NIEHS, National Toxicology Program
NIOSH, Industrywide Studies Branch
Interagency Agreement

Update on Current Collaborative Research

Elizabeth Whelan
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NTP and NIOSH: Common Goals

• To provide scientific data and knowledge necessary for making appropriate decisions that protect and improve public health.

• Establish and maintain partnerships with other federal agencies to leverage resources and reduce undue overlap
Goals of the NTP/NIOSH Collaboration

• Conduct exposure and health assessments of priority agents of mutual interest to NTP and NIOSH

• Capitalize on NIOSH access to human populations and work sites to provide real-world context for toxicology studies

• Guide decision-making for NIOSH epidemiologic studies

• Toxicology and epidemiology studies provide evidence-base for guidance documents
  • Report on Carcinogens, OHAT reviews, NIOSH Criteria Documents
Impact of the Collaboration

- Findings inform testing priorities
- Guides selection of relevant laboratory test exposures and doses (e.g., CNT)
- Has led to development of methods for generation of laboratory test exposures (e.g., welding fume, asphalt fume)
Update of Current Studies

- Indium
- Manganese Fractions In Welding Fume
- Carbon Nanotubes and Carbon Nanofibers
- Bisphenol A
- PAHs in Coal Tar Sealant Applications
- Flame Retardants
- 1-Bromopropane
Use of and Occupational Exposure to Indium in the United States

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Background

- **Indium**
  - A metal with limited use historically; however, use of indium tin oxide (ITO) in flat panel displays has increased substantially over the past decade

- **Toxicity**
  - ITO exposure associated with lung disease in Asian and U.S. workers
  - Similar lung effects seen in animals in the 1960s for related indium compounds
  - Toxicity appears to vary by type of indium compound
  - Indium appears to persist in the body (i.e. eliminated slowly)

- **Data Gap**
  - Little known about indium use in the U.S. and worker exposure levels

- **NIOSH Study**
  - Contacted a range of companies to obtain information about indium use
  - Requested indium air sampling data, if available
  - Conducted site visits and collected air samples at selected companies
Findings

- **U.S. Uses**
  - solder (most common)
  - thin film of ITO
  - indium phosphide (InP) in semiconductor fabrication
  - some photovoltaic cells
  - sputter target manufacturing (as ITO or metal alloys)
  - some alkaline batteries

- **Elevated Indium Exposure**
  - Tasks involving mechanical abrasion of ITO
  - Handling indium salts and powders
  - Some indium air concentrations exceeded the NIOSH REL & ACGIH TLV

- **Minimal Indium Exposure**
  - Processes where indium remained a molten metal
  - Processing InP semiconductor substrates (due to engineering controls for preventing phosphine exposure)
  - Alkaline battery manufacturing

Occupational Exposure Assessment Of Manganese Fractions In Welding Fume

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Objective: to characterize welders’ exposures to 4 manganese fractions based on chemical solubility of different Mn oxidation states

NIOSH evaluated novel method for soluble Mn; Mn (0, 2+); Mn (3+, 4+); insoluble Mn; (& Mn-sum)

Conducted 10 monitoring surveys: Construction at oil refineries; shipyard; steel fabricators; heavy equipment & appliance mfg

Over 300 full-shift worker-day breathing zone TWA measurements were collected (required > 650 samples; x5 analytes = ~3250 data pts.)
Occupational Exposure Assessment Of Manganese Fractions In Welding Fume

- Refinery construction, SMAW (stick welding)
- GM Mn-sum levels ranged 5.7 – 210 µg/m³
- Welders’ exposures > ACGIH TLV, total Mn
  > 10x ACGIH TLV, respirable – confined space
- Manuscript accepted for January 2017 publication, *Annals Work Exp & Health*
- Heavy equipment – GMAW (MIG welding)
- Mn 0,2+ and Mn 3+,4+ most abundant (~85% of Mn-sum)
- Evaluated method for Mn sequential extraction
Industrywide Exposure Assessment Study of Workers Exposed to Carbon Nanotubes and Carbon Nanofibers

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Objective: conduct exposure assessments for carbon nanotubes and carbon nanofibers (CNT/CNF) in a representative sample of US workplaces.

Conducted 19 Site Visits (12 with cross-sectional epi study)
- CNT/CNF Primary Manufacturers
- CNT/CNF Secondary Manufacturers (Electronics and Composites Facilities)
  - 128 Workers Sampled (2 days each)
    - 480 Full Shift, Personal Respirable and Inhalable Elemental Carbon Samples
    - 256 Full Shift, Personal Samples analyzed by TEM
    - ~105 Dermal Samples (analyzed by SEM)
    - ~90 Sputum Samples (analyzed by hyperspectral imaging)

Overall Personal Exposures (from 12 most recent site visits)
- Respirable- mean 1.0 µg/m³ (median 0.10 µg/m³)
- NIOSH Recommended Exposure Limit (REL) = 1 µg/m³ (exceeded by 7% of workers)
- Inhalable- mean 6.2 µg/m³ (median 0.24 µg/m³)
Few single fibers

- Most respirable exposures well below the NIOSH REL
- Much higher inhalable exposures (unclear toxicological implications)
- TEM structure concentrations exhibited more sensitivity to detection (but more costly—and no REL)
- Most agglomerate structures were in the 2-5 or 5-10 μm size class
Carbon Nanotube Feasibility Study
NTP Funding FY12-14

• Impact

  • 2014 IARC meeting evaluated CNT carcinogenicity
  • Nordic Expert Group for Criteria Documentation of Health Risks to develop OELs
  • Dahm et al. 2015 received NIOSH Alice Hamilton Award in 2016 for best exposure assessment paper
  • NTP selected a MWCNT for tox testing based on MWCNT types found in Dahm study

• Publications:


Urinary Bisphenol A Concentrations Among Manufacturing Workers in the United States

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Background

• **BPA**
  - Used in making polycarbonate, epoxy and phenolic resins, in certain foundry casting waxes, and in thermal paper (largely discontinued)

• **Metabolism and Toxicity**
  - After ingestion, BPA is rapidly conjugated in the liver and excreted into the urine
  - BPA is considered weakly estrogenic
  - A cross-sectional study of BPA-exposed manufacturing workers in China reported decrements in male sexual function in several domains

• **Data Gap**
  - Absence of published data on BPA exposure among U.S. manufacturing workers.

• **NIOSH Study**
  - Recruited 78 workers at 6 companies making or using BPA
  - Collected seven, timed spot urine samples over two consecutive days
  - Measured both free (unconjugated) and total BPA (free + conjugated)
  - Collected information on non-occupational BPA sources & exposure modifiers
Findings

• **Total BPA Concentrations**
  - Clear evidence of occupational exposure
  - Total BPA increased during work on both days
  - Total BPA, on average, was ~70 times higher than adults in NHANES 2013-2014

• **Determinants of Increased BPA Exposure**
  - Handling sacks, bags etc. of raw BPA
  - Taking process samples containing BPA
  - Increased body mass index
  - Time point (when sample collected, i.e. higher at end-shift than pre-shift)
  - Job: Highest: working with molten BPA-filled wax; Lowest: flaking phenolic resins

• **Other Findings**
  - Any dietary BPA exposure was overshadowed by occupational exposure
  - Suggestion that BPA elimination in workers was slower than in oral dosing studies
  - Total BPA concentrations were comparable to those reported in Chinese workers

Assessment of Exposure to Polycyclic Aromatic Hydrocarbons in Coal Tar Sealant Applicators

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Assessment of Exposure to Polycyclic Aromatic Hydrocarbons in Coal Tar Sealant Applicators

- Coal tar (CT); CT Distillates; CT Pitch – complex mixtures, variable PAH composition and concentrations

- “refined” Coal Tar Sealants (“RTS”; RT12) – blended emulsion using 30-35% processed CT pitch in water, clay & sand

- Known human carcinogens – NTP, IARC, ACGIH, NIOSH
  - Except refined-Coal Tar Sealants – No Data

- US Geological Survey research publications have reported PAHs in CTS products, nearby streams, flaked debris, & house dust

- Bans - Cities, states, water basins, universities & hardware stores

- Pavement Coating Technology Council (PCTC) contends that CT-based sealants are safe and lobby against CTS bans

- US EPA settled a lawsuit regarding industrial storm water run-off
Assessment of Exposure to Polycyclic Aromatic Hydrocarbons in Coal Tar Sealant Applicators

- Two site surveys conducted during pavement sealant jobs in FY16; six more expected in FY17
- Pavement sealing tasks & concurrent PAH exposures:
  - Vehicles; gas blowers & generators; asphalt crack fill
  - Apply CT sealant: manually; spraying or vehicles for large areas
- Exposures will be measured by breathing zone air, skin wipes, and metabolites in pre/post-shift urine & blood
- Air samples and skin wipes will be analyzed for 16 PAHs & 4 N-heterocyclics; BSF - limited
- Urine specimens will be analyzed for 1-hydroxypyrene; 1- & 2-Hydroxynaphthalene; total OH-PAH metabolites; cotinine; creatinine
Assessment of Occupational Exposure to Flame Retardants

Cheryl F. Estill, PhD

Widey added to U.S. products; changing rapidly due to polybrominated diphenyl ethers (PBDEs) phase-out

Flame Retardants

- tetrabromobisphone A (TBBPA)
- 2,3,4,5 – tetabromobenzoate (TBB)
- 2,3,4,5 – tetrabromophthalate (TBPH)
- decabromodiphenyl ethane (DBDPE)
- hexabromocyclododecane (HBCD)
- tris (1,3-dichloro-2-propyl) phosphate (TDCPP)
- tris (1-chloro-2-propyl) phosphate, (TCP)
- tricresyl phosphate (TCP)
- triphenyl phosphate (TPP)
Assessment of Occupational Exposure to Flame Retardants

Methods

• Characterize exposures in various industries:
  • spray polyurethane foam
  • nail salons
  • manufacture and installation of insulation
  • manufacture of automotive interiors
  • gymnasiums
  • manufacture of carpet padding
  • fire service

• Collect exposure information from workers over two days

• Samples to Collect:
  • urine
  • serum
  • air
  • hand wipe
  • bulk of product being used
Assessment of Occupational Exposure to Flame Retardants

Current Status

- Conducting year three of data collection
- Collected data from 14 workplaces
- Enrolled 106 workers in the study
- Samples are being analyzed
Occupational Exposure to 1-Bromopropane

- NTP-funded studies (2003-2006) contributed to 13th Report on Carcinogens
- NIOSH participated this year in IARC Monograph 115 where 1-BP classified as 2B
- NIOSH Criteria Document – public meeting this year
- EPA, ATSDR draft assessments
- ACGIH TLV lowered from 10 ppm to 0.1 ppm
Thank You
Questions?