Short-Term Guidelines

GUIDELINES WITH EXPOSURE AVERAGING PERIODS OF 24 HOURS OR LESS

Concern

- An ABC based on a chronic REL, RfC, or MRL is considered protective of humans (including susceptibles) for long-term, 24-hr/d exposures
  - As a "not to exceed" annual average {form}
- But what if an ABC is repeatedly exceeded for short periods but the annual average remains below that ABC?
  - Do these short, repetitive, higher exposures pose an adverse health risk?
  - If so, don't we need short-term guidelines (STG) to protect us against these types of exposures?

Acute, Intermediate, and Long-Term Exposure

Although definitions may vary somewhat between sources, in general:

Acute exposure = up to 14 days of exposure

Intermediate exposure = 14 days to 1 year

Long-term exposure = greater than 1 year; also typically used when discussing a lifetime of exposure

Endpoints

- Cancer
  - Risk of 10^{-6}, given a unit risk estimate (URE)
- Non-cancer
  - Acute (Physical)
    - Irritation, runny eyes, skin rash, etc.
  - Chronic (Toxicity) – non-occupational
    - Developmental, reproductive, etc.
    - Preferred - David Farrer presentation (2011)
    - EPA's School Air Toxics Monitoring Initiative used acute endpoints to assess short-term exposures

Cancer

- STG for cancer (STGc) derived from annualization of lifetime exposure value
- Adjust existing cancer-based ABC by 70-year exposure duration
  - ABC = Risk [10^{-6}]/Unit Risk Estimate (URE)
  - STGc = ABC × 70
- Approach consistent with that used by EPA's School Air Toxics Monitoring Initiative

Non-Cancer

- Basis for STGnc = chronic toxicity testing
  - Dosing typically 6 h/d, 5 d/w for 90+ days
  - Result is typically a NOAEL or LOAEL
- Adjustment for animal-human respiration
  - Human equivalent concentration (HEC)
- Application of uncertainty factors
  - LOAEL>NOAEL, interspecies, intraspecies, etc.
- Adjustment for exposure
  - Intermittent dosing regime to 24-hour exposure
  - REL, RfC, and cMRL are all 24-hour values

Challenges

- Different exposure durations may involve somewhat different Mechanisms of Action (MOAs) by a chemical
  - Timing of peak tissue concentration and total tissue dose matters greatly for developmental toxins
- Issues arise when a chemical is one
  - that accumulates in the body (long internal half-life)
  - that causes cumulative tissue damage or toxicity
  - that activates or deactivates enzyme induction
  - where the response is concentration-dependent rather than time-dependent
  - where large pharmacokinetic uncertainties exist

Options (1)

- Accept that existing ABCs are protective of higher but shorter exposures
  - OEHHA suggests a chronic REL may be sufficient as a guideline for repeated, shorter exposures
  - An STG for an averaging period < 24-hr will always be larger than an existing 24-hr ABC based on long-term exposure
- Use someone else's STG values
  - Most other states with STGs use acute endpoints
  - TCEQ has different STGs based on chronic endpoints for permitting and monitoring
  - OEHHA has 8-hr chronic RELs

Options (2)

- Apply Haber's Rule (TCEQ, OEHHA)
  - $ABC^n \times T1 = STG^n \times T2$; n = 1 default; T1=time (duration) of exposure related to ABC; T2=time of exposure related to STG; solve for STG
  - Not if MOA has rate-limiting critical steps or toxicity testing did not reach steady state
- Adjust for volume inhaled (OEHHA)
  - Chronic (24-hr) REL × fraction inhaled during exposure period (20/10 for 8-hr exposure)
- Change the "form"
  - Apply existing ABC, or multiple of ABC, to an exposure averaging period of less than one year

Form

- Defines terms of compliance with a given guideline or criterion value

- Example: Sulfur dioxide NAAQS
  - Primary [75 FR 35520, Jun 22, 2010]: 75 ppb
    - Averaging time: 1 hour
    - Form: 99th percentile of 1-hour daily maximum concentrations, averaged over 3 years
  - Secondary [38 FR 25678, Sept 14, 1973]: 3,000 ppb
    - Averaging time: 3 hours
    - Form: Not to be exceeded more than once per year