Toxicity Tests: Calculated Endpoints

Calculated Endpoints in Toxicity Tests

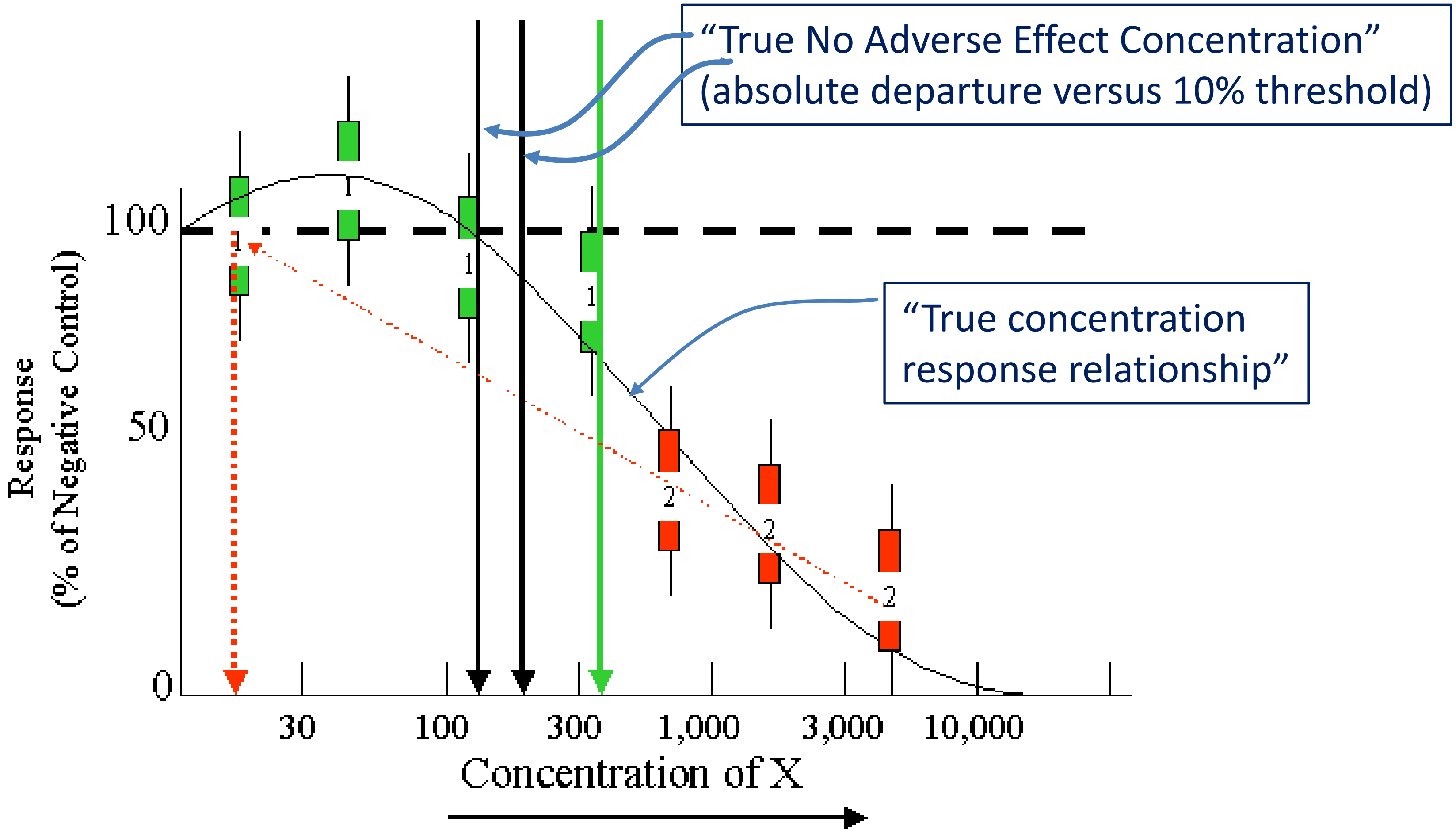
- Point Estimates — Analysis of Variance Designs
  - No Observable Adverse Effect Concentration (NOAEC)
  - Lowest Observable Adverse Effect Concentration (LOAEC)
  - MATC — Maximum Allowable Toxic Concentration = Geometric Mean of the NOAEC and LOAEC
  - Predicted No Effects Concentration (PNEC)
- Point Estimates — Regression Designs
  - EC_X — Effect Concentration; X = a designated percentage of controls
  - IC_X — Inhibitory Concentration; X = a designated percentage of controls

N.B.: NOAECs and LOAECs (or equivalent terms) have been criticized. See Bailer and Oris (1997); Chapman *et al*. (1996); Hoeskstra and van Ewijk (1993); Kapustka (2008); Laskowski (1995); OECD (1998)

Tools to Calculate Endpoints

- The US EPA (http://www.epa.gov/nerleerd/stat2.htm) offers free downloads of software programs to calculate endpoints
  - Dunnett's Procedure
  - Probit Analysis
  - Trimmed Spearman-Karber Method
  - Linear Interpolation (Icp) Method
- Environment Canada (2005) — *Guidance Document on Statistical Methods for Environmental Toxicity Tests*
- Most standardized test methods (e.g., ASTM-I, OECD, ISO) for specific tests include recommended statistical methods

Why we should use all the data!



Note different "NOAEC" from a study with just the green data points (green arrow) and the red data points (red arrow)

Adapted from Kapustka (2006)

Constraints of Point Estimates

- Point estimates are useful with respect to identifying a threshold concentration. However, much information is lost by reducing the full range of data obtained in a test to a single value.
- For example, what is the effect of having 2-times the EC_x? One needs to know the slope of the response to answer this question.
- Consider the markedly different answers one would get from the different point estimates illustrated on the previous slide.
  - Point estimates approximately 15, 150, 200, 320 mg/kg
  - Compared to "true response relationship" the 2-times concentrations would result in
    - No detectable response
    - Minimal detectable response
    - Modest decrease
    - Major decrease

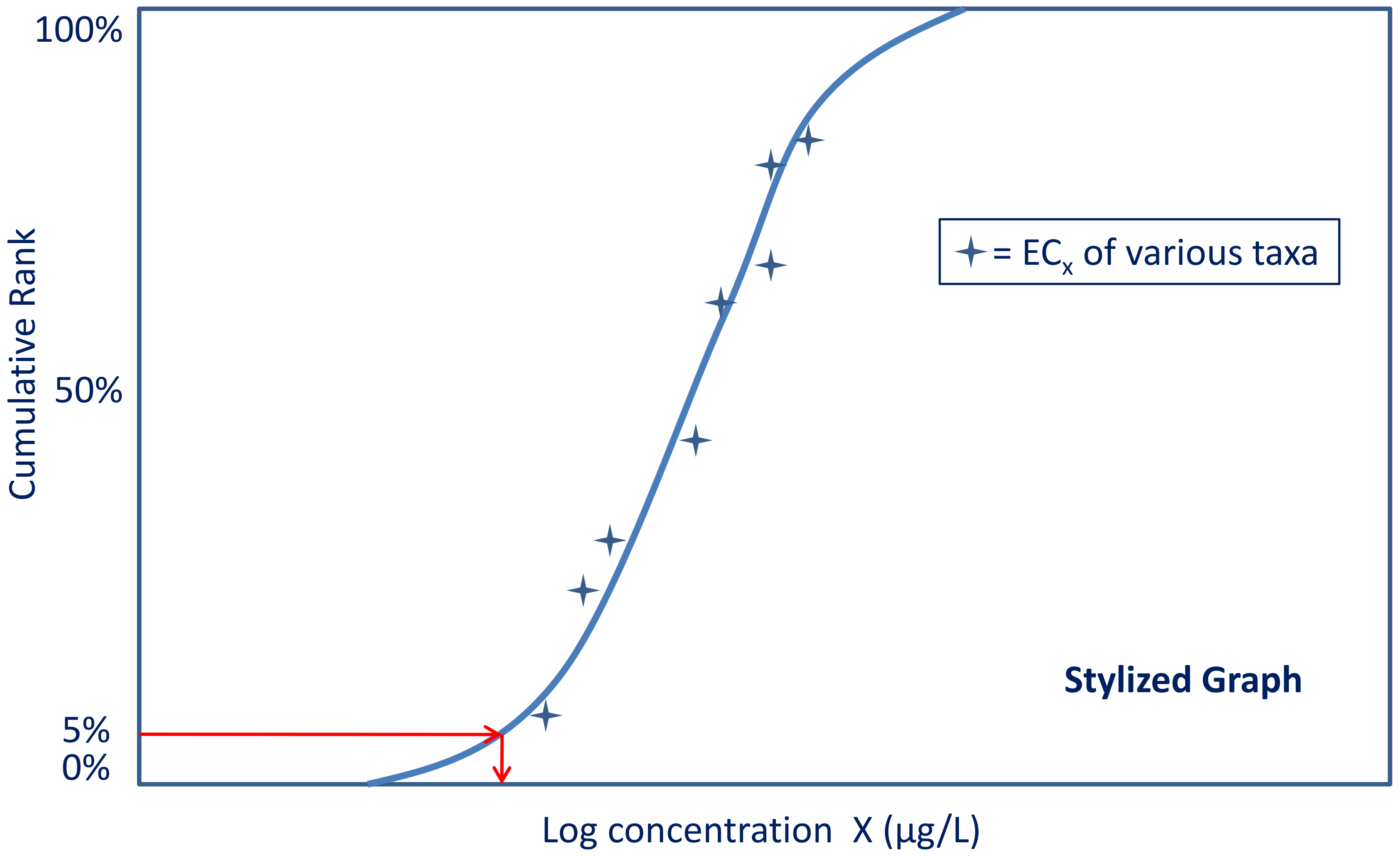
Species Sensitivity Distributions

- Point estimates of toxicity (e.g., EC_x) from multiple taxa are displayed in cumulative rank order where the X-axis is concentration of a toxicant
- Resulting fitted curves (e.g., Weibull, lognormal) are assumed to represent the distribution of all taxa, not just those tested
- The 5^{th} percentile is considered to be represent the most sensitive species, hence if the data set is robust the corresponding concentration should be protective of all taxa

Adapted from Posthuma et al. (2002)

See graph on next slide

Species Sensitivity Distributions



EPA Acute Ecotoxicity SSDs

Chemical	Four Most Sensitive Genus	
Cu	4. Amphipod	2. Cladoceran (Ceriodaphnia)
	3. Snail	1. Cladoceran (Daphnia)
Cd	4. Trout (Oncorhynchus)	2. Trout (Salvelinus)
	3. Bass	1. Trout (Salmo)
NH3	4. Trout (Oncorhynchus)	2. Shiner
	3. Darter	1. Whitefish
Atrazine	4. Trout (Oncorhynchus)	2. Trout (Salvelinus)
	3. Stonefly	1. Hydra
Diazinon	4. Amphipod	2. Cladoceran (Daphnia)
	3. Cladoceran (Simocephalus)	1. Cladoceran (Ceriodaphnia)
CN	4. Perch	2. Trout (Salvelinus)
	3. Salmon	1. Trout (Oncorhynchus)

EPA Chronic Ecotoxicity SSDs

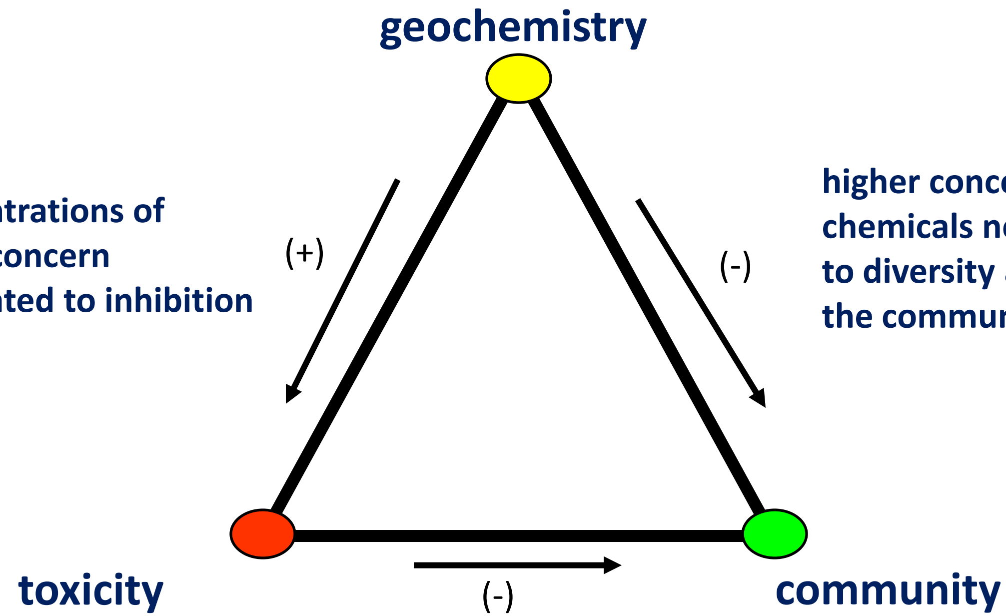
Chemical	Four Most Sensitive Genus	
Cu	4. Snail	2. Caddisfly
	3. Cladoceran (Daphnia)	1. Rotifer
Cd	4. Midge	2. Cladoceran (Daphnia)
	3. Trout (Oncorhynchus)	1. Amphipod
NH3	4. Bluegill	2. Rainbow trout
	3. Amphipod	1. Freshwater mussel
Atrazine	4. Trout (Salvelinus)	2. Fathead minnow
	3. Trout (Oncorhynchus)	1. Bluegill
Diazinon	4. Flagfish	2. Trout (Salvelinus)
	3. Fathead minnow	1. Cladoceran (Ceriodaphnia)
CN	4. Bluegill	2. Amphipod
	3. Fathead minnow	1. Trout (Salvelinus)

Environmental Quality Triad

- Sample locations are characterized in terms of biological community composition/structure
- Co-located samples measures for analyte concentrations for chemicals of concern and toxicity to relevant organisms

Correlations:

higher concentrations of chemicals of concern positively related to inhibition of organisms



higher concentrations of chemicals negatively related to diversity and vigour of the community

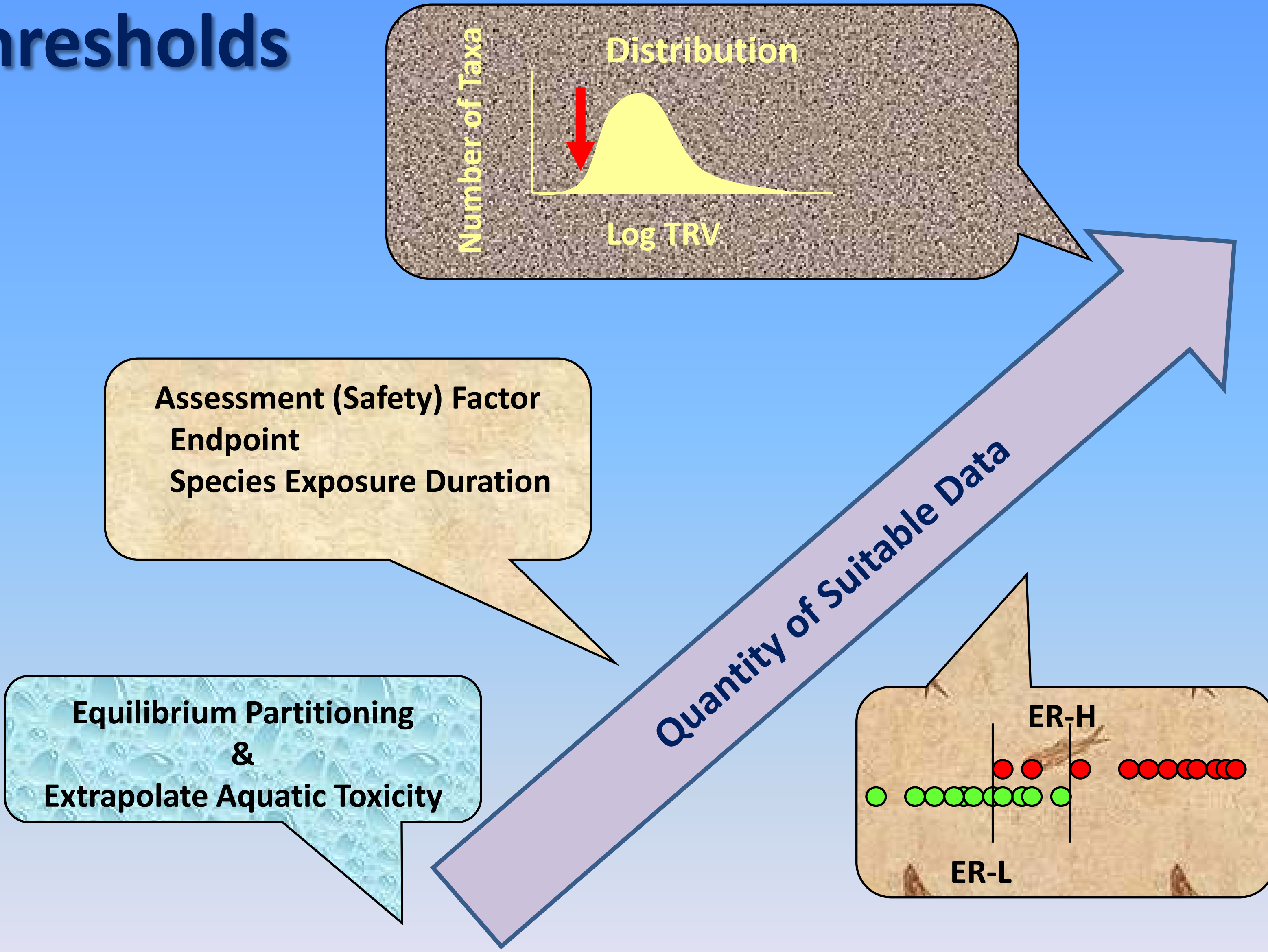
greater inhibition of organisms negatively related to diversity and vigour of the community

For background information, see Chapman et al. (1987, 1992) Kapustka (2002)

Jurisdictional Issues

- Sovereignty has resulted in many different approaches to risk assessment including
  - specificity of protection goals
  - data quality acceptability criteria
  - methods of assessment
- International trade has lead to efforts to harmonize and standardize across these differences
  - challenge to avoid "lowest common denominator"
  - challenge to establish effective and consistent enforcement
- Bi-lateral and multi-lateral agreements attempt to establish commonality, but differences persist

Thresholds



Increasing quality and quantity of data reduces uncertainty regarding effects threshold.

Examples of Assessment Factors Used

Assessment factors for determination of soil quality criteria (Europe)	
Information available	**Assessment Factor**
Only acute LC_{50} data are available and the data set is small or represents only a few genera (<3)	1,000
Only acute LC_{50} data are available, but there is an extensive phylogenetic range represented ($\geq$3)	100
Chronic test data are available but from a limited data set (<4)	10

Uncertainty factors for determination of soil quality criteria using the weight of evidence approach (Canada)	
Information available	**Suggested Uncertainty Factor**
Only the minimum of 3 studies is available	5
> 3 studies are available, but <3 taxonomic groups are represented	3
> 25% of the data below the 25th percentile are definitive effects data (i.e., not LOAECs)	1

The differences reflect policy with respect to the degree of precaution taken.

These assessment, safety, or uncertainty factors inject risk management decision into the science-based assessment activities.

Recapping

Procedural Details

- Site-specific conceptual models guide the choices made in characterizing a site
  - Assessment endpoints
  - Measurement endpoints
  - Methods used to obtain measurements
  - Data quality objectives
- The project-specific Sampling and Analysis Plan lays out the choices made—this workplan or roadmap guides work
- The project-specific Quality Assurance Project Plan establishes the steps that will be taken to establish acceptable levels of quality in all aspects of work

Toxicity Test Options

- There are numerous standardized test procedures available to evaluate the effects of test substances or site sample in terms of their adverse effects on organisms living in
  - Aquatic or marine systems
  - Sediments
  - Soils
- Interpretation of toxicity data, especially of older test reports can be challenging and subject to considerable error
- Integrative methods can be useful to establish weight-of-evidence lines among chemical measurements, toxicity test results, and community structure.

Relevant Websites

- ASTM-I (Standards): www.astm.org
- European Chemicals Bureau: http://ecb.jrc.it/reach/
- European Chemicals Agency: http://ec.europa.eu/echa/home_en.html
- European Commission
  http://ec.europa.eu/environment/chemicals/reach/reach_intro.htm
  http://ec.europa.eu/enterprise/reach/index_en.htm
- http://ecb.jrc.it/DOCUMENTS/REACH/REACH_in_brief_0207.pdf
- Helpdesks EU member states: http://www.reachright.ie
  http://www.senternovem.nl/reach
- US EPA on Risk Assessment: http://www.gov/oswer/riskassessment
- US EPA on hazardous waste cleanup and training: http://www.clu-in.org
- US EPA on DQOs: http://epa.gov/quality/dqos.html
- DQO training: http://epa.gov/quality//trcourse.html#intro_dqos
- http://www.library.uiuc.edu/envi/toxigateway.htm
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