Risk Assessment -- Overview

National Tribal Forum on Environmental Science

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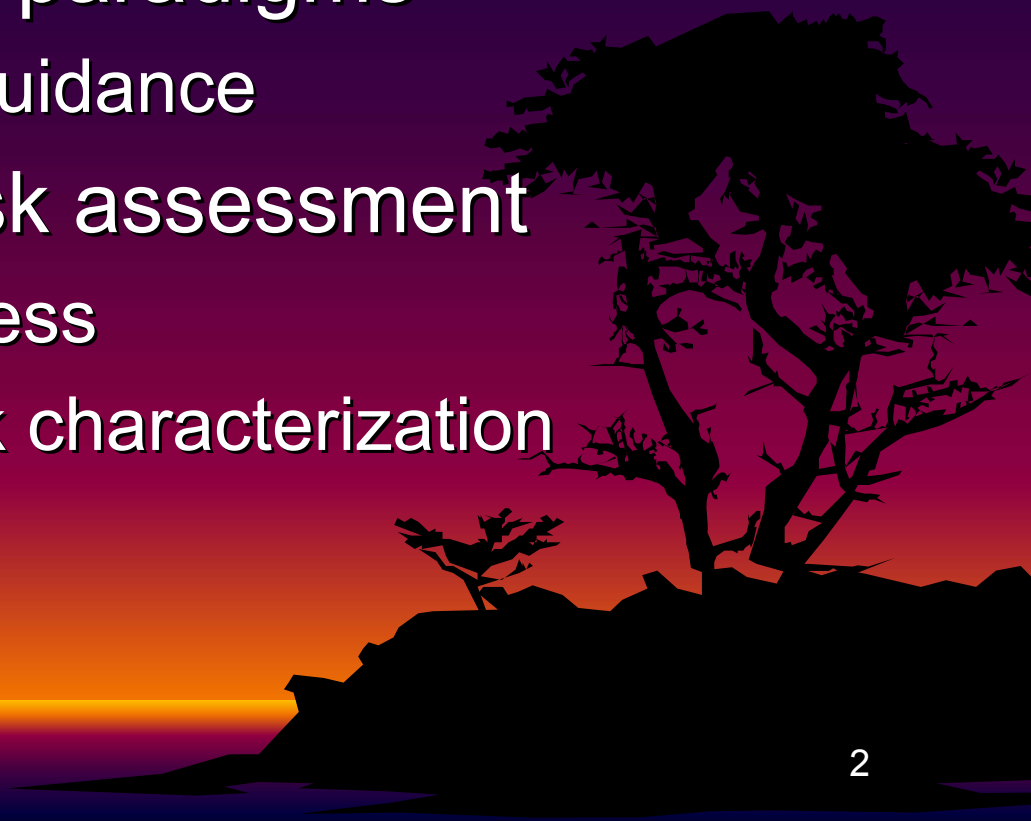
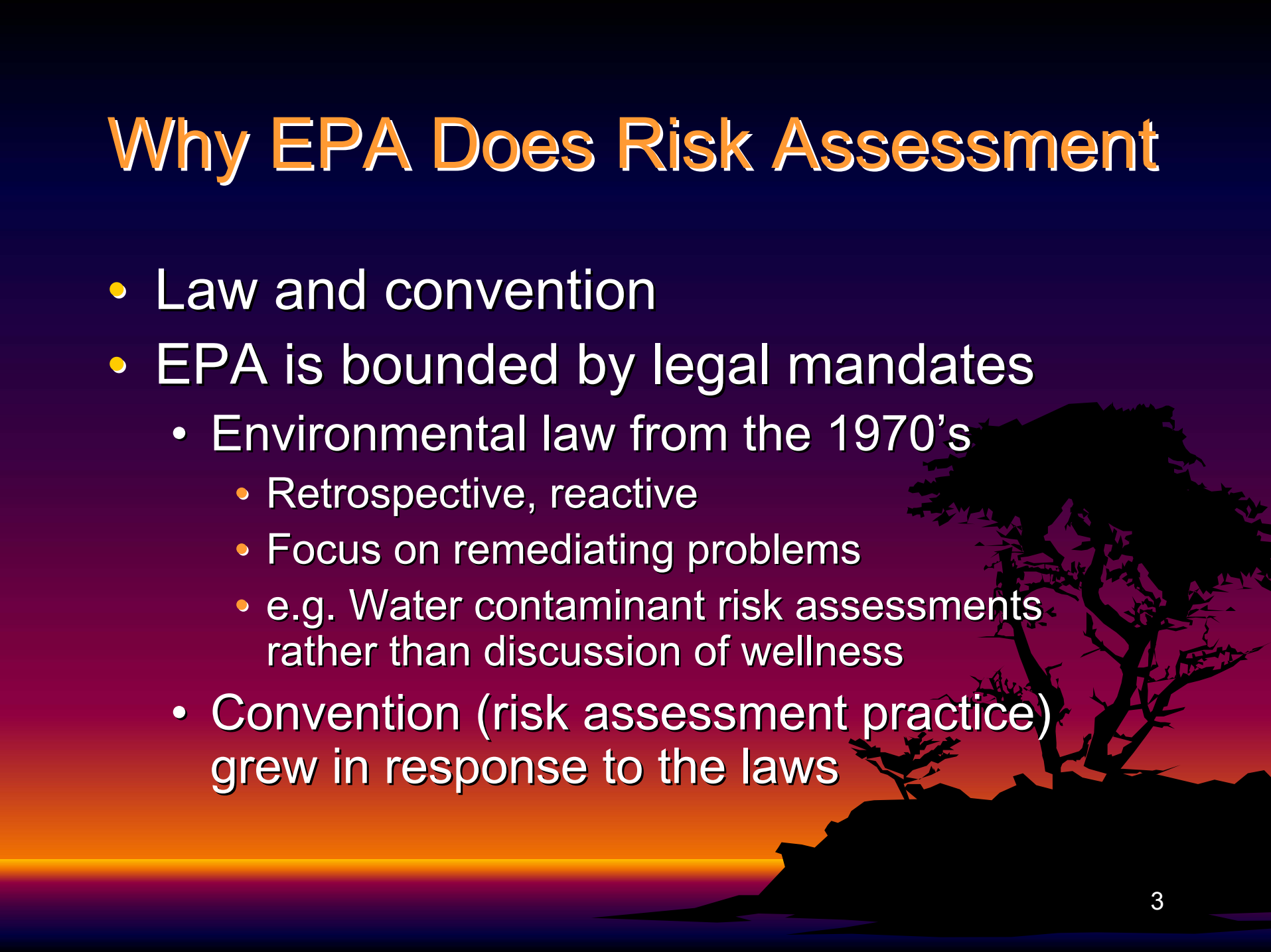
Outline

- Why EPA does risk assessment
- Risk assessment paradigms
  - Guidelines and guidance
- Human Health risk assessment
  - Parts of the process
  - Example of a risk characterization



Why EPA Does Risk Assessment

- Law and convention
- EPA is bounded by legal mandates
  - Environmental law from the 1970's
    - Retrospective, reactive
    - Focus on remediating problems
    - e.g. Water contaminant risk assessments rather than discussion of wellness
  - Convention (risk assessment practice) grew in response to the laws



Example – SDWA '96

Does the contaminant adversely affect public health?

Is the contaminant known or likely to occur in PWSs with a frequency and at levels posing a threat to public health?

Will regulation of the contaminant present a meaningful opportunity for health risk reduction?

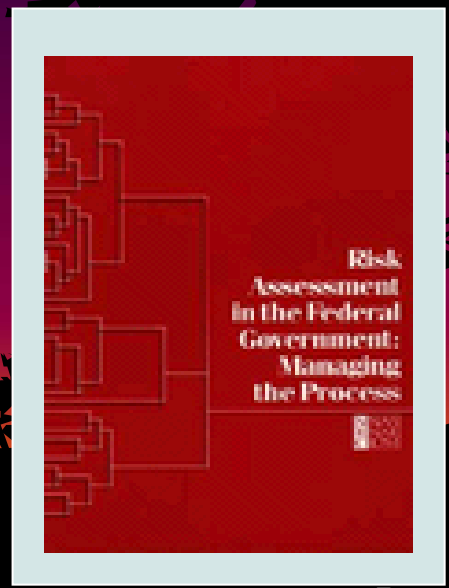
Regulate with NPDWR

These are questions, demonstrations of risk

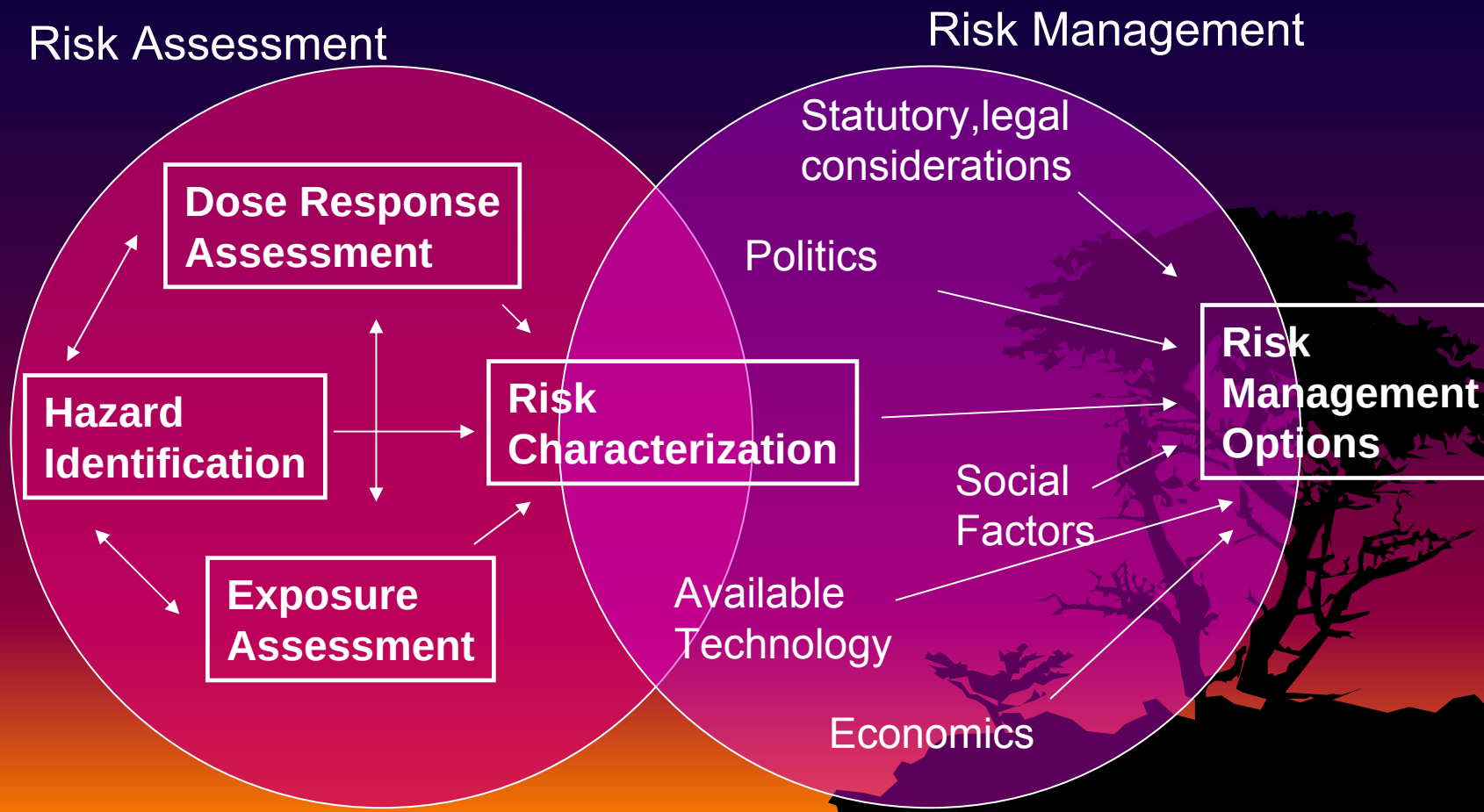
NRC 1983

- To impart consistency and transparency to U.S. Government risk assessments
- Major points
  - Human Health RA paradigm
  - RA ≠ RM
  - Feds should write and use their own Guidelines

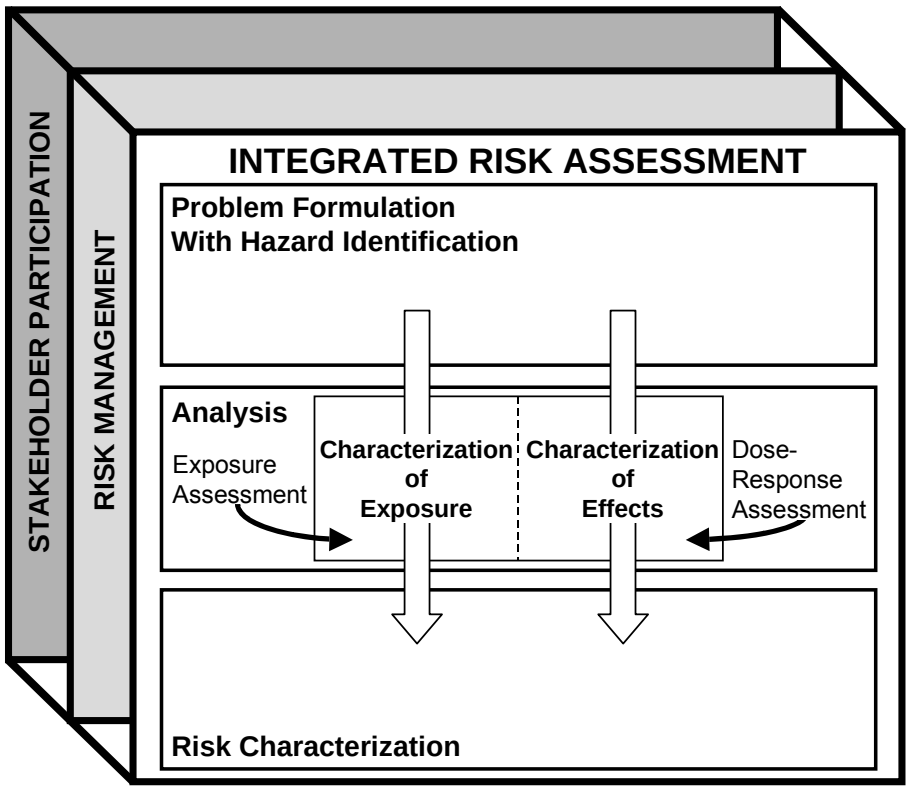
Convention = Guidelines + common practice



’83 Risk Assessment Paradigm ‘06



Ecological Risk Assessment Uses a Different Paradigm



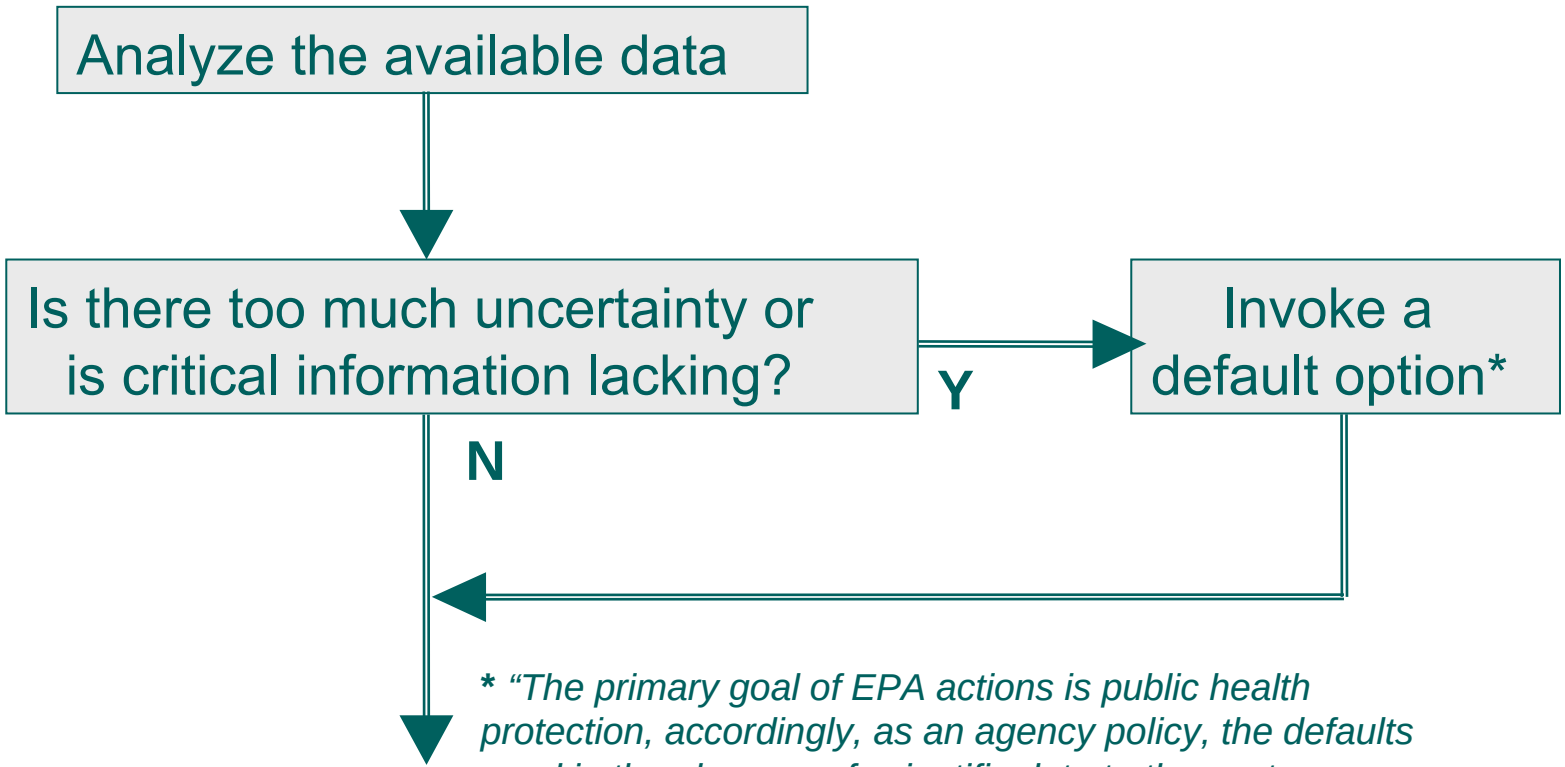
U.S. EPA RA Guidelines

- Guidelines for Carcinogen Risk Assessment (2005)
- Guidelines for Chemical Mixtures Risk Assessment (1986)
- Guidelines for Ecological Risk Assessment (1998)
- Guidelines for Neurotoxicity Risk Assessment (1998)
- Guidelines for Reproductive Toxicity Risk Assessment (1996)
- Guidelines for Exposure Assessment (1992)
- Guidelines for Developmental Toxicity Risk Assessment (1991)
- Guidelines for Mutagenicity Risk Assessment (1986)

Paradigm Shift in 2005

Use of Default Options

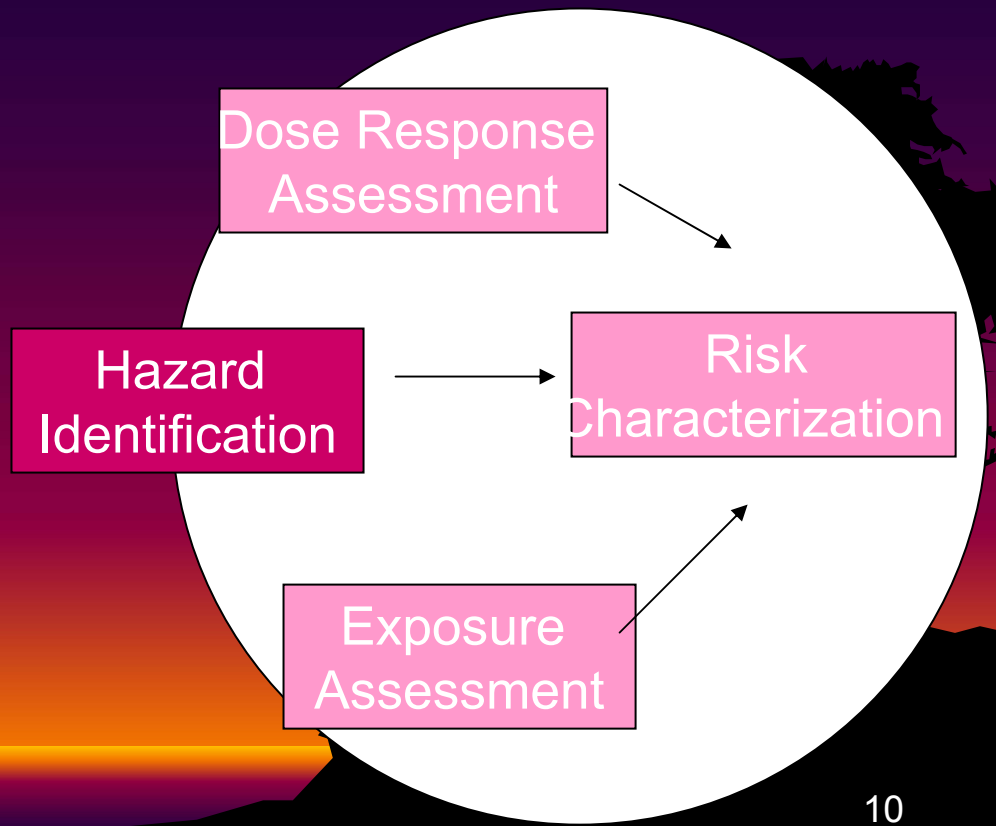
Guidelines ***emphasize analysis of data before use of default options.***



***** *"The primary goal of EPA actions is public health protection, accordingly, as an agency policy, the defaults used in the absence of scientific data to the contrary should be health protective (SAB 1999)."*

Hazard Identification

- Is there potential for harm, adverse effects?
- What does it do?
- (How does it do it?)



Hazard Identification

- Weight of Evidence Judgment
  - Common to all the HI Guidelines
  - Guidelines describe data quality objectives
  - Provide guidance for weight to be given to types of data (e.g. human > animal, *in vivo* > *in vitro*)
  - Both negative and positive data considered

2005 Weight-of-Evidence Narrative

Informative discussion of the scientific evidence:

- Conclusions, including a weight-of-evidence descriptor:
  - *Carcinogenic to humans*
  - *Likely to be carcinogenic to humans*
  - *Suggestive evidence of carcinogenic potential*
  - *Inadequate information to assess carcinogenic potential*
  - *Not likely to be carcinogenic to humans*
- Conditions of carcinogenicity:
  - *Route, magnitude, and duration of exposure*
  - *Susceptible populations and lifestages*
- Summary of key evidence supporting conclusions
- Summary of key default options invoked
- Summary of potential Modes of Action (MOA)

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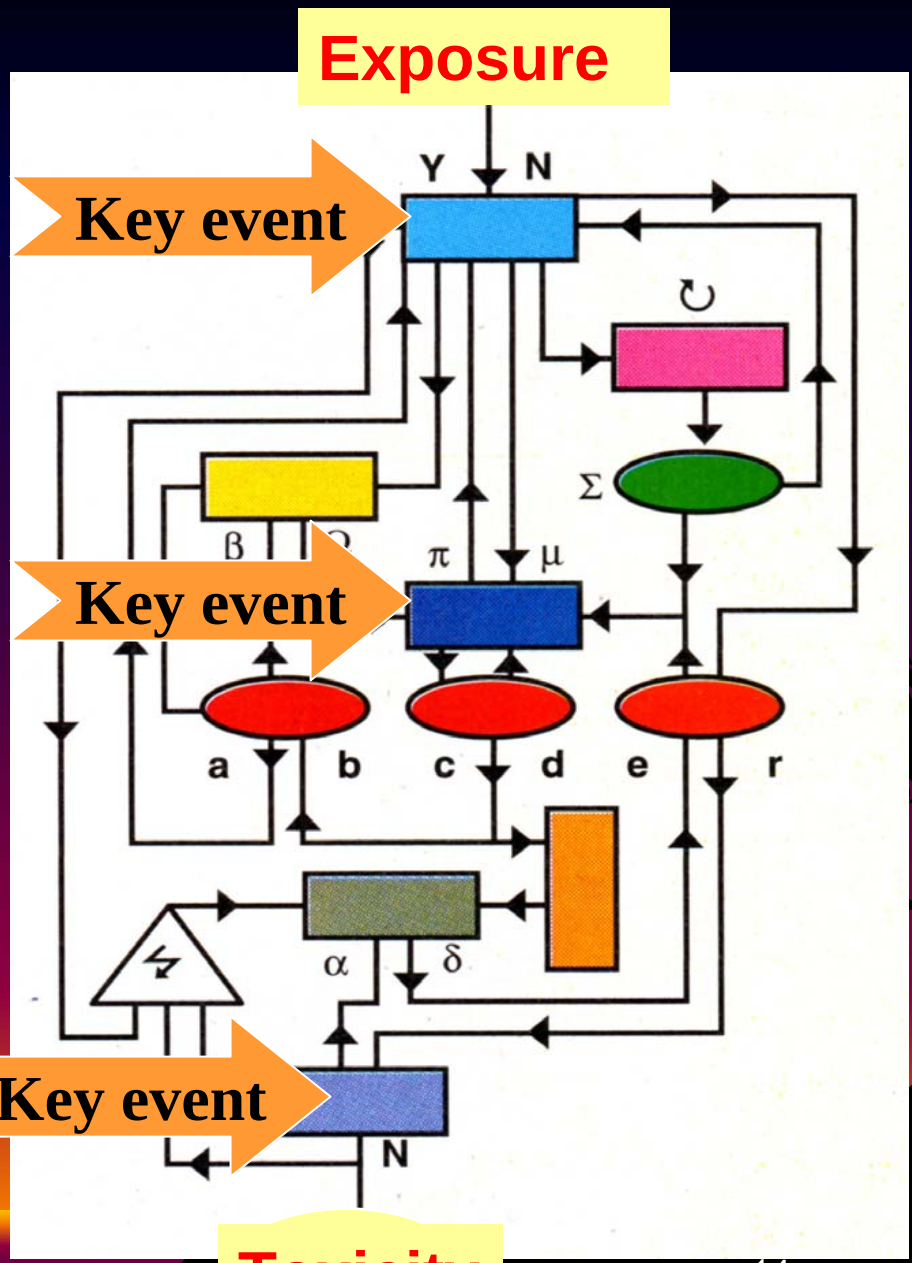
MOA is key in Hazard Identification

- Describe circumstances under which agent is carcinogenic (High dose? Route?)
- Relevance of data for humans
  - Alpha-2-u-globulin & kidney cancer -- male rats only
  - Atrazine effect on hypothalamic-pituitary-ovarian function -- female Sprague Dawley rat mammary tumors (but likely reproductive toxicant)

"Mechanism of action"
(more detailed understanding at biochemical & molecular level)
vs
"Mode of action"
(identification of **key & obligatory** steps)



Mode Of Action

Oxidative CYP2E1 Metabolism

Chloroform

Phosgene

Sustained Toxicity

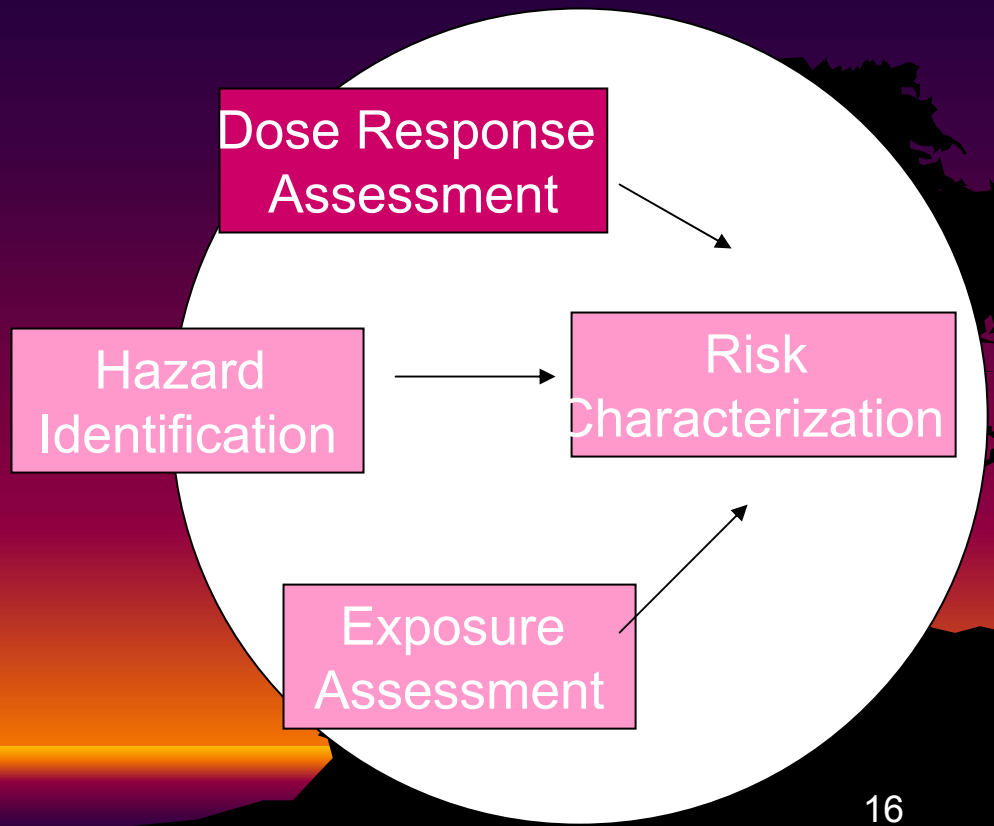
Regenerative Cell Proliferation

Tumor Development

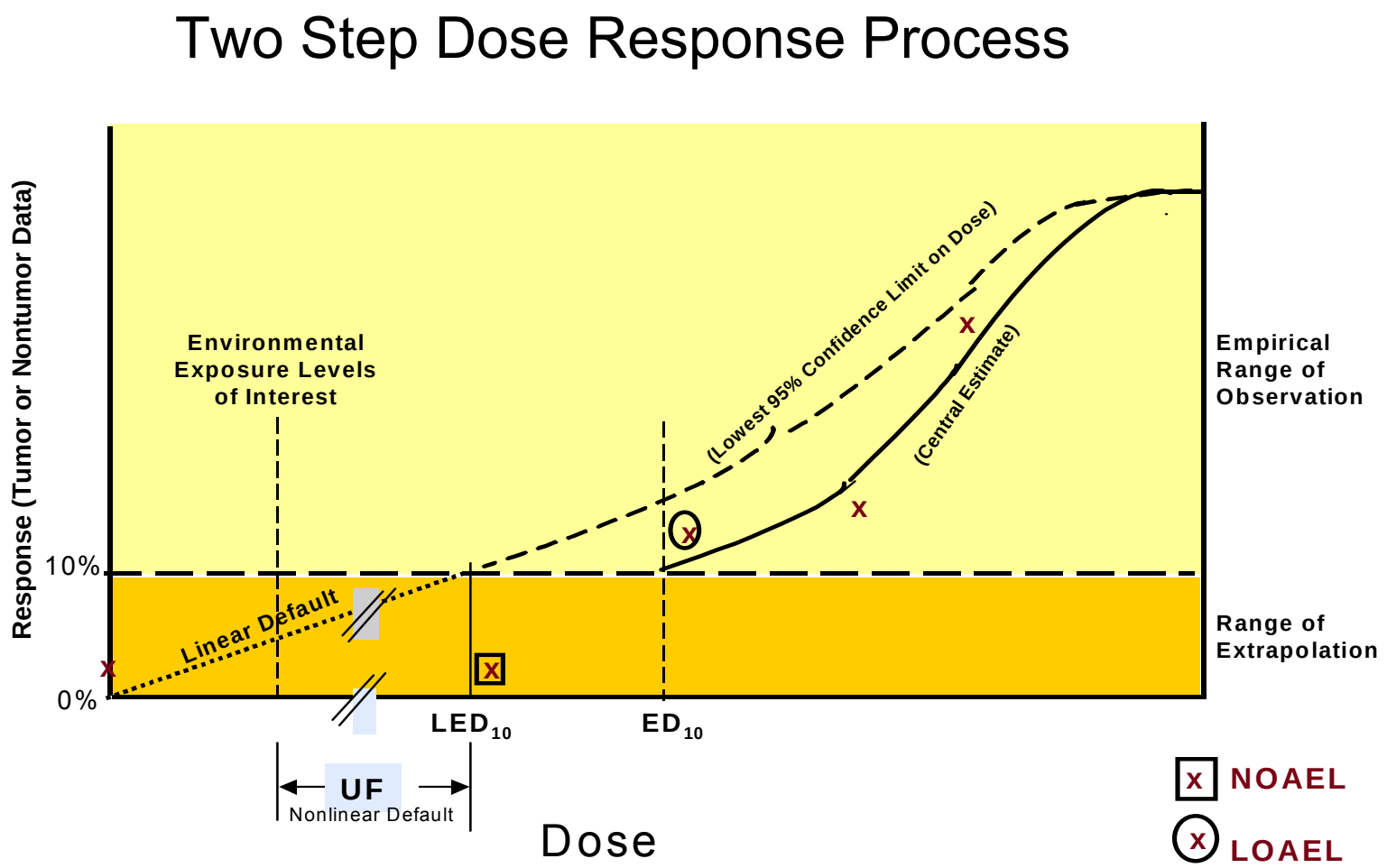
Key Events

Dose Response

- How much of it causes what degree (or type) of effect?
- How much is “safe”?
- What risk is associated with x amount?



MOA and Dose Response



Quantitative Risk Assessments

- RfD/ RfC = “safety assessment”
  - Amount with order of magnitude uncertainty that can be ingested (including sensitive human subpopulations) on a daily basis for a lifetime without expectation of adverse effect
- Slope factor = estimate of risk

Dose Response -- 2

- Choice of low dose extrapolation depends on MOA
- Nonlinear extrapolation
  - When there is no evidence of linearity, and
  - Sufficient info to support MOA nonlinear at low doses
- Linear extrapolation
  - Mutagenic MOA or another MOA expected to be linear at low doses, or
  - Linear extrapolation is default when data do not establish the MOA

MOA and Kids

- *Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens*
  - Effects observed in childhood
  - Early life exposures contributing later life effects

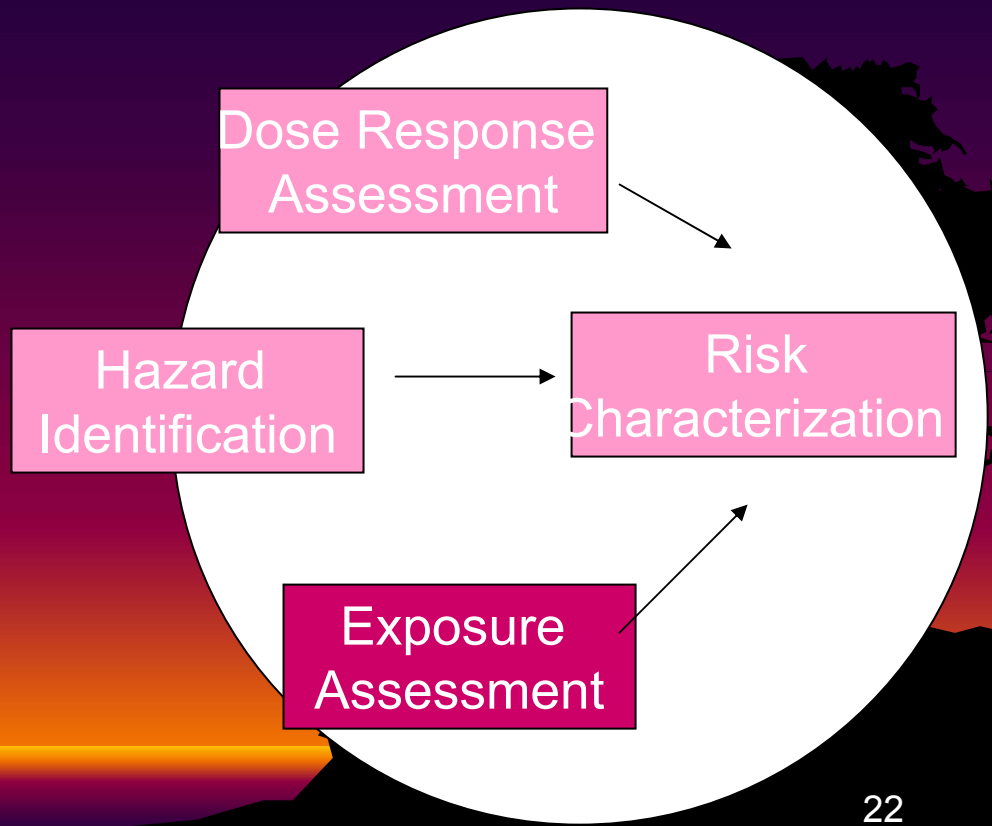
http://cfpub.epa.gov/ncea/raf/recordisplay.cfm?deid=116283

Kids Guidance

- Use age-specific values for exposure and potency
- When data permit, develop separate potency estimates for childhood exposure
- In risk characterization, mutagenic MOA risk is increased by age-dependent adjustment factor (used with exposure info for age group)
  - <2 yrs old, 10 fold
  - 2 to < 16yrs, 3 fold
- No MOA, use linear extrapolation without ADAF; non-linear MOA, do not use ADAF

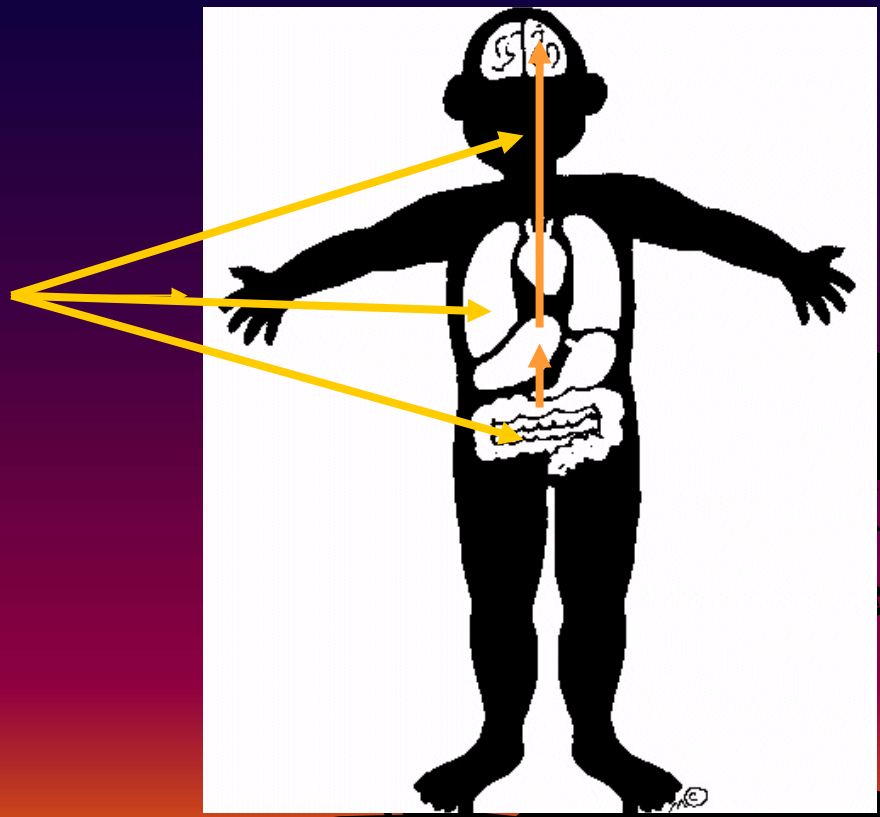
Exposure Assessment

- How much of an agent reaches an individual? (How much gets to the target tissue?)
- How does it reach the individual?
- How long does exposure last?
- How frequently does the exposure occur?
- How many people are exposed?



Exposure-Dose

- ***Exposure*** - how much of an agent is available to a human
- ***Dose*** - how much of that agent is absorbed through the skin, lungs or GI tract that reaches an organ



Sources → Pathways → Routes

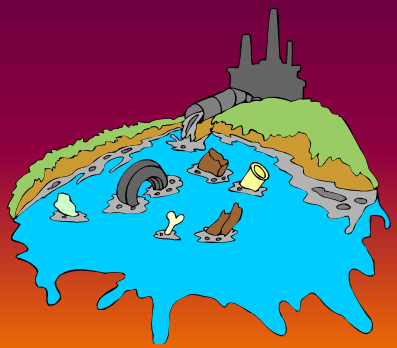
Food

Drinking Water

Breast feeding

Hand-to-mouth

Ingestion



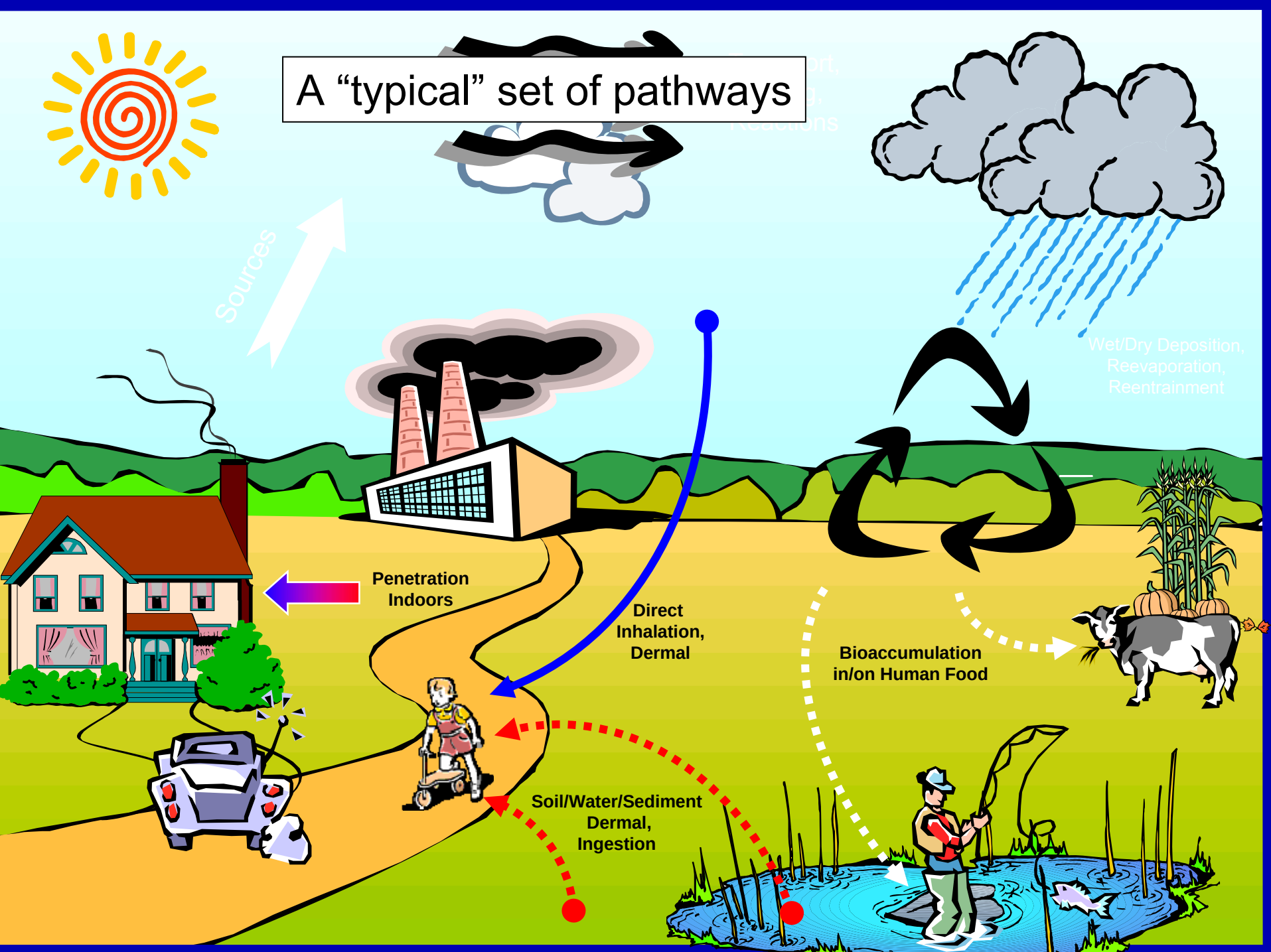
Air

Contact with hazardous substances

Inhalation

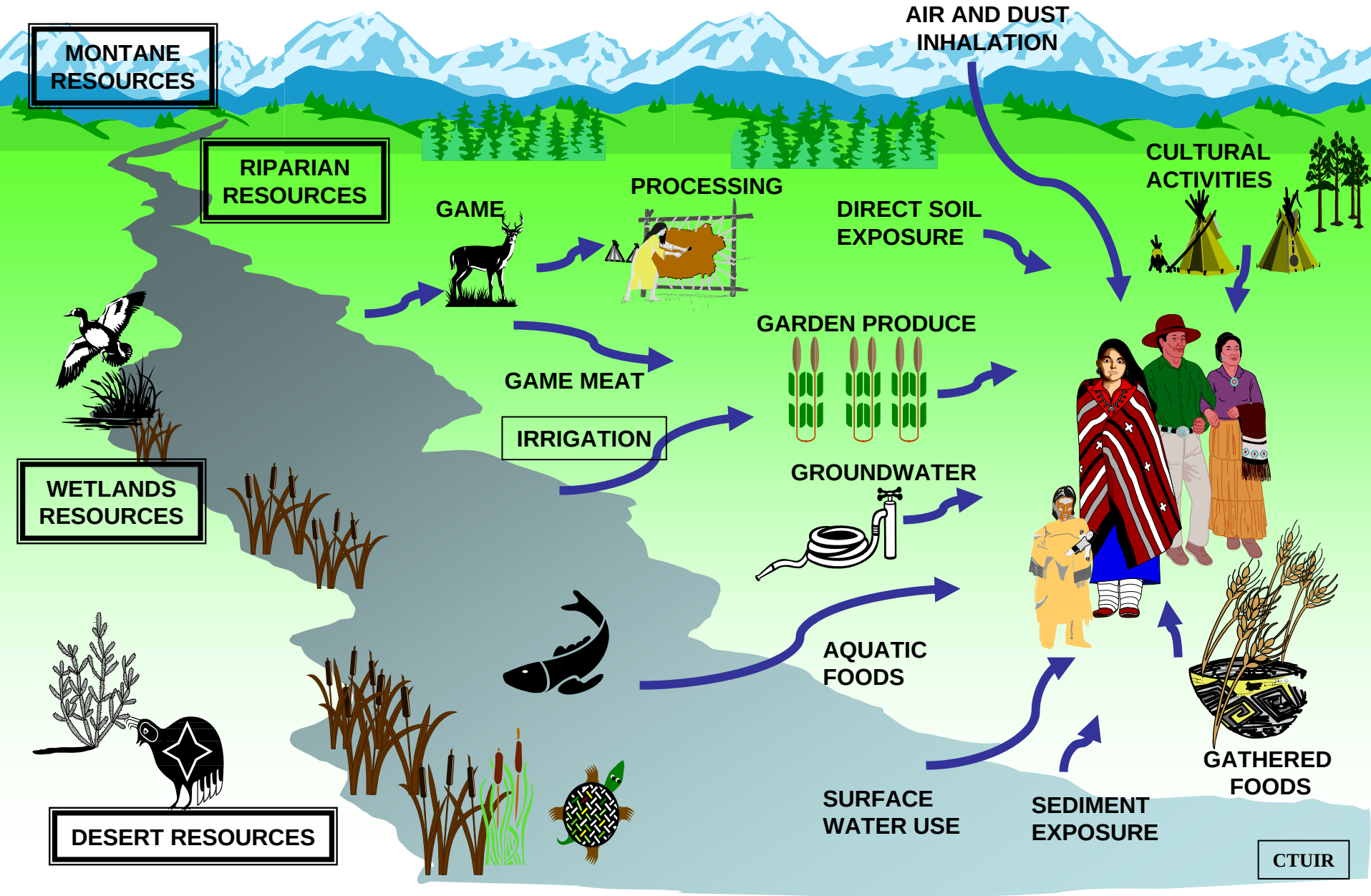
Dermal


All pathways are not common to all people.


A “typical” set of pathways
Sources
Wet/Dry Deposition,
Reevaporation,
Reentrainment
Penetration
Indoors
Direct
Inhalation,
Dermal
Bioaccumulation
in/on Human Food
Soil/Water/Sediment
Dermal,
Ingestion

Your “typical” pathways may be different.

Tribal EXPOSURE SCENARIO = numerical description of a traditional lifestyle.



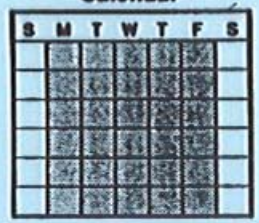
ASSESS EXPOSURE

Five Basic Variables Used to Estimate Intake

- Exposure Point Concentrations:

- Contact Rate:

- Exposure Frequency/Duration:



- Body Weight:

- Exposure Averaging Time:

II-14

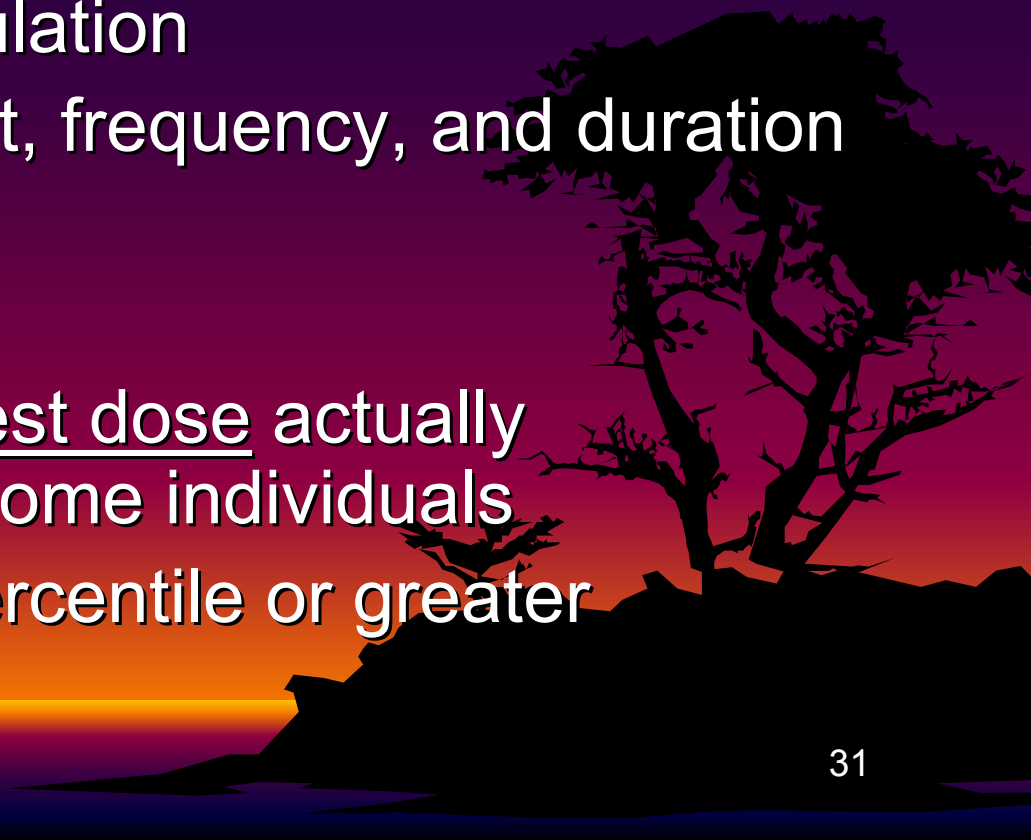
Exposure Equation

$$\text{Dose} = \frac{C \times CR \times EFD}{BW \times AT}$$

Dose = Daily intake of contaminant (Exposure)
C = Concentration in medium
CR = Contact rate with medium
EFD = Exposure frequency and duration
BW = Body weight
AT = Averaging time

Exposure Assessments

- Central Tendency
  - Estimate of average amount of exposure for exposed population
  - Based on amount, frequency, and duration of exposure.
- High End
  - Estimate of highest dose actually experienced by some individuals
  - Generally 90th percentile or greater

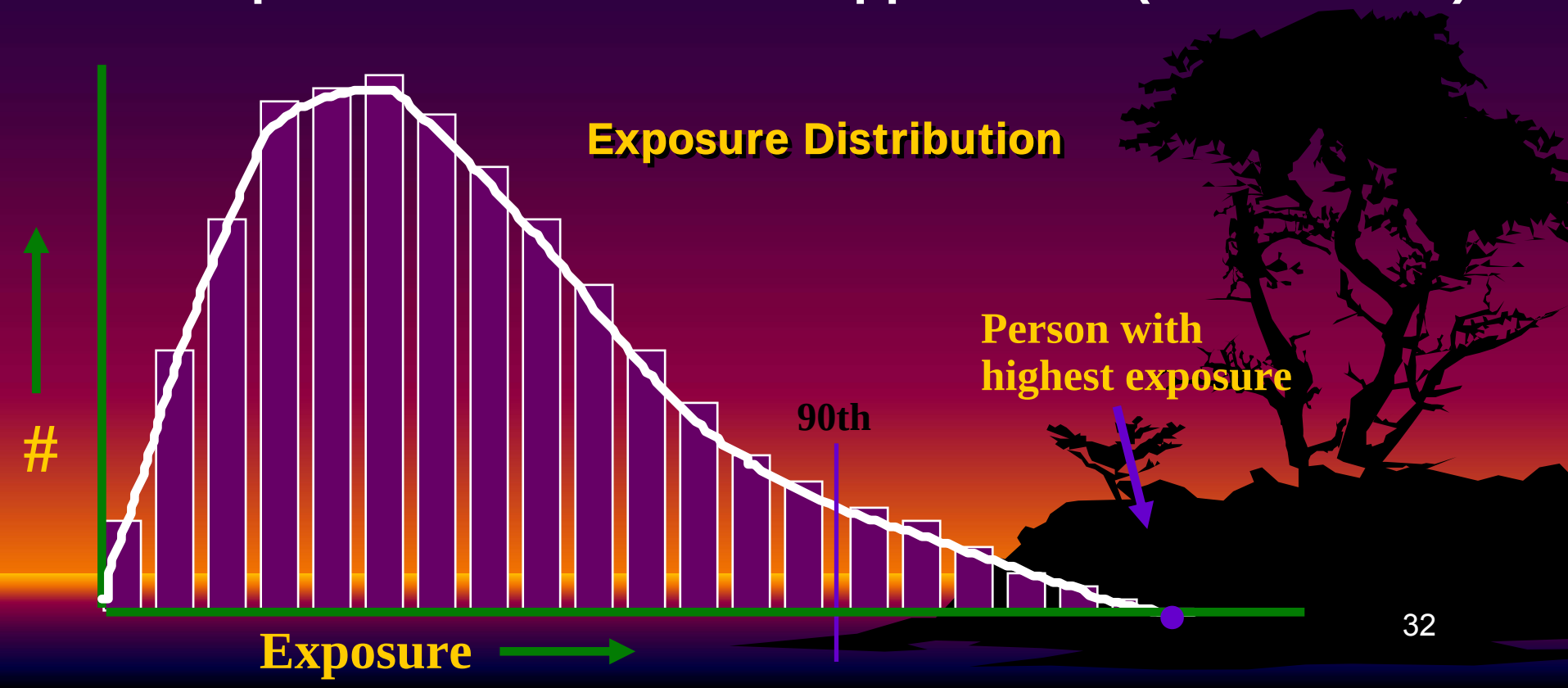


Use Data in Modeled Estimates

Risk Descriptors

- Central Estimates
- High End
- Reasonable Worst Case
- Theoretical Upper Bound Estimate (TUBE)

Development of Probabilistic Approaches (Monte Carlo)



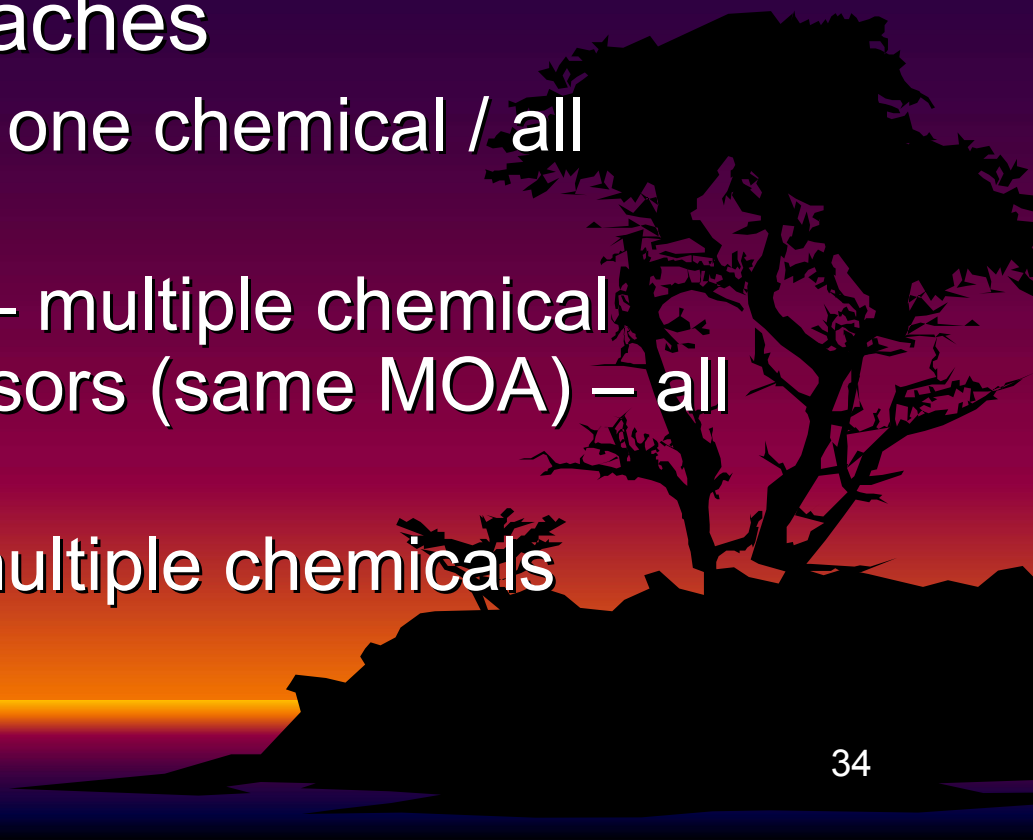
Use of Defaults when no Data

Superfund Defaults vs. Tribal Assumptions Used by Region

	Superfund Adult Defaults	Tribal Adult Assumptions
Years of Adult Exposure	24 years	64 years
Soil Ingestion	100 mg/day	300 mg/day
Sweat Lodge (inhaling volatiles)	No Superfund default	365 day/year, 2 hours per day
Hunting (meat consumption)	No Superfund default	1,185 grams/day (2.6 lbs per day)
Fish consumption	No Superfund default (17.5 grams per day (0.26 lbs/week) is low end)	97.5 grams per day (1.5 lb/week) 175 grams per day (2.7 lbs/week) 598 grams per day (9.2 lbs/week)

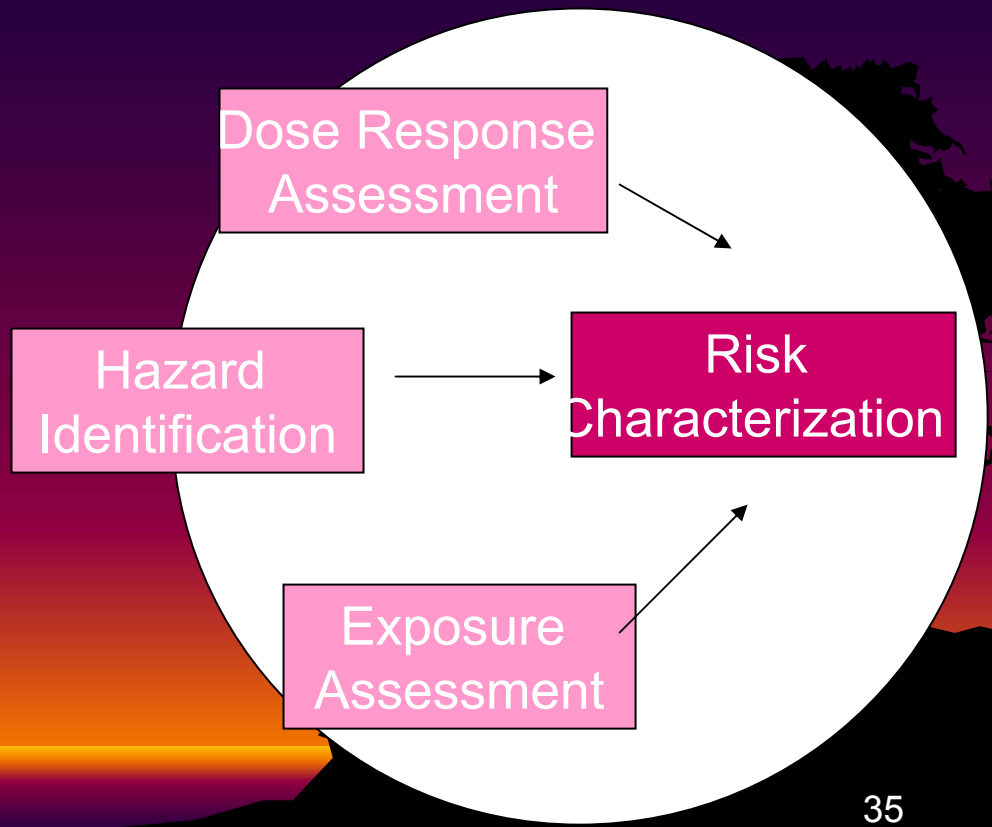
Exposure Assessment

- Most common
  - One chemical – one route
- Newer approaches
  - Aggregate – one chemical / all routes
  - Cumulative – multiple chemical agents/stressors (same MOA) – all routes
  - Mixtures – multiple chemicals



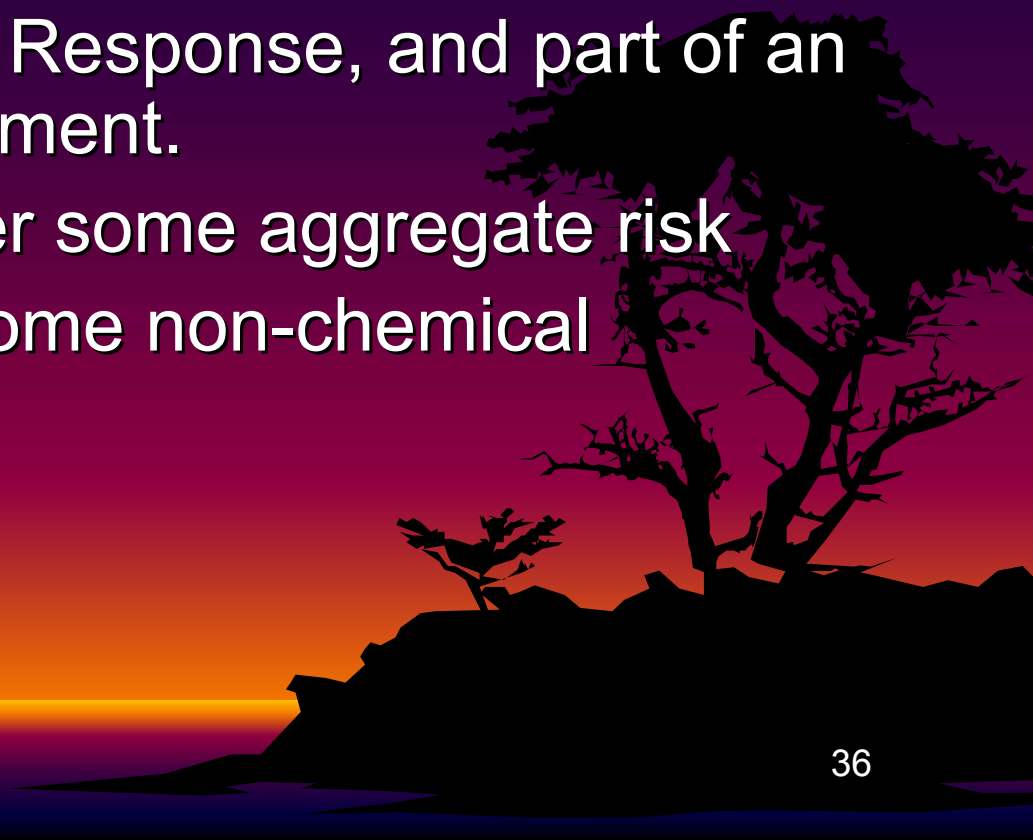
Risk Characterization

- Is there a risk from a specific scenario?
  - Spill
  - Point source
  - Drinking water source
- What is the degree of hazard?
- What are the uncertainties?
- What are the assumptions?



Not all EPA "risk assessments" Cover All 4 Components

- CWA criteria
  - Hazard ID, Dose Response, and part of an exposure assessment.
  - But does consider some aggregate risk
  - And deals with some non-chemical stressors

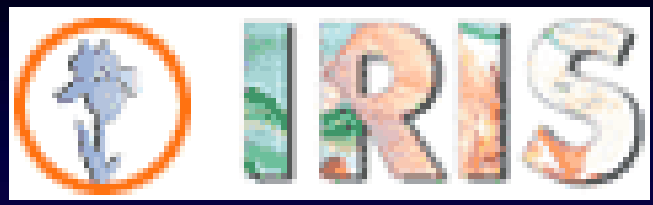


National Ambient Water Criterion Equation

$$AWQC = RfD \cdot RSC \cdot \left(\frac{BW}{DI + \sum_{i=2}^{4} (FI_i \cdot BAF_i)} \right)$$

RSC	= Relative Source Contribution
DI	= Drinking Water Intake
FI	= Fish Intake
BAF	= Bioaccumulation Factor

Hazard ID and Dose Response on



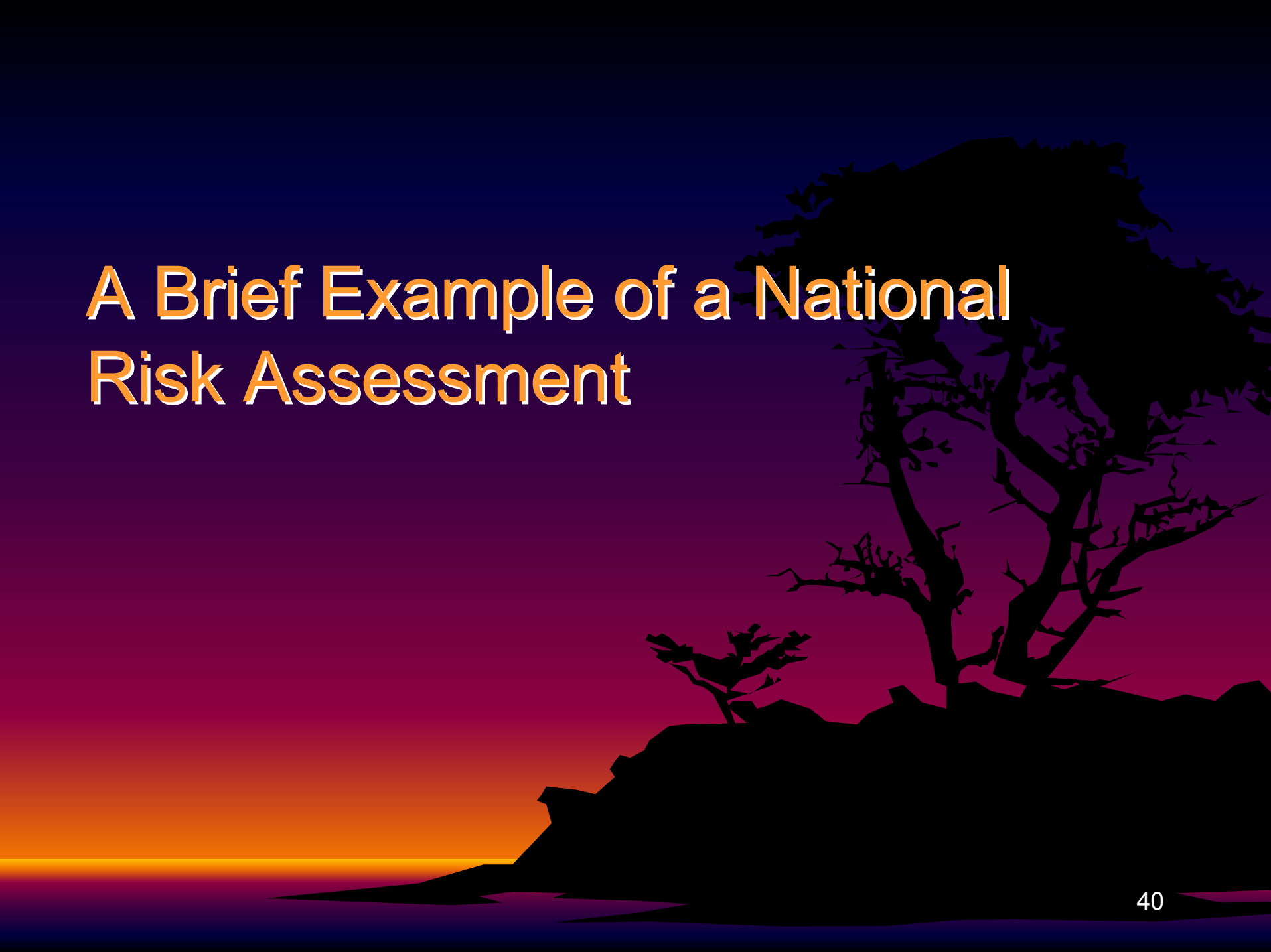
- Cancer classification
- Reference Dose / Concentration and description of toxicity
- Link to supporting documents
- These are consensus assessments of EPA
  - Peer reviewed

IRIS - 2

- Deals only with chronic (lifetime exposure)
- Does not focus on developmental, repro., immunotox.
- Some are more current than others
- Few MOA

A	*Human carcinogen*	*Sufficient* human evidence
B1 B2	*Probable human carcinogen*	*Limited* human evidence *Sufficient* animal evidence
C	*Possible human carcinogen*	*Limited* animal evidence
D	*Not classifiable*	*Inadequate* human and animal evidence
E	*Evidence of noncarcinogenicity*	Sufficient negative evidence

A Brief Example of a National Risk Assessment



National MeHg Advice

- National advice on fish consumption to reduce exposure to methylmercury
- Advice is not a risk assessment but used RA as one of the bases for advice
- Jointly issued by FDA and EPA
  - Incorporated stakeholder input
  - Incorporated peer review
  - Incorporated policy at several levels

MeHg Hazard Characterization

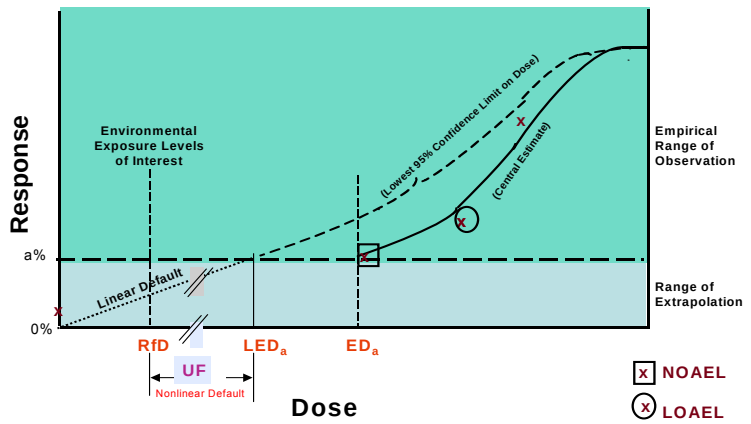
- Effects of adult exposure or during development range from mortality through subtle effects on ability to learn
  - **Effects on adults** included death, paresthesia, tremors, ataxia, hearing and vision impairment, balance and speech disturbances, motor difficulties
    - Cases of neurological effects in adults have been seen in the U.S.
  - **Children** born to mothers exposed during pregnancy exhibited cerebral palsy-like symptoms, delayed walking/talking, delayed startle responses, subtle neurological effects, effects on tests related to ability to learn and process information
  - **Not likely to be a human carcinogen** (Tumors are seen in animals only at extremely toxic doses; neurological effects are observed at orders of magnitude lower exposures)
- Developing nervous system is a sensitive target for low dose MeHg exposure
- Human and animal evidence of cardiovascular effects – from adult and *in utero* exposure
- Animal evidence of immune and reproductive effects
- Mode of action is not established

MeHg Dose Response

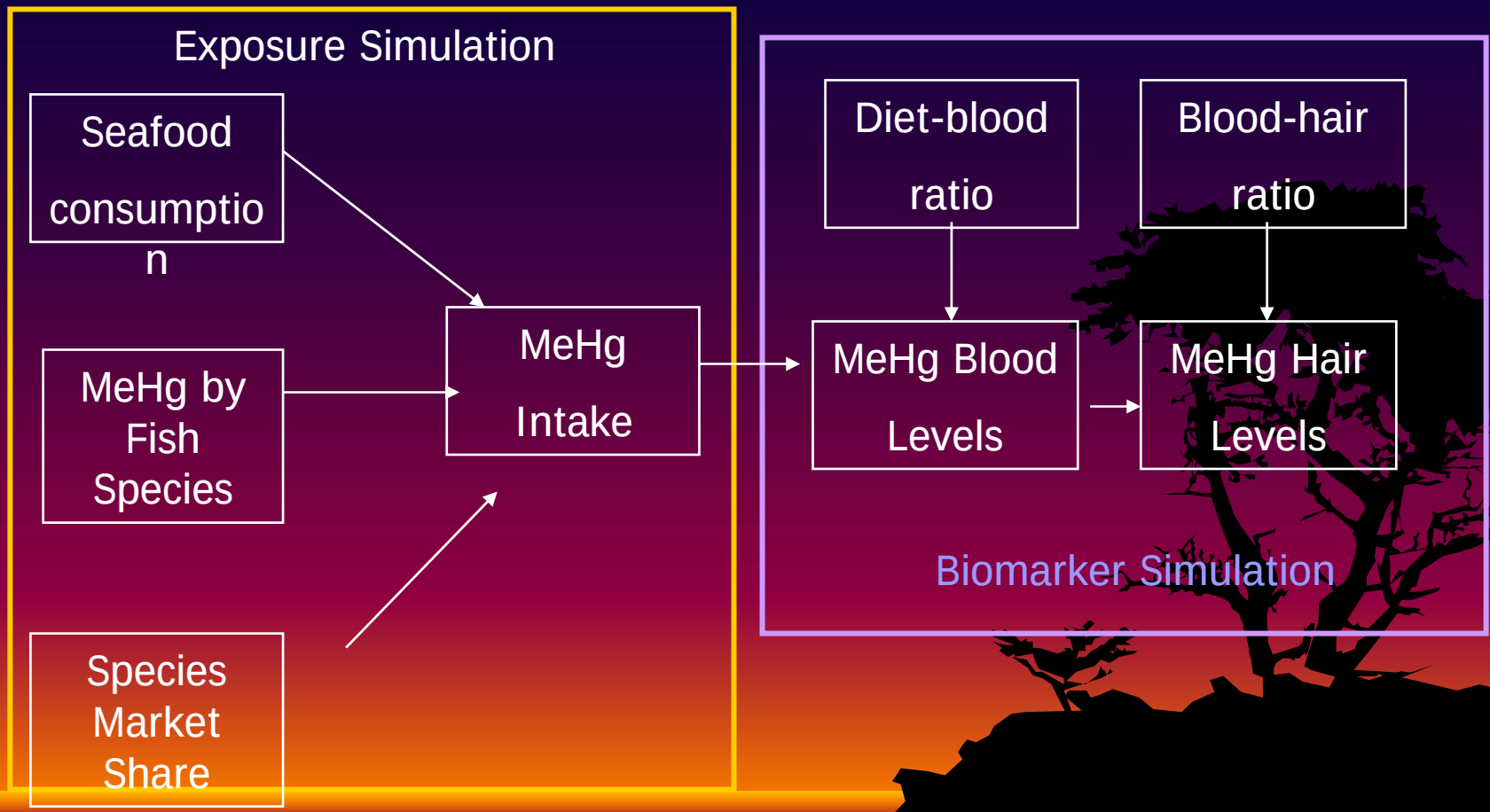
- **RfD = 0.1µg/kg/day** (about 1.1 ppm hair, 5.8 ug/L blood) neuropsychological effects in children exposed *in utero* through maternal seafood consumption; includes consideration of Faroes, Seychelles, New Zealand data. “The test scores are all indications of neuropsychological processes involved with a child’s ability to learn and process information.” (NRC 2001)
  - The benchmark dose for methylmercury is a level at which one would expect a doubling of the number of poor performers on these tests (from 5% to 10% of the population)
  - Used Boston Naming Test as example–

BMDL = 58 ug mercury / L blood

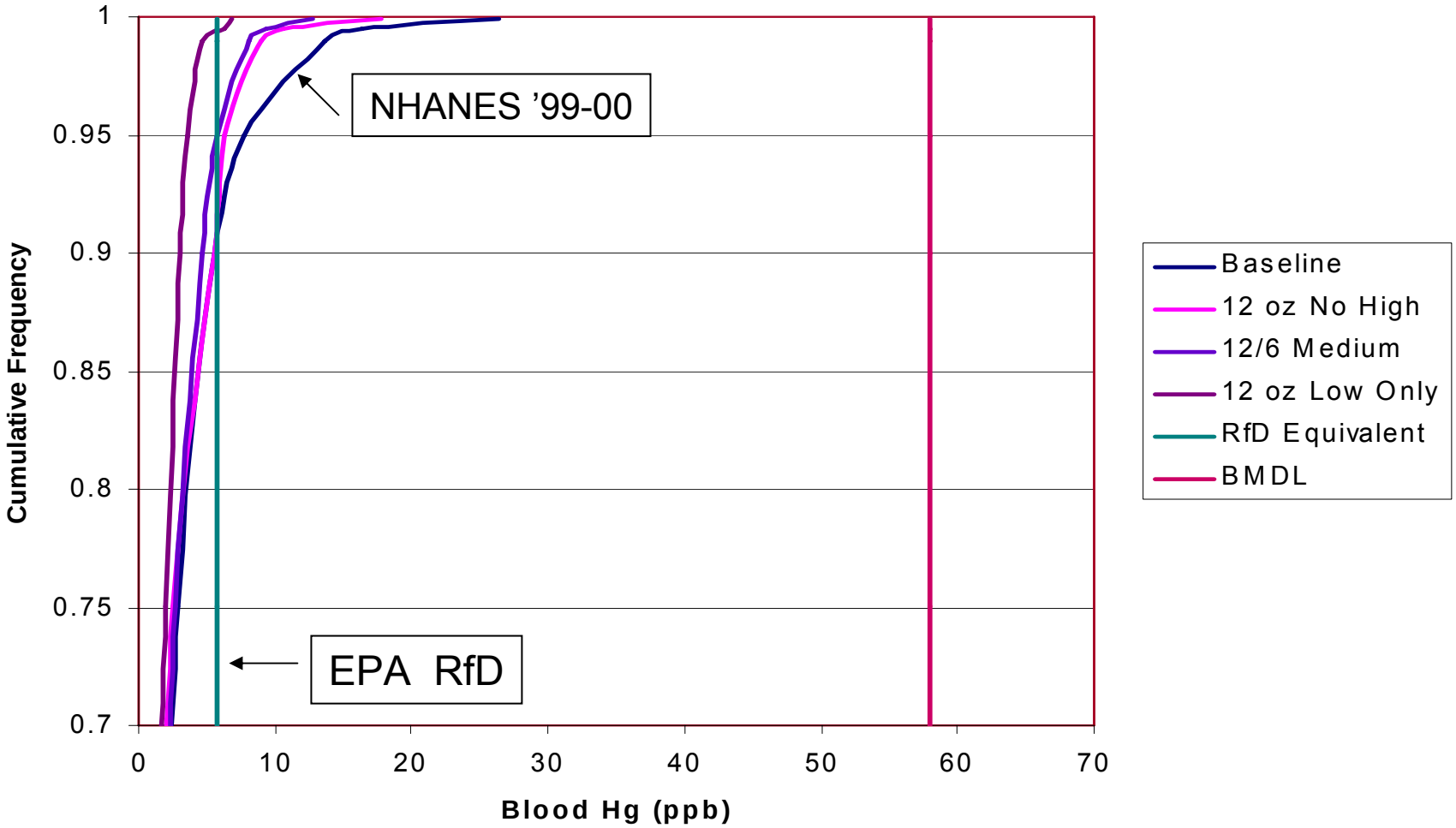
Uncertainty factor is small – 10; thus there is not much of a margin of exposure between an effect level and the RfD



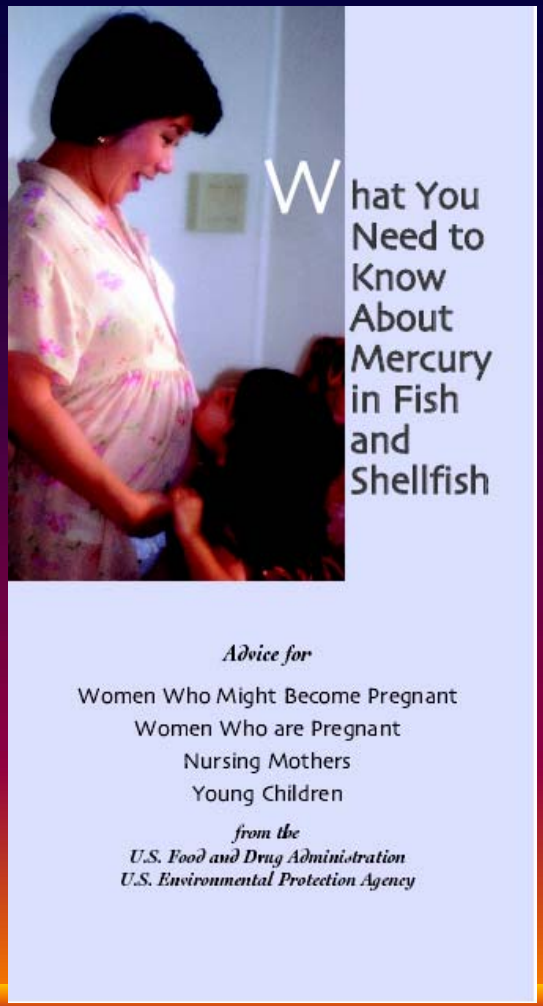
MeHg Exposure Model Overview



Risk Characterization



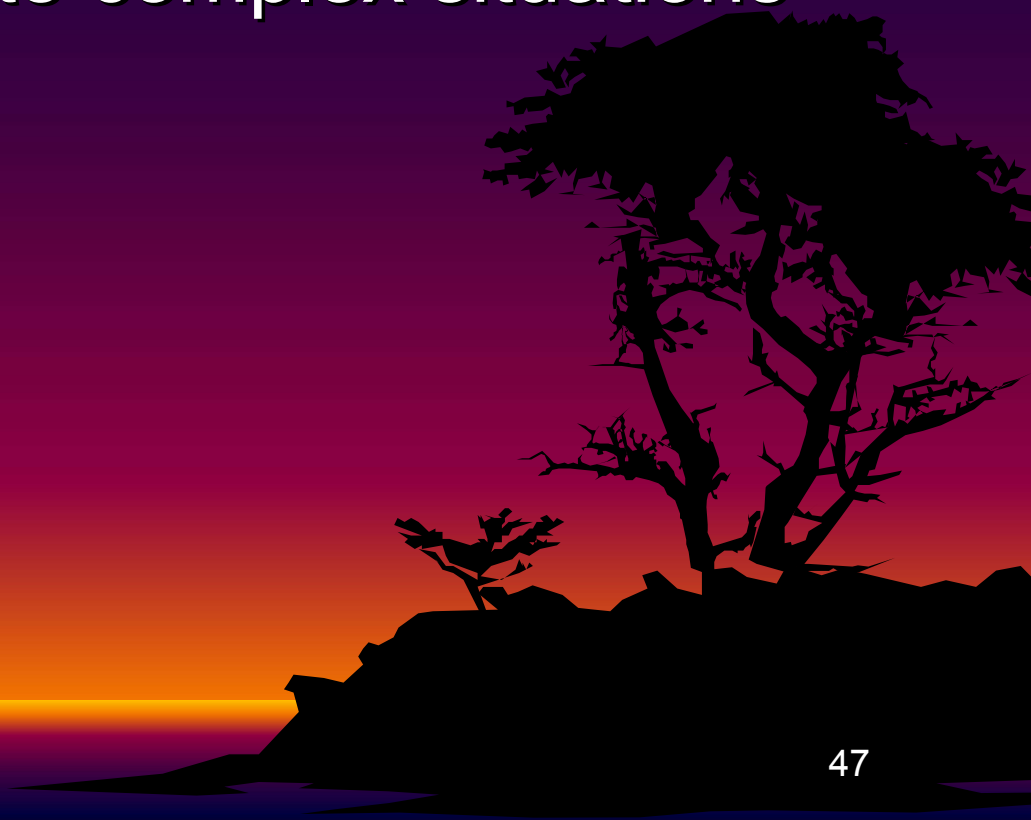
Risk Management



These efforts to avoid exposure must be coupled with actions to reduce mercury contamination of the environment

Risk Communication

- Would take another day long course
- Must communicate complex situations
  - Simply
  - Consistently
  - Completely
  - Respectfully



Useful Websites

- Guidelines
  - http://cfpub.epa.gov/ncea/raf/recordisplay.cfm?deid=55907
- Cancer guidelines
  - http://cfpub.epa.gov/ncea/raf/recordisplay.cfm?deid=116283
- IRIS
  - http://www.epa.gov/iris/index.html

What's Different from 1986?

- Analyze data before invoking default options.
- Mode of action is key in decisions
- Weight-of-evidence narrative replaces the previous "A-B-C-D-E" classification scheme.
- Two step dose response assessment
  - Model in observed range
  - Extrapolate from point of departure
- Consider linear and non-linear extrapolation
- Address differential risks to children