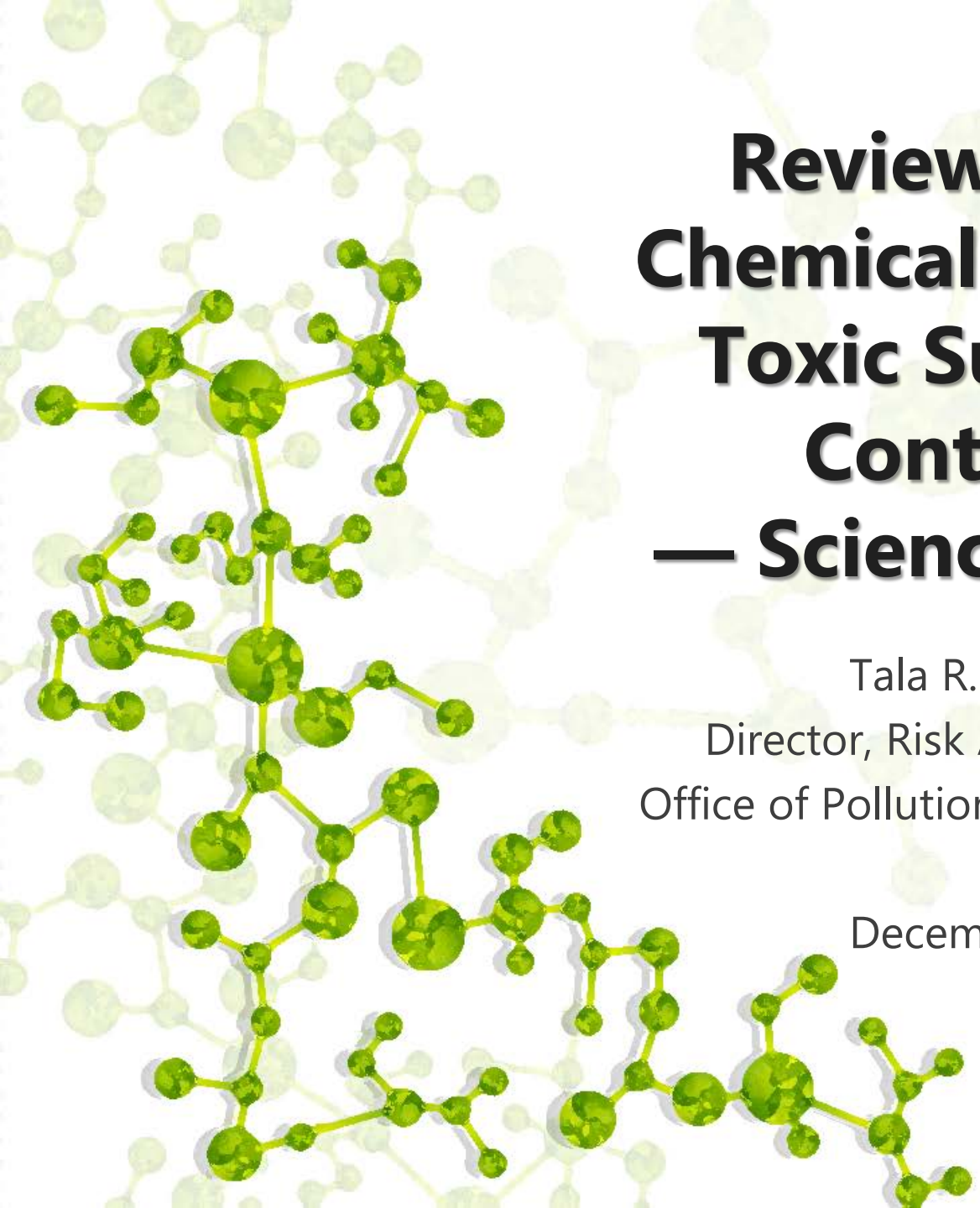

Reviewing New Chemicals under the Toxic Substances Control Act — Science Issues —

Tala R. Henry, Ph.D.
Director, Risk Assessment Division
Office of Pollution Prevention and Toxics

December 14, 2016

PMN Review Process

- Chemical Review/Search Strategy Meeting
- Structure Activity Team (SAT) Meeting
- Development of Exposure/Release Assessments
- FOCUS – Initial Risk Management Preliminary Decision Meeting
- Further Assessment, if needed
  - "Standard Review"
- Final Risk Management Decision meeting

PMN Review Process: Chemical Review/Search Strategy (CRSS)

Day 8-12

- Physical-Chemical Properties
  - PMN Data
  - Model Estimates
  - Data from literature
- Conditions of Use Identified in PMN
- *Identify* Foreseen Uses
  - Uses for structural and/or functional Analogs/Similar Chemistries

PMN Review Process: Structure Activity Team (SAT)

Day 9-13

- Conditions of Use, P-Chem, Fate, Health Hazard, Eco Hazard Data & Information PMN Data considered:
  - Data Submitted for PMN
  - Data Submitted for Analog(s) identified by submitter
  - Data for Analog(s) identified by EPA experts
  - (Quantitative) Structure Activity Relationships ((Q)SAR), EPA New Chemical Categories, Expert Systems, Structural Alerts, Best Professional Judgement used when test data are absent
- Determine whether/what scope of exposure assessment to conduct, e.g., occupational, general population, consumers, environment

Exposure/Release Assessments Day

Day 10-19

- Based on Modeling
  - Well known/publicly available models
  - Well known/publicly available exposure scenarios for occupational (ESDs), general population, and consumer exposures
  - Use both default (reasonable worst-case; upper-end; typical) and case-specific (if data are provided in PMN) input parameters
  - All exposure pathways/routes may not be assessed quantitatively; attempt to characterize these uncertainties qualitatively, but may need data if uncertainty is great

PMN Review Process: FOCUS

Day 15-19

- Conditions of use, environmental fate, exposure, health & eco hazard and initial risk estimates presented;
- Assessment adequate or "Standard Review"?
  - determine whether further assessment/analysis will be conducted

PMN Review Process: Standard Review

Day 21-70

- "Full Life-Cycle Assessment – all exposure pathways/populations scoped at SAT
  - Highly dependent on Analog data for human health hazard
  - Highly dependent on QSAR estimates for eco hazard, as applicable; also analogs
  - Quantify Risks for as many endpoints as possible; qualitatively identify others
  - Identify Data Gaps
  - Characterize Uncertainties, generally and especially as associated with data gaps and/or structural alerts
  - Identify/quantify risk reductions associated with certain/standard risk mitigation strategies (e.g., PPE, engineering controls), e.g., "fold-factor" for Respirators
  - Identify testing strategies for addressing data gaps and reducing uncertainties

Science Issues & Approaches for Addressing Chemical Review/Search Strategy

- Forseen Uses: *Identify* whether chemical characterization changes under different production conditions
  - Physical/chemical properties for residuals of concern, smaller MW components
  - Consider whether a change in residuals/smaller MW components is forseen if manufacturing conditions change
  - CRSS Timeline has not changed

- EPA does not conduct "risk assessment" for all foreseen uses

Science Issues & Approaches for Addressing Health Hazard

- **Issue:** No Data; Insufficient information to conduct a reasoned evaluation
  - Approach: Recommend Testing to fill data gap

- **Issue:** Structural Alerts (qualitative) without toxicity data (quantitative benchmarks) for PMN nor Analog (e.g., dermal & respiratory sensitization; lung effects: particle overload, cationic binding, surfactancy, waterproofing
  - Approach: Participating in national and international efforts (ICCVAM; OECD) to assess performance of alternative (non-animal) methods for assessing dermal & respiratory sensitization
  - Approach: EPA conducting literature search/reviews on lung effects: particle overload, cationic binding, surfactancy, waterproofing) with goal of identifying quantitative benchmarks and/or risk reduction 'rules of thumb'
  - Approach: Opportunity for discussion on findings and collaboration on data collection and/or testing

- **Issue:** Analogs with high uncertainty (e.g., structural components not well matched; multiple analogs for different endpoints)
  - Approach: Reviewing Category Documents/Definitions; goal of adding existing test data and underpinning with in vitro and mechanistic data (e.g., HTP Tox)

Science Issues & Approaches for Addressing Eco Hazard

- **Issue:** Whether Foreseen Uses May Change Hazard/Risk
  - Approach: Flag whether other conditions or manufacture or use would change risk (e.g., will lower MW components or residuals alter risk profile?)
- **Issue:** (Additional/New) data highlight uncertainties with assumptions regarding Mitigation Factors (e.g., humic acid)
  - Approach: Targeted testing of compounds for which mitigation factors were previously applied, e.g., cationic polymers, aliphatic amines, surfactants
  - Approach: Revisiting environmental mitigation factors application procedures (e.g., humic acid)
- **Issue:** (Additional/New) data highlight uncertainties with assumptions regarding environmental speciation (e.g., "Tight Ion Pairs" causing unexpected toxicity)
  - Approach: Tiered Testing to elucidate environmental fate and toxicity; chemistry then fate (measured concs) then toxicity

Science Issues & Approaches for Addressing Fate

- **Issue:** (Additional/New) data highlight uncertainties with assumptions regarding environmental speciation (e.g., "Tight Ion Pairs" causing unexpected toxicity)
  - Approach: Tiered Testing to elucidate environmental fate and toxicity; chemistry then fate (measured concs) then toxicity

- **Issue:** Improving multi-compartment analysis
  - Approach: Exploring/deploying additional models for estimating more realistic distribution to water vs sediment compartment(s) [Model]
  - Approach: EPA conducting literature search/review for anaerobic biodegradation; potentially develop scaling/adjustment factors to apply to more data-rich aerobic degradation

Science Issues & Approaches for Addressing Exposure/Release Assessments

- **Issue:** "Potentially Exposed and Susceptible Subpopulations"
  - Have previously done some, e.g., pregnant workers; children for general population & consumer uses; fish consumption for general population
  - Approach: Expanded Subpopulations under new legislation, e.g., more age groups for general population & consumer populations
  - Approach: Developed scaling factors for ease/efficiency
  - Approach: Developing more systematic & transparent procedures and protocols (in progress)

Opportunities

- Now:
  - Suspend PMNs with inhalation testing for lung effects
  - Provide data / expertise on Lung Effects: particulate overload; cationic binding; surfactancy; water-proofing
- Near Term (early 2017):
  - When EPA completed data/information gathering/summaries, initiate discussions