TOXICITY

EVALUATION
(1)

ENVIRONMENTAL TOXICOLOGY

EMISSION – TRANSPORT – FATE – EFFECT

MAJOR CLASSES OF POLLUTANTS (CHEMICALS)

INORGANIC IONS

*** metals & anions**

ORGANIC POLLUTANTS

* hydrocarbons

* polychlorinated biphenyls (PCBs)

* pesticides (organochlorines, organophosphates, carbamates, pyrethroids, etc)

* detergents

RADIOACTIVE ISOTOPES

GASEOUS POLLUTANTS


environmental toxi...
eTOX - Principles o...
New Tab
ttp://www.epa.gov/ebtpages/pollutants.html
Agricultural Chemicals
Air Pollutants
Aerosols, Asbestos, Carbon Monoxide, Chlorofluorocarbons (CFCs), Criteria Air Pollutants, Ground Level Ozone, Hazardous Air Pollutants (HAPs), Hydrochlorofluorocarbons (HCFCs), Lead, Mercury, Methane, Nitrogen Oxides (NOx), Particulate Matter (PM), Propellants, Radon, Refrigerants, Sulfur Oxides (SOx), Volatile Organic Compounds (VOCs)
Biological Contaminants
Carcinogens
Chemicals
Benzene, Chlorofluorocarbons (CFCs), Chromated Copper Arsenate (CCA), Dichloroethylene (DCE), Dioxins, Endocrine Disruptors, Ether, Ethylbenzene, Furans, Halons, Hazardous Air Pollutants (HAPs), Heavy Metals, Hydrochlorofluorocarbons (HCFCs), Inorganic Cyanides, Ketones, Methane, Methyl Bromide, Methyl Chloride, Methyl-T-Butyl-Ether (MTBE), Nitrogen Oxides (NOx), Organic Cyanides, Particulate Matter (PM), Perchloroethylene (PCE), Phthalates, Polychlorinated Biphenyls (PCBs), Radionuclides, Styrene, Sulfur Hexafluoride (SF6), Sulfur Oxides (SOx), Toluene, Trichloroethylene (TCE), Volatile Organic Compounds (VOCs)
Microorganisms
Coliform, Cryptosporidium, Viruses
Multimedia Pollutants
Arsenic, Asbestos, Benzene, Cyanide, Lead, Mercury, Methyl Tertiary Butyl Ether (MTBE), Polychlorinated Biphenyls (PCBs)
Ozone
Radiation
Ionizing Radiation, Radiation Detection, Radiation Exposure, Radiation Protection, Radionuclides, Radon
Soil Contaminants
Acetone, Arsenic, Barium, Benzene, Cadmium, Chloroform, Cyanide, Lead, Mercury, Polychlorinated Biphenyls (PCBs), Tetrachloroethylene, Toluene, Trichloroethylene (TCE)
Toxic Substances
Persistent Bioaccumulative Toxic Pollutants (PBTs), Persistent Organic Pollutants (POPs), Toxicological Profiles
Water Pollutants
Arsenic, Contaminated Sediment, Disinfection Byproducts, Dredged Material, Lead, Microbial Pathogens

UNIVERSITAS KATOLIK SOEGIJAPRANATA

United States
Environmental Protection
Agency

Air

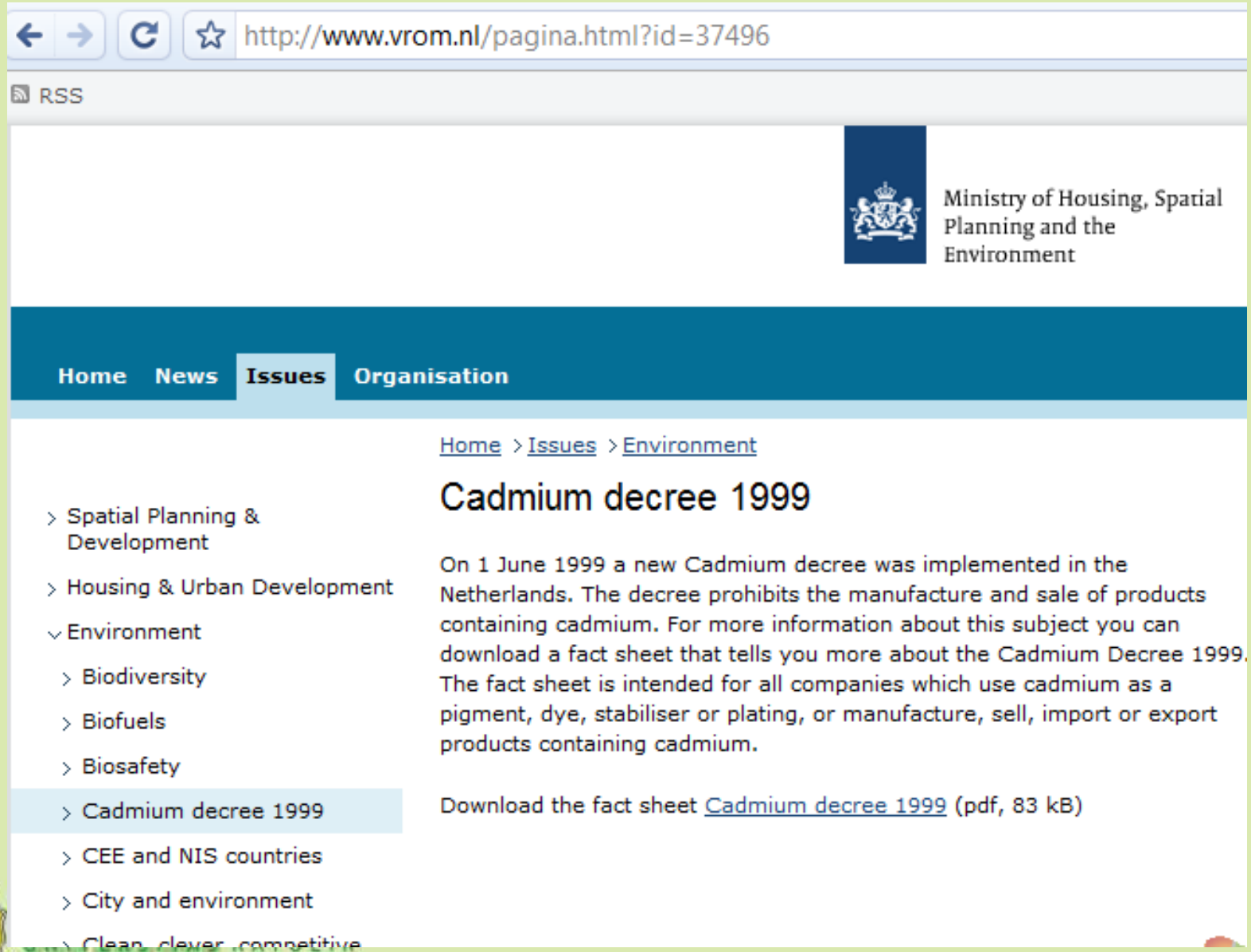
EPA-452/R-97-005
December 1997

Mercury Study Report to Congress

Volume III: Fate and Transport of Mercury in the Environment

EPA

Office of Air Quality Planning & Standards
and
Office of Research and Development



SOEGIJAPRANATA

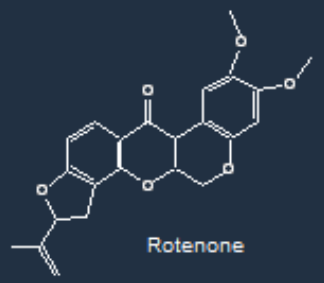
Pesticides

- Insecticides.
- Herbicides.
- Fungicides.
- Rodenticides.
- Bactericides.
- Biopesticides.
- Special application.

Special Application Chemicals

- Acaracides, Algicides, Avicides, Bactericides, Piscicides, Virucides, Molluscicides.
- Insect attractants, Insect repellants, Bird repellents, Mammal repellents.
- Plant growth activators.
- Synergists.

- Antibiotic insecticides.
  - Abamectin, Spinosad.
- Arsenical insecticides.
  - Lead arsenate.
- Botanical insecticides.
  - Nicotine, Pyrithrins, Rotenone.



Rotenone

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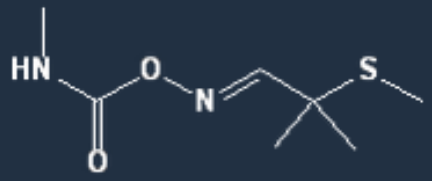
KELOMPOK2

PESTISIDA

- Bacterium
  - *Bacillus thuringiensis* (Bt)
- Carbamate insecticides.
  - Aldicarb, Carbaryl, Carbofuran, Oxamyl.
- Organochlorine insecticides.
  - Aldrin, Dieldrin, DDT, Endrin, Methoxychlor, Pentachlorophenol.



Aldicarb

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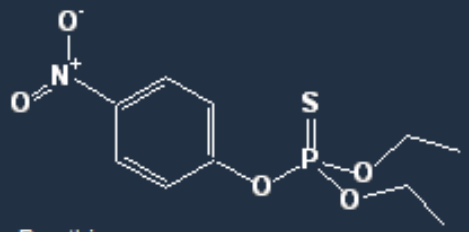
- Organophosphorus insecticides.
  - Azinphos-methyl, Dichlorvos, Chlorpyriphos, Fenthion, Diazinon,
  - Malathion, Parathion.
- Pyrethroid insecticides.
  - Fenvalerate, Permerthrin, Resmethrin.



Parathion

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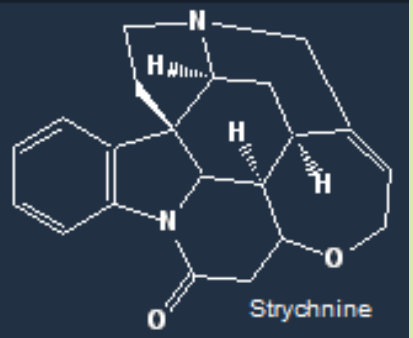
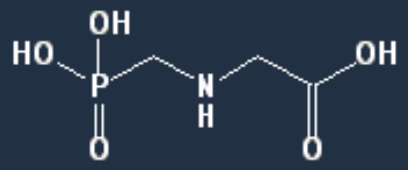
- Botanical rodenticides.
  - Strychnine.
- Coumarin rodenticides.
  - Brodifacoum, Bromodialone, Warfarin.
- Inorganic rodenticides.
  - Zinc Phosphide.
- Unclassified rodenticides.
  - Ergocalciferol, Sodium Fluoroacetate.



Strychnine

- Amide herbicides.
  - Metolachlor.
- Dinitrophenol herbicides.
  - Dinoseb.
- Imidazolinone herbicides.
  - Imazethapyr.
- Organophosphorus herbicides.
  - Glyphosate.



Glyphosate

Hormones:
biochemicals produced by endocrine glands, travel through the bloodstream and cause responses in other parts of the body

Hormones of primary concern:
Estrogen, androgen and thyroid hormones

Classification of Toxicants (1)

Target organ

Hepatotoxin, neurotoxin

Intended use

Pesticide, solvent

Source

Natural, synthetic

Special effect

Carcinogen, mutagen, endocrine disruptor

Classification of Toxicants (2)

Physical state.

Gas, solid

Toxicity

Extremely, slightly.

Chemical composition.

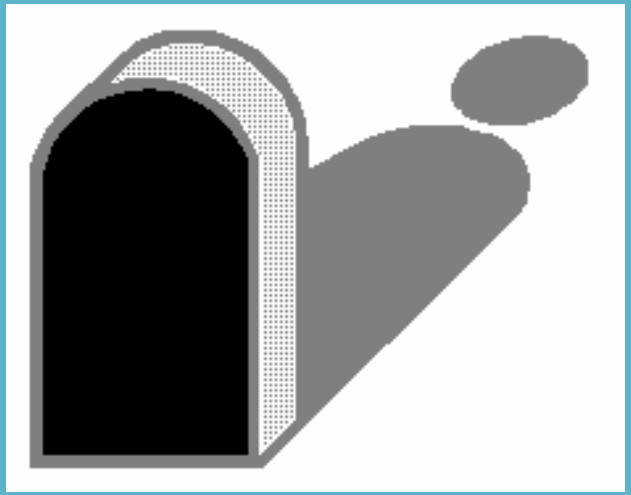
Heavy metal, organophosphate.

Mechanism of action.

Anticholinergic, inhibitor, uncoupler.

TOXICOLOGICAL (BIOLOGICAL) PARAMETERS AT THE INDIVIDUAL LEVEL

- **Direct damaging effects (acute & chronic effects)**
- **Accumulation**



<u>Toxic Effects</u>

- ***Reversible* – go away after the toxicant ceases to be active**

- ***Irreversible* – permanent damage (death)**

Key measurement parameters in laboratory effects tests

TERM	DESCRIPTION
Acute Parameter	indicated as LC_{50} or LD_{50}
Mortality	number of dead individuals

LD50 = lethal dose 50

LC50 = lethal concentration 50

TERM	DESCRIPTION
Chronic Parameter	indicated as NOEC, EC_x (x= proportion of affected test organism)
Growth	change in biomass or body size
Reproduction	number of eggs or young animals (clutch size, hatching rate)
Juvenile development	included in reproduction test
Morphological effects	external damages: wound in animals, cholrosis in plants
Biochemical/ physiological effects	e.g. changes in enzyme synthesis or activity or in respiration *etc*
Behavioral effects	observation of non-typical behavior (e.g. unccordinated swimming of fish)
Teratogenicity, carcinogenicity, mutagenicity	defects in embryos, formation of tumors, irreversible changes of the genome

TOXIC RESPONSES (PÜSA, 2008)

- Direct injury of cell or tissue
- Biochemical damage
- Neurotoxicity
- Immunotoxicity
- Teratogenicity
- Genotoxicity
- Carcinogenicity
- Endorine disruption

Endocrine Disrupters

- Chemicals which interfere with endocrine system function.
- Endocrine system consists of glands and the hormones they produce.
  - Pituitary, thyroid, and adrenal glands, the female ovaries and male testes.

Estradiol

Endocrine disruptors
(hormone mimicking substances)

Detergents in urban water streams: male fishes with increased level of vitallogenin

LD50 = lethal dose 50
LC50 = lethal concentration 50

EDx = effect dose
ECx = effect concentration

NOEC = no observed effect concentration
NEL = no effect level
NOAEL = No Observed Adverse Effect Level

Life-History Parameters

- Survival
- Growth
- Reproduction

ACUTE TOXICITY TEST

A. Mammals (including human beings)

- **Oral or demal application in milligrams of toxicant per kilogram body weight (mg/kg)** ppm (w/w)

- **Inhalation milligram toxicant per liter inhaled air (mg/l)** ppm (w/v)

B. Other animals

Exposure primarily takes place via the surrounding substrate (water, sediment, soil)

TWO STEPS

(1) preliminary (range finding) test – several levels of concentration

(2) actual toxicity test – usually 5 levels of concentration

LC50/LD50 (24, 48, 96 hours)

The mean lethal volume or concentration of a substance or its formulation that cost death in half of the test animals after exposure through the stomach, skin or respiratory pathways within a specific period of time

Toxicity profile

- Websites:
  - TOXNET
  - ASTDR
  - HIGHWIRE (portal of free journals, Stanford University)

  NAME AND DESCRIPTION OF THE TOXICANT

  PHYSICO-CHEMICAL PROPERTIES

  TOXICITY ON HUMAN/ANIMALS

  LC50, NOEC

TEST ANIMALS

should be homogeneous (age, size, sex etc)

CONCENTRATION (***a geometric series)***

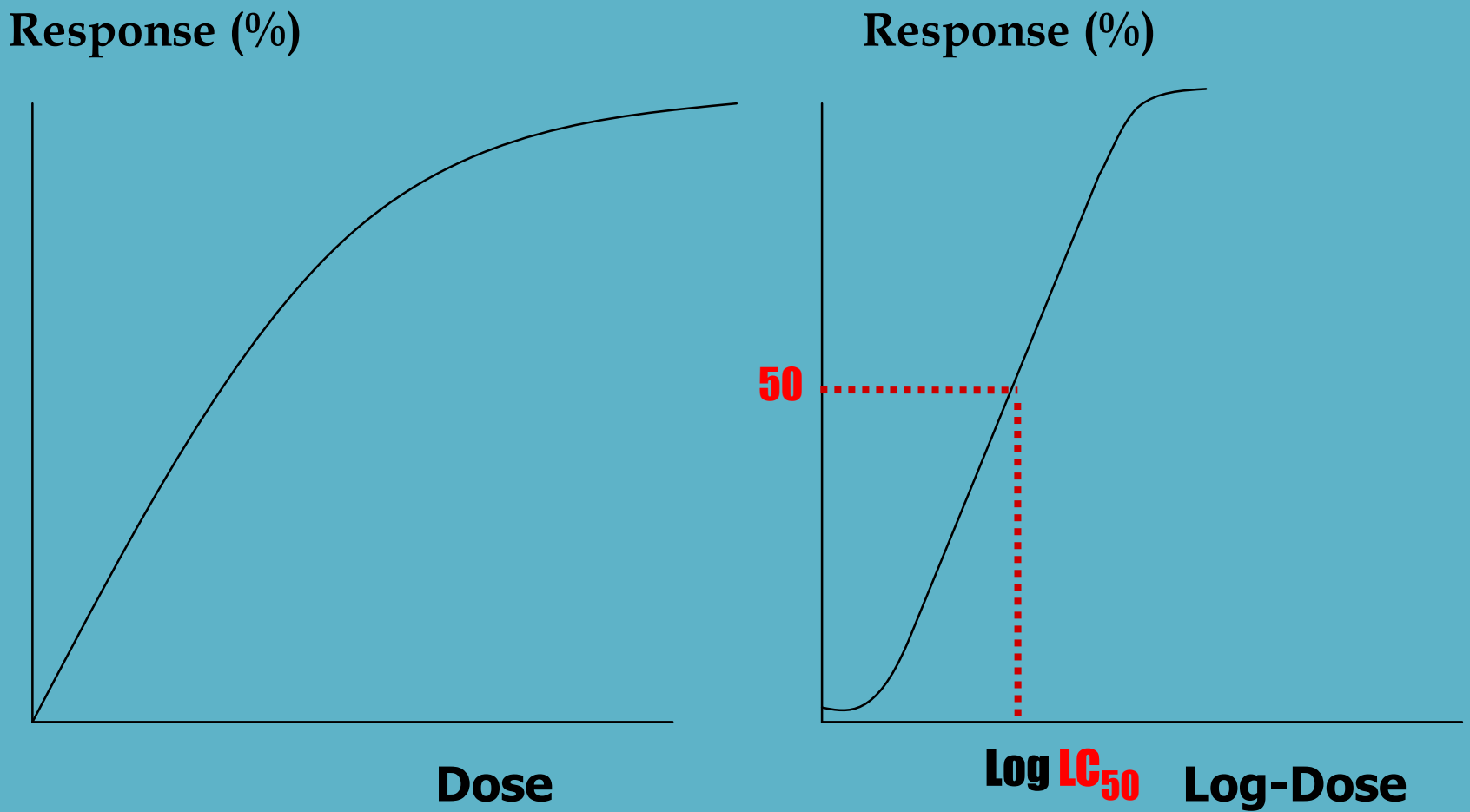
2mg/l – 2√2 mg/l – 4 mg/l - 4√2 mg/l - 8 mg/l

D A T A A N A L Y S I S

Quantal response = all-or-none, binary response

if the response is quantal, the organism is classified at a given time after dosage as <u>having responded</u> or <u>not</u> (in the organism the quantal response is a qualitative phenomenon)

DOSE-RESPONSE CURVE



LC50/EC50 Calculation

Transformation of response percentages to probits

%	0.0	0.1	0.2	.	0.5	.	.	0.9
0	..	1.91	2.12	..	2.42	..	..	2.63
1	..							..
2	..							..
3	..							..
.	..							..
.	..							..
50	5.00	..	..	..	..	..	..	..
.	..	..	..					
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KOMPUTASI LC_{50}

TOXICITY OF NICOTINE ON *Aphis rumicis*

Concentration of Nicotine (C)	Log C	Proportion of affected animals (%)	Probit Response
2.5	0.4	3.7	3.21
5	0.7	2.4	3.02
10	1.0	0	-
20	1.3	18.7	4.11
30	1.48	39.6	4.74
40	1.60	60.7	.
60	1.79	78.6	.
80	1.90	85.0	.
100	2.00	95.7	.
150	2.18	95.7	.
200	2.30	100	-

REGRESSION EQUATION

- Log concentration - as - the independent variable (X)
- Probit response - as - the dependent variable (Y)

$$Y = a + b X$$

probit response – Y

Log C – X

$$b = \frac{\Sigma XY - \frac{(\Sigma X)(\Sigma Y)}{n}}{\Sigma X^2 - \frac{(\Sigma X)^2}{n}}$$

$$a = \bar{Y} - b\bar{X}$$

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LC_{50} = ?

To find

X* ..... i.e. X value where Y = 5

$LC_{50} = 10^{X*}$

DETERMINATION OF NO EFFECT

No Observed Effect Concentration (NOEC)
No Adverse Effect Level (NOAEL)
No Effect Level (NEL)

Can be obtained from ANOVA (*analysis of variance*) of the dose response data involving a control treatment…..followed by a post hoc test e.g. THE DUNNETT'S TEST

TYPICAL DATA OF NO EFFECT DETERMINATION

Example: a toxicity experiment using hamster

(dietary exposure of Cd - 4 weeks)

Treatment*	Body Weight (g)	Average
Control	55.1, 55.2, 55.3, 54.9, 58.3	$\boxtimes_0$
Cd-1 ppm	54.1, 54.2, 55.4, 53.9, 56.3	$\boxtimes_1$
Cd-2 ppm	49.1, 47.2, 45.3, 42.9, 47.3	$\boxtimes_2$
Cd-3 ppm	38.1, 37.2, 37.3, 36.9, 38.3	$\boxtimes_3$
Cd-4 ppm	24.1, 25.2, 25.3, 34.9, 29.3	$\boxtimes_4$

ANOVA

*) Cd-1 to 4 ppm = cadmium concentration in the diet (1 ppm to 4 ppm)

$\boxtimes_0$ vs $\boxtimes_1$

$\boxtimes_0$ vs $\boxtimes_2$

$\boxtimes_0$ vs $\boxtimes_3$ **

$\boxtimes_0$ vs $\boxtimes_4$ **

NOEC = 2 ppm

NOAEL as a foundation of food safety measures:
ADI & MTWI

NOAEL → ADI → MTWI
(exp. animal) (human) (human)

ADI = acceptable daily intake

MTWI = maximum tolerable weekly intake

ADI = NOAEL/100 --------> *Safety Factor*

ADI

the maximum amount of toxic substance that can be consumed by human in one day (mg per kg body weight) without any impact on health

$$MTWI = 7 \times ADI$$

MTWI

the maximum amount of toxic substances that can be consumed by human in one week (mg per kg body weight) without any impact on health