NTP Research Concept: NIEHS-EPA collaborative project to improve characterization of personal care product and home exposures

Project leader

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Background

A critical research priority identified in the NIEHS Strategic Plan (NIEHS 2012) is to advance characterization of environmental exposures through improved exposure assessment, at both the individual and population level. Leading up to the Strategic Plan, specific research priorities related to exposure assessment were identified in the 2011 NIEHS workshop "Advancing Research on Mixtures: New Perspectives and Approaches for Predicting Adverse Human Health Effects", including the need to evaluate the utility of existing instruments that classify or quantify exposures, develop better tools to improve exposure assessment, and to better understand the nature of combined exposures (e.g., mixtures). This project will inform research priorities identified in the NIEHS strategic plan[1] and several specific research needs discussed during the 2011 NIEHS workshop on mixtures:

- Evaluate current exposure assessment technologies, including questionnaires
- Develop better models that link source with behavior to predict exposure
- Analyze combined exposures
- Evaluate usefulness of commercially available product use/marketing databases
- Evaluate prediction models
- Characterize behavior that impact exposures using new technologies (cell phone/internet use)

The proposed research concept represents a collaboration between NIEHS (Division of the National Toxicology Program, Division of Intramural Research, and the Clinical Research Unit) and the EPA Office of Research and Development (ORD). The partnership includes co-funding with EPA, the sharing of equipment and expertise, and the use of EPA field teams for extensive collection of exposure information.

[1] Research goals in the NIEHS Strategic Plan that correspond with this study's objectives are as follows:

- Theme 2: Transform exposure science by enabling consideration of the totality of human exposures and links to biological pathways, and create blueprint for incorporating exposure science into human health studies.
- Goal 3: Exposure research to advance characterization of environmental exposures through improved exposure assessment, at both the individual and population levels.

The initial motivation for this project stemmed from NIEHS's interest in characterizing the personal care product questionnaire administered in the NIEHS Sister Study as an exposure assessment tool when compared to a daily diary or biomonitoring data. The Sister Study is a large cohort study of 50,000 women who had at least one sister diagnosed with breast cancer and were breast cancer-free themselves at time of enrollment (http://sisterstudy.niehs.nih.gov). Enrollment ended in 2009 and analyses are currently underway to look at associations between personal care product usage and breast cancer and other health outcomes. Thus it is important to characterize the Sister Study personal care product questionnaire as an exposure assessment tool with the purpose of aiding the interpretation of the health outcome analyses as well as for potential use of the questionnaire, or subset of questionnaire items, in other epidemiology studies (Objective 1). In addition to the personal care product questionnaire, the Sister Study has a household/residential questionnaire that captures exposure to products that may also contain potential endocrine disrupting and other chemicals (e.g., household pesticides). Since these questionnaires will also be used to assess and categorize exposures in epidemiological analyses we expanded the original concept to include the household/residential questionnaire. Because exposures to the same chemicals that come from personal care and household/residential products can also come from food packaging and processed foods we decided to assess a third questionnaire based on food packaging and food processing (Rudel et al. 2011). The initial goal of characterizing these questionnaires was expanded based on discussions with our EPA collaborators to include collecting additional exposure information (e.g., air and dust samples, and household inventories of consumer products) for the purposes of evaluating and improving exposure prediction models used in EPA's ExpoCast and High Throughput Stochastic Human Exposure and Dose Simulation (SHEDS-HT) initiatives (Objective 2).

Objective and Specific Aims

Objective 1.

Evaluate the utility of existing questionnaire instruments to assess exposure from personal care products, household chemicals, and packaged and processed food. Knowledge gained from the evaluation of the existing questionnaires will aid the interpretation of analyses using these questionnaires.

This objective focuses on NIEHS's interest in the effectiveness of existing exposure assessment tools in the context of epidemiologic studies. We are specifically interested in evaluating the effectiveness of three questionnaires in classifying exposure to chemicals found in food and consumer products. Two of these questionnaires are currently being used in the NIEHS Sister Study. The Sister Study's Personal Care questionnaire and Residential History and Exposures questionnaire were designed to capture patterns of current exposure to personal care products and common exposures in the home (e.g., pesticides, cleaning products, etc.). The third questionnaire will be based on Rudel et al (2011) and captures another potential source of exposure: food packaging and processed food.

We will not be using participants or samples from the NIEHS Sister Study in our study. Rather, we will be using the questionnaires, as well as daily diaries and biomonitoring data, to gather exposure information from a new group of participants. We will gauge the effectiveness of these questionnaires by comparing exposure estimates between the questionnaires, daily diary, and biomonitoring data.

To the best of our knowledge, no other longitudinal study assessing use patterns of personal care products, household chemicals, and food packaging/processed food has paired the analysis with a daily dairy and human biomonitoring data. Knowledge gained from this exercise may make it easier for researchers to gather exposure data without the cost of conducting biomonitoring studies, which often limits the extent of exposure information that can be collected, or could guide improvement of current questionnaires.

Specific Aim 1.1: Personal care products

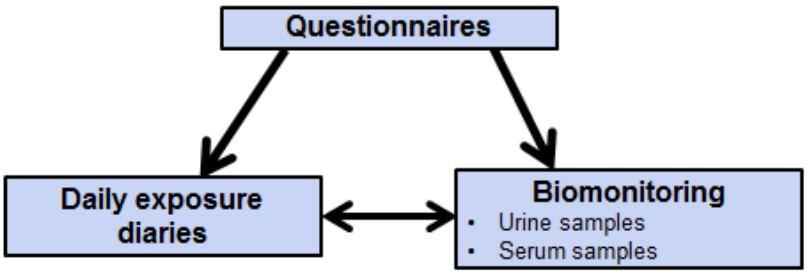
Compare exposure estimates from the Personal Care questionnaire (Appendix 1), a daily diary, and biomonitoring data of several chemicals associated with personal care products (e.g., phthalates, phenols, and parabens).

Specific Aim 1.2: Household chemicals

Compare exposure estimates from the Residential History and Exposures questionnaire (Appendix 2), a daily diary, and biomonitoring data of several chemicals associated with household exposures (e.g., several semi-volatile organic compounds (SVOCs), organophosphate insecticides, pyrethroid insecticides).

Specific Aim 1.3: Food packaging and processed food

Compare exposure estimates from the food packaging and processing questionnaire (Rudel et al. 2011) (Appendix 3), a daily diary, and biomonitoring data of several chemicals associated with food packaging and processed food (e.g., phthalates, bisphenol A).



Hypothesis: When compared to the questionnaires we expect the biomonitoring data to better reflect the daily diary results. We expect certain items from the personal care product questionnaire, the household exposure questionnaire, and the food packaging/food processing questionnaire to correlate with daily diary and biomonitoring data. This could provide support for developing improved questionnaires for future epidemiological studies.

Objective 2

Inform and evaluate models designed to predict exposure to chemicals in the environment.

This objective focuses on EPA's interest in analysis models that predict exposures, i.e. how reliable are models that require varying data input in predicting actual exposure. The EPA will be responsible for the following aims:

Specific Aim 1: Test a variety of modeling approaches designed to predict chemical exposures from consumer products. These model applications include the following:

- Empirical evaluation of high throughput exposure models and information within chemical use databases via the ExpoCast framework
    - The ability of models to predict exposure has been evaluated systematically with respect to human chemical exposure biomonitoring data provided by CDC (National Health and Nutrition Examination Survey) NHANES for the aggregate U.S. populations – pilot study data will provide evaluation of exposure variability as estimated from NHANES
    - In order to evaluate ability to extrapolate inferences from known chemicals to unknown chemicals; previously uninvestigated chemicals predicted to be similar to those with very high and very low exposures in reproductive-aged women monitored by NHANES will be investigated
- Evaluation will focus on predictions made with models for proximate sources of chemical exposure (*i.e*., near field exposure), especially EPA's High Throughput Stochastic Human Exposure and Dose Simulation (SHEDS-HT)
    - SHEDS-HT is a stream-lined version of SHEDS for chemical prioritization – pilot study data will be used to evaluate the SHEDS-HT main assumptions and inputs
    - SHEDS model predicts human exposures using mechanistic exposure algorithms in conjunction with human activity information obtained from EPA's Consolidated Human Activities Database (CHAD). CHAD contains more than 50,000 individual diary entries collected over the years as part of19 different nationwide studies
    - SHEDS-HT can be used to rapidly generate specific (e.g., by gender, age group, location, and activity type and level), population distributions of potential exposures from selected consumer products

Specific Aim 2: Test and demonstrate measurement methods to more fully and accurately characterize consumer product chemical exposure including:

- UPC scan and Nielsen HomeScan determination of consumer product use, household inventory of existing consumer products within the home
- House dust collection and analysis
- GPS and accelerometer measurements integrated with MicroTrac (Breen MS 2014) to monitor daily time-activity patterns, e.g., time in and out doors.
- Direct-reading personal total volatile organic compound (TVOC) monitoring using recent sensor technology
- Indoor residential temperature measurements and questionnaire on building characteristics to estimate residential air exchange rates (Breen et al. 2010).

Specific Aim 3: Based on models and measurements described above, (1) evaluate patterns of co-exposure and, (2) consider approaches for mass balance analysis.

Proposed Approach

The proposed research concept includes collecting an extensive amount of exposure-related information from a single set of participants. This research concept is large in scope and participants will be assigned a considerable amount of work. Therefore it is necessary that we start with a pilot phase to determine whether a larger post-pilot study phase is feasible with respect to practicality and participant burden. The EPA field teams have experience in successfully implementing exposure assessment protocols that are of similar complexity to the outlined approach. This experience comes from conducting a pilot study to estimate human exposures to pyrethroids using an exposure reconstruction approach (the Ex-R Study) (Morgan et al. 2013).

The proposed pilot study will be used to guide and refine procedures for a larger exposure study, and inform sample size and power calculations for post-pilot study phases. It will also help highlight areas where there is a large degree of uncertainty, such as potential discordance between the questionnaire, daily diary, and biomonitoring data for specific types of chemicals. Pilot data will be used by EPA collaborators to evaluate and refine current predictive exposure models. It is possible the study outlined below may not be feasible. In this case subsequent work would focus on specific elements determined by practicality, cost, and impact of analysis.

Pilot Study Design: Major Elements

- 10-day pilot study
- Enroll 10-15 eligible women of reproductive age (25-40 years) using Clinical Research Unit's (CRU's) sample registry
- At enrollment, participants will take the three questionnaires
    - Personal care product questionnaire (Sister Study)
    - Household and environmental exposure questionnaire (Sister Study)
    - Food packaging and processing questionnaire (adapted from Rudel et al.)
- Participants will have their blood drawn at the CRU the first day and last day
- Participants will collect all urine samples at home using a cooler with a temperature data logger
- Participants will complete a daily exposure diary of all consumer products used (e.g., personal care products, household cleaners, pesticides) over a ten-day period.
- On the morning of the first day a technician will visit the participants and use a smartphone or UPC scanner to record all personal care and household products in the home.
- A technician will visit the participants the morning of the second day and each subsequent day in the study to collect urine, collect household samples (i.e., dust, air)

Samples and Measures

- Questionnaires
- Daily diary
- Serum samples:
    - Cotinine
    - Polybrominated diphenyl ethers (PBDEs)
    - Perfluorinated Chemicals (PFCs)
- Urine samples
    - Phytoestrogens

    - Creatinine
    - Phthalates
    - Phenols
    - Parabens
    - Perchlorate
    - organophosphate insecticides (dialkyl phosphate; non-specific metabolites)
    - pyrethroid insecticides and organophosphorus pesticide specific metabolites
    - hydroxylated polycyclic aromatic hydrocarbons (OH-PAHs)
- Nielson HomeScan
- Smartphone/UPC Scanners
- Surface wipe samples
- Vacuum dust samples
- Air pollution, volatile organic compounds (VOCs), locational/micro-environmental monitoring with GPS

Significance

This project is a strong collaborative effort between NIEHS, EPA, and the CDC[2]. . The objectives above inform a number of research goals identified in the NIEHS Strategic Plan and the NIEHS 2011 workshop; they also inform a number of EPA research needs identified by the Chemical Safety for Sustainability (CSS) program.

[2] Chart of contributions

NIEHS (DNTP, DIR, Clinical Research Unit)	• Study design • Clinical research unit facilities • NIEHS Sister Study questionnaires • Characterize questionnaires as exposure assessment tools
EPA Office of Research Design	• Study design • Co-funding • Share equipment and expertise • EPA field times for extensive collection of exposure information • Data analysis for evaluating • exposure prediction models
CDC	• Study design • Analyze a sub-set of NHANES chemicals

Appendices

Appendix 1: NIEHS Sister Study Personal care questionnaire

Appendix 2: NIEHS Sister Study Environmental exposures questionnaire

Appendix 3: Food packaging questionnaire (Rudel 2011)

References

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