



Severity

Developing a Scoring Scale
for Screening Contaminants
(PCCL to CCL)

Severity

- ◆ One of the five NRC recommended attributes that will be used to characterize a contaminant's known or potential ability to cause a health effect
- ◆ Answers the question: How bad is the effect?

Process

- ◆ Used NRC proposed scale as starting point
- ◆ Applied scale to sample data set
- ◆ Assessed scoring difficulties
- ◆ Revised scale to resolve difficulties
- ◆ Completed three cycles of review/revision process

Guiding Principles

- ◆ Severity was scored based on the critical effect associated with the selected potency value (e.g.- RfD, NOAEL, LOAEL, LD₅₀)
- ◆ Definition:
 - **Critical Effect-** The first adverse effect, or its known precursor, that occurs to the most sensitive species as the dose rate of an agent increases.
- ◆ Descriptions of critical effects were used exactly as found in IRIS database.
- ◆ For chemicals having multiple critical effects, each effect was scored. The highest score prevailed.

Types of Critical Effect Descriptors

Chemical Contaminant	RfD	IRIS critical effect
Fenamiphos	2.5E-04	Cholinesterase inhibition (ChE)
2,4-dinitrophenol	2.00E-03	Cataract formation
Chlordane	5.00E-04	Hepatic necrosis
Dicamba	3.00E-02	Maternal & Fetal toxicity
2,4-dinitrotoluene	2.00E-03	Neurotoxicity, Heinz bodies and biliary tract hyperplasia

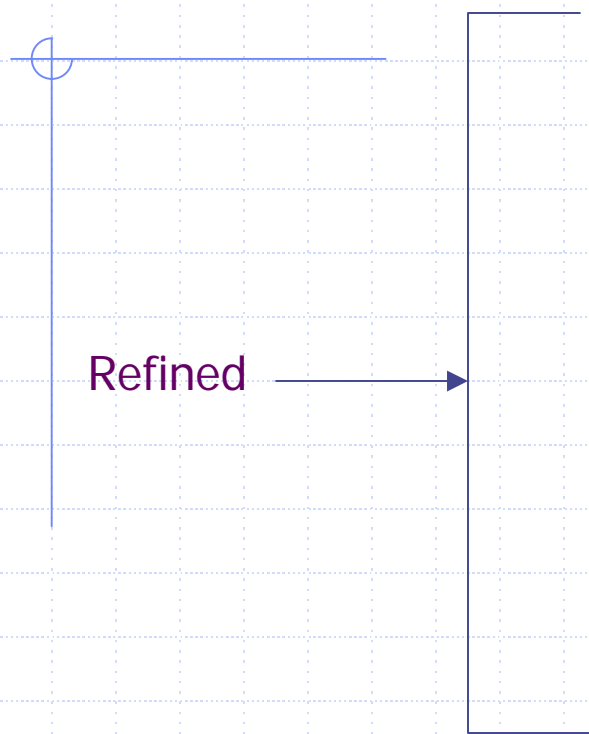
NRC Scoring Scheme*

0	No Effect	6	Irreversible changes; treatable disease
1	Changes in organ weights with minimal clinical significance	7	Single organ system pathology and function loss
2	Biochemical changes with minimal clinical significance	8	Multiple organ system pathology and function loss
3	Pathology of minimal clinical significance	9	Disease likely leading to death
4	Cellular changes that could lead to disease; minimal functional change	10	Death
5	Significant functional changes that are reversible		

* See Table I

Scoring Scale: Revision 1

(Table II)



- 0 No Effect
- 1 Cosmetic Effects
- 2 Transient, reversible effects
- 3 Cellular/physiological changes that could lead to disease/disorder (risk factors or precursor effects)
- 4 Mild, permanent functional changes
- 5 Curable diseases or disorders
- 6 Treatable, uncurable diseases or disorders
- 7 Chronic, untreatable, nonlethal diseases or disorders
- 8 Effects leading to sterility, miscarriage, stillbirths (population effects)
- 9 Disease likely leading to death
- 10 Death

Scoring Scale: Revision 2

(Table III)

0	No Effect	5	Significant, irreversible disorders that can be managed by medical treatment
1	Cosmetic Effects	6	Significant, irreversible, non-lethal conditions or disorders that cannot be managed by medical treatment
2	Transient, reversible effects; differences in organ weights, body weights or changes in biochemical parameters with minimal clinical significance	7	Developmental or reproductive effects leading to major dysfunction
3	Cellular/physiological changes that could lead to disorders (risk factors or precursor effects)	8	Disorder likely leading to death
4	Significant functional changes that are reversible or permanent changes of minimal toxicological significance	9	Death

Scoring Scale: Revision 3

(Table IV)

- | | | | |
|---|--|---|--|
| 1 | No adverse effect | 6 | Significant, irreversible, nonlethal conditions or disorders |
| 2 | Cosmetic effects | 7 | Developmental or reproductive effects leading to major dysfunction |
| 3 | Reversible effects; differences in organ weights, body weights or changes in biochemical parameters with minimal clinical significance | 8 | Tumors or disorders likely leading to death |
| 4 | Cellular/physiological changes that could lead to disorders (risk factors or precursor effects) | 9 | Death |
| 5 | Significant functional changes that are reversible or permanent changes of minimal toxicological significance | | |

Scoring/Binning Exercise (Table IV)

- ◆ 100 chemicals with RfDs in IRIS database

- ◆ Purpose
 - Further improve scoring scheme by scoring actual effects as they can be downloaded from IRIS
 - Experiment with “binning” of critical effects
 - Begin developing a “working vocabulary” or glossary of critical effect descriptors

Examples of Critical Effects: Results of "Binning Exercise"

- 1 No adverse effects
No observed adverse effects
- 2 Abnormal appearance
- 3 Cholinesterase inhibition
Salivation, Clinical parameters,
Increased relative organ
weights, Increased enzymes
- 4 Decreased blood counts,
Hypothermia, Liver cell
enlargement
- 5 GI irritation, GI bleeding,
Tremors
- 6 Kidney damage(unspecified),
Cardiac toxicity, Spleen
toxicity
- 7 Testicular effects,
Spermatogenic arrest, Lower
ovarian weight
- 8 Decreased longevity
- 9 Mortality, Increased mortality,
Decreased survival

On-going Issues

- ◆ Middle scores remain difficult to differentiate
- ◆ Difficulties in placing different types of reproductive and developmental effects
- ◆ How to score chemicals lacking critical effects

Next Steps

- ◆ Expand “binning” exercises to include data sources other than IRIS and continue to develop a glossary of terms
- ◆ Continue to revise scoring scheme based on lessons learned

Questions to Consider

- ◆ Should scale be condensed to contain fewer categories?
- ◆ Should “death” be included as separate category? (possibly useful for LD₅₀)