Regulatory Risk Assessment

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    - *OMB Memorandum 9/20/01*

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Types of Risk Assessment

- Qualitative
  - Potential hazard
  - Actual or potential exposure
  - Mass
- Quantitative
  - Probabilistic (eg, engineering systems, LPHC events)
  - Extrapolation from toxicological dose-response (eg, cancer)
  - Scale extension from epidemiology
- Pseudo-quantitative (Safety Assessment)
  - Reference Doses, Reference Concentrations, Acceptable Daily Intakes, etc.

Qualitative Risk Assessment

- Variants
  - Potential hazard
    Actual or potential exposure
  - Emission
  - Body burden

Quantitative Risk Assessment: Cancer Slope Factors (I)

- Linearized multistage model (LMS)
  - *Not* the MLE of best curve, but a numerically calculated envelope of several 95th percentile upper bounds
    - Numerical method makes the linear term ('*q1**') in the model as large as possible
    - *q1** is best predicted by the highest dose tested, not D-R
  - Overstates likely risk at low doses
    - More for sublinear D-R, less for superlinear D-R
    - Can be several orders of magnitude
    - Infinitely overstates risk of chemicals with thresholds
  - Monotonically increasing function is often wrong (eg, ethanol, certain nutrients)

Quantitative Risk Assessment: Cancer Slope Factors (II)

- Conversion to 'benefits' is easy (but biased)
  - Estimates of baseline risk are exaggerated
  - Potential benefits of regulation are exaggerated
- New biases added by agency economists
  - Risk model: R = f (cumulative exposure)
  - *But* benefit model: B = f (instantaneous exposure reduction)
    - Biological lag effects are ignored (eg, repair mechs)
    - Cumulative exposure risk model is ignored
  - WTP defaults overstate actual WTP

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Scale Extension from Epidemiology

RR of Covariates Different from Fine PM in All-Causes Mortality Association (Based on Pope, et al., HEI Reanalysis)		
RR	COVARIATE	DESCRIPTION
1.19*	PM	RR for fine PM used in NAAQS revision
1.18*	Temperature variation	Variation in maximum daily temperature (F) averaged by month for 1980 through 1989; the aver-age of the monthly variation was used as the ecologic covariate
1.15*	Water hardness	Concentration of $CaCO_3$ (ppm) in drinking water
1.03	Relative humidity	Minimum daily relative humidity (%) averaged by month for 1984 through 1989; the mean of all monthly averages was used as the ecologic covariate
0.96	Relative humidity variation	Variation in minimum daily relative humidity (%) averaged by month for 1984 through 1989; the average of the monthly variation was used as the ecologic covariate
0.94*	Education	Percentage of the number of persons 25 years of age or older who indicated they had completed 4 years of high school or some years of college divided by the total number of persons 25 years and older
0.86*	Temperature	Maximum daily temperature (F) averaged by month for 1980 through 1989; the average of all monthly averages was used as the ecologic covariate
0.85*	Income disparity	Gini coefficient calculated from income group data for 1979 (0 = maximum equality, 1 = maximum inequality)
* = statistically significant at 0.05. Sources: HEI Reanalysis II, Tables 34 and 37		

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Pseudo-quantitative (Safety Assessment): RfD Example

- Terminology
  - NOEL/LOEL: No/Lowest Observed Effect Level
  - NOAEL/LOAEL: No/Lowest Observed Adverse Effect Level
  - Point of Departure: Choice of NOAEL or NOAEL
  - Uncertainty Factors (1, 3, or 10 each)
    - Less-than-chronic to chronic
    - Animal to human
    - LOAEL to NOAEL
    - Inter-human variability
    - Completeness of the database
- Definition of ‘adverse’ effect may be policy-driven

Pseudo-quantitative (Safety Assessment): RfD Example

- Definition
  - An estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It can be derived from a NOAEL, LOAEL, or benchmark dose, with uncertainty factors generally applied to reflect limitations of the data used. Generally used in EPA's noncancer health assessments.

Source: EPA IRIS Glossary at http://www.epa.gov/iris/gloss8.htm#r

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Pseudo-quantitative (Safety Assessment): RfD Example

- NOAEL/LOAEL Approach
  - Critical effect
    - First adverse effect or [immediate] precursor
    - What's 'adverse'?
  - Point of departure
    - NOAEL/LOAEL from 'best' study
    - What is the 'best' study? Who chooses?
  - 'Uncertainty' factors (5 possible)
  - RfD = POD / $\prod_i \{UF_i\}$

Pseudo-quantitative (Safety Assessment): RfD Example

- Benchmark Dose (BMD) Approach
  - Statistical tool for curve-fitting data
    - Benchmark response: P_{effect} = x%
    - Is x% a biologically meaningful of 'adverse' effect?
  - Biased or unbiased?
    - MLE is unbiased <u>if</u> correct functional form is used
      - Typical BMD functions assume no threshold
    - BMDL is biased to overstate likelihood of harm
      - 95th percentile lower confidence interval on MLE
  - Cancer and noncancer risks "harmonized' at LCD

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  - What is the 'best' study? Who chooses?
- 'Uncertainty' factors (5 possible)
  - 1, 3 or 10x
  - Scientific uncertainty or public health precaution?
  - RfD = POD / $\prod_i \{UF_i\}$

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Exposure Assessment

- Default values commonly used in lieu of data
  - Typically 90th to 95th percentiles
  - Sometimes exceed 100th percentile
- When empirical data are available, agencies typically select values from the upper tail
  - FQPA example, with obvious incentive effects
- Converting dose to exposure
  - Averages in numerator, upper-bounds in denominator yield downwardly biased factors

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Applying Risk Assessment to BCA

- Almost all versions are incompatible with BCA
  - Outputs are biased, overstate both baseline risk and health benefits of exposure reduction
  - Benefits are highly exaggerated when risk estimates are multiplied by upper bound WTP
- Easiest to probe exposure assessment and exposure scenario design
- Do not assume toxicology and epidemiology were performed correctly

Questions?

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