
T	TRR	Cell transformation, RLV/Fischer rat embryo cells
T	T7R	Cell transformation, SA7/rat cells
T	T7S	Cell transformation, SA7/Syrian hamster embryo cells
T	TEV	Cell transformation, other viral enhancement systems
T	TVI	Cell transformation, treated *in vivo*, scored *in vitro*
		Human cells in vitro
D	DIH	DNA strand breaks, cross-links or related damage, human cells *in vitro*
D	RIH	DNA repair exclusive of unscheduled DNA synthesis, human cells *in vitro*
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	UIH	Unscheduled DNA synthesis, other human cells *in vitro*
G	GIH	Gene mutation, human cells *in vitro*
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	SIH	Sister chromatid exchange, other human cells *in vitro*
M	MIH	Micronucleus test, human cells *in vitro*
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	CIH	Chromosomal aberrations, other human cells *in vitro*
A	AIH	Aneuploidy, human cells *in vitro*
T	TIH	Cell transformation, human cells *in vitro*
		Body fluid and host-mediated assays
F	BFA	Body fluids from animals, microbial mutagenicity
F	BFH	Body fluids from humans, microbial mutagenicity
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 ahimal hosts
		Animals in vivo
D	DVA	DNA strand breaks, cross-links or related damage, animal cells *in vivo*
D	RVA	DNA repair exclusive of unscheduled DNA synthesis, animal cells *in vivo*
D	UPR	Unscheduled DNA synthesis, rat hepatocytes *in vivo*
D	UVC	Unscheduled DNA synthesis, hamster cells *in vivo*
D	UVM	Unscheduled DNA synthesis, mouse cells *in vivo*

Appendix 3A (contd)

End-point[a]	Code	Definition
		MAMMALIAN SYSTEMS (contd)
		Animals in vivo *(contd)*
D	UVR	Unscheduled DNA synthesis, other rat cells *in vivo*
D	UVA	Unscheduled DNA synthesis, other animal cells *in vivo*
G	GVA	Gene mutation, animal cells *in vivo*
G	MST	Mouse spot test
G	SLP	Mouse specific locus test, postspermatogonia
G	SLO	Mouse specific locus test, other stages
S	SVA	Sister chromatid exchange, animal cells *in vivo*
M	MVM	Micronucleus test, mice *in vivo*
M	MVR	Micronucleus test, rats *in vivo*
M	MVC	Micronucleus test, hamsters *in vivo*
M	MVA	Micronucleus test, other animals *in vivo*
C	CBA	Chromosomal aberrations, animal bone-marrow cells *in vivo*
C	CLA	Chromosomal aberrations, animal leucocytes *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	COE	Chromosomal aberrations, oocytes or embryos treated *in vivo*
C	CVA	Chromosomal aberrations, other animal cells *in vivo*
C	DLM	Dominant lethal test, mice
C	DLR	Dominant lethal test, rats
C	MHT	Mouse heritable translocation test
A	AVA	Aneuploidy, animal cells *in vivo*
T	TVI	Cell transformation, treated *in vivo*, scored *in vitro*
		Humans in vivo
D	DVH	DNA strand breaks, cross-links or related damage, human cells *in vivo*
D	UBH	Unscheduled DNA synthesis, human bone-marrow cells *in vivo*
D	UVH	Unscheduled DNA synthesis, other human cells *in vivo*
S	SLH	Sister chromatid exchange, human lymphocytes *in vivo*
S	SVH	Sister chromatid exchange, other human cells *in vivo*
M	MVH	Micronucleus test, human cells *in vivo*
C	CBH	Chromosomal aberrations, human bone-marrow cells *in vivo*
C	CLH	Chromosomal aberrations, human lymphocytes *in vivo*
C	CVH	Chromosomal aberrations, other human cells *in vivo*
A	AVH	Aneuploidy, human cells *in vivo*
		Test systems not shown on activity profiles
D	BID	Binding (covalent) to DNA *in vitro*
D	BIP	Binding (covalent) to RNA or protein *in vitro*

Appendix 3A (contd)

End-point[a]	Code	Definition
	Test systems not shown on activity profiles (contd)	
D	BVD	Binding (covalent) to DNA, animal cells *in vivo*
D	BVP	Binding (covalent) to RNA or protein, animal cells *in vivo*
D	BHD	Binding (covalent) to DNA, human cells *in vivo*
D	BHP	Binding (covalent) to RNA or protein, human cells *in vivo*
I	ICR	Inhibition of intercellular communication, animal cells *in vitro*
I	ICH	Inhibition of intercellular communication, human cells *in vitro*
P	SPF	Sperm morphology, F1 mice *in vivo*
P	SPM	Sperm morphology, mice *in vivo*
P	SPR	Sperm morphology, rats *in vivo*
P	SPH	Sperm morphology, humans *in vivo*

Appendix 3B: 1. Summary table of genetic and related effects of 2,7-dichlorodibenzo-*para*-dioxin

Non-mammalian systems				Mammalian systems			
Proka-ryotes	Lower eukaryotes	Plants	Insects	*In vitro*		*In vivo*	
				Animal cells	Human cells	Animals	Humans
D G	D R G A	D G C	R G C A	D G S M C A T I	D G S M C A T I	D G S M C DL A	D S M C A
$-^1$				$-^1$			

A, aneuploidy; C, chromosomal aberrations; D, DNA damage; DL, dominant lethal mutation; G, gene mutation; I, inhibition of intercellular communication; M, micronuclei; R, mitotic recombination and gene conversion; S, sister chromatid exchange; T, cell transformation

In completing the table, the following symbols indicate the consensus of the Working Group with regard to the results for each end-point:

+ considered to be positive for the specific end-point and level of biological complexity
$+^1$ considered to be positive, but only one valid study was available to the Working Group
– considered to be negative
$-^1$ considered to be negative, but only one valid study was available to the Working Group
? considered to be equivocal or inconclusive (e.g. there were contradictory results from different laboratories; there were confounding exposures; the results were equivocal)

Appendix 3B: 2. Summary table of genetic and related effects of 2,3,7,8-TCDD

Non-mammalian systems				Mammalian systems			
Proka-ryotes	Lower eukaryotes	Plants	Insects	*In vitro*		*In vivo*	
				Animal cells	Human cells	Animals	Humans
D G	D R G A	D G C	R G C A	D G S M C A T I	D G S M C A T I	D G S M C DL A	D S M C A
–				? –[1] ?	–[1] +[1] +[1] ?	+ – –[1] –[1]	–[1] –

A, aneuploidy; C, chromosomal aberrations; D, DNA damage; DL, dominant lethal mutation; G, gene mutation; I, inhibition of intercellular communication; M, micronuclei; R, mitotic recombination and gene conversion; S, sister chromatid exchange; T, cell transformation

In completing the table, the following symbols indicate the consensus of the Working Group with regard to the results for each end-point:

+ considered to be positive for the specific end-point and level of biological complexity
+[1] considered to be positive, but only one valid study was available to the Working Group
– considered to be negative
–[1] considered to be negative, but only one valid study was available to the Working Grou p
? considered to be equivocal or inconclusive (e.g. there were contradictory results from different laboratories; there were confounding exposures; the results were equivocal)

Appendix 3B: 3. Summary table of genetic and related effects of octachlorodibenzo-*para*-dioxin

Non-mammalian systems				Mammalian systems			
Proka-ryotes	Lower eukaryotes	Plants	Insects	*In vitro*		*In vivo*	
				Animal cells	Human cells	Animals	Humans
D G	D R G A	D G C	R G C A	D G S M C A T I	D G S M C A T I	D G S M C DL A	D S M C A
–[1]							

A, aneuploidy; C, chromosomal aberrations; D, DNA damage; DL, dominant lethal mutation; G, gene mutation; I, inhibition of intercellular communication; M, micronuclei; R, mitotic recombination and gene conversion; S, sister chromatid exchange; T, cell transformation

In completing the table, the following symbols indicate the consensus of the Working Group with regard to the results for each end-point:

\+ considered to be positive for the specific end-point and level of biological complexity
+[1] considered to be positive, but only one valid study was available to the Working Group
– considered to be negative
–[1] considered to be negative, but only one valid study was available to the Working Group
? considered to be equivocal or inconclusive (e.g. there were contradictory results from different laboratories; there were confounding exposures; the results were equivocal)

Appendix 3B: 4. Summary table of genetic and related effects of 2,3,4,7,8-PeCDF

Non-mammalian systems				Mammalian systems			
Proka-ryotes	Lower eukaryotes	Plants	Insects	*In vitro*		*In vivo*	
				Animal cells	Human cells	Animals	Humans
D G	D R G A	D G C	R G C A	D G S M C A T I	D G S M C A T I	D G S M C DL A	D S M C A
					$+^1$ $+^1$		

A, aneuploidy; C, chromosomal aberrations; D, DNA damage; DL, dominant lethal mutation; G, gene mutation; I, inhibition of intercellular communication; M, micronuclei; R, mitotic recombination and gene conversion; S, sister chromatid exchange; T, cell transformation

In completing the table, the following symbols indicate the consensus of the Working Group with regard to the results for each end-point:

+ considered to be positive for the specific end-point and level of biological complexity
$+^1$ considered to be positive, but only one valid study was available to the Working Group
– considered to be negative
$-^1$ considered to be negative, but only one valid study was available to the Working Group
? considered to be equivocal or inconclusive (e.g. there were contradictory results from different laboratories; there wer e confounding exposures; the results were equivocal)

APPENDIX 3C

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 end-point, 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 the relative molecular masses 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. 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

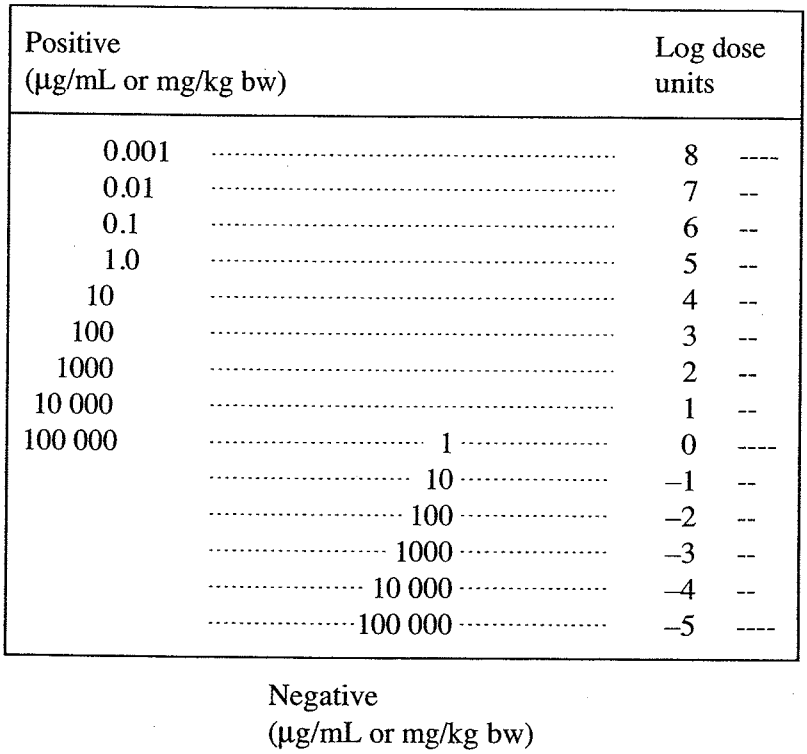
$$LDU_{ij} = -\log_{10} (\text{dose}), \text{ for HID values; LDU} \leq 0$$

and (1)

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

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 doses (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



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 a caret (^). 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. Naming conventions are described below.

Data listings are presented in the text and include end-point and test codes, a short test code definition, results, either with or without an exogenous metabolic system, the associated LED or HID value and a short citation. Test codes are organized phylogenetically and by end-point from left to right across each activity profile and from top to bottom of the corresponding data listing. End-points 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 2.7-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 if the actual top agar volume is not reported. For spot tests, a 1-ml volume is used in the calculation.

(*f*) Conversion of particulate concentrations given in $\mu g/cm^2$ is 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-letter 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 letter may be used to define the tester strain (e.g. SA8 for *S. typhimurium* TA1538, ECW for *E. coli* WP2*uvr*A). When strain designation is not indicated, the third letter is used to define the specific genetic end-point 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 end-point 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 end-point 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 leukocytes or lymphocytes *in vitro* (-AL, animals; -HL, humans), -L- for leukocytes *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 mutation, postspermatogonia; SLO, mouse specific locus mutation, other stages; DLM, dominant lethal mutation in mice; DLR, dominant lethal mutation in rats; MHT, mouse heritable translocation.

The genetic activity profiles and listings were prepared in collaboration with Integrated Laboratory System (ILS) under contract to the United States Environmental Protection Agency; ILS 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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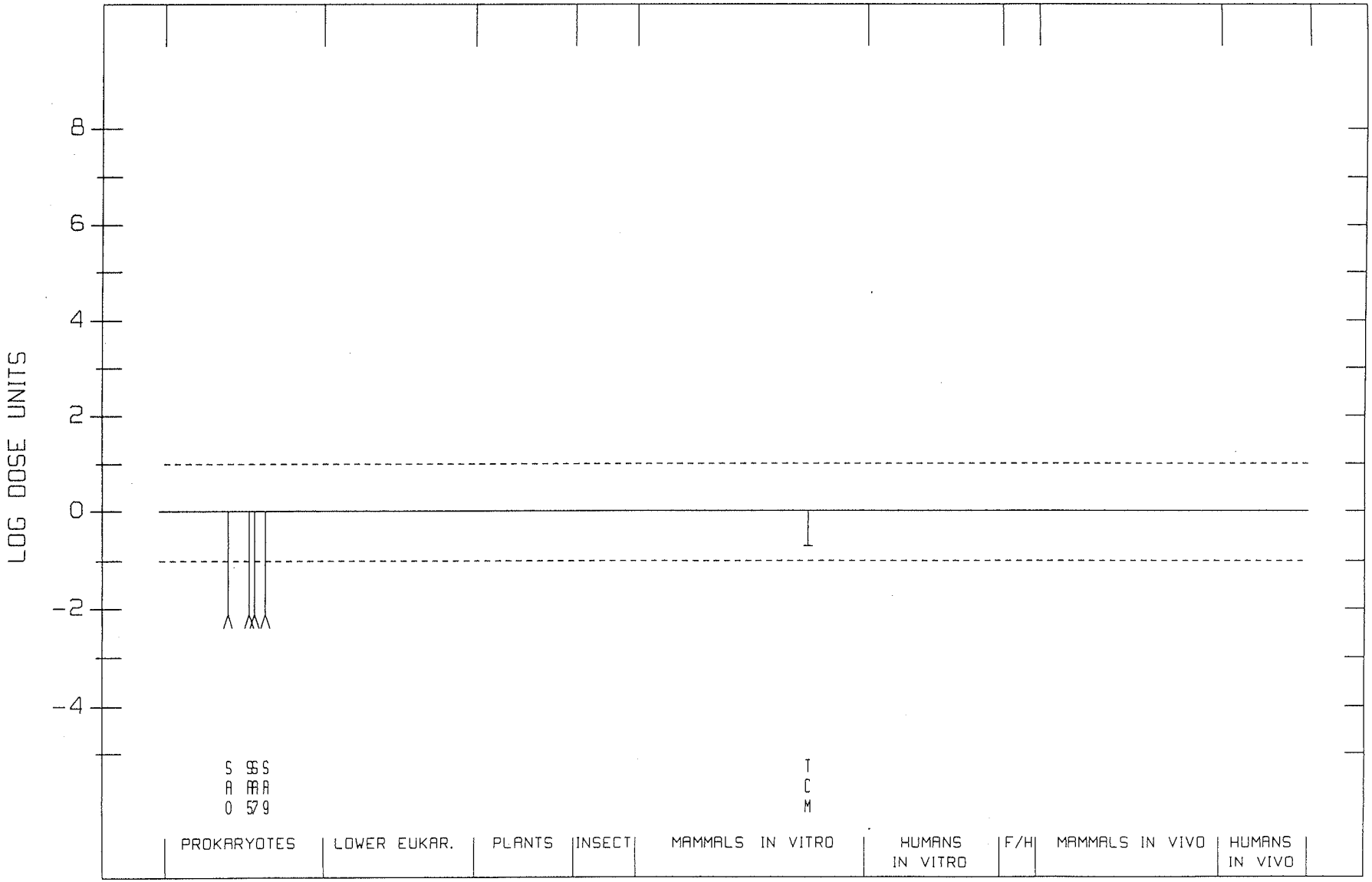
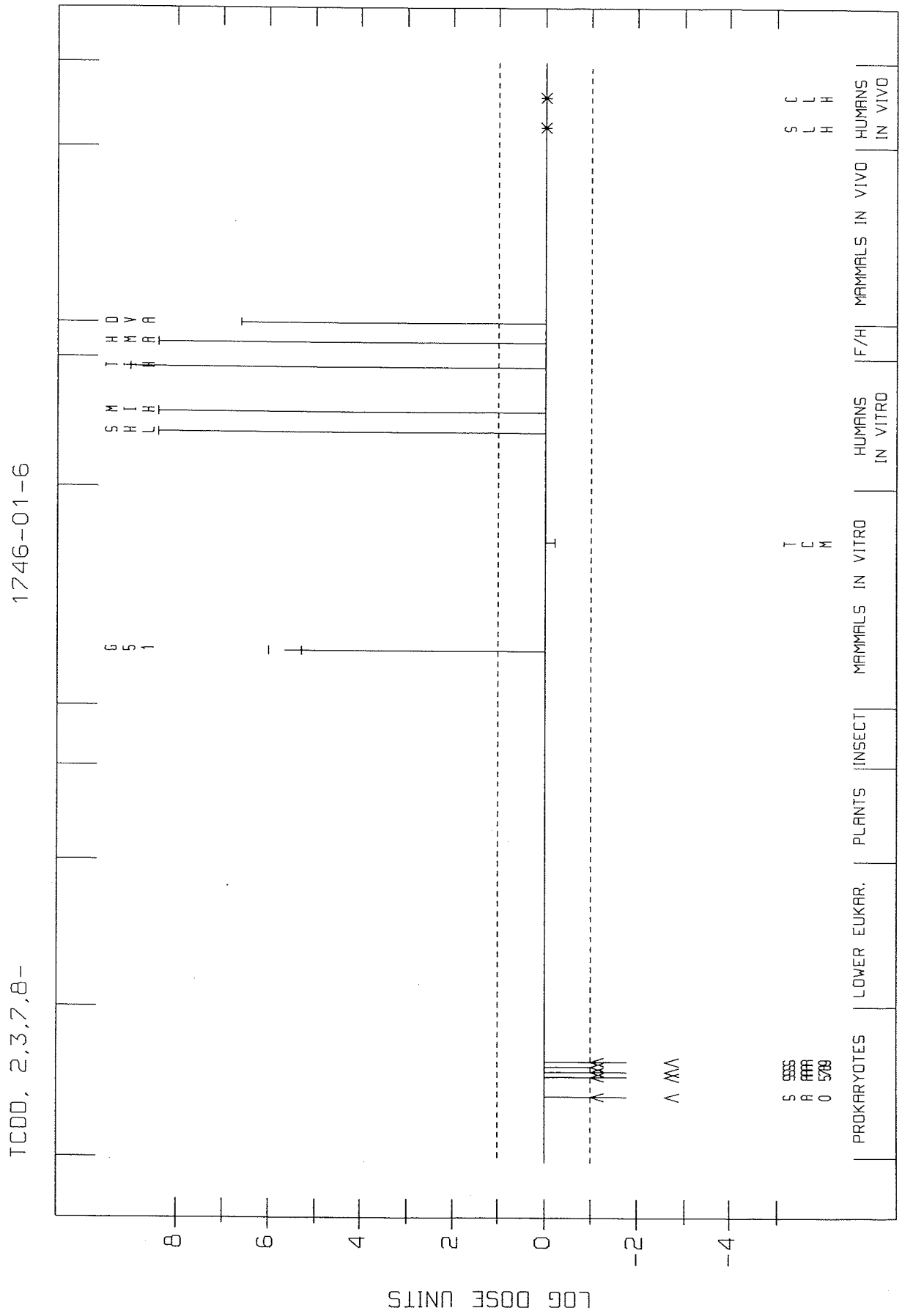
DICHLORODIBENZO-p-DIOXIN, 2,7- 33857-26-0

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-2
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LOWER EUKAR.
PLANTS
INSECT
MAMMALS IN VITRO
HUMANS IN VITRO
F/H
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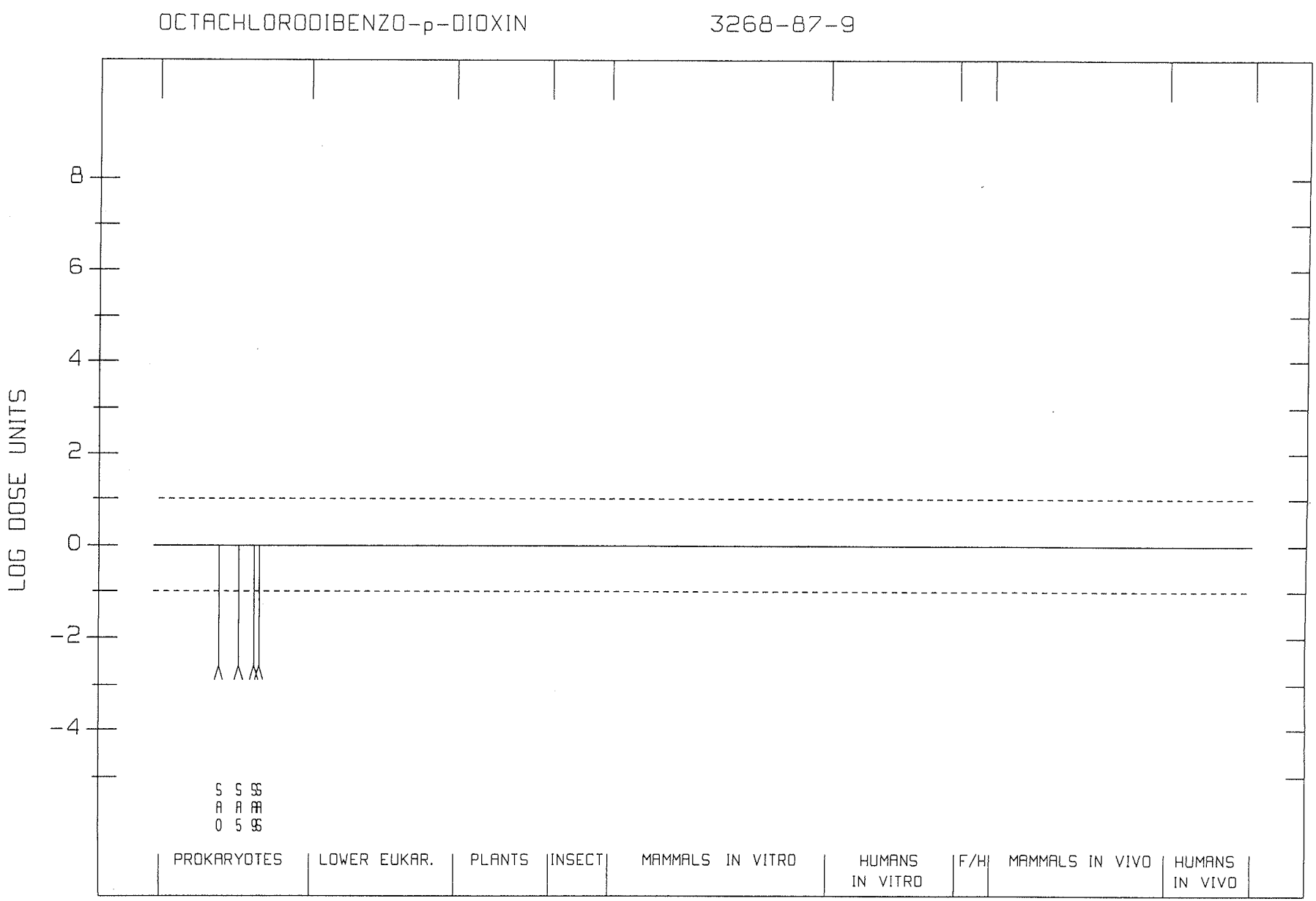
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0 5 55
PROKARYOTES
LOWER EUKAR.
PLANTS
INSECT
MAMMALS IN VITRO
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PeCDF, 2,3,4,7,8– 57117–31–4