Agency for Toxic Substances and Disease Registry (ATSDR)

EPA Reportable Quantity Methodology Used to Establish Toxicity/Environmental Scores for the Substance Priority List

This document contains the methodology used to determine the Toxicity/Environmental Scores (TESs) for the ATSDR Substance Priority List. The TESs were based on the methodology used to determine Reportable Quantities (RQs). The RQ methodology was applied to those candidate substances without final CERCLA RQs in order to establish a TES. These scores were developed for use only in the ranking methodology and do not represent regulatory values. The Substance Priority List is available at www.atsdr.cdc.gov/SPL and more information on the determination of the toxicity component can be found in the Support Document located at www.atsdr.cdc.gov/SPL/resources.

Five Components of the Reportable Quantity (RQ) Methodology

● Ignitability/Reactivity ● Aquatic Toxicity ● Mammalian Toxicity ● Chronic Toxicity ● Carcinogenicity

IGNITABILITY AND REACTIVITY SCALES

CATEGORY	IGNITABILITY (FIRE)	REACTIVITY		RQ (pounds)
		With Water	Self-Reaction	
D	FP 100°-140°F	Moderate reaction, e.g. NH_3	Slight; may polymerize with low heat release	5000
C	FP <100°, BP ∃100°F	High reaction, e.g. oleum	Moderate; contamination may cause polymerization; no inhibitor required	1000
B	FP <100°, BP <100°F	Extreme reaction, e.g. SO_3	High; may polymerize; requires stabilizer	100
A	Pyrophoric or self-ignitable	Inflames	Extreme self-reaction; may cause explosion or detonation	10
X	RQ of 1 not assigned based on ignitability/reactivity.			1

FP = Flash Point; BP = Boiling Point

AQUATIC TOXICITY SCALE

CATEGORY	AQUATIC TOXICITY	RQ (pounds)
D	100 mg/l ≤ LC_{50} < 500 mg/l	5000
C	10 mg/l ≤ LC_{50} < 100 mg/l	1000
B	1 mg/l ≤ LC_{50} < 10 mg/l	100
A	0.1 mg/l ≤ LC_{50} < 1 mg/l	10
X	LC_{50} < 0.1 mg/l	1

LC_{50} = Lethal Concentration (50% kill)
Note: Use fathead minnow (Pimephales promelas) or bluegill (Lepomis macrochirus) as standard choice for test species.

MAMMALIAN TOXICITY SCALE

CATEGORY	MAMMALIAN TOXICITY (ORAL)	MAMMALIAN TOXICITY (DERMAL)	MAMMALIAN TOXICITY (INHALATION)	RQ (pounds)
D	100 mg/kg ≤ LD_{50} < 500 mg/kg	40 mg/kg ≤ LD_{50} < 200 mg/kg	400 ppm ≤ LC_{50} < 2000 ppm	5000
C	10 mg/kg ≤ LD_{50} < 100 mg/kg	4 mg/kg ≤ LD_{50} < 40 mg/kg	40 ppm ≤ LC_{50} < 400 ppm	1000
B	1 mg/kg ≤ LD_{50} < 10 mg/kg	0.4 mg/kg ≤ LD_{50} < 4 mg/kg	4 ppm ≤ LC_{50} < 40 ppm	100
A	0.1 mg/kg ≤ LD_{50} < 1 mg/kg	0.04 mg/kg ≤ LD_{50} < 0.4 mg/kg	0.4 ppm ≤ LC_{50} < 4 ppm	10
X	LD_{50} < 0.1 mg/kg	LD_{50} < 0.04 mg/kg	LC_{50} < 0.4 ppm	1

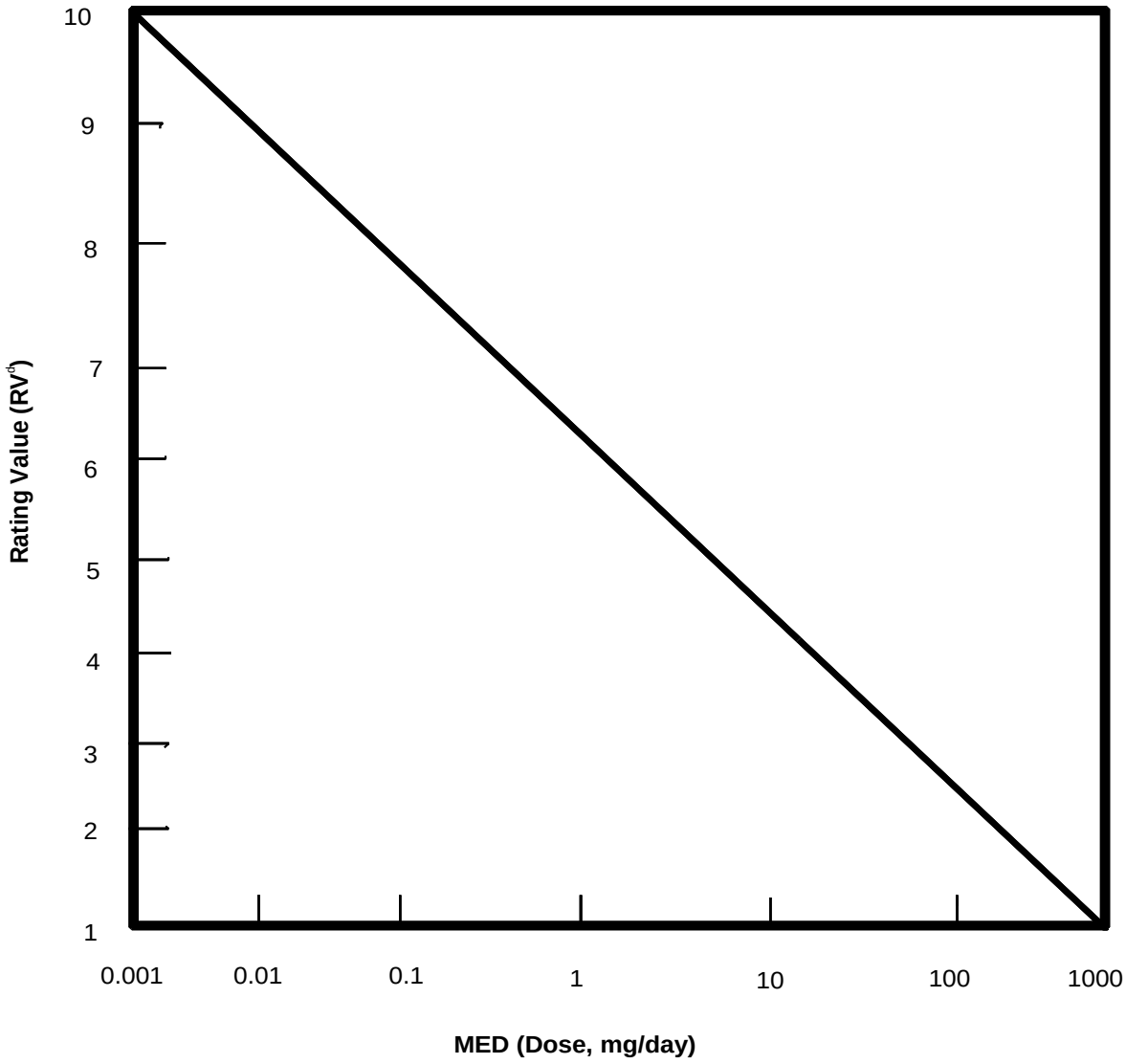
LD_{50} = Lethal Dose (50% kill)
Use rat data wherever available. Use other species in the absence of (or in conjunction with) rat data. If data from multiple species are not consistent, then use the most conservative values, unless the preponderance of data indicates otherwise.

CHRONIC TOXICITY

Based on two primary attributes of each substance:

- The minimum effective dose (MED) levels for chronic exposures (mg/day for 70-kg man) via alternative environmental media (air, water, etc.)
- Type of effect (liver necrosis, teratogenicity, etc.)

The MED is the lowest effective dose level that can be identified having any effect on an organism under study. In order to have consistent values, animal MEDs are converted to human MEDs by a conversion factor that relates animal body weight to human body weight. For the human body weight, 70 kilograms is used. The human MED is then used to determine a rating value by dose (RV_d) for each of the substances evaluated for chronic toxicity. MEDs are converted to RV_ds using the following scale:



Note: All MED values of 1000 or greater are assigned a rating value of 1; all MED values of 0.001 or less are assigned a rating value of 10.

CONVERSION TABLE FOR ANIMAL TO HUMAN EQUIVALENT DOSE

Multiply the administered dose by the following factor to derive human equivalent dose:

Species	Dose in mg/day:	Dose in mg/kg/day:
Rhesus monkey	3.5	37.6
Chimpanzee	2.4	45.5
Mouse [mean body weight (BW) of 2 strains]	169.6	5.4
Rat (mean BW of 5 strains)	28.1	13.2
Guinea pig	18.36	16.3
Hamster, golden Syrian (default)	64.9	8.7
Hamster, Chinese	142.9	5.9
Gerbil	88.6	7.4
Dog	3.5	37.5
Cat	7.2	26.2
Rabbit	7.0	26.4
Chicken	14.3	18.5
Pig, domestic (default)	0.5	103.3
Pig, miniature	1.0	70.6
Mink	11.9	20.3

For animal dose in mg/day:

$$\textit{animal dose (mg/day)} \; X \; \left(\frac{70kg}{\textit{animal weight}} \right)^{2/3}$$

For animal dose in mg/kg/day:

$$\textit{animal dose (mg/kg/day)} \; X \; \left(\frac{\textit{animal weight}}{70kg} \right)^{1/3} \; X \; 70kg$$

Similarly, the type of effect produced by a particular hazardous substance is given a rating value based on effect (RV_e). These RV_e values range from one to ten depending on the severity of the effect, with ten being the most severe:

RATING VALUES FOR TOXIC EFFECTS

RATING	EFFECT
1	Enzyme induction or other biochemical change with no pathologic change and no change in organ weights.
2	Enzyme induction and subcellular proliferation or other changes in organelles but no other apparent effects.
3	Hyperplasia, hypertrophy, or atrophy, but no change in organ weights.
4	Hyperplasia, hypertrophy, or atrophy with changes in organ weights.
5	Reversible cellular changes: cloudy swelling, hydropic change, or fatty changes.
6	Necrosis, or metaplasia with no apparent decrement in organ function. Any neuropathy without apparent behavioral, sensory, or physiologic changes.
7	Necrosis, atrophy, hypertrophy, or metaplasia with a detectable decrement in organ functions. Any neuropathy with a measurable change in behavioral, sensory, or physiologic activity.
8	Necrosis, atrophy, or metaplasia with definitive organ dysfunction. Any neuropathy with gross changes in behavior, sensory, or motor performance. Any decrease in reproductive capacity. Any evidence of fetotoxicity.
9	Pronounced pathologic changes with severe organ dysfunction. Any neuropathy with loss of behavioral or motor control or loss of sensory ability. Reproductive dysfunction. Any teratogenic effect with maternal toxicity.
10	Death or pronounced life-shortening. Any teratogenic effect without signs of maternal toxicity.

A composite score is determined for each substance by multiplying the rating value for dose (RV_d) by the rating value for effect (RV_e). The possible range of composite scores is 1 to 100. These resulting composite scores are then correlated with the five RQ levels as follows:

CHRONIC TOXICITY SCALE

CATEGORY	COMPOSITE SCORE (RV_d X RV_e)	RQ (pounds)
D	1 - 5	5000
C	6 - 20	1000
B	21 - 40	100
A	41 - 80	10
X	81 - 100	1

CARCINOGENICITY SCALES

EPA WEIGHT-OF-EVIDENCE CATEGORY	EPA CANCER CLASSIFICATION	DEFINITION
Group A	Known human carcinogen	Substances for which "sufficient" evidence from human epidemiologic studies supports a causal connection between exposure to the substance and cancer.
Group B1	Probable human carcinogen (limited human evidence)	Weight of evidence of human carcinogenicity based on epidemiologic studies is "limited."
Group B2	Probable human carcinogen (no human evidence)	Substances for which there is "no data," or "no evidence" from human epidemiologic studies, but for which the weight of evidence of carcinogenicity based on animal studies is "sufficient."
Group C	Possible human carcinogen	Substances with "limited" evidence of carcinogenicity in animals, and "inadequate evidence," "no data," or "no evidence" from human epidemiologic studies.
Group D	Not evaluated	Not classifiable for human carcinogenicity (insufficient data).
Group E	Noncarcinogenic	Evidence of noncarcinogenicity in humans.

The substances also receive a potency classification of Group 1, 2, or 3, with Group 1 representing the potential carcinogens with the highest relative potencies. The following matrix is used to yield a relative hazard ranking of "high," "medium," or "low" which correspond to RQ levels of 1, 10, and 100 pounds, respectively:

WEIGHT-OF-EVIDENCE GROUP	POTENCY GROUP		
	1 (HIGHEST)	2	3 (LOWEST)
A	High (1)	High (1)	Medium (10)
B	High (1)	Medium (10)	Low (100)
C	Medium (10)	Low (100)	Low (100)
D	No hazard ranking is made. The other primary criteria are used to assign the RQ.		
E	No hazard ranking is made. The other primary criteria are used to assign the RQ.		

BIODEGRADATION/ HYDROLYSIS/ PHOTOLYSIS ADJUSTMENT

RQ is raised one level (multiplied by 10) if biodegradation, hydrolysis, and/or photolysis (BHP) results in degradation when the substance is released into the environment. However, if the degradation products are themselves hazardous substances, the RQs for the substances are assigned the RQ of the degradation product. Furthermore, the biodegradation RQ adjustment is not considered for substances that are highly volatile (boiling point of 100°F or lower). Substances are considered to be rapidly degraded by photolysis/hydrolysis if its half-life is 5 days or less. If a substance is highly water soluble (infinitely miscible), adjustment to the RQ is made based on biodegradation. BHP adjustment to potential carcinogens is done just like the other four RQ components.