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, LD_{50})
- 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

1 Changes in organ weights with minimal clinical significance

2 Biochemical changes with minimal clinical significance

3 Pathology of minimal clinical significance

4 Cellular changes that could lead to disease; minimal functional change

5 Significant functional changes that are reversible

6 Irreversible changes; treatable disease

7 Single organ system pathology and function loss

8 Multiple organ system pathology and function loss

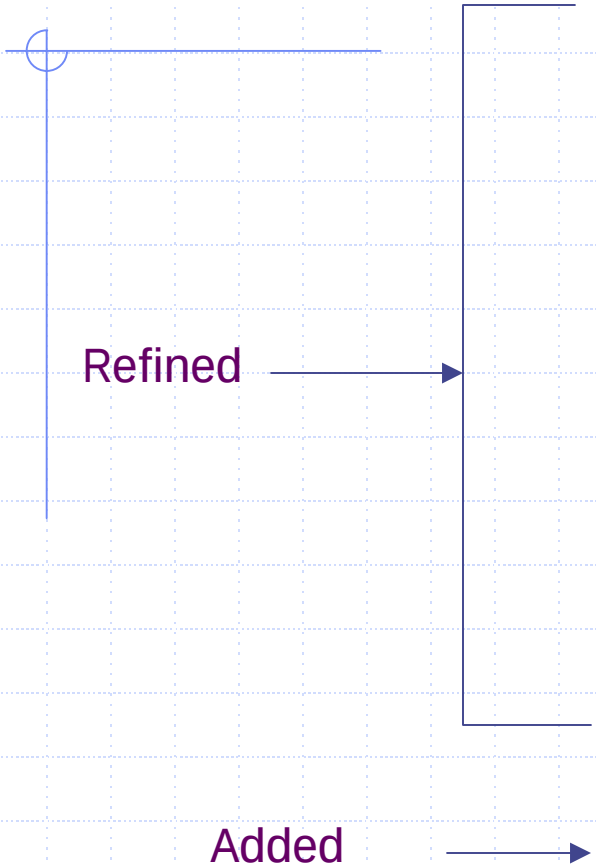
9 Disease likely leading to death

10 Death

*** 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

1 Cosmetic Effects

2 Transient, reversible effects; differences in organ weights, body weights or changes in biochemical parameters with minimal clinical significance

3 Cellular/physiological changes that could lead to disorders (risk factors or precursor effects)

4 Significant functional changes that are reversible or permanent changes of minimal toxicological significance

5 Significant, irreversible disorders that can be managed by medical treatment

6 Significant, irreversible, non-lethal conditions or disorders that cannot be managed by medical treatment

7 Developmental or reproductive effects leading to major dysfunction

8 Disorder likely leading to death

9 Death

Scoring Scale: Revision 3
(Table IV)

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

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 LD_{50})