An Overview of NCD's Risk Assessment Process

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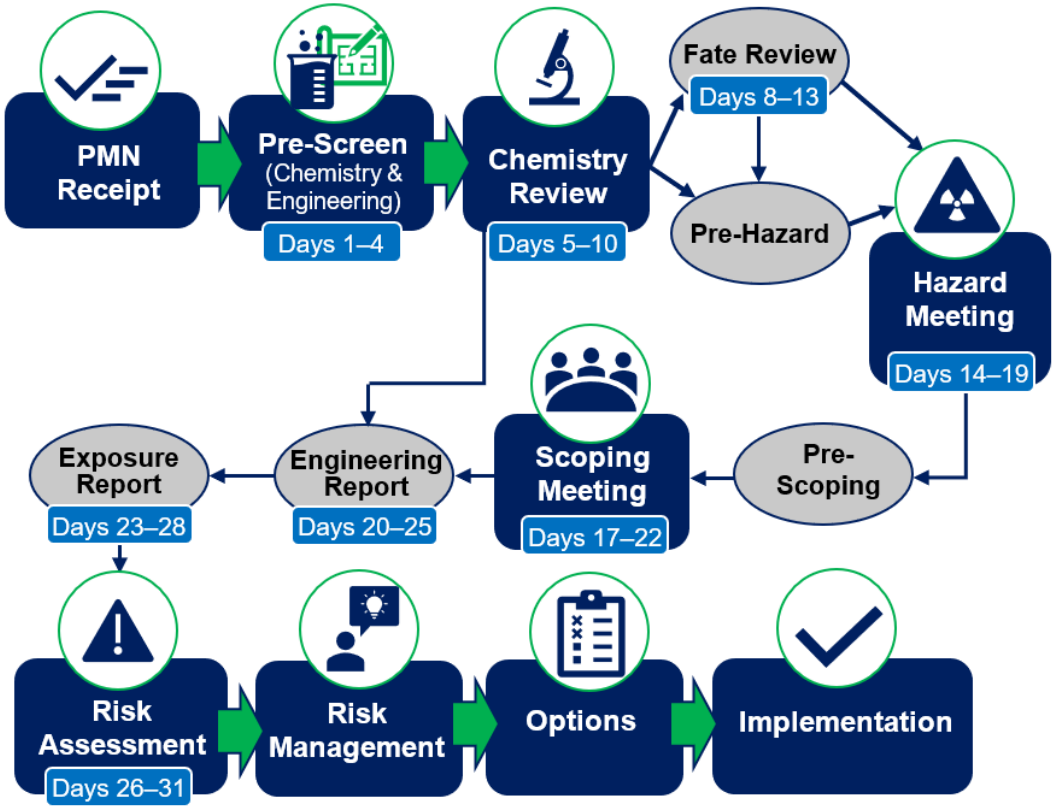
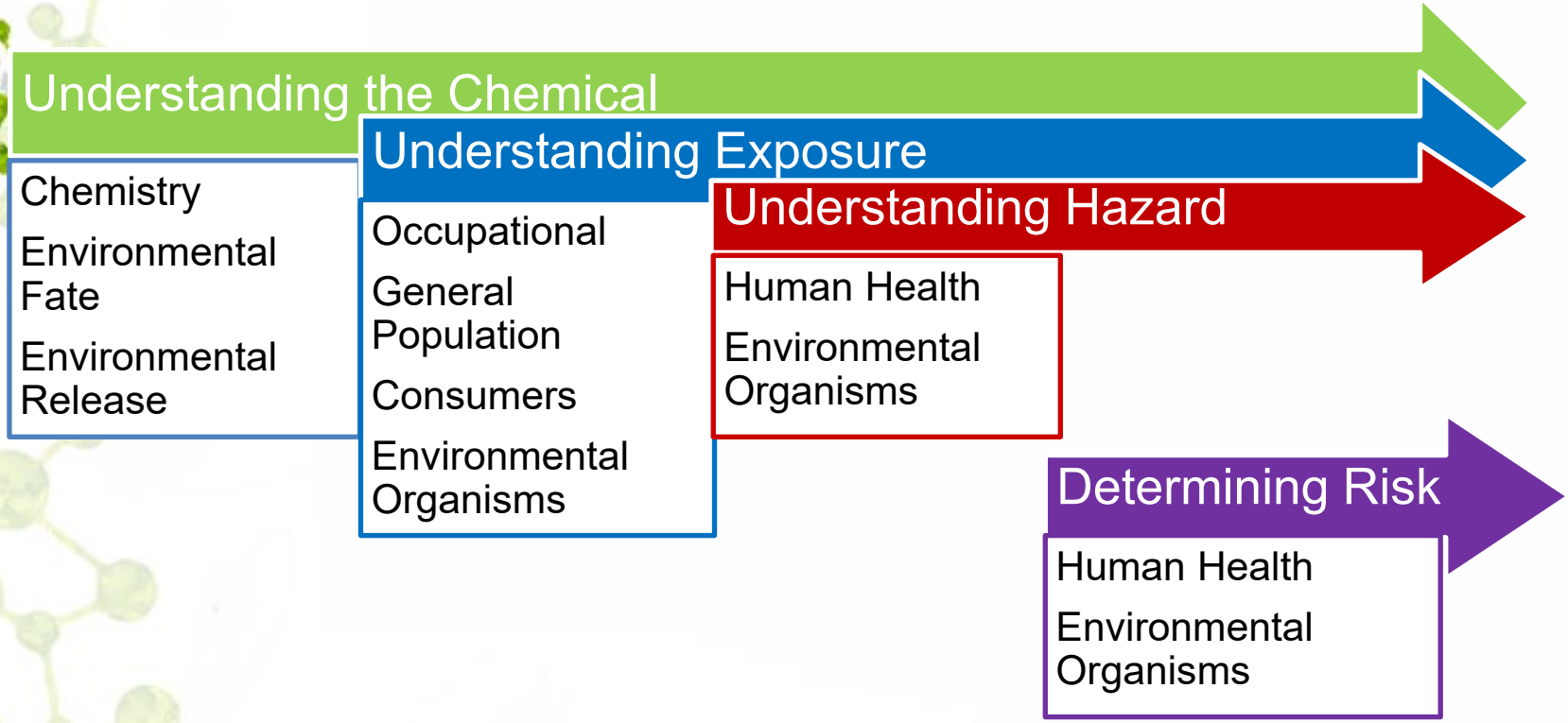
NCD Risk Assessment / Management review process



Office of Chemical Safety and Pollution Prevention

Risk Assessment Overview



Purpose

- This presentation will focus on the risk assessment process for new chemicals, examining the following disciplines:
- Pre-screen review
- Chemistry review
- Engineering (Environmental Releases and Occupational Exposure)
- Environmental Fate and Transport
- Environmental Exposure (Non-Occupational)
- Environmental Hazard and Risk Assessment
- Human Health Hazard and Risk Assessment

Note: This presentation is primarily extracted from EPA's Points to Consider document: https://www.epa.gov/sites/production/files/2018-06/documents/points_to_consider_document_2018-06-19_resp_to_omb.pdf

Information Manufacturers Must Submit

- Chemical Identity
- By-products and impurities
- Estimated production/import volume
- Proposed uses and amounts for each use
- Human exposure information
- Disposal methods and estimates of releases to the environment
- Existing test data in notifier's possession or control (or otherwise reasonably ascertainable) concerning human health and environmental effects

Engineering Pre-screen Process

- Engineering Pre-screening[1] of PMN submission is performed to determine if submission is complete with regards to engineering information as per the **40 CFR § 720.65(c)(1)(vi):**

  > *A submission is not complete, and the notification period does not begin, if the submitter does not provide information required on the notice form and by § 720.45 or indicate that it is not known to or reasonably ascertainable by the submitter.*

- Pre-screening review is limited to whether information that is required per the **40 CFR § 720.45,** such as process description, identity of sites, worker exposure, environmental releases, and controls, is included in the submission or not.

- Pre-screening review does **NOT** involve confirming whether supporting information/documentation is provided NOR any evaluation to determine, if information/documentation is acceptable. This more detailed review is performed during the engineering assessment of the case.

[1] Engineering prescreening is independent of prescreening performed by Industrial Chemistry Branch

ONCE ACCEPTABLE, REVIEW STARTS WITH CHEMISTRY

Chemistry Assessment

- Check for chemical/case history/Inventory status
  - Evaluate chemical and physical properties (e.g., boiling point, melting point, vapor pressure, water solubility, and Kow values)
  - Provides insight into hazard, fate and exposure
  - Measured preferred, estimated with Estimation Programs Interface Suite (EpiSuite™) where data are lacking
- Evaluate synthesis; including residuals and impurities
- Review provided uses(s), compare with any existing uses, and identify other reasonably foreseen use(s)
- Identify pollution prevention opportunities and benefits
- Preference: Chemical-specific test data >> Analogue data > Modeled data

ENGINEERING ASSESSMENT

Engineering: Environmental Release

- Evaluates when and where the chemical is released to the environment: Manufacture (or import), processing, distribution, and use for land, air, water

- ChemSTEER -Chemical Screening Tool for Exposures and Environmental Releases
  - Estimates industrial and commercial releases for a chemical

- Generic Scenarios / OECD Emission Scenario Documents: Documents containing information about specific industrial or commercial setting and models and assumptions for estimating releases

Engineering: Occupational Exposure

- ChemSTEER is used to estimate workplace exposures (inhalation and dermal)
- Generic Scenarios/OECD Emission Scenario Documents: Documents containing information about specific industrial or commercial settings and models and assumptions for estimating worker exposures
- Other data sources (ex: OSHA Permissible Exposure Limits, ASTM method for glove permeation testing, NIOSH guidance on nanomaterials, and other published literature)

FATE ASSESSMENT

Environmental Fate Assessment: Purpose

- Characterize environmental partitioning
- Identify the persistence and bioaccumulation potential:

	Limited Persistence (P1)	**Persistent (P2)**	**Very Persistent (P3)**	
Persistence	< 2 months	2 to 6 months	≥ 6 months	**Half-life**
	Low (B1)	**Moderate (B2)**	**High (B3)**	
Bioaccumulation potential	< 1000	1000 to 5000	≥ 5000	**BCF and/or BAF**

- The higher of the bioconcentration factor (BCF) or bioaccumulation factor (BAF) is provided for use in the Exposure assessment; however, when the models disagree EPA considers the applicability of each model including factors such as metabolism
- Exceptions to the persistence and bioaccumulation scoring system are made as appropriate
- See PBT policy documents (https://www.epa.gov/reviewing-new-chemicals-under-toxic-substances-control-act-tsca/policy-statement-new-chemicals)

Environmental Fate Assessment: Approach

- Review structure, physicochemical properties, and structural alerts:
  - Potential for degradation via biodegradation, hydrolysis or photolysis
  - Structural fragments that may affect metabolism (e.g., esters)
  - Fugacity models based on equilibrium parameters give indication of potential partitioning in WWTPs and the environment
- Review submitted environmental fate test data
  - Most new chemical submissions do not contain degradation or bioaccumulation data
  - Non-guideline studies may be acceptable if sufficiently conducted and documented
  - If an analogue with test data is submitted, provide:
    - Rationale for consideration of the analogue
    - Chemical name, structure and CAS numbers of analogue(s)
  - 40 CFR 720.50 (a) requires complete reports or standard literature citations on the new chemical
- EPA frequently uses modeling to estimate environmental fate endpoint values in the absence of reliable & relevant data
  - EPISuite™

EXPOSURE ASSESSMENT

Environmental Exposure Assessment

- Identify concentrations of the chemical in environmental media, typically using the Exposure and Fate Assessment Screening Tool (E-FAST) model, for surface water in the absence of data; see https://www.epa.gov/tsca-screening-tools/e-fast-exposure-and-fate-assessment-screening-tool-common-questions-and-answers

- Calculate an acute environmental exposure concentration for surface water
  - One day surface water concentration based on releases from one site and the 7Q10 flow for the receiving water body
    - 7Q10 : lowest 7-day flow over a period of 10 years

- Calculate a chronic environmental exposure concentration for surface water
  - Based on 10^{th} and 50^{th} percentile of flows for a site or a group of sites (industrial code)

Preference: Chemical-specific test data >> Surrogate data > Modeled data

General Population Exposure Assessment

- Exposure to populations living near industrial facilities
  - Drinking Water Exposures
    - Surface water concentrations resulting from water releases in the engineering report
    - Ground water concentrations resulting from landfill releases in the engineering report
  - Fish Ingestion Exposures
    - Fish tissue concentrations (mg/kg) result from the multiplication of surface water concentrations (mg/L) times the bioconcentration (L/Kg)
  - Inhalation exposures to communities living near industrial facilities that result from air emissions at industrial sites described in the engineering report

Preference: Chemical-specific test data >> Surrogate data > Modeled data

General Population Exposure Assessment (continued)

- Both E-FAST and the Integrated Indoor Outdoor Air Calculator (IIOAC) model are used to determine air concentrations for human receptors. However, E-FAST is usually run first (see https://www.epa.gov/tsca-screening-tools/e-fast-exposure-and-fate-assessment-screening-tool-common-questions-and-answers)
- If the air exposures for fugitive, stack, and incineration releases need to be refined, IIOAC may be used
- IIOAC is site-specific, uses more model inputs and parameters
- IIOAC is a higher tier model that has been used in the new chemical program to refine E-FAST air exposures (see https://www.epa.gov/tsca-screening-tools/iioac-integrated-indoor-outdoor-air-calculator)

Preference: Chemical-specific test data >> Surrogate data > Modeled data

Consumer Exposure Assessment

- E-FAST contains 6 consumer exposure models (CEM v 1.2)
  - Dermal and inhalation routes of exposure
  - Built with a representative household and pre-programmed consumer behavior patterns
- Expanded Consumer models in updated version of CEM (CEM v 3.2) in 2019 see https://www.epa.gov/tsca-screening-tools/approaches-estimate-consumer-exposure-under-tsca#consumer

Preference: Chemical-specific test data >> Surrogate data > Modeled data

ENVIRONMENTAL ASSESSMENT

Environmental Hazard Assessment Purpose

- Identify potential aquatic hazard concerns, using acute and chronic toxicity endpoint values

- Standard aquatic toxicity profile includes 6 endpoints:
  - Fish 96-hr LC_{50}
  - Daphnid 48-hr EC_{50}
  - Green algae 96-hr IC_{50}
  - Fish Chronic toxicity value (ChV)
  - Daphnid ChV
  - Green algae ChV

- Weight of evidence and best available science are used in TSCA chemical assessments
  - Review chemical structure, physicochemical and fate properties, and structural alerts
  - Review submitted test data for the submitted substance
  - Search for measured hazard data for appropriate analogues of the new chemical
  - Ecological Structure Activity Relationships (ECOSAR) Predictive Model

Environmental Hazard Assessment Purpose (continued)

- Use acute and chronic toxicity endpoint values (*i.e.*, LC_{50}, EC_{50}, ChV) to identify potential aquatic hazard concern levels

Hazard Concern Level	Ecotox Rating	Acute Endpoints	Chronic Endpoints
Low	1	≥100 mg/L	≥10 mg/L
Moderate	2	1 to <100 mg/L	0.1 to <10 mg/L
High	3	< 1 mg/L	< 0.1 mg/L

- Identify the environmental **Hazard Concern Level** and **Ecotox Rating**
  - An Ecotox Rating of 2 or 3 will require quantification of environmental exposure and risk
    - Environmental exposure (via water) is also quantified when there is human health concern for drinking water or fish ingestion, even when the Ecotox Rating is 1.
- Derive acute and chronic concentrations of concern (COC)
  - Harm to the aquatic environment may occur if the COC is exceeded

Environmental Risk Assessment Approach

- EPA evaluates environmental risk by comparing the acute and chronic COCs to potential environmental concentrations (PECs) of the chemical
  - PEC information is provided in the Exposure assessment generated using the E –FAST exposure model (https://www.epa.gov/tsca-screening-tools/e-fast-exposure-and-fate-assessment-screening-tool-version-2014)
- *(If there are no exposures, no need for risk calculation)*
- Evaluation of environmental **risk** from **acute aquatic exposure**
  - EPA compares acute COCs directly to the PECs using the Risk Quotient method
  - Potential for risk from acute exposure exists if the PEC > acute COC

Environmental Risk Assessment Approach (continued)

- Evaluation of environmental **risk** from **chronic aquatic exposure**
  - If the PEC is greater than the **chronic** COC, then potential chronic risk may exist.
  - Aquatic risk from chronic exposures is further evaluated by determining the number of days per year that the estimated PEC exceeds the chronic COC.
- Evaluation of environmental risk from soil/sediment exposures
  - Acute and chronic risks to soil and/or sediment-dwelling organisms are assessed by EPA when physical-chemical and fate properties indicate that the new chemical substance will partition into soils and/or sediments

HUMAN HEALTH ASSESSMENT

Human Health Hazard Assessment: Purpose

- Identify/Characterize the following:
  - Absorption by exposure routes based on experimental data or physicochemical properties for the new chemical or an analogue
  - Hazards associated with the new chemical substance based on the following:
    - Data provided in the notification
    - Analogues for informing the identification of potential hazards
      - Analogue search conducted for every submission
    - Structural alerts, physicochemical and fate properties
    - Metabolites and/or hydrolysis products
  - Relevant routes of exposure (e.g., dermal, inhalation, fish ingestion, and/or drinking water)
  - Determine if the data are suitable for the identification of a point of departure (e.g., NOAEL, LOAEL, or BMDL) for quantitative risk estimation, or if they can be used for qualitative risk estimation

Human Health Risk Assessment: Overall Approach

- Risk characterization is part of the risk assessment and takes the form of a conclusion about the chemical substance's potential for health risk.

- It embodies the effects of potential concern, the route and magnitude of potential exposure, and the population estimated to be exposed.

Human Health Risk Assessment: Quantitative Approach

- If a point of departure (POD) is identified during the human health hazard/toxicity data review, then risks are quantified.
- Risks are generally calculated using the Margin of Exposure (MOE) approach.
- The MOEs are then compared to a benchmark MOE to determine if potential risks are present.
- Potential risks are identified if the calculated MOE is below the benchmark MOE.

Human Health Risk Assessment: Quantitative Approach (continued)

- The benchmark MOE is obtained by multiplying together the uncertainty factors (UFs) associated with each POD.
- These UFs typically include:
  1. The variation in susceptibility among members of the human population (i.e., inter-individual or intraspecies variability or UF_H = default of 10),
  2. The uncertainty in extrapolating animal data to humans (i.e., interspecies uncertainty or UF_A = default of 10)
  3. An additional UF may be added if the POD is based on a LOAEL, rather than a NOAEL (i.e., LOAEL-to-NOAEL extrapolation or UF_L = 10)
- Benchmark MOEs are typically 100 or 1000

Human Health Risk Assessment: Quantitative Approach (continued)

- EPA may refine the risk calculations based on:
  - Absorption (e.g., measured data vs prediction)
  - If relevant, % of chemical substance that represents the structural alert for hazard.
    - e.g., if the hazard identified for a polymer is due to a particular moiety that is 2% of the molecular weight of the polymer, then the exposure may be adjusted to 2% of the total estimated dose and risk estimated accordingly.
  - Specific data are available to justify changes to UFs

Human Health Risk Assessment: Qualitative Approach

- In some cases, hazards are identified based on a structural alert, which need to be supported by experimental scientific evidence.
- If data are not available to derive a quantitative POD, a qualitative approach may be considered.
- In such cases, if there are populations that may be exposed, EPA may qualitatively identify a potential hazard and consider whether data are sufficient for a reasoned evaluation.
- Examples:
  - Skin and respiratory sensitization
  - Skin and eye irritation

Human Health Risk Assessment: Insufficient Data

- When there are no quantitative hazard information available on the new chemical substance for certain hazards (e.g., cancer) and exposures are expected, EPA cannot perform a reasoned evaluation of potential risks and will generally request testing on the new chemical substance, unless exposures for the relevant route(s) can be eliminated or mitigated.

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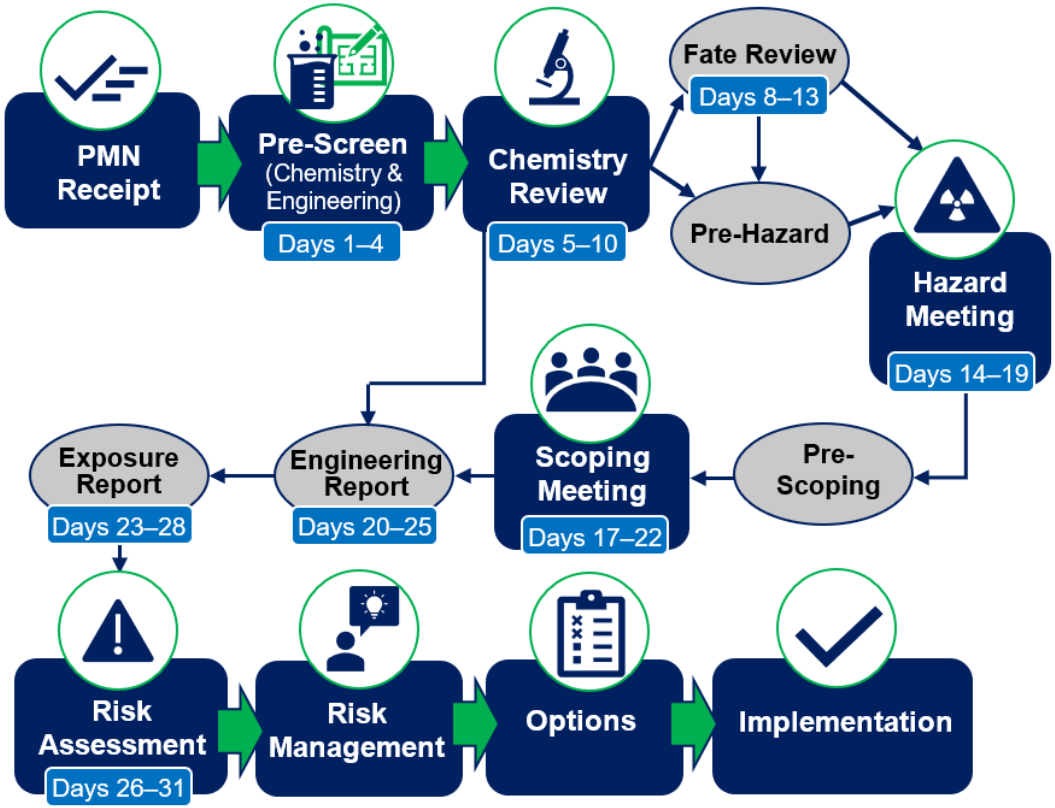

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Questions?

Thank You!

Contact me: cox.jamesw@epa.gov