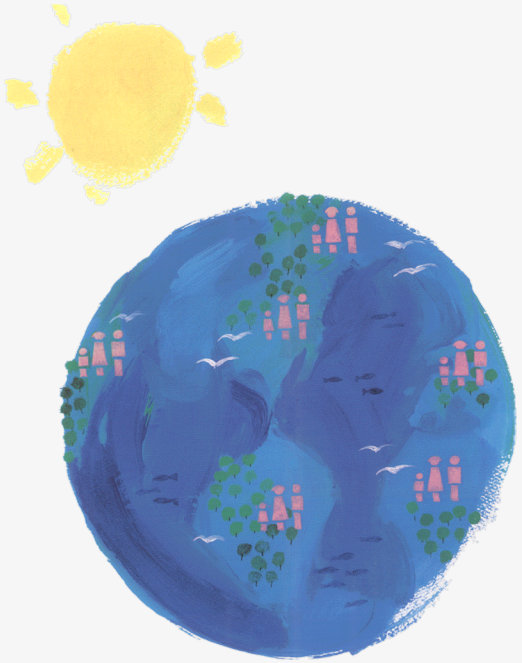
NICEATM — *National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods*

ICCVAM — *Interagency Coordinating Committee on the Validation of Alternative Methods*



Data Currently Collected During Acute Systemic Toxicity Tests

Gary Wnorowski

President

Eurofins | Product Safety Labs

Acute Chemical Safety Testing Workshop

February 6 & 7, 2008

National Toxicology Program

NIEHS

National Institutes of Health

Department of Health & Human Services • USA

Regulatory Drivers

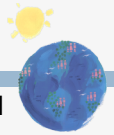
- Current technical guidance is provided by EPA's OPPTS 870 series and OECD's Guidelines for Testing of Chemicals.
- From a regulatory perspective, the primary reason for conducting these studies is to allow for the proper labeling of pesticides and antimicrobials.
- Common Acute Toxicity Studies that continue to be conducted on a regular basis.
  - Oral
  - Dermal
  - Inhalation

Acute Oral Toxicity

- Several alternative methods have been introduced over the last 5 years that have significantly reduced the number of animals used in this testing.
- Test compound administered to rats by oral gavage at appropriate dose
- Following administration, and for the next 14 days animals are closely monitored for clinical signs. Animals are weighed at study initiation, day 7 and day 14. At the end of 14 days the animals are sacrificed and subjected to gross necropsy.

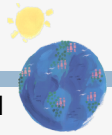
Acute Dermal Toxicity

- Test compound applied dermally to rats.
- Test site covered with gauze held in place by tape. Patches removed and sites cleaned after 24 hours of exposure.
- Animals are closely monitored for clinical signs over the 14 day test period beginning from the application of test compound. Animals are weighed at study initiation, day 7 and day 14. At the end of 14 days the animals are sacrificed and subjected to gross necropsy.



Acute Inhalation Toxicity

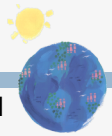
- Rats exposed to aerosolized test compound for a period of one or four hours.
- Following exposure, animals are closely monitored for clinical signs over the 14 day test period. Animals are weighed at study initiation, day 7 and day 14. At the end of 14 days the animals are sacrificed and subjected to gross necropsy.



Endpoints Assessed

Although current OPPTS and OECD guidelines emphasize the importance of reducing the numbers of animals used for these studies, the criteria for assessing toxicity has remained generally unchanged.

Abdominal Distention	Desquamation	Hunched Posture	Piloerection
Aggressive	Diarrhea	Hyperactivity	Prolapsed Penis
Ano-Genital Staining	Dyspnea	Hyperkeratosis	Prolapsed Uterus
Alopecia	Edema	Hypoactivity	Prone
Ataxia	Emaciation	Hypothermia	Prostrate
Blanching	Erythema	Irregular Respiration	Rales -Moist
Convulsions - Clonic	Eschar	Moribund	Rales - Dry
Convulsions - Tonic	Exophthalmos	Mouth Discharge	Reduced Fecal Volume
Corneal Opacity	Facial Stains	Nasal Discharge	Reduced Food Consumption
Cyanosis	Fissuring	Normal	Soft Feces
Dead	Necrosis	Ocular Discharge	Tremors
Enophthalmos	Gasping	Pannus	Unthrifty



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