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# Managing Contaminants of Emerging Concern: Human Health Effects

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# Chemicals in Commerce

Synthetic chemicals are created for their beneficial properties. Sometimes they have unanticipated consequences and become subjects of emerging concern.

## **Benefits**

Plastics

Synthetic fibers

Pharmaceuticals

Antibiotics

Employment

Economic Growth



## **Unanticipated Consequences**

Love canal

Thalidomide

Smog

Antibiotic resistance

Species loss

**Balance is important**

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# Contaminants of Emerging Concern

- **Contaminants identified in unintended media**

- Bis phenol A in baby formula
- Methyl mercury in fish
- Pharmaceuticals in drinking water
- Brominated flame retardants in the arctic

- **Problem:** often initially difficult to link occurrence to an environmental effect

- Requires research

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# Contaminants of Emerging Concern

- **Pollution accompanied by an environmental change**
  - Intersex changes in fish
  - Cancer clusters in industrial areas
  - Fish kills
  - Endangered species
  - Climate change
- **Problem:** Difficult to link the effect to the chemical or group of chemicals present
  - Requires research

# Impact

- Public anxiety
- Uncertainty and debate
- Calls for government action
- Expert work groups and meetings
- Research
  - Health effects
  - Ecological impact
  - Monitoring
  - Remediation options
- Risk management challenges
- Risk communication needs



A collage of news articles. At the top, there's a handwritten note: "Seattle Times 4/11/07". Below it, a newspaper clipping with the headline "Hormonal chemicals may be imperiling fish" and sub-headline "PERVERSIVE IN AREA'S WATER | Even at the low level detected, scientists worry about the possible...". To the right, another clipping with the headline "&lt; Hormones FROM B1 FISH MAY BE AT RISK" and sub-headline "hemicals in water may affect growth and reproduction". Below these, a large headline reads "AP: Drugs found in drinking water". Underneath this headline, it says "Updated 31d ago | Comments 147 | Recommend 76" and "E-mail |". At the bottom left of the collage is a small image of a person's face, and at the bottom right is a text block: "By Jeff Donn, Martha Mendoza and Justin Pritchard, Associated Press" followed by a paragraph: "A vast array of pharmaceuticals — including antibiotics, anti-convulsants, mood stabilizers and sex hormones — have been found in the drinking water supplies of at least 41 million Americans, an Associated Press investigation shows."

# Human Health Concerns

## ■ Health

- Endocrine disruption
- Birth defects
  - Physical deformities
  - Neurological
    - Autism
    - Attention deficit disorder
- Sterility/miscarriages



## ■ Disease

- Cancer
- Heart disease
- Diabetes



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# Human Health Benchmark Approaches

- Approach depends on the available data
- **Quantitative Risk Assessment**
  - Requires comprehensive data on toxicokinetics, hazard identification, and dose-response
    - Reference dose
    - Reference concentration
    - Cancer slope factor
- “Gold” standard
- Complete data sets often lacking for contaminants of emerging concern

# Human Health Benchmark Approaches (2)

- Other Alternatives
- **Class Based**
  - Pool data from similar chemicals based on structures and common effects
  - Use the quantitative risk value for the most toxic and data-rich member of the group as a benchmark
  - NSF/ANSI Drinking Water Standards 60/61
    - Direct and indirect drinking water additives
- **Structure Based**
  - QSAR models
  - Structure-based decision rules estimates
    - Cramer classification
  - Projections derived from large data sets of chemicals with known toxicities
  - New product development

# Human Health Benchmark Approaches (3)

## ■ **Distribution Based**

- default uncertainty factors

## ■ EPA's CCL3 Point of Departure (POD) for Health Reference Levels (HRLs)

- UF based on the mode for the distribution of the rounded log of the toxicity value compared to that from the RfDs for the same chemicals

- $\text{NOAEL} \div 1000$

- $\text{LOAEL} \div 3000$

- $\text{LD50} \div 100,000$

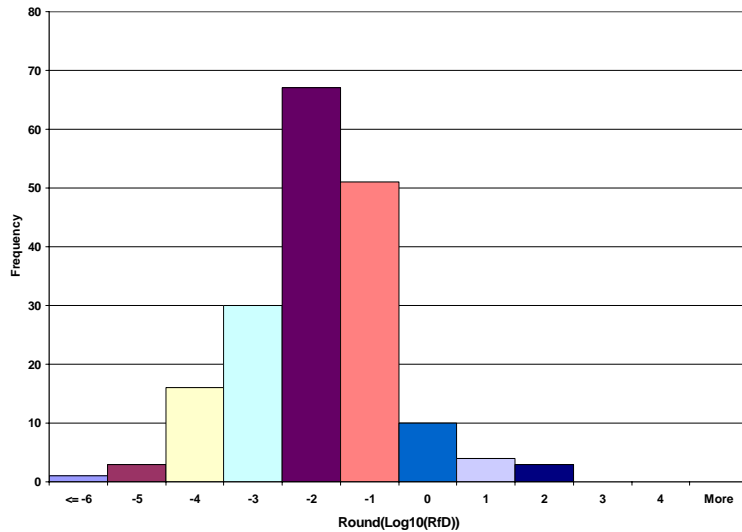
## ■ Virtually Safe Dose (Gaylor and Gold 1998)

- Maximum Tolerated Dose  $\div 740,000$

- Cancer endpoint

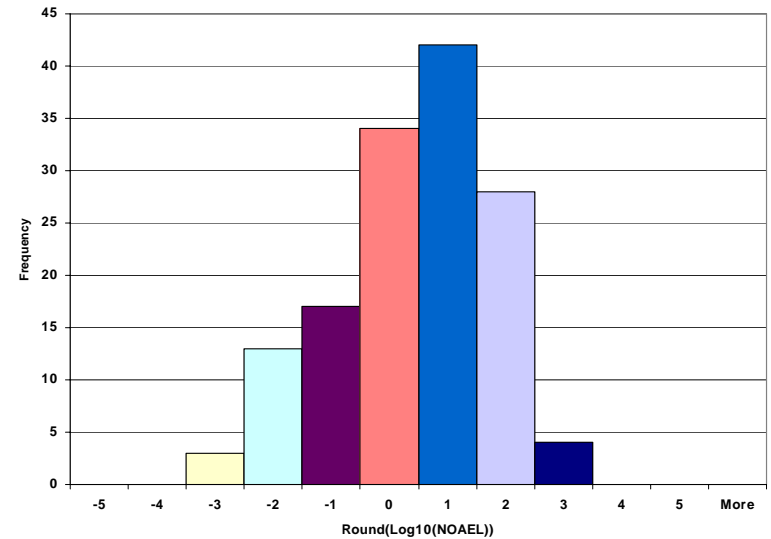
# Example

## RfD Distribution



Mode =  $10^{-2}$

## NOAEL Distribution



Mode = 10

**Difference =  $10^3 = 1000$**   
**Average RfD UF 1000**

# Human Health Benchmark Approaches (3)

- **Threshold of Evaluation**
- Level at which toxicity testing not required
  - Substances having structural alerts, known, or potent toxins are not eligible
  - Supporting evidence used by FDA based on the high toxicity bounds for the data in the distribution
    - FDA (indirect additives)
      - 1.5 µg/day
    - NSF/ANSI Standards 60/61 (indirect additives)
      - 0.3 µg/L normalized to at-the-tap

# Human Health Benchmark Approaches (4)

## ■ Qualitative

- Modified application of the precautionary principle
- Tier 1
  - Weight of evidence from required genotoxicity data indicates the chemical is not a hazard
  - $\leq 10 \mu\text{g/L}$
  - Minimum data requirement: one mutagenicity study and one clastogenicity study
- Teir 2
  - Teir 1 data and a repeated-dose study of less < 90-day duration indicates the chemical is not a hazard
  - $\leq 50 \mu\text{g/L}$
- NSF/ANSI Standards 60/61

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# Advantages of Multiple Approaches

- Provide a variety of options that can accommodate differences in available data
- The approach can be tailored to the chemical, the type of data, and the concentration in water
- Every approach includes adjustments for uncertainty
- Transparent explanations available for the data that support most options
- Can vary the core approach to fit the exposure scenario

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# Other Considerations

- Mixtures
  - Interactions between chemicals can influence their potency where there is a common target tissue or mode of action
  - Adds complexity to the risk assessment
    - Different chemical mixtures in different places
    - Different chemical mixtures at different times
- Other sources of exposure to the same chemicals
  - Total exposure important not exposure to one media such as water
- Sensitive population groups