Webinar Magistrali 2022

Società Italiana di Medicina del Lavoro

1994-2022: ABOUT THE OPPORTUNITY OF CRITICALLY REVIEWING THE METHODOLOGY OF OCCUPATIONAL RISK ASSESSMENT

Risk Assessment History and Perspectives

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Disclaimer: The findings and conclusions in this report are those of the author and do not necessarily represent the official position of the National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention.

- Critical in occupational safety and health is making decisions about “safe” levels of exposures to hazards for workers
- This process is based on risk assessment

Risk is a construct

Before risk there was fate

(Bernstein 1996)

What is risk?

Risk = *f* (Hazard, Consequence, Opportunity)

Risk assessment sets out to answer three questions:

1. What can happen?
2. What are the consequences if it does happen?
3. How likely is it that it will happen?

Risk example: What is the lifetime risk of dying at work?

- 5,190 U.S. workers were killed on the job in 2016
  - 142,000,000 full-time equivalent workers in 2016
  - 3.7 per 100,000 full-time equivalent workers per year
- For an individual working 45 years, lifetime risk of on-the-job fatality is:
  - Cumulative incidence (risk) = 1 - exp(-R*t)

    = 1 - exp(-3.7 x 10^{-5} x 45 years)

    = 1.6 x 10^{-3}
  - Lifetime risk =1.6 fatalities per 1000 workers

Source, BLS: www.bls.gov

Lifetime Fatality Risks by Occupation

Occupation	Fatalities	Rate (per 100,000 FTE)	Lifetime Risk (per 1,000 workers)*
Management	672	1.2	0.54
Protective services	281	8.4	3.8
Installation, maintenance	470	9.4	4.2
Construction and extraction	970	12.4	5.6
Transportation	1,388	15.4	6.9
Farming, fishing, forestry	290	24.9	11.1
Logging workers	91	135.9	59.3

* 45 Year Working Life Exposure

Source, BLS: www.bls.gov

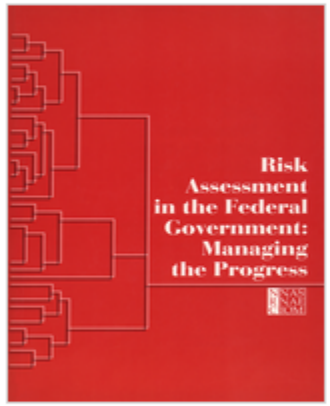
Risk assessment

- Tool for society and decision-makers
  - Utilizes the available evidence to estimate risk and characterize uncertainty
- Focus of risk assessment
  - When social policy decisions are in dispute
  - When consequences of options are not subject to direct measurement
- Challenges in risk assessment application
  - Incomplete data to characterize dose-response relationship

(Hattis and Silver 1993)

Risk assessment – selected history

- 3200 BC – The Asipu in Tigris-Euphrates Valley: first recorded instance of a simplified form of risk assessment
- ~400 BC – Athenians developed capacity to assess risks before making decisions
- Mid-1600's– development of classical probability theory
- 1883 – Gruber concluded after exposing 2 hens and 12 rabbits and himself that "the boundary of injurious actions of carbon monoxide lies at a concentration probability of 500 ppm but certainly no less than 200 ppm."
- 1930s – protection of human health from chemicals
  - Identification of some form of dosage versus response relationship
- 1970s – major health, safety, and environmental legislation



Risk Assessment in the Federal Government: Managing the Process

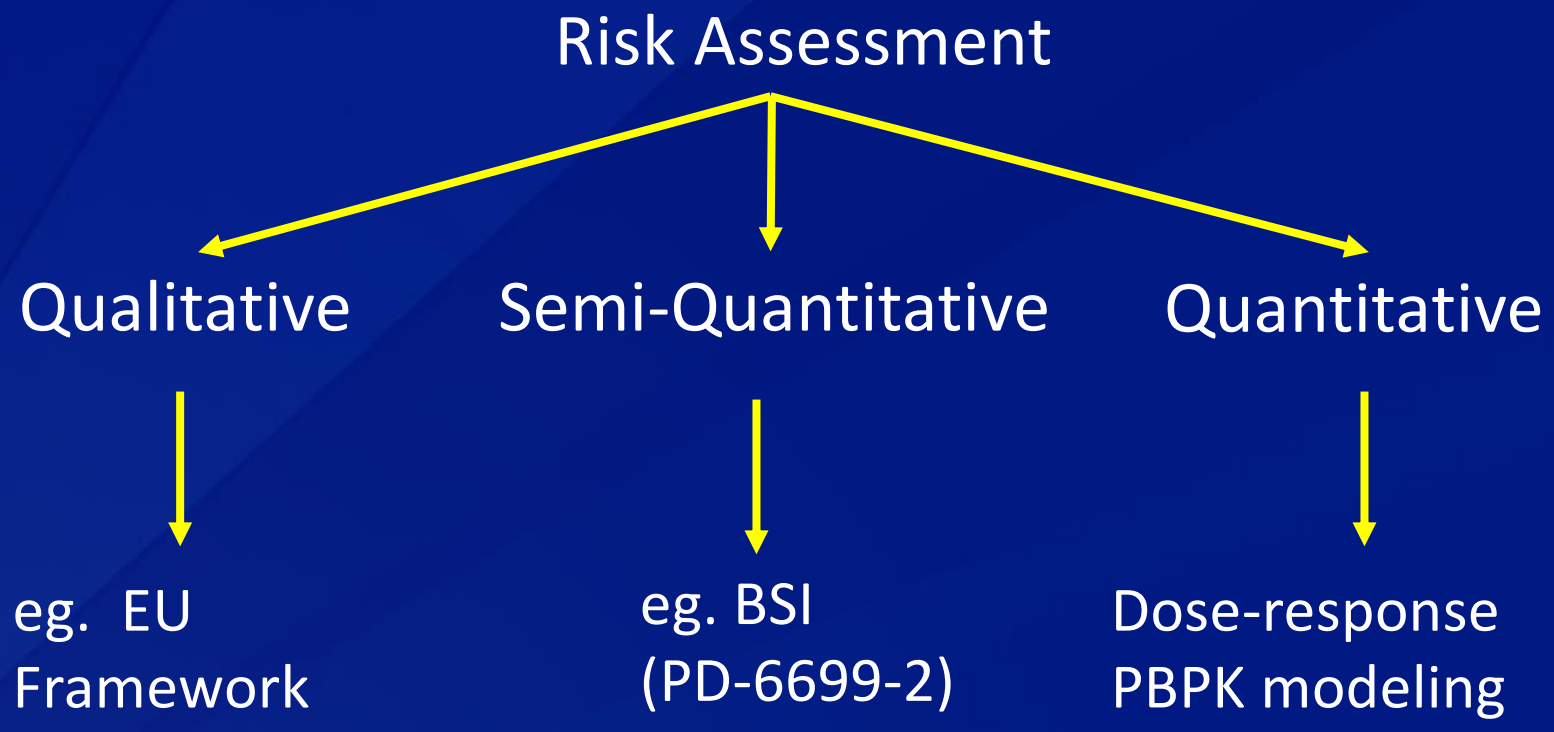
National Research Council (US) Committee on the Institutional Means for Assessment of Risks to Public Health.

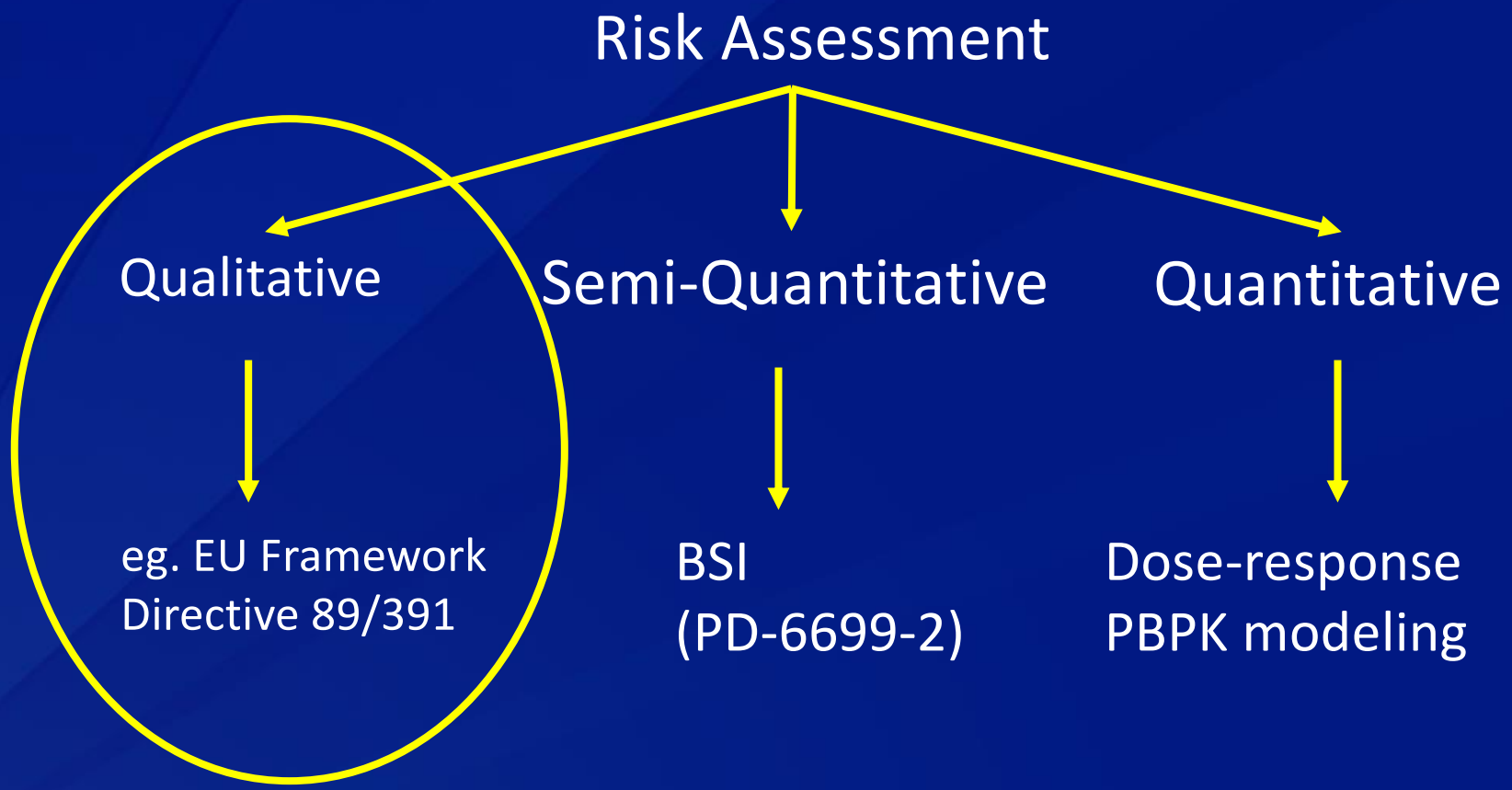
Washington (DC): National Academies Press (US); 1983.
ISBN: 0–309–03349–7

The regulation of potentially hazardous substances has become a controversial issue. This volume evaluates past efforts to develop and use risk assessment guidelines, reviews the experience of regulatory agencies with different administrative arrangements for risk assessment, and evaluates various proposals to modify procedures. The book's conclusions and recommendations can be applied across the entire field of environmental health.

Risk assessment – selected history

- 1983 – NRC “Red Book”
- 1989 – Framework Directive 89/391
- 1996 E Guidance – the process of evaluating the risk to health and safety of workers while at work arising from the circumstance of the occurrence of a hazard at the workplace
- 2002 – ECETOC – tiered and targeted risk assessment of chemicals
- 2006 – REACH (EC No 1907/2006) and ECHA Risk Assessment Committee
- 2009– NRC– science & decisions: advancing risk assessment


Risk Assessment
Qualitative
Semi-Quantitative
Quantitative
eg. EU Framework Directive 89/391
eg. BSI (PD-6699-2)
Dose-response PBPK modeling


Risk Assessment
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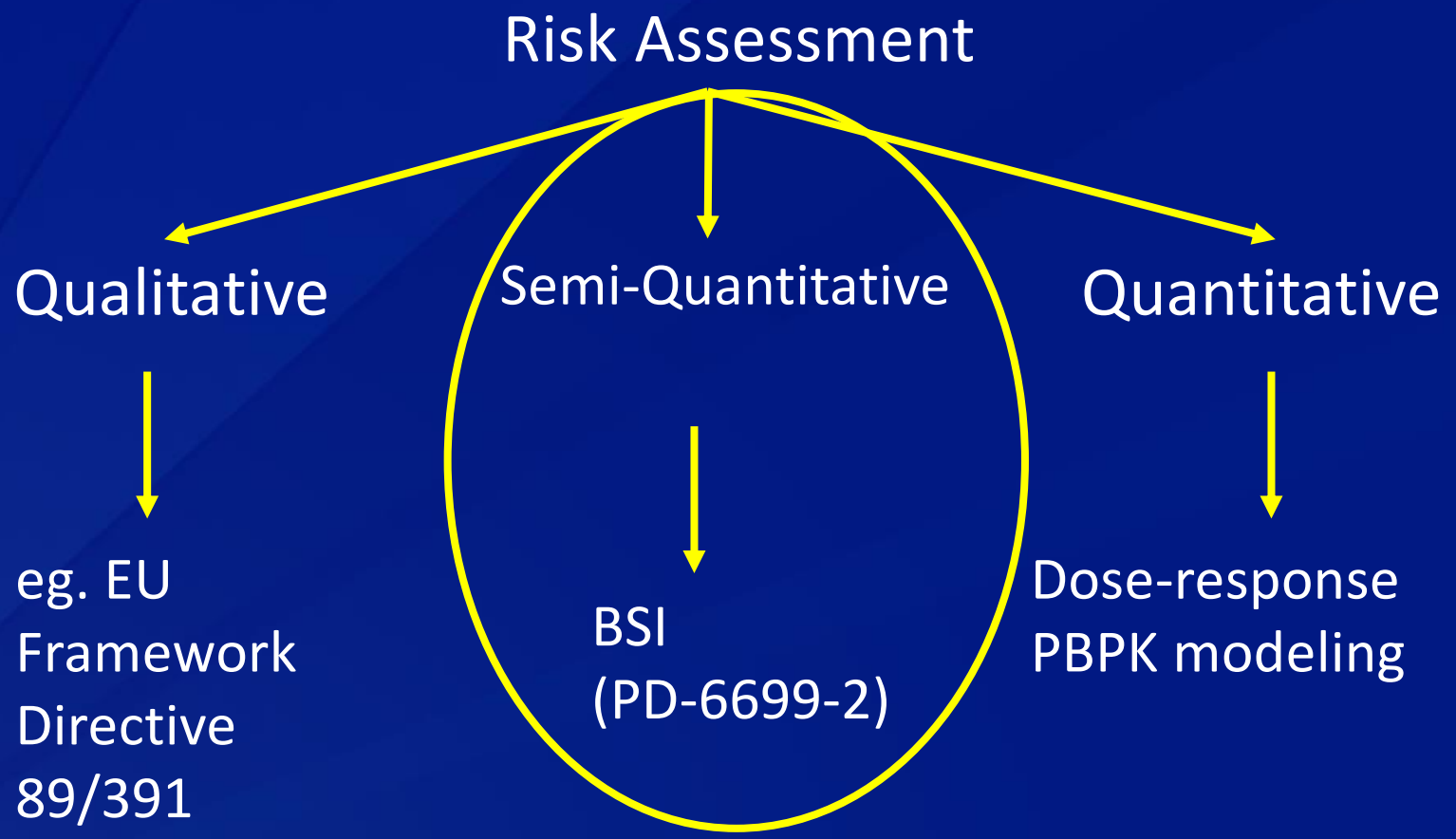
European Agency for Safety and Health at Work

OiRA: free and simple tools for a straightforward risk assessment process

Risk assessment is the essential first step in the prevention of occupational accidents and ill health. OiRA — Online interactive Risk Assessment — makes this process easy.

It provides the resources and know-how required to enable micro and small organisations to assess their risks themselves. Available free on the web, OiRA tools are easily accessible and easy to use.

OiRA offers a step-by-step approach to the risk assessment process, beginning with the identification of workplace risks, then taking the user through the process of implementing preventive actions, and finally to monitoring and reporting risks.


Risk Assessment
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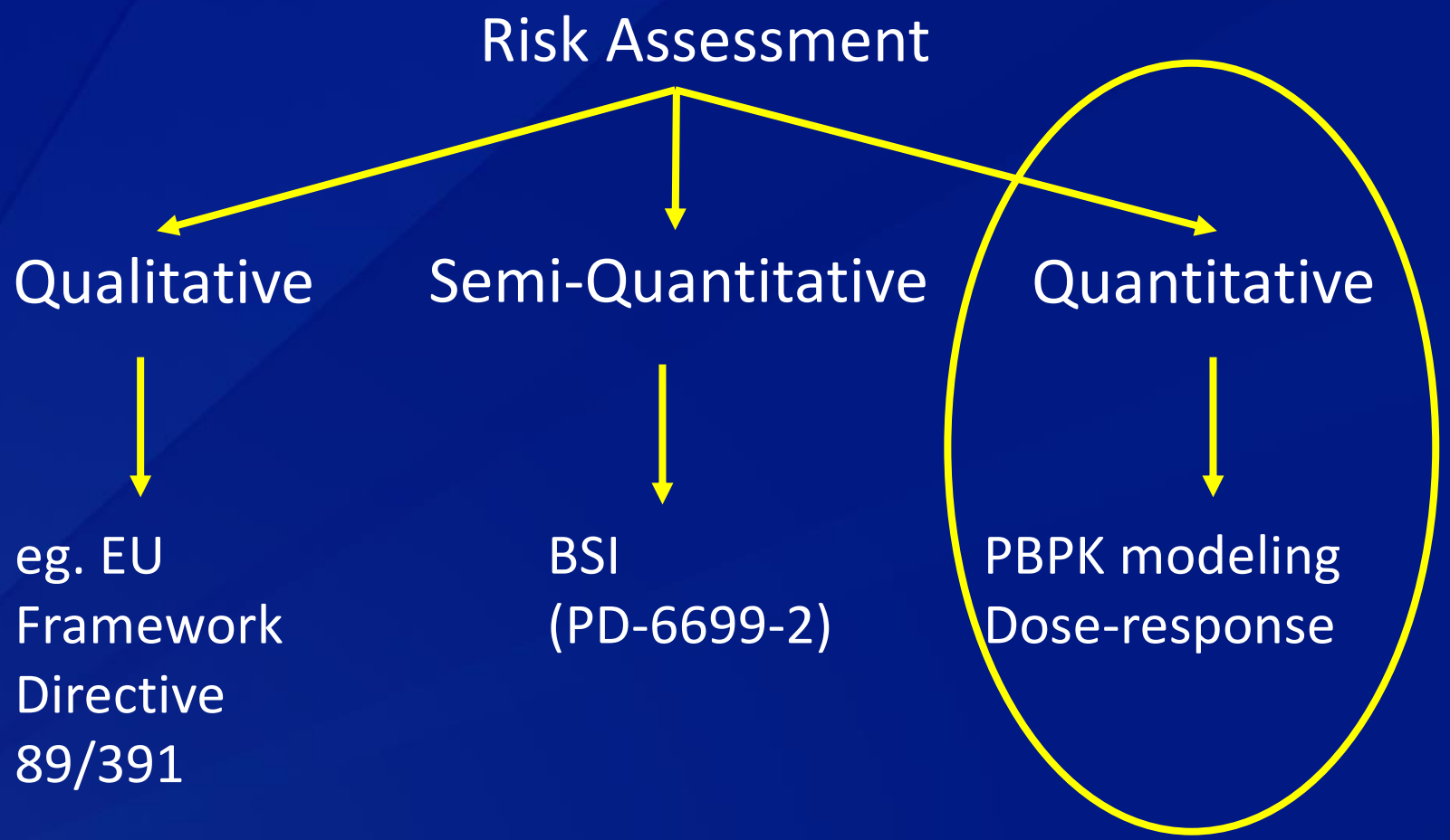
eg. EU Framework Directive 89/391
BSI (PD-6699-2)
Dose-response PBPK modeling

Hazard Categories in British Standards Institute (PD - 6699-2)

Category	Definition	Benchmark Exposure Limit (BEL)
Fibrous	Insoluble Aspect ratio >3:1 >5000 nm	0.01 f/cm
CMAR*	Already classified in larger particle form as CMAR	0.1 of mass-based OEL for its larger particle form
Insoluble	Insoluble or poorly soluble nanomaterial not in fibrous or CMAR category	0.066 of mass-based OEL for its larger particle form or 10,000 particle/cm^3
Soluble	Soluble nanomaterial not in fibrous or CMAR category	0.5 of mass-based OEL for its larger particle form

BSI [2009]

*Carcinogenic, mutagenic, asthmatogenic, or reproductive toxicant


Risk Assessment
Qualitative
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eg. EU Framework Directive 89/391
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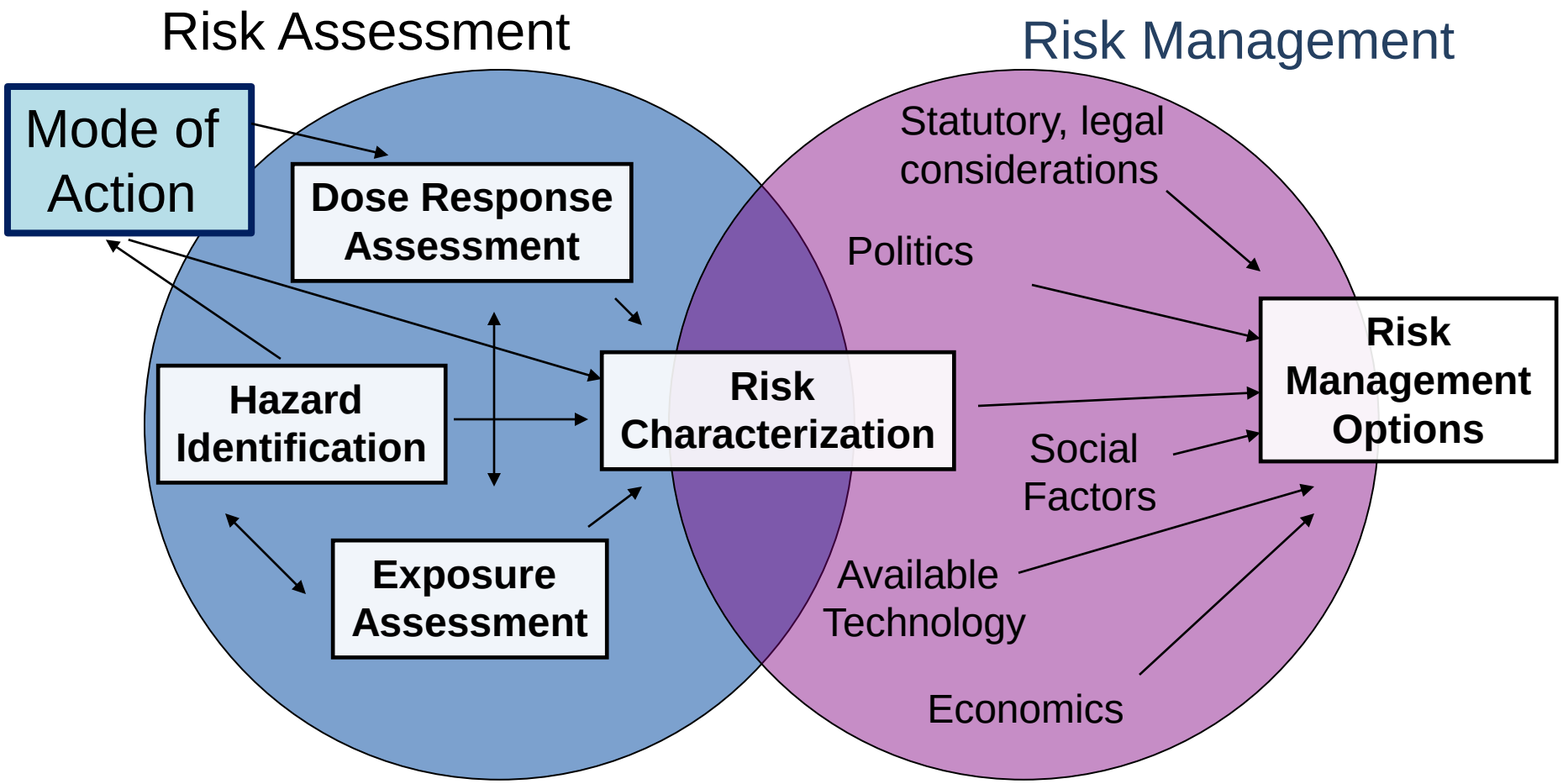
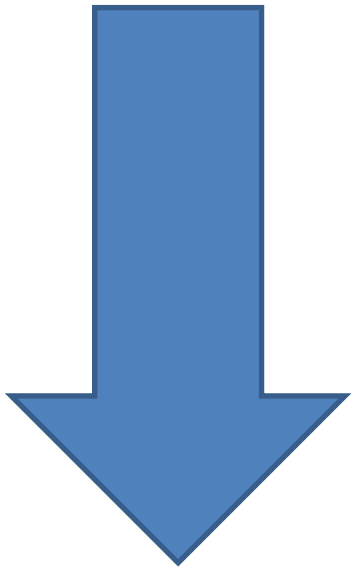
PBPK modeling
Dose-response

Risk Assessment Paradigm



Quantitative Risk Assessment



Occupational Exposure Limits (OELs)

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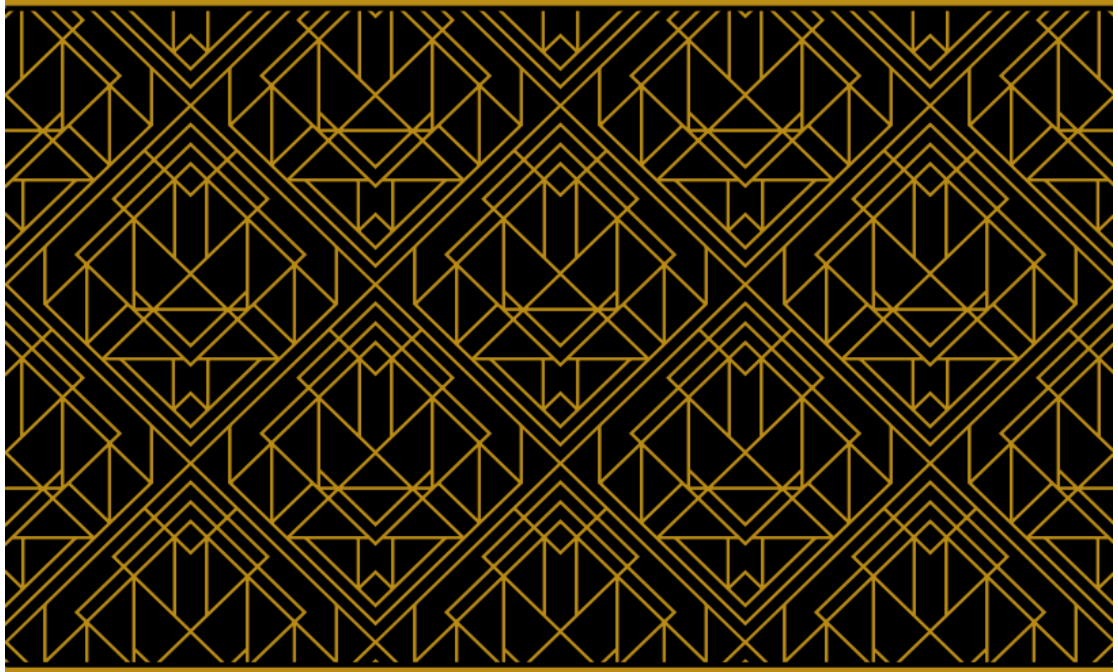
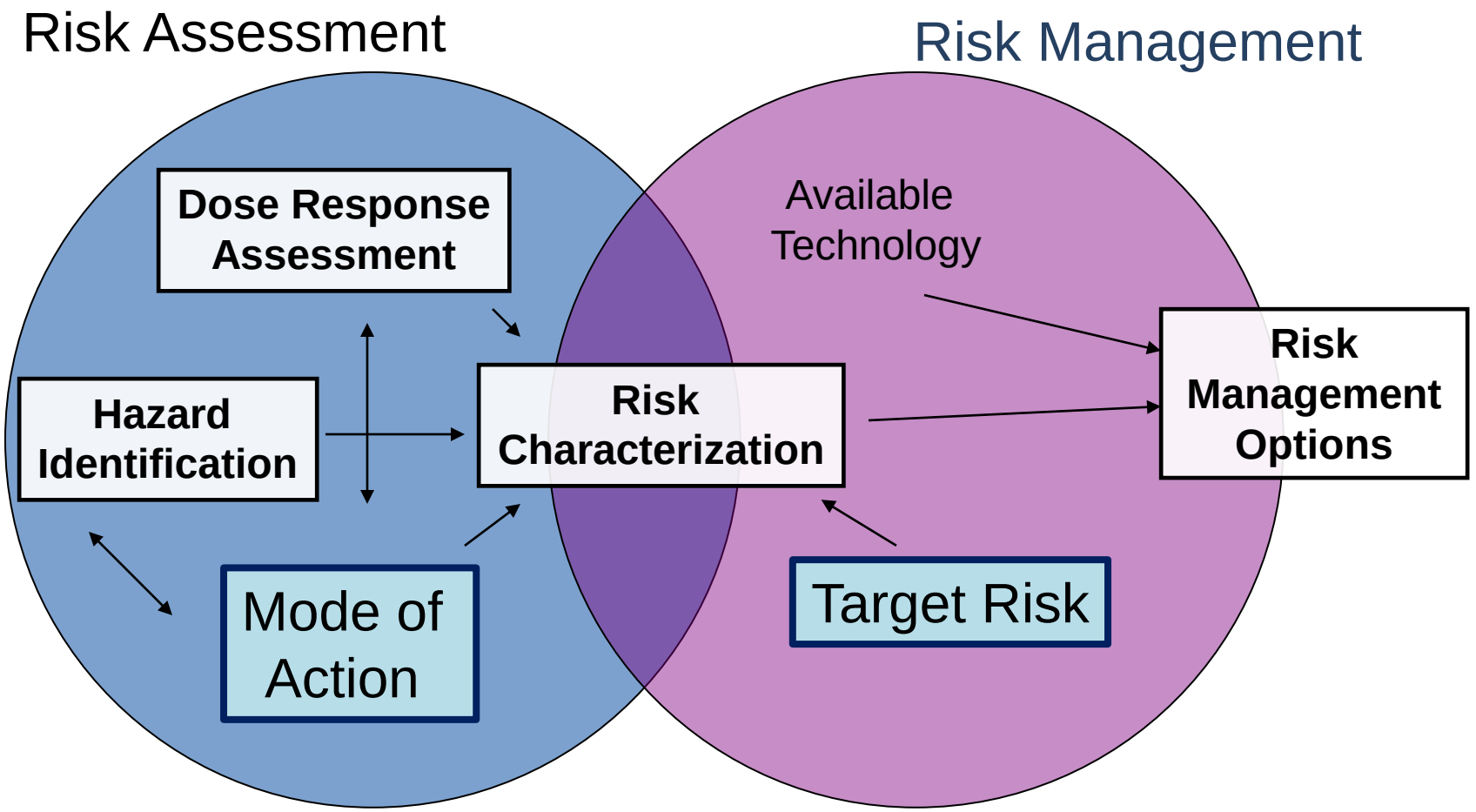


NIOSH Practices in Occupational Risk Assessment

Centers for Disease Control and Prevention
National Institute for Occupational Safety and Health

NIOSH Risk Assessment Paradigm



Selected History of NIOSH Quantitative Risk Assessment

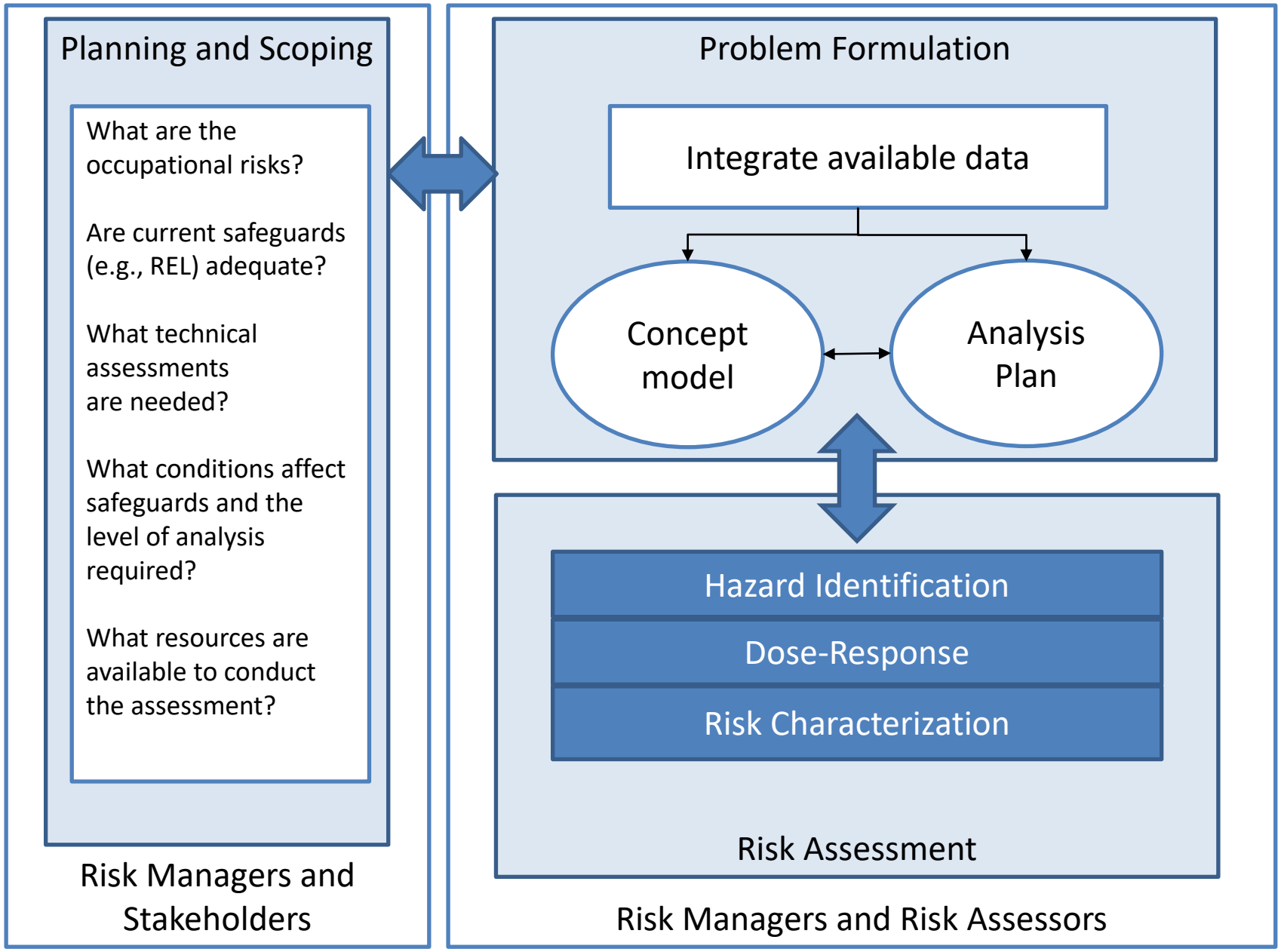
Agent	Adverse Effect[1]	Dose-response assessment[2]	Risk Characterization	Reference
1,3-butadiene	leukemia	toxicologic, Weibull time-to-tumor regression model, animal to human extrapolation epidemiologic and toxicologic, literature review	extrapolation, excess lifetime risk, target risk unspecified	[Dankovic et al. 1993]
asbestos	lung cancer, asbestosis	epidemiologic, Poisson regression, additive relative rate function (cancer), power function (asbestosis)	extrapolation, excess lifetime risk, target risk unspecified	[Stayner et al. 1997]
cadmium	lung cancer	epidemiologic, Poisson and Cox PH regression, additive relative rate function	extrapolation, excess lifetime risk, target risk unspecified	[Stayner et al. 1992a; Stayner et al. 1992b]
carbon nanotubes and nanofibers	non-malignant adverse lung effects	toxicologic, NOAEL and BMD assessments	PoD/UF	[NIOSH 2013b]
coal mine dust	coal workers' pneumoconiosis, progressive massive fibrosis, pulmonary dysfunction	epidemiologic, logistic and multiple linear regression	extrapolation, excess lifetime risk, target risk unspecified	[Kuempel et al. 1997]
diacetyl and 2,3-pentanedione	pulmonary dysfunction	epidemiologic, linear extrapolation, multiple regression	extrapolation, excess lifetime risk, 10^{-3} target risk	[NIOSH 2016a]
diesel exhaust	lung cancer	toxicologic and epidemiologic (review)	extrapolation, excess lifetime risk, target risk unspecified	[Stayner et al. 1998]

History of NIOSH Quantitative Risk Assessment Continued

Agent	Adverse Effect[1]	Dose-response assessment[2]	Risk Characterization	Reference
EGME, EGEE, EGMEA, EGEEA	reproduction developmental, hematotoxic effects	toxicologic, NOAEL and LOAEL assessments	PoD/UF	[NIOSH 1991]
hexavalent chromium	lung cancer	epidemiologic, Poisson regression linear ERR model	extrapolation, excess lifetime risk, 10^{-3} target risk	[NIOSH 2013a; Park et al. 2004]
noise	material hearing impairment	epidemiologic, logistic regression	extrapolation, excess lifetime risk with no target risk level specified	[NIOSH 1998; Prince et al. 2003]
radon	lung cancer	epidemiologic, Cox proportional hazards regression	extrapolation, excess lifetime risk, target risk unspecified	[Hornung and Meinhardt 1987; NIOSH 1987]
silica	lung cancer	epidemiologic, Poisson regression, additive relative rate function	extrapolation, excess lifetime risk, target risk unspecified	[Rice et al. 2001]
silica	non-malignant lung disease	epidemiologic, Poisson regression, additive relative rate function	extrapolation, excess lifetime risk, target risk unspecified	[Park et al. 2002]
titanium dioxide	lung cancer	toxicologic, nonlinear extrapolation, BMD model averaging quantal endpoint	extrapolation, excess lifetime risk, 10^{-3} target risk	[NIOSH, 2011]

1. Analysis may have considered multiple adverse effects. The adverse effect shown in the table was selected as the primary effect in the risk assessment.
2. The dose-response assessment refers to the primary source supporting final models and/or recommendations on risk-based exposure limits.

Abbreviations: BMD, benchmark dose; EGEE, ethylene glycol monoethyl ether; EGEEA, ethylene glycol monoethyl ether aceate; EGME, ethylene glycol monomethyl ether; EGME, ethylene glycol monomethyl ether acetate; ERR, excess relative rate; LOAEL, lowest observable adverse effect level; NOAEL, no observable adverse effect level; PH, proportional hazards; PoD, point of departure, UF, uncertainty factor.


Planning and Scoping
What are the occupational risks?
Are current safeguards (e.g., REL) adequate?
What technical assessments are needed?
What conditions affect safeguards and the level of analysis required?
What resources are available to conduct the assessment?
Risk Managers and Stakeholders
Problem Formulation
Integrate available data
Concept model
Analysis Plan
Hazard Identification
Dose-Response
Risk Characterization
Risk Assessment
Risk Managers and Risk Assessors

Planning and Scoping

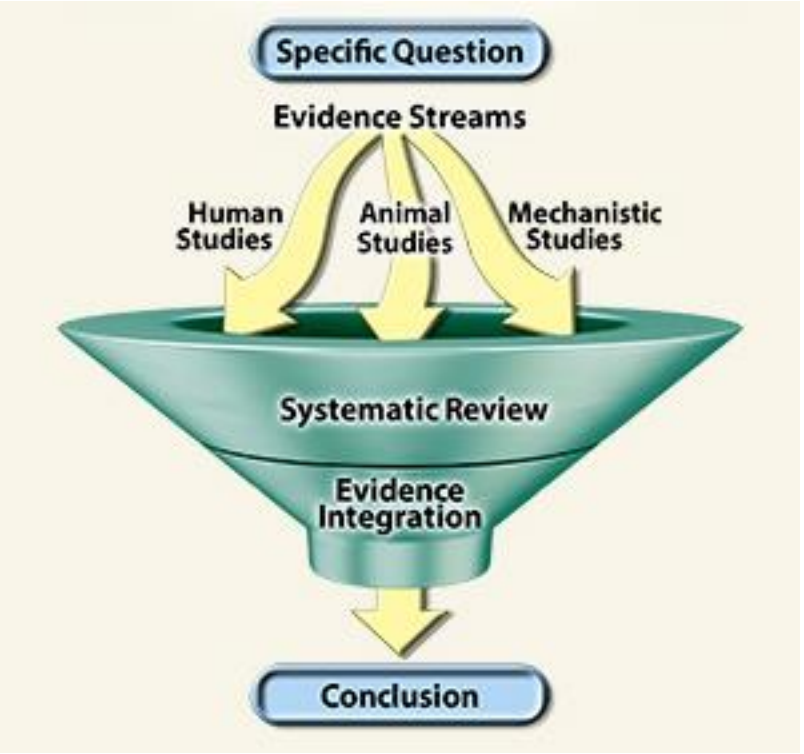
- Who is affected?
- Where does the problem exist?
- What are the potential adverse effects and how measured?
- How are adverse effects defined and measured?
- What are the causal agents and how measured?
- What are risk management needs?
- What are stakeholder needs?

Hazard Identification

The identification of the type and nature of adverse effects that an agent has an inherent capacity to cause in an organism, system, or population.

Hazard Identification Approach

1. Define questions of interest and develop criteria for study (data) selection
2. Review, identify, and select relevant information
3. Evaluate and integrate evidence across studies
4. Synthesize and interpret findings

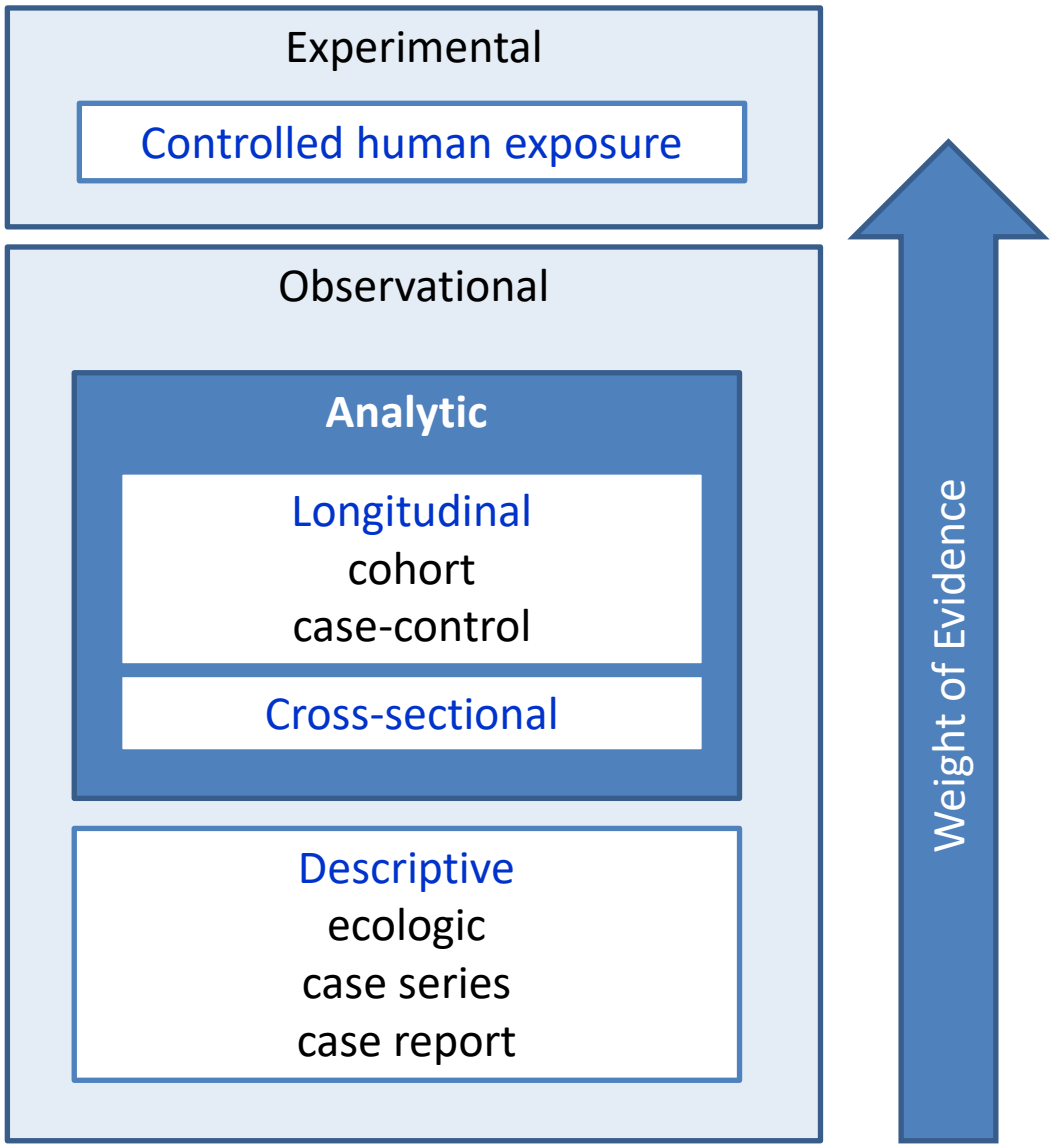


https://ntp.niehs.nih.gov/pubhealth/hat/review/index-2.html

Hazard Identification: Gather Data

- Human data (always preferred)
  - Controlled human exposure studies (experimental)
  - Analytic observational studies
  - Descriptive studies (e.g., case reports)
- Animal data
  - Systemic toxicity studies (e.g., pathology, dose-response)
- Mechanistic data
  - Structure-activity relationships
  - Metabolic data
  - Genomics, epigenomics
- In vitro data

Human Data



The best model for human is human!

Hazard Identification: Identify Toxicity

- **Effects:** What effects are observed from the data?
  - Toxicokinetics: What does the body do to the agent (ADME)?
  - Toxicodynamics: What does the agent do to the body?
- **Mode of Action:** How does the agent act to produce an effect?
- **Causality Framework:** A way to organize and evaluate causality given toxicity data (e.g., Hill guidelines)
- **Weight of Evidence:** How likely is this agent to cause adverse effects and under what conditions?

Hazard Identification: Identify Effects

Adverse effect: A specified change in the morphology, physiology, growth, development, reproduction, or life span of an organism, system, or population that results in an impairment of functional capacity, an impairment of the capacity to compensate for additional stress, or an increase in susceptibility to other influences.

- What are the affected organs or tissue systems?
- What is the severity of effects?
- Who is more sensitive or susceptible?
- What factors affect susceptibility?

Hazard Identification: Identify Uncertainties

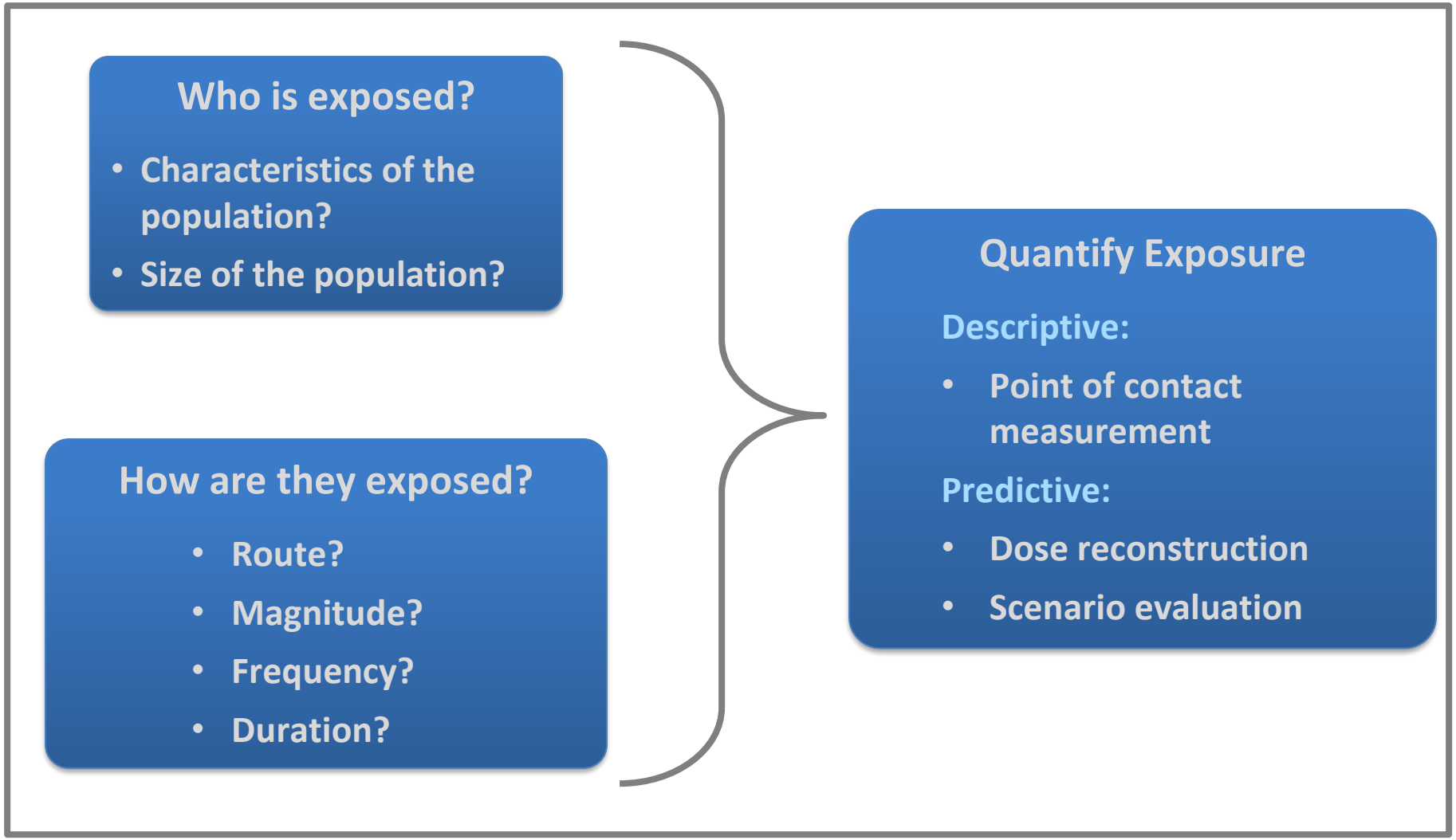
- Animal to human extrapolation
- Variability within the human population (susceptibility)
- Extrapolation below observed data
- Size and quality of the database

Exposure Assessment

The process of estimating or measuring the magnitude, frequency, and duration of exposure to an agent, along with the number and characteristics of the population exposed.

Not explicitly performed in NIOSH risk assessment.

Exposure Assessment



Dose-Response Assessment

The relationship between the amount of an agent administered to, taken up by, or absorbed by an organism, system, or population and the change developed in that organism, system, or population in reaction to the agent.

Paracelsus (1493-1541): “All things are poison and nothing without poison; only the dose makes that a thing is not a poison.”

Dose-Response Terminology

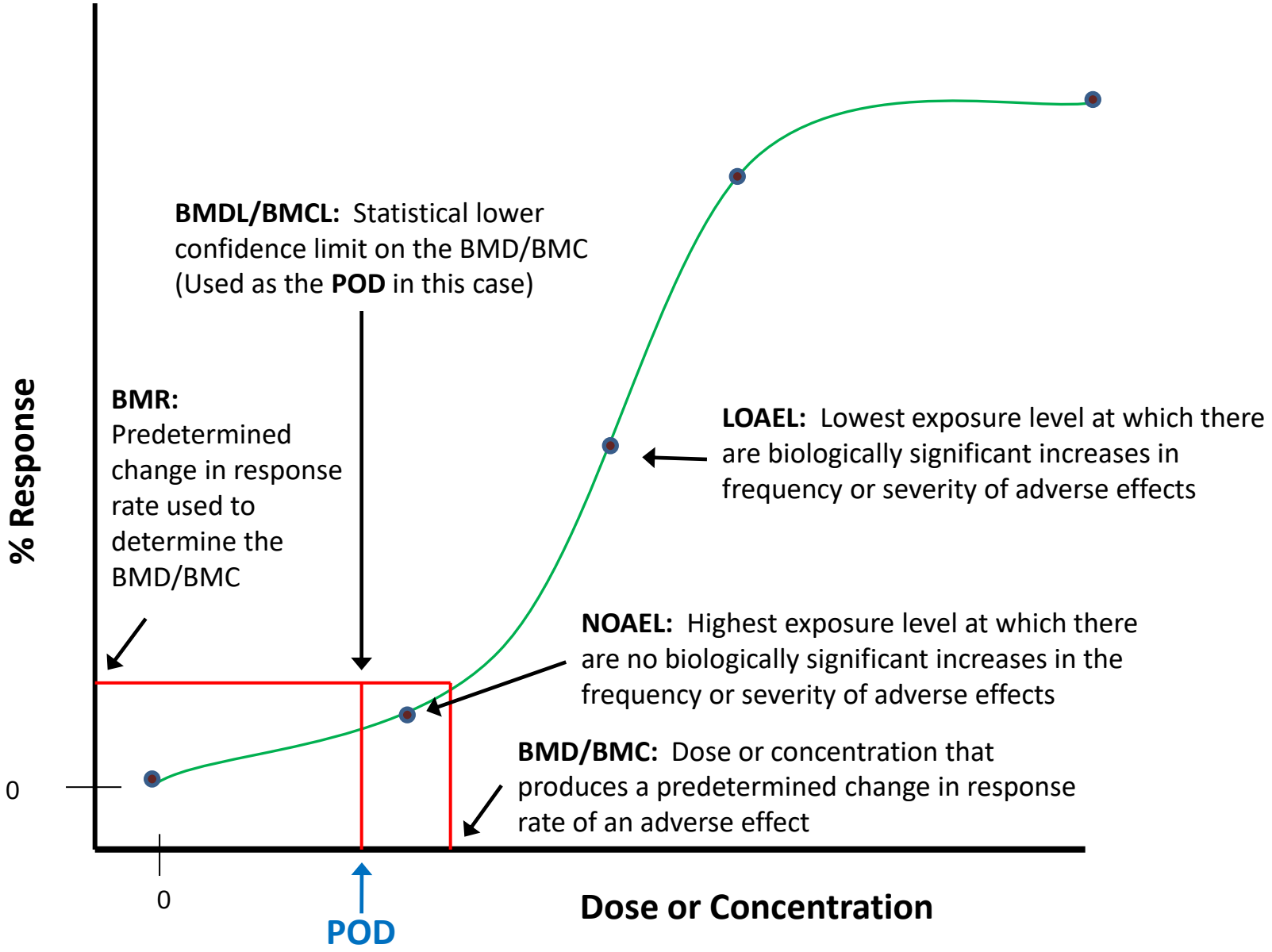
LOAEL
Lowest-Observed-Adverse-Effect Level. Lowest dose at which significant adverse effects are observed.

NOAEL
No-Observed-Adverse-Effect Level. Highest dose at which no significant adverse effects are observed.

BMD
Benchmark Dose. An exposure to a low dose of a substance that is linked with a low (1-10%) risk of adverse health effects, or the dose associated with a specific biological effect.

BMDL
A lower, one-sided confidence limit on the BMD.

Point of Departure
The dose-response point that marks the beginning of a low dose extrapolation.


BMDL/BMCL: Statistical lower confidence limit on the BMD/BMC (Used as the POD in this case)
BMR: Predetermined change in response rate used to determine the BMD/BMC
LOAEL: Lowest exposure level at which there are biologically significant increases in frequency or severity of adverse effects
NOAEL: Highest exposure level at which there are no biologically significant increases in the frequency or severity of adverse effects
BMD/BMC: Dose or concentration that produces a predetermined change in response rate of an adverse effect
% Response
0
0
POD
Dose or Concentration

Risk Characterization

The qualitative and, wherever possible, quantitative determination, including attendant uncertainties, of the probability of occurrence of known and potential adverse effects of an agent in persons under defined exposure conditions.

For NIOSH risk assessments, risk characterization is the integration of the hazard identification and dose-response assessment with other information necessary to complete the basis for the REL.

Uncertainty Factors

- UF_H – Human variability
- UF_A – Animal-to-human extrapolation
- UF_S – Subchronic-to-chronic extrapolation
- UF_L – LOAEL-to-NOAEL extrapolation
- UF_D – Database deficiencies

$$REL = \frac{PoD}{(UF_H \times UF_A \times UF_S \times UF_L \times UF_D)}$$

Illustration of Quantitative Risk Assessment for Engineered Nanomaterials

Regulatory Toxicology and Pharmacology
Volume 95, June 2018, Pages 207-219

Characterizing risk assessments for the development of occupational exposure limits for engineered nanomaterials

P.A. Schulte, E.D. Kuempel, N.M. Drew

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https://doi.org/10.1016/j.yrtph.2018.03.018

Abstract

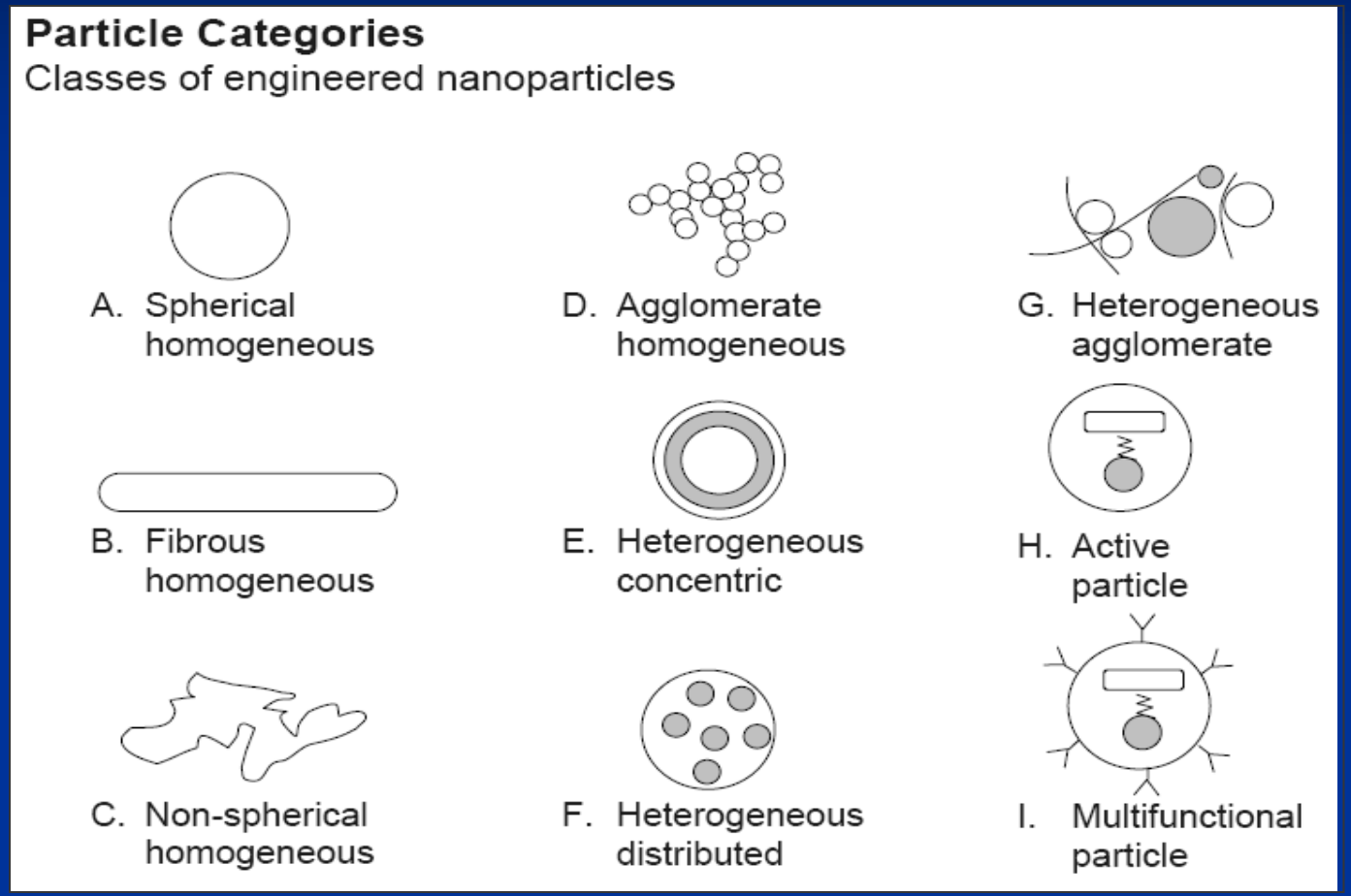
The commercialization of engineered nanomaterials (ENMs) began in the early 2000's. Since then the number of commercial products and the number of workers potentially exposed to ENMs is growing, as is the need to evaluate and manage the potential health risks. Occupational exposure limits (OELs) have been developed for some of the first generation of ENMs. These OELs have been based on risk assessments that progressed from qualitative to quantitative as nanotoxicology data became available. In this paper, that progression is characterized. It traces OEL development through the qualitative approach of general groups of ENMs based primarily on read-across with other materials to quantitative risk assessments for nanoscale particles including titanium dioxide, carbon nanotubes and nanofibers, silver nanoparticles, and cellulose nanocrystals. These represent prototypic approaches to risk assessment and OEL development for ENMs. Such substance-by-substance efforts are not practical given the insufficient data for many ENMs that are currently being used or potentially entering commerce. Consequently, categorical approaches are emerging to group and rank ENMs by hazard and potential health risk. The strengths and limitations of these approaches are described, and future derivations and research needs are discussed. Critical needs in moving forward with understanding the health effects of the numerous EMNs include more standardized and accessible quantitative data on the toxicity and physicochemical properties of ENMs.

How little is “nano?”

If the diameter of the Earth represented
1 meter…

…1 nanometer
would be the size of a dime.

What could a "nanoparticle" be?



Source: Dr. A . Maynard: Woodrow Wilson International Center for Scholars

Parameters That Could Affect Nanoparticle Toxicity

- Size
- Shape
- Composition
- Solubility
- Crystalline structure
- Charge
- Surface characteristic
- Agglomeration
- Impurities
- Attached functional groups

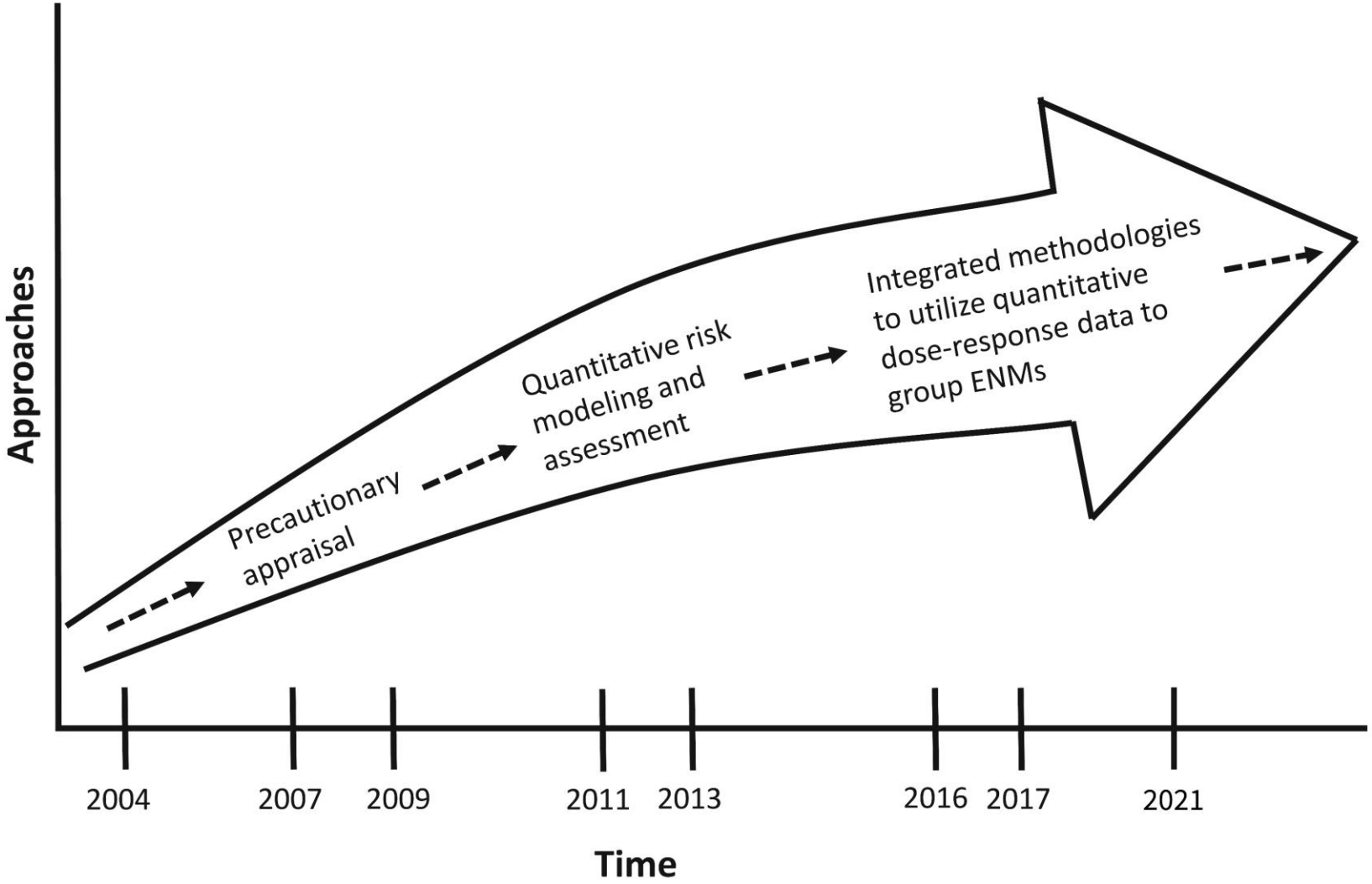
Basis for Concern about Health and Safety Effects of Nanoparticles

- Findings from air pollution epidemiology
  - Particles < 2.5 μm associated with respiratory and cardiovascular effects
- Studies of industrial fumes (e.g., welding fumes) and combustion (e.g., diesel) products
  - Wide range of effects: pulmonary and eye irritation, fever, lung cancer

Basis for Concern about Health and Safety Effects of Nanoparticles (cont'd)

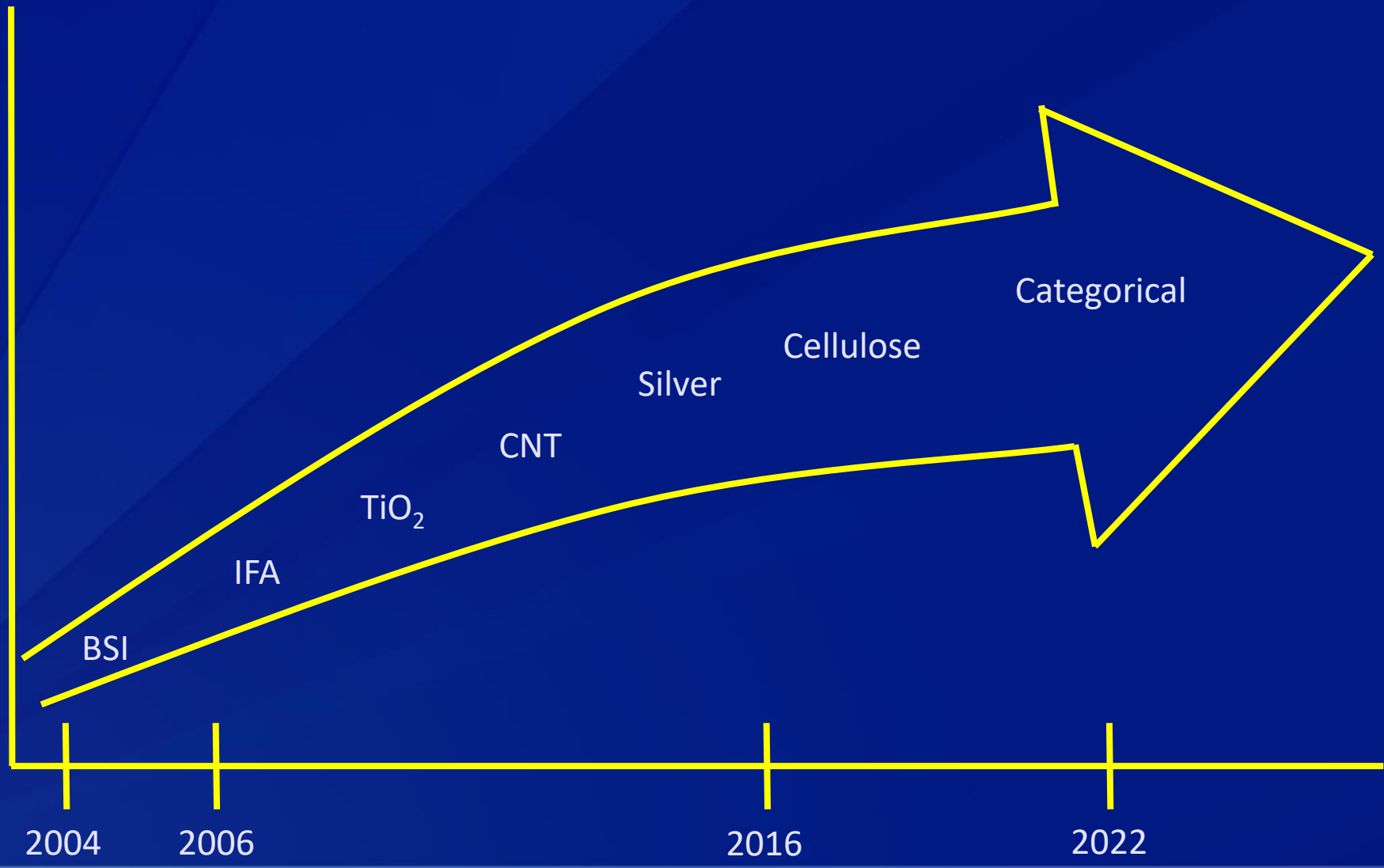
- Initial animal inhalation studies of engineered nanomaterials
  - Pulmonary fibrosis, granulomas, and inflammation
  - Lung cancer, mesothelioma-like effects
  - Cardiovascular effects: oxidative stress, plaque

History or Risk Assessment for EMNs



[Schulte et al. 2018, Reg Tox Pharm 95:207]

Trajectory of risk assessments and OEL development for nanomaterials



Quantitative Risk Assessment Steps for Inhaled Particles

1. Identify relevant animal model, dose metric, and disease response.
2. Evaluate dose-response relationship & estimate dose associated with a specified risk of adverse effect.
3. Extrapolate the animal critical dose to humans by adjusting for differences in breathing parameters & lung morphology
4. Estimate airborne exposure that would result in the human-equivalent dose.

[Kuempel et al. Inhal Toxicol 2006]

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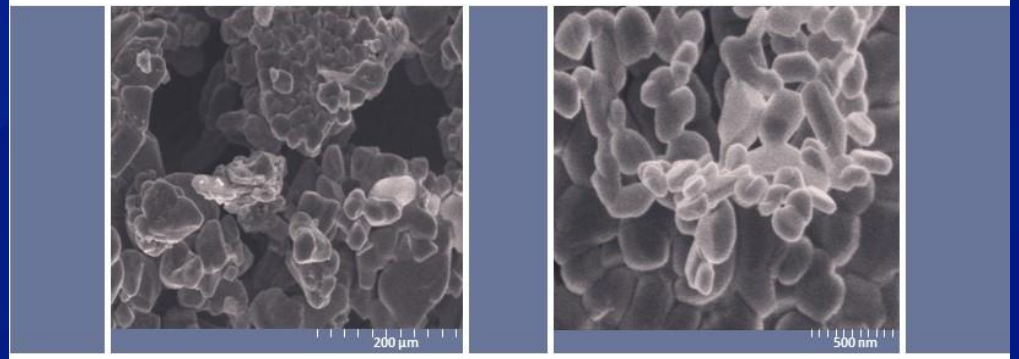
Occupational Exposure to Titanium Dioxide



DEPARTMENT OF HEALTH AND HUMAN SERVICES
Centers for Disease Control and Prevention
National Institute for Occupational Safety and Health

Two size ranges: <100nm ultrafine
> 100nm fine

Public draft – 2004
Published 2011

Hazard Classification for Ultrafine (Nanoscale) TiO_2 <100nm

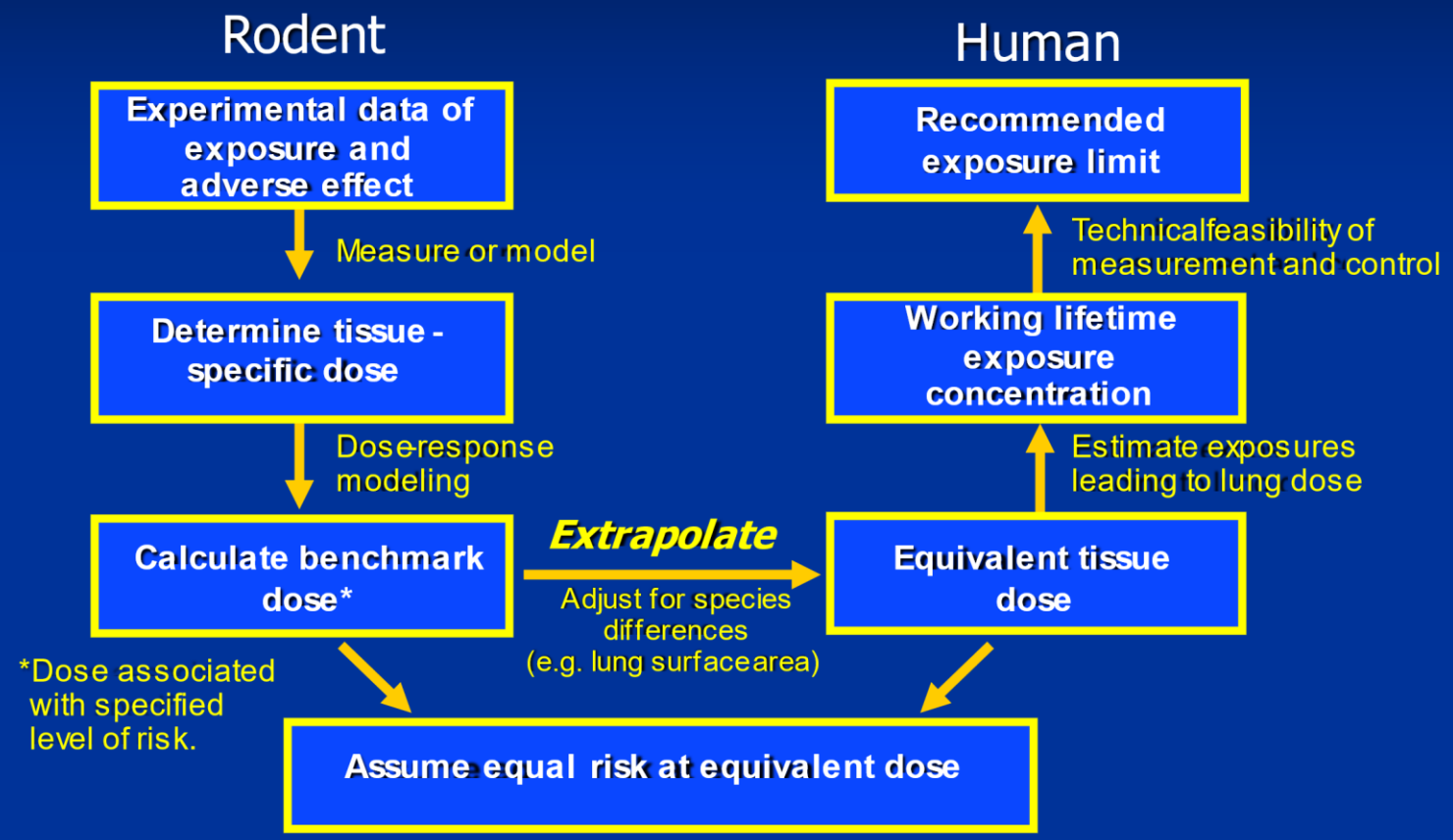
- Weight of evidence suggests rat tumor response to ultrafine TiO_2
  - Results from secondary genotoxic mechanism
  - Related to physical form of inhaled particle (i.e., particle surface) rather than the chemical compound itself
  - Rat tumorigenic data are sufficient and appropriate for making preventive recommendations
- Classification
  - Potential Occupational Carcinogen

Ultrafine (Nanoscale, <100nm) TiO_2

- Recommended Exposure Limit (respirable fraction)
  - Estimated to reduce risk of lung cancer below 1 in 1,000 over a 45-year working life time
  - OEL: 0.3 mg/m^3 (TWA for up to 10 hrs/day during a 40 hour week for a working lifetime)

Quantitative Risk Assessment (QRA) Methods to Develop Recommended Exposure Limits for Inhaled Particles

Based on Kuempel et al. [2006]

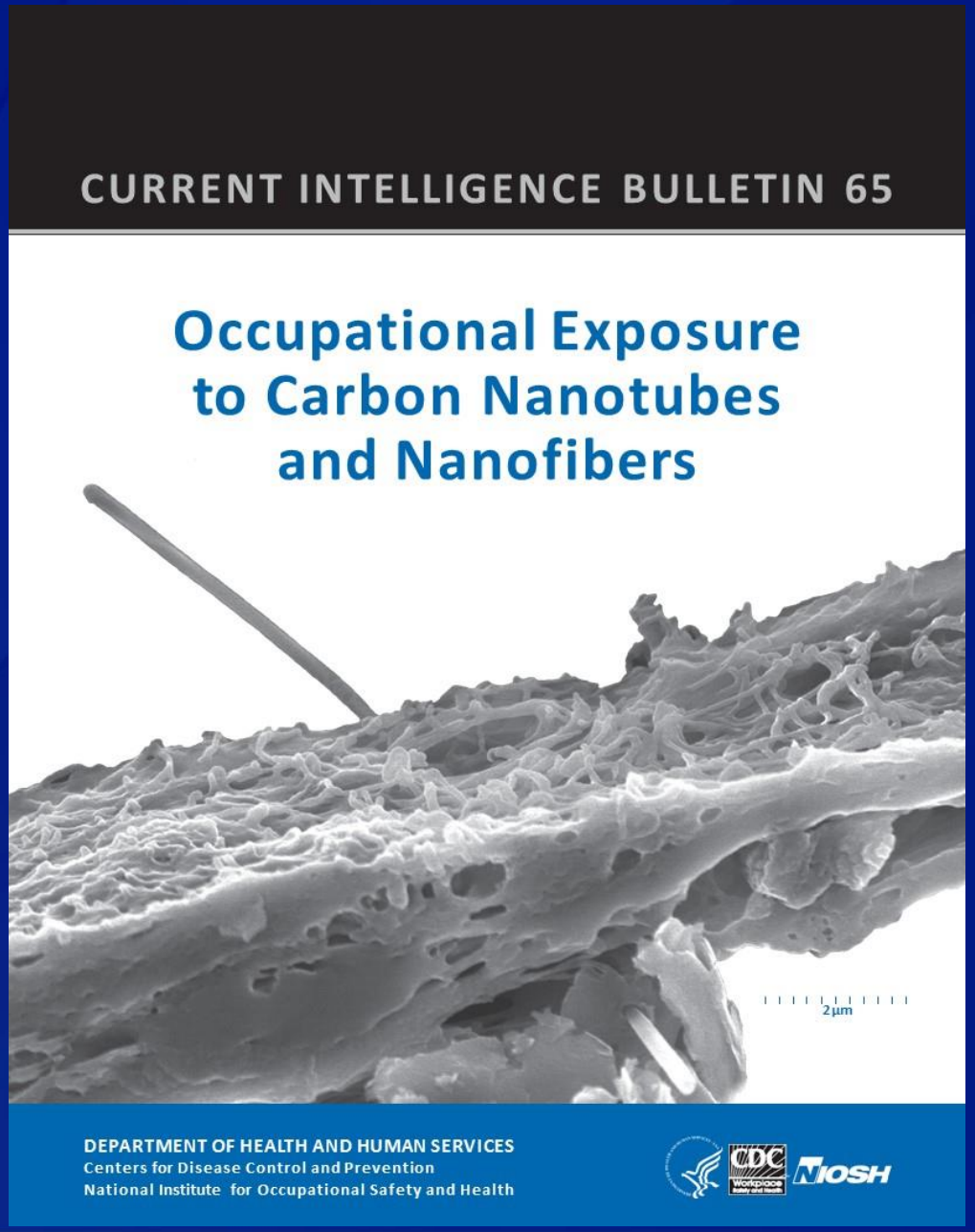


Fine TiO_2

- Recommended Exposure Limit (respirable fraction)
  - NIOSH used all tumor data when conducting dose-response modeling
    - *Excluding squamous cell keratinizing cystic tumors
  - OEL: 2.4 mg/m^3 (TWA for up to 10 hrs/day over a working below 1 in 1,000)
  - QRA indicates lifetime risk of lung cancer of 1 in 1,000 at 2.4 mg/m^3 (95% Lower Confidence Limit)

Critical Issues

- Generalizability to all types of TiO_2
  - Crystal structure (anatase, rutile) appears not to modify significantly TiO_2 inflammation or tumor response; depends on particle surface area
  - TiO_2 toxicity does not appear attenuated by coatings
- Risk assessment should be used as a baseline
  - Toxicity may be increased by particle treatment or process modification



Public draft – 2010
Published 2013

Rationale for Development of OEL

- Several animal studies showed pulmonary fibrosis (early onset, persistent) and granulomatous inflammation from carbon nanotube (CNT) exposure
- Associated with both unpurified and purified CNT (raw metal contaminated)
- Effects occurring at relatively low dose
- Ability of CNT to persist and migrate to pleura
- Other adverse effects (e.g. aneuploidy)

Carbon Nanotube Risk Assessment

- Focus: Preventing chronic occupational lung disease over a working lifetime
- No epidemiology studies yet in CNT workers

Carbon Nanotube Risk Assessment

- Animal dose-response data available
  - Several single- or short-term exposure studies in rats and mice
  - Two subchronic (13 wk) inhalation studies in rats
  - Responses: Early-stage inflammation, granuloma, and fibrosis; persistent or progressive after the end of exposure

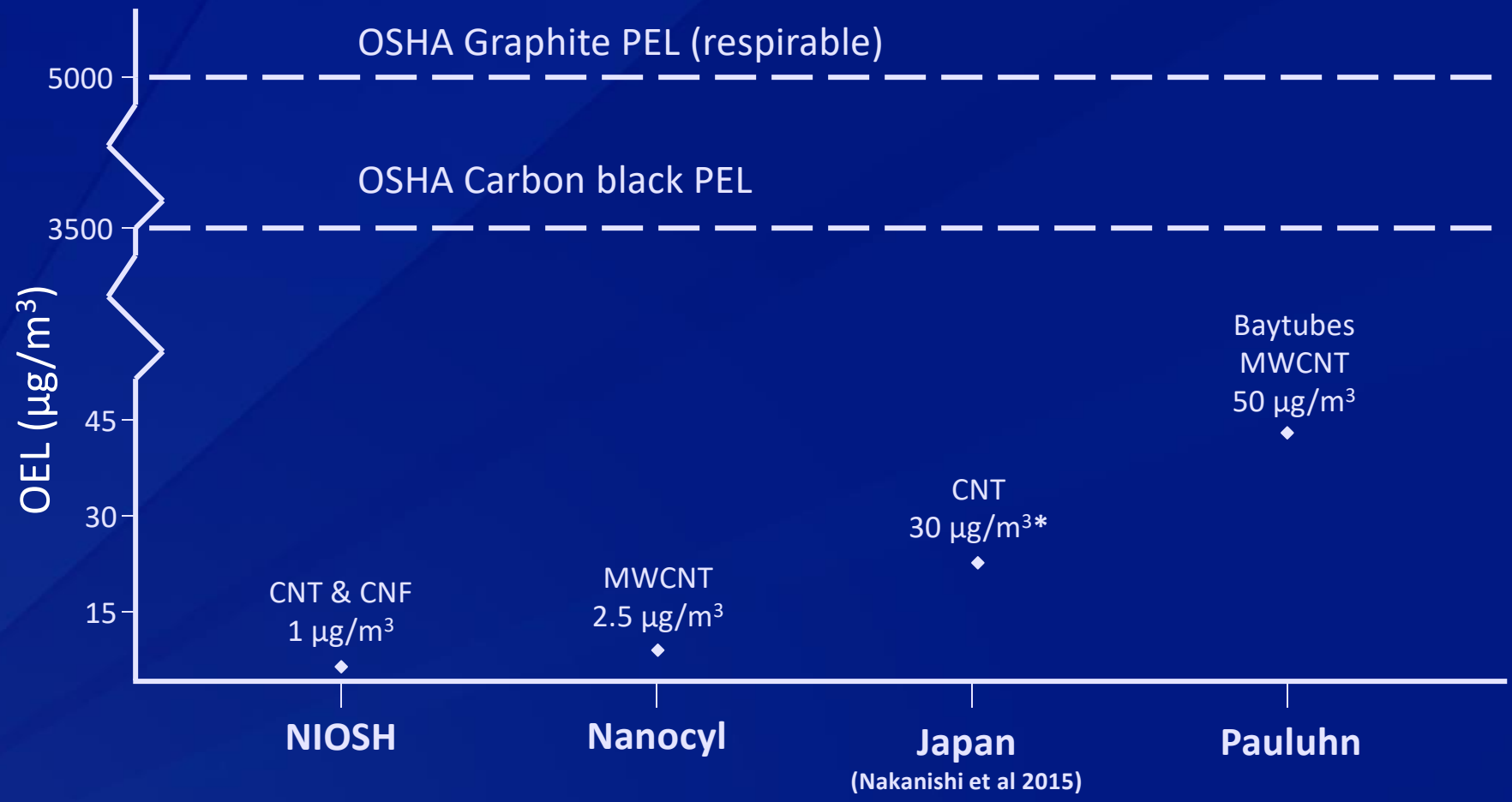
Issues in the Quantitative Risk Assessment (QRA) for CNT

- Interpretation of fibrosis data
  - Endpoint: Alveolar connective tissue (septal) thickening of minimal or higher grade
    - Observed in short-term and subchronic studies
    - Persisted for six months post exposure
  - Do not consider this response—if it happened in worker—to be acceptable

Issues in the Quantitative Risk Assessment (QRA) for CNT (cont'd)

- Use of benchmark dose methodology versus NOAEL/LOAEL
  - Statistical advantage of BMD
  - BMD(L) estimates similar to NOAEL or LOAEL values
- Mass-based versus CNT count-based OEL

OELs for Carbon Nanotubes



BSI—0.01 f/ml [benchmark exposure limit-BEL] high aspect ratio nanomaterials –established at 1/10 asbestos OEL

*Period-limited (15-yr).

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ISSN: 1743-5390 (print), 1743-5404 (electronic)

Nanotoxicology

Nanotoxicology, 2016; 10(7): 945–956
 DOI: 10.3109/17435390.2016.1148793

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ORIGINAL ARTICLE

Occupational exposure limit for silver nanoparticles: considerations on the derivation of a general health-based value

Brittany A. Weldon[1,2], Elaine M. Faustman[1,2], Günter Oberdörster[3], Tomomi Workman[1,2], William C. Griffith[1,2], Carsten Kneuer[4], and Il Je Yu[5]

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Abstract

With the increased production and widespread commercial use of silver nanoparticles (AgNPs), human and environmental exposures to silver nanoparticles are inevitably increasing. In particular, persons manufacturing and handling silver nanoparticles and silver nanoparticle containing products are at risk of exposure, potentially resulting in health hazards. While silver dusts, consisting of micro-sized particles and soluble compounds have established occupational exposure limits (OELs), silver nanoparticles exhibit different physicochemical properties from bulk materials. Therefore, we assessed silver nanoparticle exposure and related health hazards in order to determine whether an additional OEL may be needed. Dosimetric evaluations in our study identified the liver as the most sensitive target organ following inhalation exposure, and as such serves as the critical target organ for setting an occupational exposure standard for airborne silver nanoparticles. This study proposes an OEL of 0.19 $\mu g/m^3$ for silver nanoparticles derived from benchmark concentrations (BMCs) from subchronic rat inhalation toxicity assessments and the human equivalent concentration (HEC) with kinetic considerations and additional uncertainty factors. It is anticipated that this level will protect workers from potential health hazards, including lung, liver, and skin damage.

Keywords

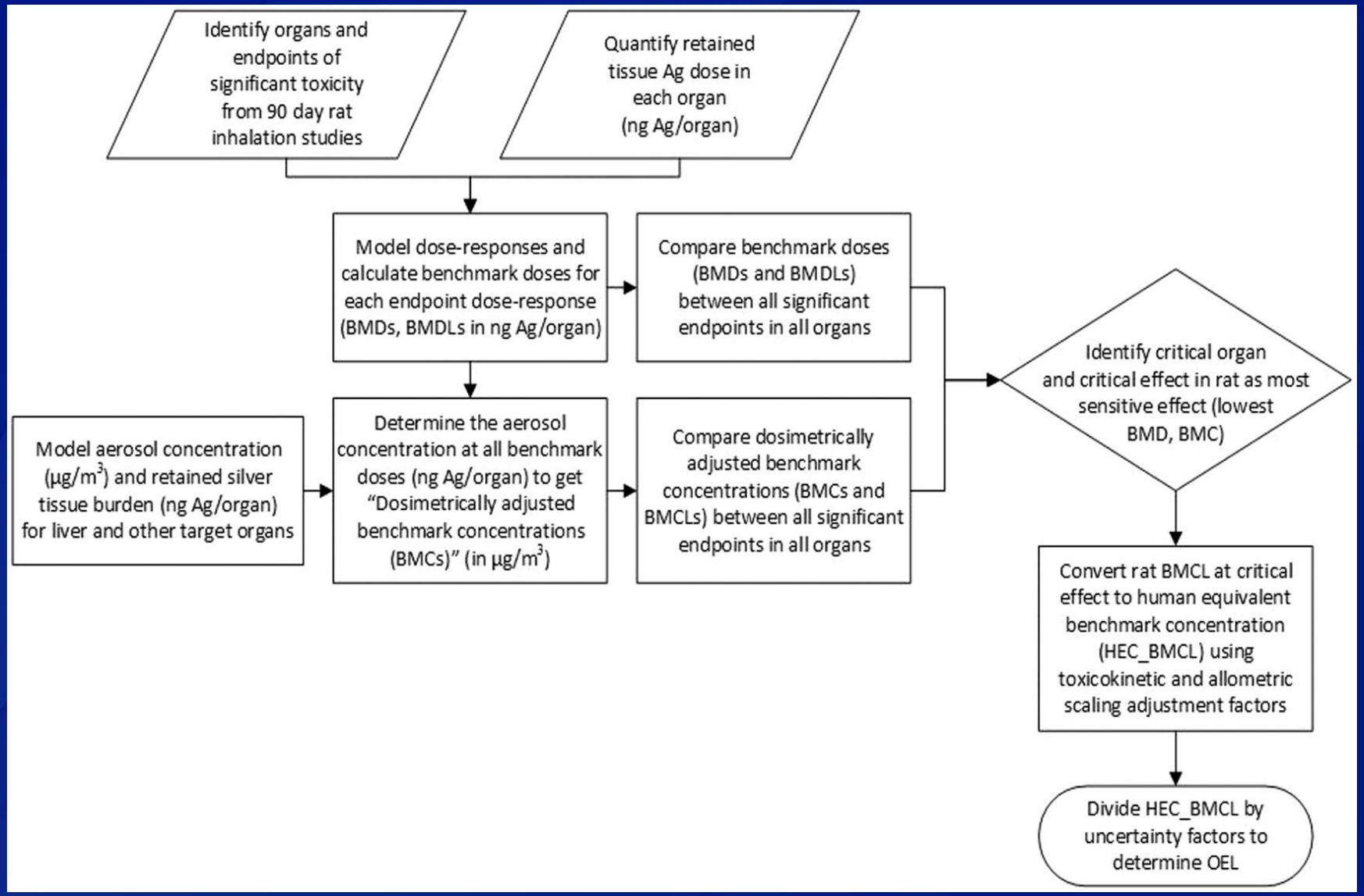
Clearance, dosimetry, occupational exposure, silver nanoparticles, subchronic inhalation

History

Received 10 November 2015
Revised 26 January 2016
Accepted 27 January 2016
Published online 9 March 2016

Nano Silver (Ag) Risk Assessment and OEL (Weldon et al. 2016)

- Identified most relevant studies and toxicity end points
- Modeled dose-response for each end point
  - Calculated benchmark dose (BMD)
- Used tissue and aerosol exposure concentration to determine aerosol concentration at each BMD
- Extrapolation to human utilizes modified human equivalent concentration equation



(Weldon et al 2016)

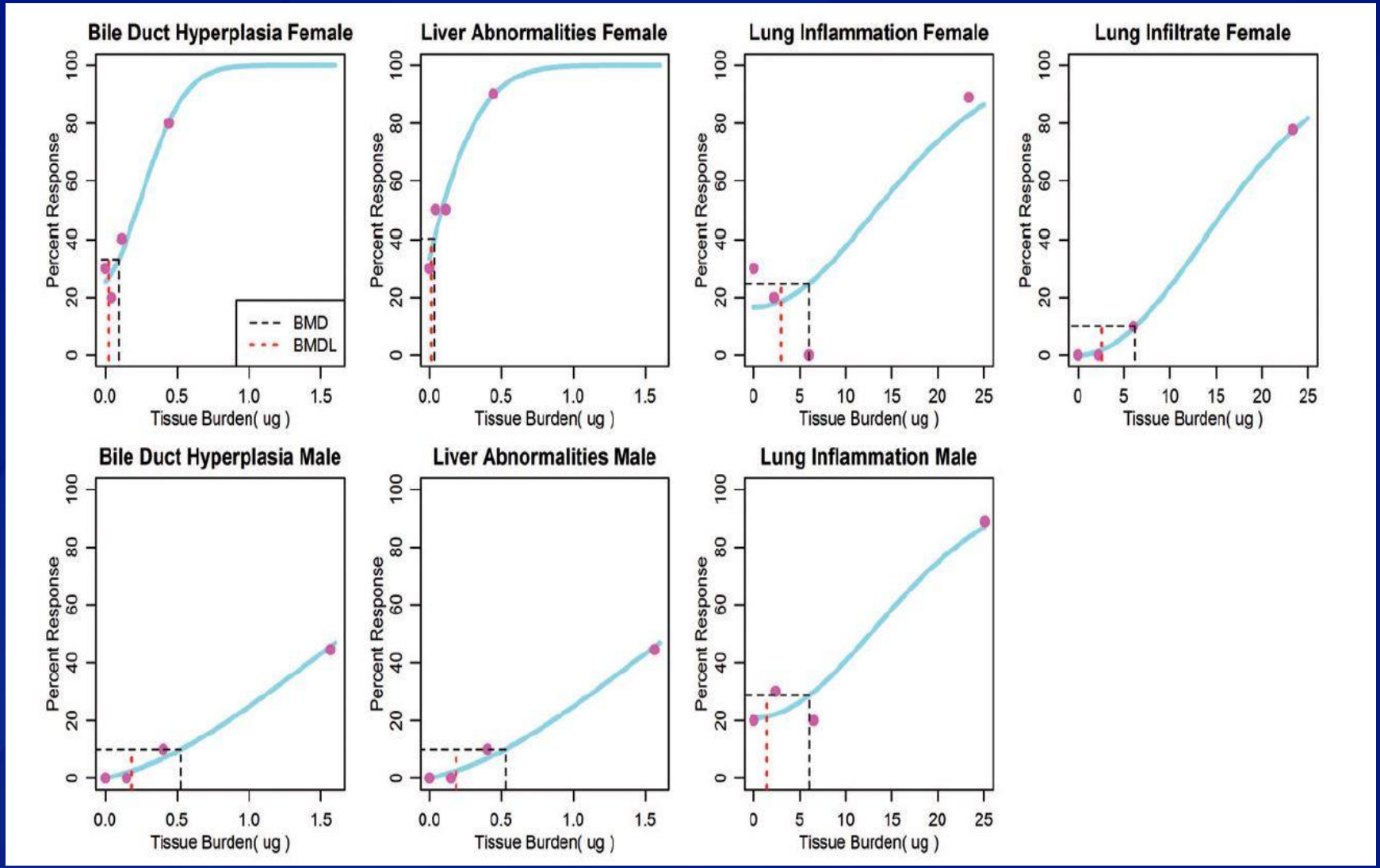


Figure 2. Benchmark dose (BMD) analysis of significant histopathology endpoints of toxicity in male and female rats after subchronic inhalation of AgNPs (Sung et al., 2009). Dose–response curves are modeled as multistage polynomial degree 2 model for dichotomous data. BMDs (upper dashed lines) and BMDLs (lower dashed lines) are calculated as a 10% change in response relative to control and are indicated as tissue burden (mg silver/ organ). BMDs and BMDLs are summarized in Table 2. (Weldon et al 2016)

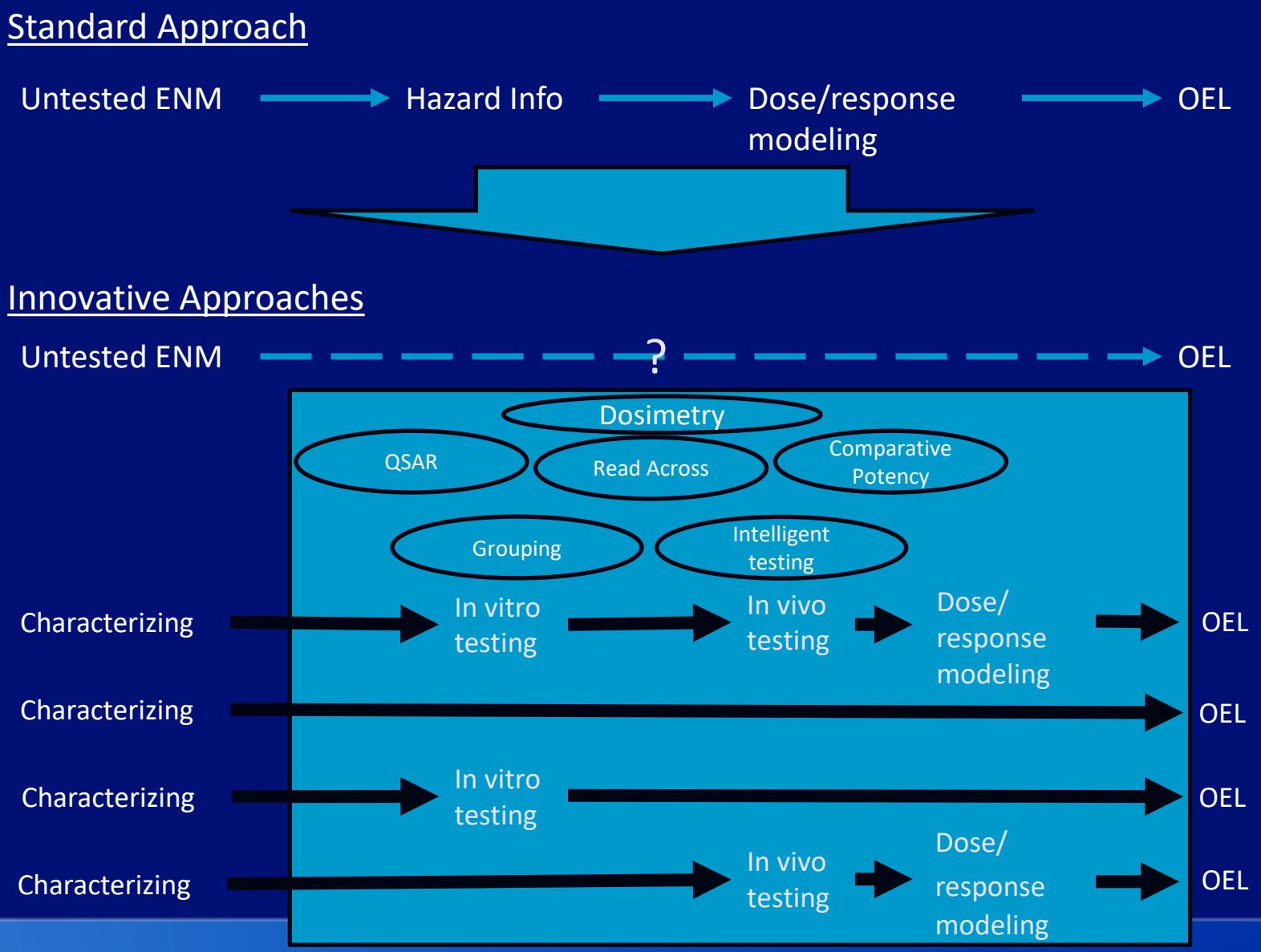
Current OEL for Silver 10 µ/m^3

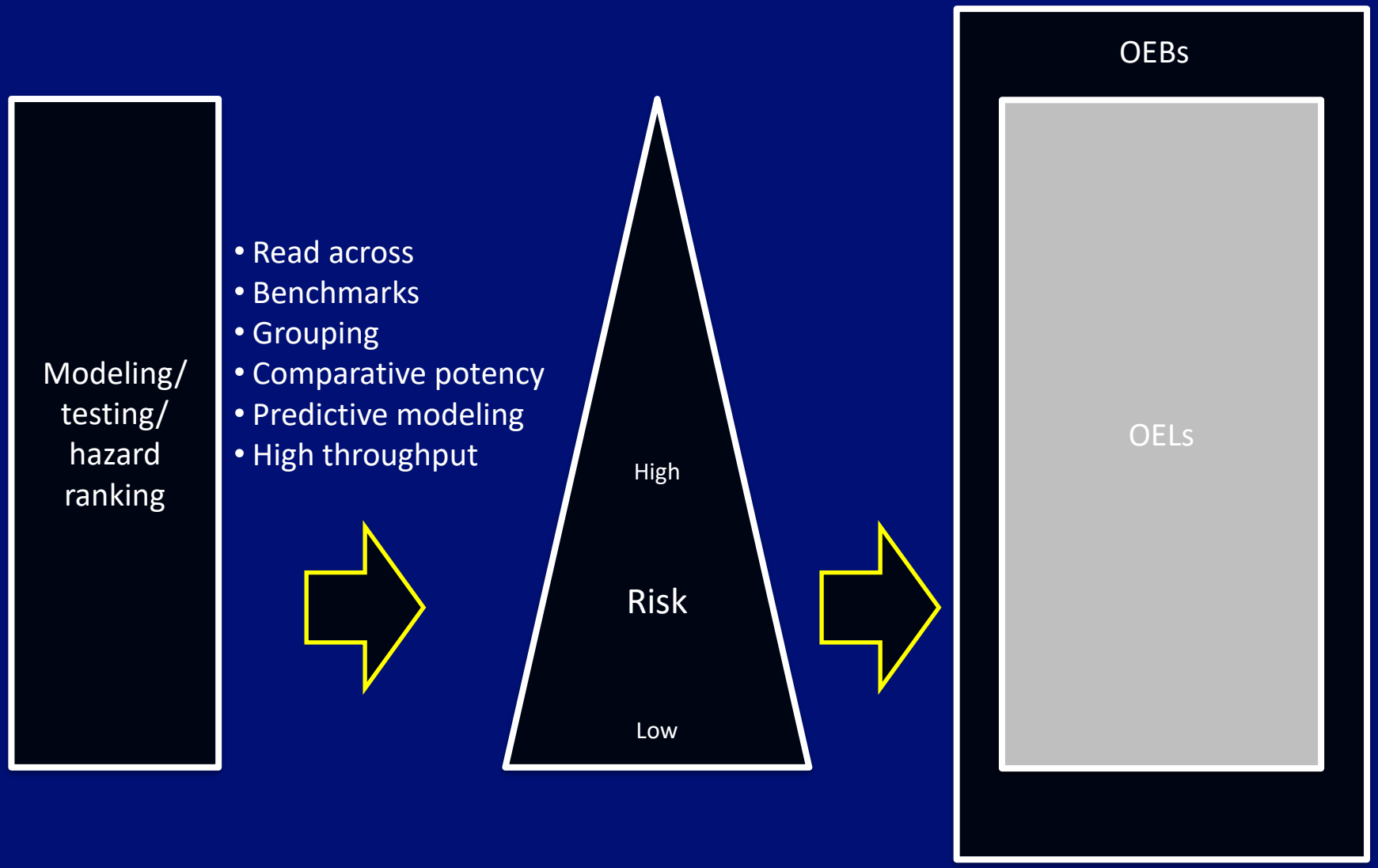
Weldon analysis:

- Used inhalation exposure of rats
- OEL derived from benchmark concentrations and human equivalent concentration
- Proposed OEL: 0.19 µ /m^3

(Weldon 2016)

Frontier of Risk Assessment For ENM OEL Development




Modeling/ testing/ hazard ranking
• Read across
• Benchmarks
• Grouping
• Comparative potency
• Predictive modeling
• High throughput
High
Risk
Low
OEBs
OELs

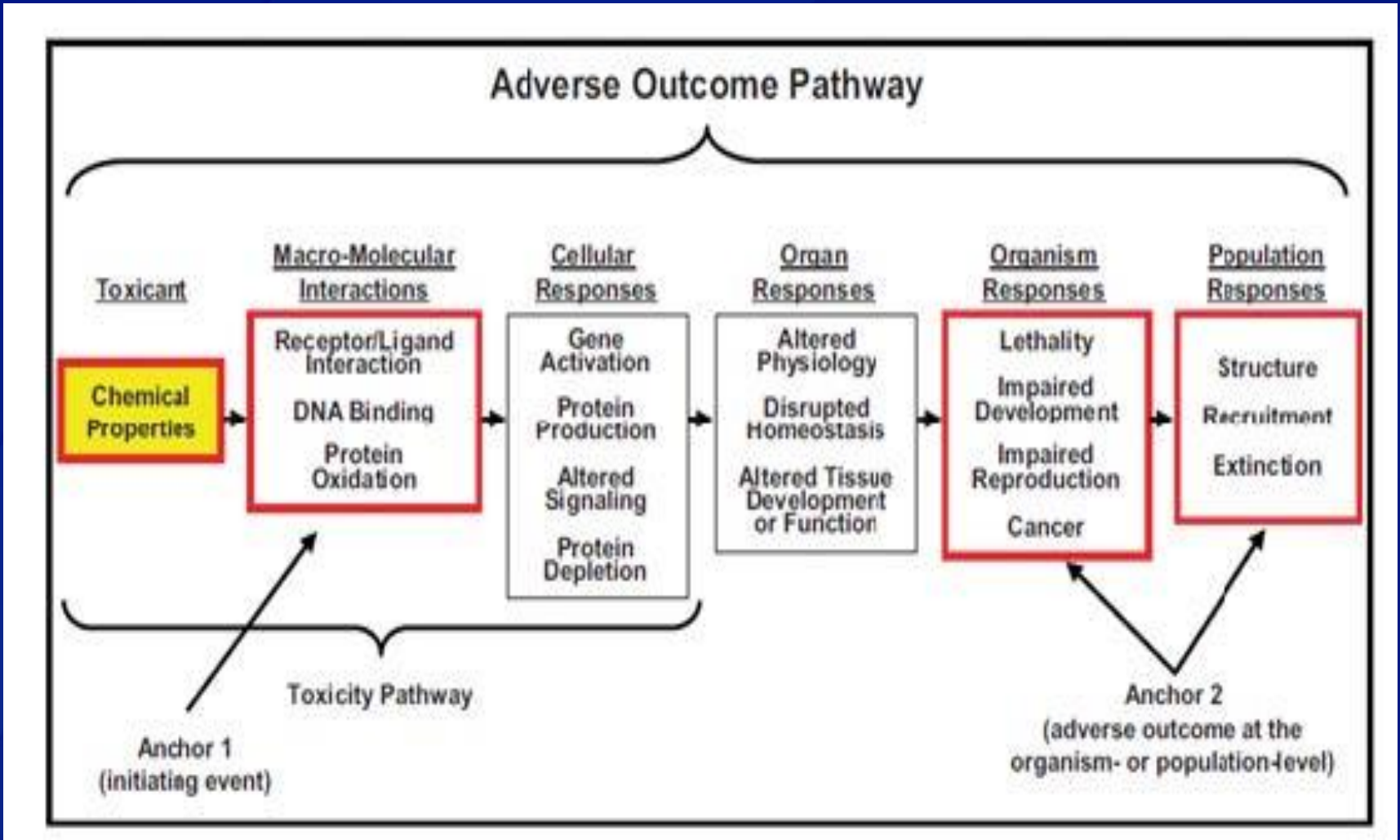


Figure 1. An Adverse Outcome Pathway is a biological map from the molecular initiating event through the resulting adverse outcome that describes both mechanism and mode of action. From: Ankley et al. (2010).

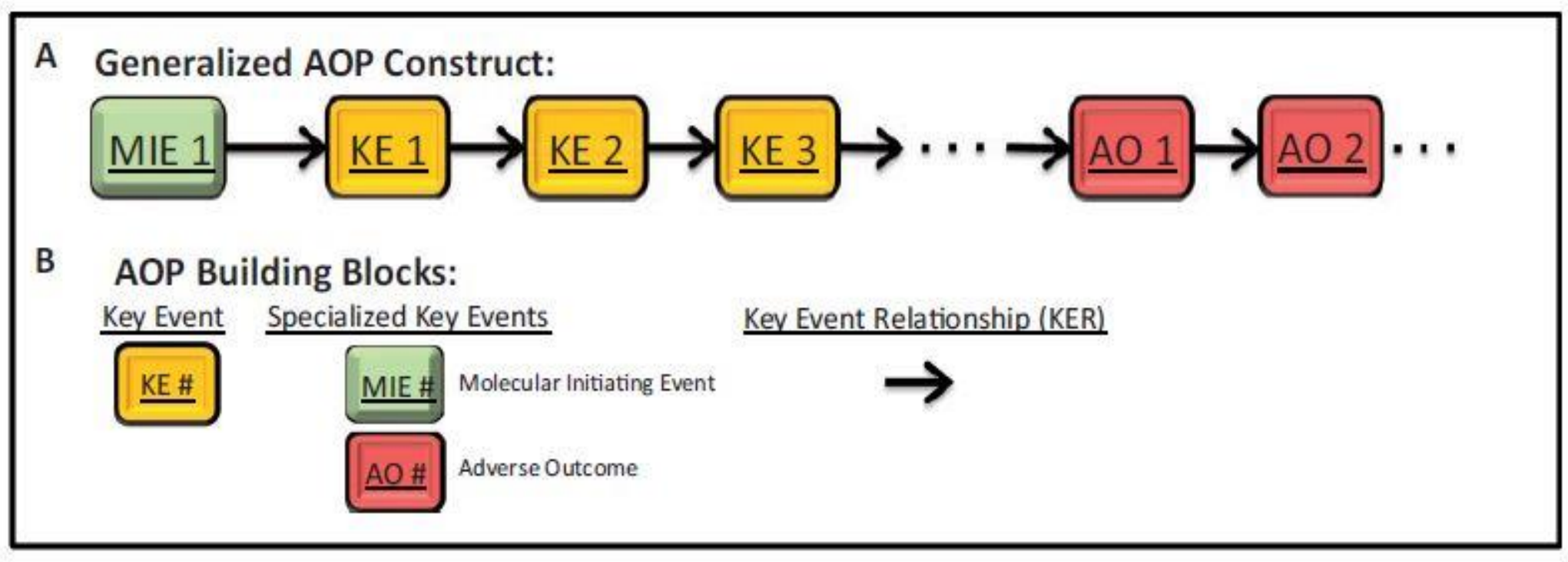
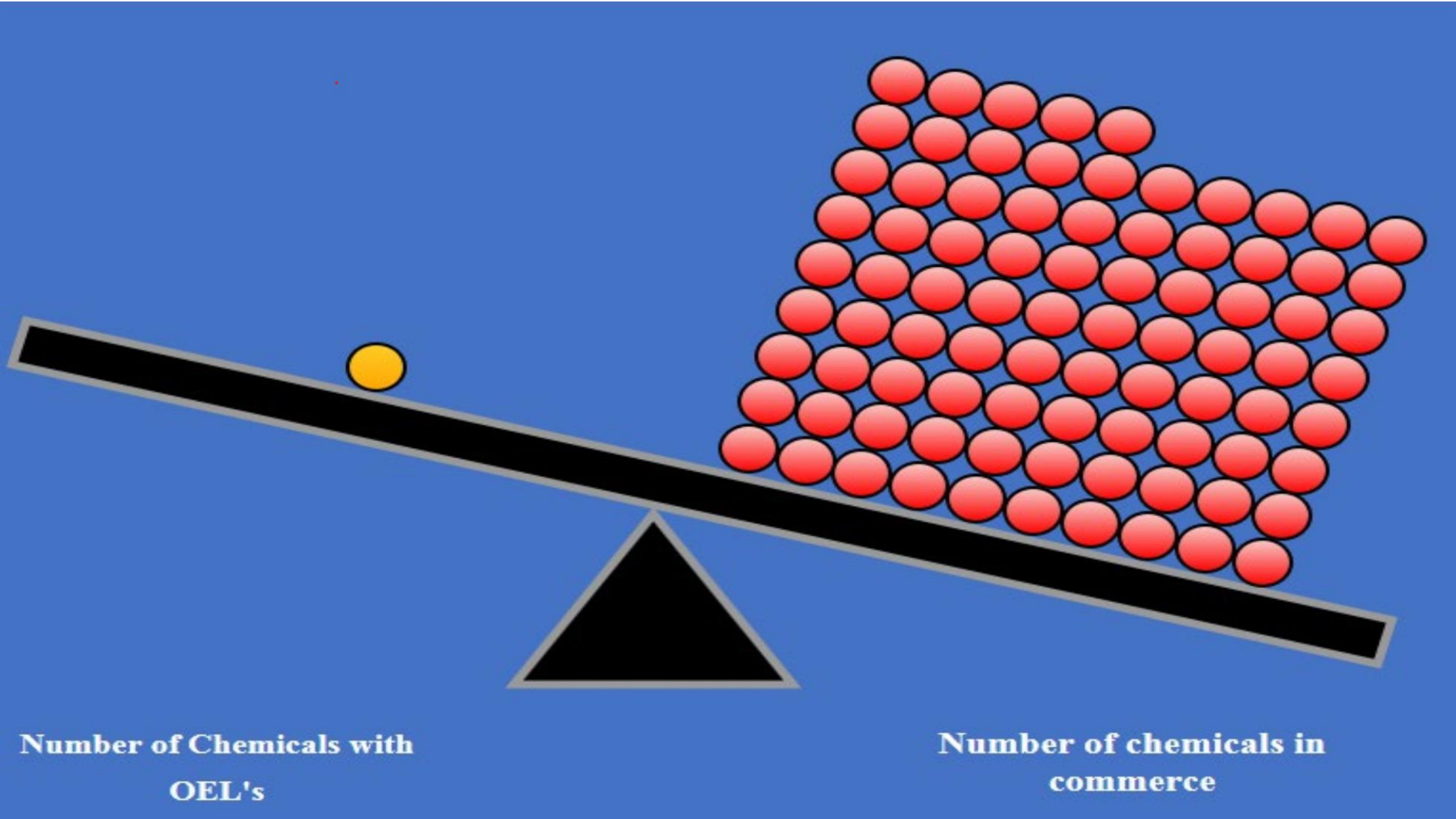


FIG. 1. Graphical representation of a generalized adverse outcome pathway (AOP; A). Each AOP is composed of two key components (B), key events (KEs) and key event relationships (KERs). Additionally, there are two specialized KEs, molecular initiating events (MIEs) and adverse outcomes (AOs) that anchor an AOP description. Individual AOPs sharing KEs or KERs can be represented as an AOP network (C). The AOP network depicted is composed of four individual AOPs, each representing a unique sequence of KEs linking an MIE to AO: AOP 1 [MIE1, KE1, KE2, KE3, AO1, AO2]; AOP 2 [MIE2, KE4, KE1, KE2, KE3, AO1, AO2]; AOP 3 [MIE1, KE1, KE2, KE5, KE6, AO3]; AOP 4 [MIE2, KE4, KE1, KE2, KE5, KE6, AO3]. Color image is available in the online version of the article.

AOP Cautionary Note

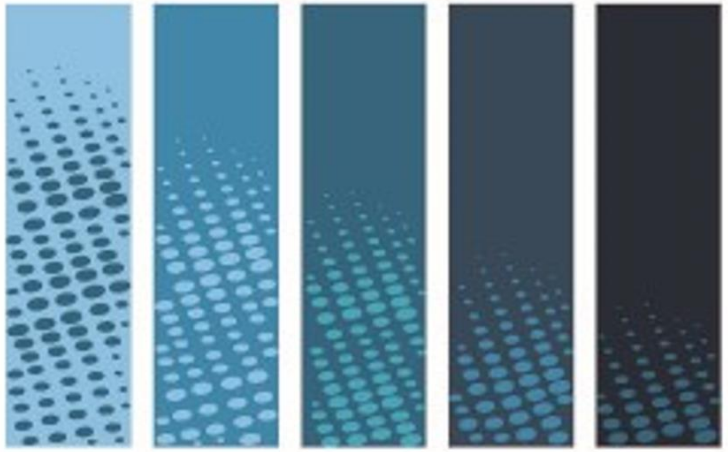
- Premature to use for Risk Management purposes
- May restrict needed toxicological investigation
- Difficult to validate
- May falsely present illusion of safety
- Need to be based on robust data when used as a predictor tool

Pesticide Action Network Europe (2016)


Number of Chemicals with OEL's
Number of chemicals in commerce

CURRENT INTELLIGENCE BULLETIN 69

The NIOSH Occupational Exposure Banding Process for Chemical Risk Management



What is Occupational Exposure Banding?

A mechanism to quickly and accurately assign chemicals into “categories” or “bands” based on their health outcomes and potency considerations

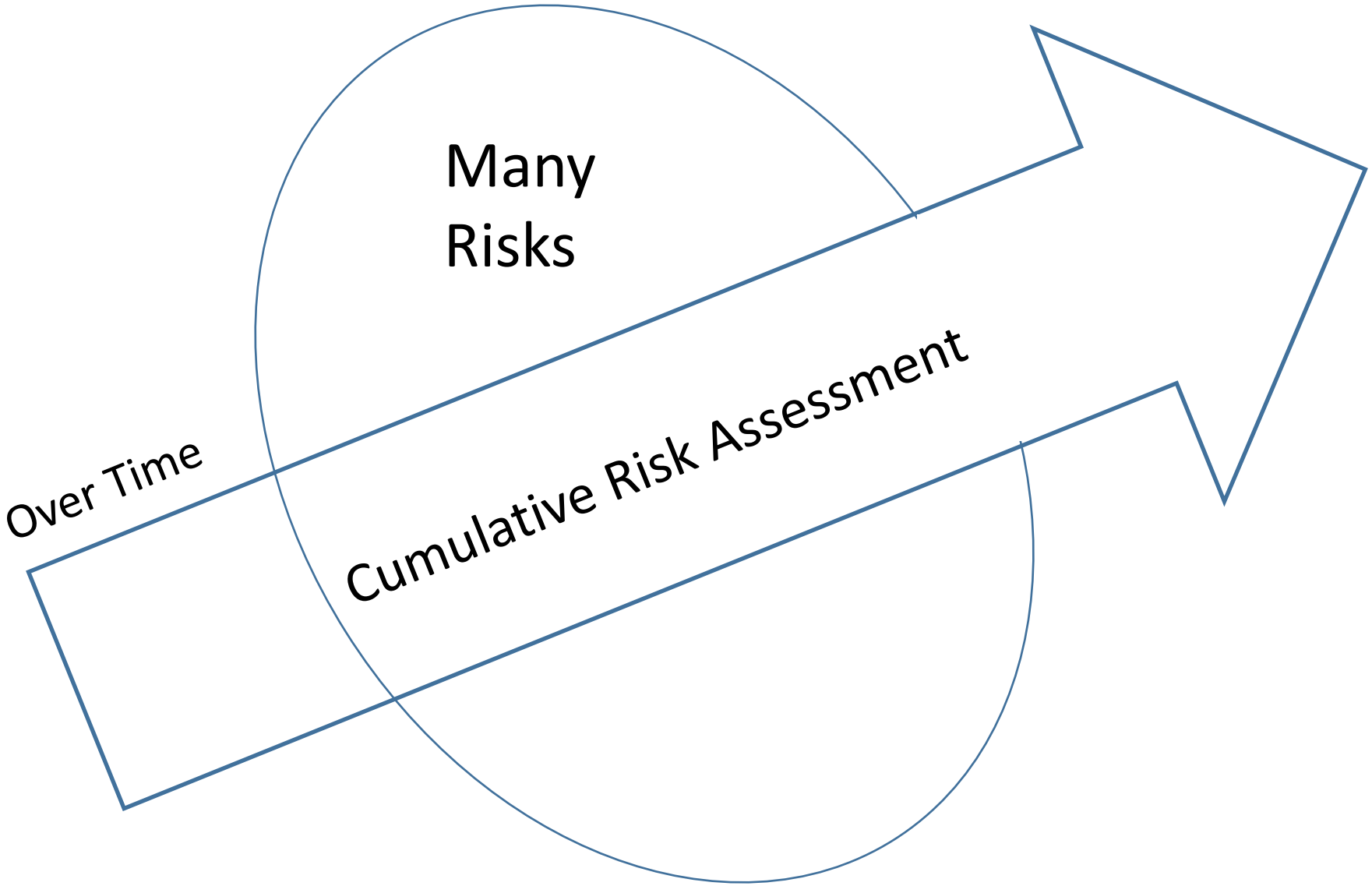
How is the process organized?

Bands are assigned based on the findings for nine standard toxicological endpoints:

- acute toxicity
- skin corrosion and irritation
- serious eye damage and irritation
- respiratory sensitization
- skin sensitization
- genotoxicity
- carcinogenicity
- reproductive/developmental toxicity
- specific target organ toxicity resulting from repeated exposure

IMPORTANT POINT

An OEB is not meant to replace an OEL, rather it serves as a starting point to inform risk management decisions.


Many
Risks
Over Time
Cumulative Risk Assessment

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Aggregate Exposure and Cumulative Risk Assessment—Integrating Occupational and Non-occupational Risk Factors

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[7]Agency for Toxic Substances and Disease Registry, Centers for Disease Control and Prevention, Atlanta, Georgia

Occupational exposure limits have traditionally focused on preventing morbidity and mortality arising from inhalation exposures to individual chemical stressors in the workplace. While central to occupational risk assessment, occupational exposure limits have limited application as a refined disease prevention tool because they do not account for all of the complexities of the work and non-occupational environments and are based on varying health endpoints. To be of greater utility, occupational exposure limits and other risk management tools could integrate broader consideration of risks from multiple exposure pathways and routes (aggregate risk) as well as the combined risk from exposure to both chemical and non-chemical stressors, within and beyond the workplace, including the possibility that such exposures may cause interactions or modify the toxic effects observed (cumulative risk). Although still at a rudimentary stage in many cases, a variety of methods and tools have been developed or are being used in allied risk assessment fields to incorporate such considerations in the risk assessment process. These approaches, which are collectively referred to as cumulative risk assessment, have potential to be adapted or modified for occupational scenarios and provide a tangible path forward for occupational risk assessment. Accounting for complex exposures in the workplace and the broader risks faced by the individual also requires a more complete consideration of the composite effects of occupational and non-occupational risk factors to fully assess and manage worker health problems. Barriers to integrating these different factors remain, but new and ongoing community-based and worker health-related initiatives may provide mechanisms for identifying and integrating risk from aggregate exposures and cumulative risks from all relevant sources, be they occupational or non-occupational.

Keywords aggregate exposure, cumulative risk, occupational

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INTRODUCTION

Occupational exposure limits (OELs) have traditionally focused on preventing morbidity and mortality arising from inhalation exposures to individual chemical stressors in the workplace. While there are other strategies for pursuing or promoting risk prevention and avoidance of occupational hazards, many of which enhance effectiveness when used in conjunction with OELs, the theme of this manuscript and its accompanying manuscripts pertains specifically to the establishment of OELs and the potential for incorporating new science into this practice. The basis and impetus for OELs

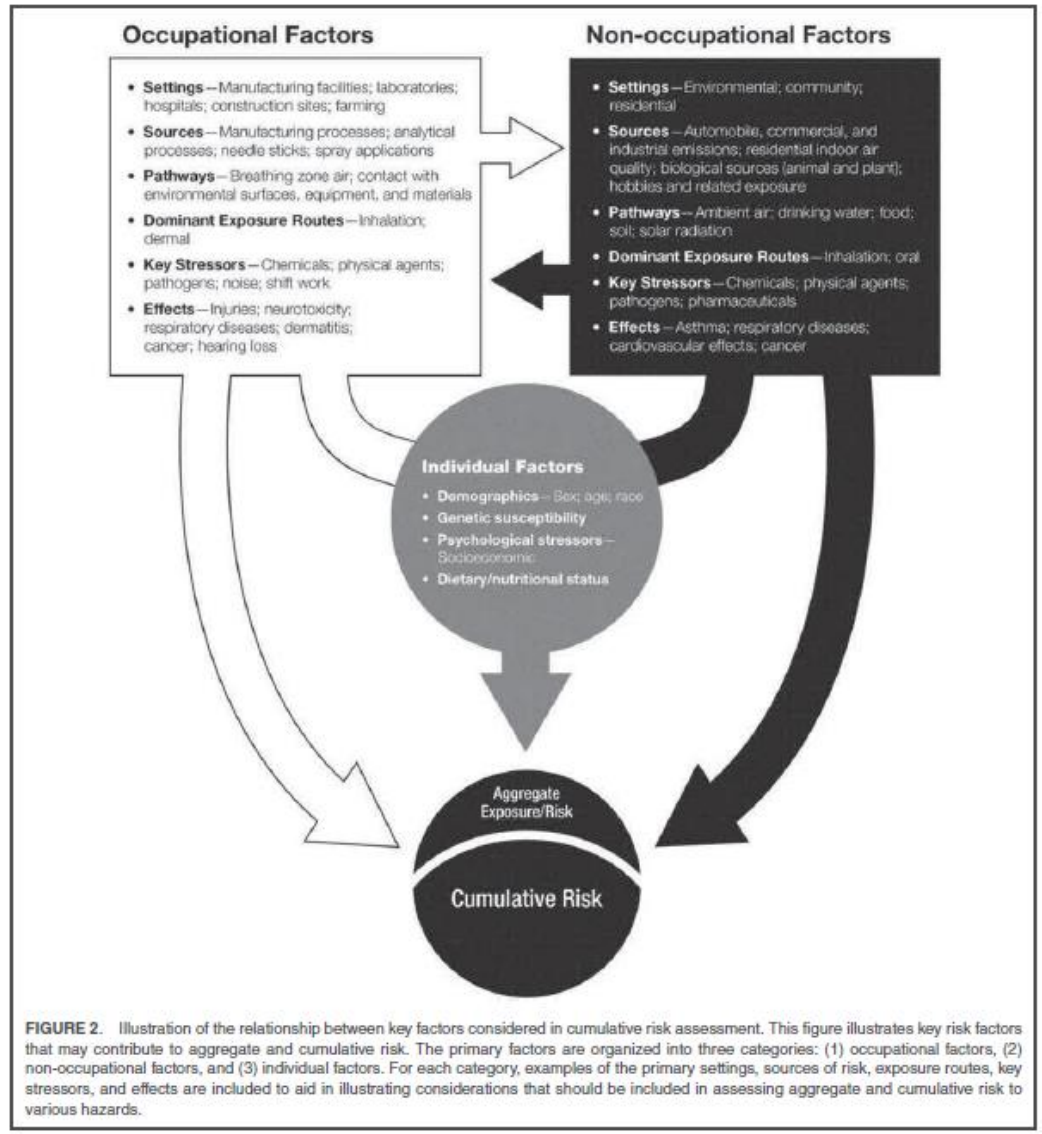

FIGURE 2. Illustration of the relationship between key factors considered in cumulative risk assessment. This figure illustrates key risk factors that may contribute to aggregate and cumulative risk. The primary factors are organized into three categories: (1) occupational factors, (2) non-occupational factors, and (3) individual factors. For each category, examples of the primary settings, sources of risk, exposure routes, key stressors, and effects are included to aid in illustrating considerations that should be included in assessing aggregate and cumulative risk to various hazards.

uncertainties associated with the assessment are described, and estimates of cumulative risk are interpreted in the context of their significance, reliability, and overall confidence. Various approaches are available for addressing the variability and uncertainty in risk estimates including sensitivity analyses and one-dimensional and two-dimensional stochastic analyses such as with Monte Carlo simulation.

With respect to the second phase of cumulative risk assessment, several techniques have been developed to examine environmental and occupational exposures. Three of the more common techniques are (1) exposure monitoring, (2) exposure modeling, and (3) biomonitoring. These methods are intended to provide estimates of the external exposure concentration to which the target population has been exposed or to provide

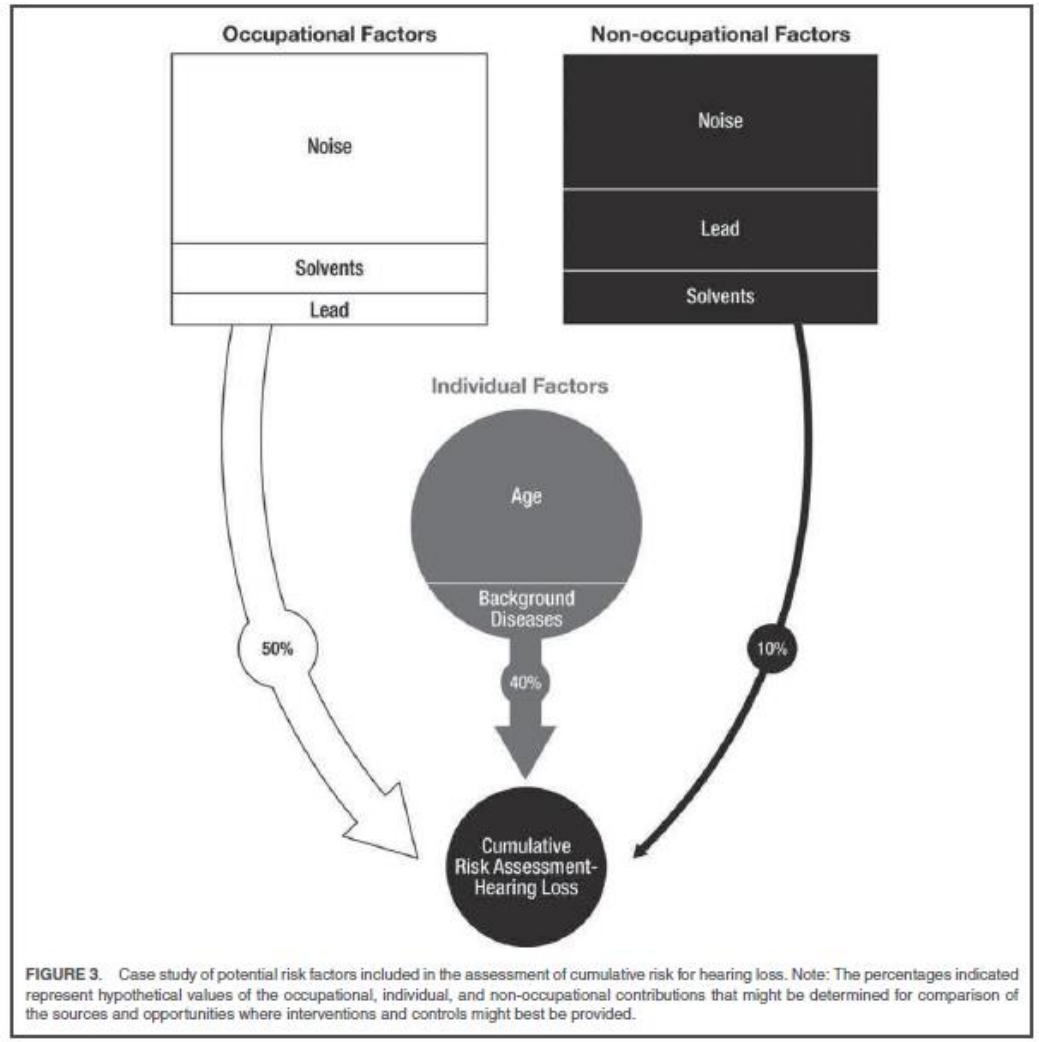

FIGURE 3. Case study of potential risk factors included in the assessment of cumulative risk for hearing loss. Note: The percentages indicated represent hypothetical values of the occupational, individual, and non-occupational contributions that might be determined for comparison of the sources and opportunities where interventions and controls might best be provided.

better reflect and characterize real-world situations. Emphasis in this area has gradually increased in the occupational safety and health community on the basis of recent frequency of symposia and information sessions on this topic; a case-in-point is the "Risk Assessment Symposium – Converging Risk Analysis, Management, and Perception" convened at the 2011 Professional Conference on Industrial Hygiene (PCIH 2011, Baltimore, MD, November 3–9). A proactive approach for accomplishing this goal is to incorporate such concepts in new chemical registration and use processes, where such techniques play an important role in preventing exposures before chemical use and introduction. With this goal in mind several steps to enhance current processes could be taken. Some of these include the following.

(a) Developing a concise review, building on descriptions above, of the degree to which:

- current risk assessment processes incorporate occupational scenarios; and
- occupational assessments incorporate considerations of risk assessment of aggregate exposures and cumulative risk assessment.

Safety Science 93 (2017) 143–151

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journal homepage: www.elsevier.com/locate/ssci

A method of identifying health-based benchmarks for psychosocial risks at work: A tool for risk assessment

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[b] Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, SE-171 77 Stockholm, Sweden
[c] Centre for Research on Ageing Health and Wellbeing, The Australian National University, Canberra, Australian Capital Territory 0200, Australia
[d] Ministry for Primary Industries, 25 The Terrace, Wellington 6140, New Zealand

ARTICLE INFO

ABSTRACT

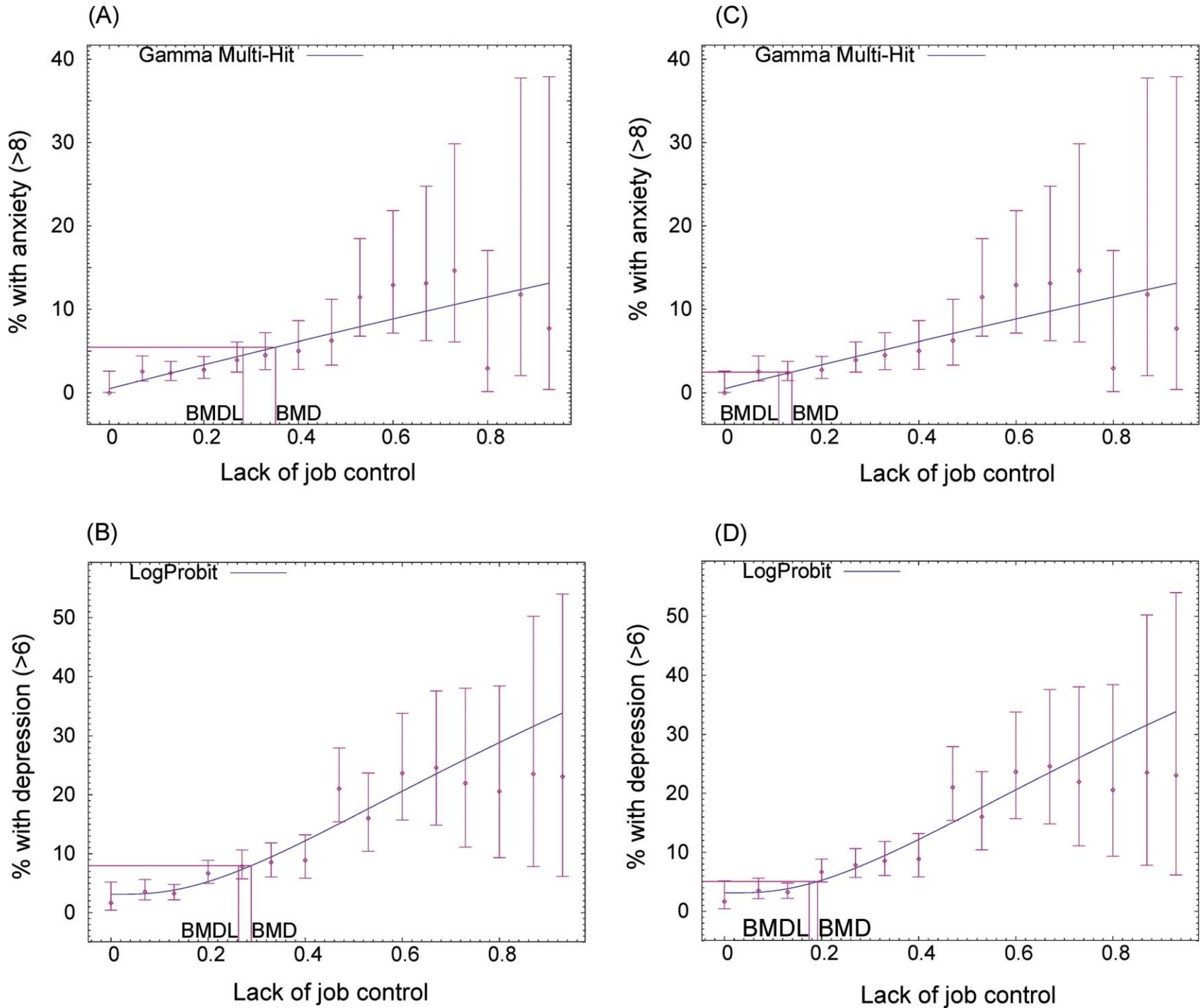
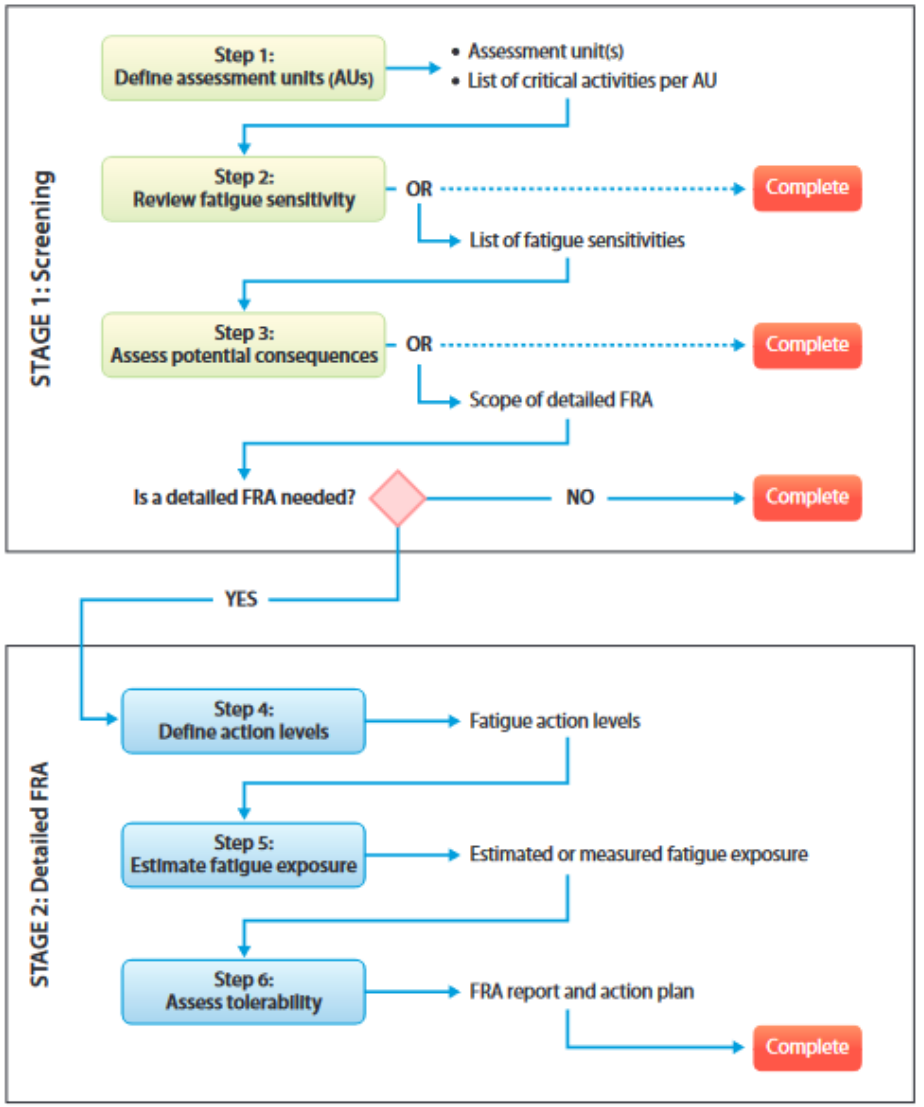

(A)
Gamma Multi-Hit
% with anxiety (>8)
Lack of job control
BMDL
BMD
(C)
Gamma Multi-Hit
% with anxiety (>8)
Lack of job control
BMDL
BMD
(B)
LogProbit
% with depression (>6)
Lack of job control
BMDL
BMD
(D)
LogProbit
% with depression (>6)
Lack of job control
BMDL
BMD

Figure 1 *Recommended process for performing a fatigue risk assessment*



(IPIECA, 2014)

International Journal of
Environmental Research and Public Health

MDPI

Article

Supporting Occupational Health and Safety Risk Assessment Skills: A Case Study of Five Companies

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Center for Safety Management and Engineering, CSME, Faculty of Management and Business, Tampere University, 33014 Tampere, Finland; maria.lindholm@tuni.fi (M.L.); sari.tappura@tuni.fi (S.T.)
* Correspondence: minna.rantala@tuni.fi

Abstract: Financial burden due to poor occupational safety practices remains high although occupational health and safety (OHS) have improved in recent years. Conducting risk assessment is one way to improve OHS. Workplaces may not have sufficient expertise in risk assessment. The aim of this study was to identify the needed OHS risk assessment skills, current support in the workplaces and the ways to improve risk assessment skills. This study was conducted with the Delphi survey for OHS experts ($n = 13$) and with interviews ($n = 41$) in the case companies. OHS experts agreed that the most significant skills were for employees to identify hazards and minimize risks in one's work; for supervisors to influence others with a good example; and for OHS experts to understand and manage the wholeness of safety practices and understand and manage the meaning, concepts, and criteria of risk assessment. The current main support methods were learning at work, training and written instructions. However, many of the interviewees felt that they had not received risk assessment training and that the support depended on their activity. Finally, the OHS experts determined that the most feasible ways to improve risk assessment skills were training, coaching and giving clear instructions. Likewise, the interviewees suggested various training methods. Based on these results, concrete development plans to improve risk assessment skills can be made.

Keywords: development; expertise; occupational health and safety; risk assessment; skill; support; training

Citation: Rantala, M.; Lindholm, M.; Tappura, S. Supporting Occupational Health and Safety Risk Assessment Skills: A Case Study of Five Companies. *Int. J. Environ. Res. Public*

Occupational Safety & Health (OSH) Risk Assessment Skills

Survey of 13 OSH Experts and 41 companies

Most significant skills

- Employees: Identify hazards and minimize risk in one's work
- Supervisors: influence others with a good example
- OSH Experts: Understand and manage the wholeness of safety practices and the meaning, concepts and criteria of risk assessment

(Rantala et al., 2022)

Figure 1. Opinions of occupational health specialists and managers on the most important risk assessment skills needed by the employee.

Figure 2. Opinions of occupational health specialists and managers on the most important risk assessment skills needed by the supervisor.

Figure 3. Opinions of the occupational health specialists and managers on the most important risk assessment skills needed by the expert.

Acknowledgements

- Robert Daniels
- Christine Whittaker
- Lauralynn McKernan
- Jenn Bakes
- Eileen Kuempel

Thank you

pschulte@cdc.gov