

The Tonawanda Health Study: An Epidemiologic Study of Health Effects and Coke Oven Emissions from Tonawanda Coke

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Abstract

The Tonawanda Coke Corporation was convicted of illegally releasing coke oven gas, a hazardous air pollutant and known human carcinogen, into the environment. In response to concerns about potential adverse health effects due to these coke oven emissions, we propose a large epidemiologic project to assist the community in understanding the health risks posed by exposures. This comprehensive project is composed of 3 components, including: 1) conducting a large prospective cohort study of 38,000 residents of the Town of Tonawanda and Grand Island, 2) conducting a retrospective occupational cohort study of Tonawanda Coke Corporation employees, and 3) establishing a Center for Environmental Health Education. The prospective cohort study will assess the cause-specific prevalence of morbidity and mortality in the community, biomonitor residents for current benzene exposure, and follow cohort members to ascertain the incidence of new cases of disease. The retrospective occupational cohort study will investigate all-cause and cause-specific mortality among past and current employees because these employees were also unwittingly exposed to coke oven emissions, and at higher concentrations than the general community. The Tonawanda Environmental Health Education Center will be established to promote health and wellness to the community as part of the Tonawanda Health Study. We anticipate that the results of the epidemiologic studies will provide the residents of Tonawanda and Grand Island with the necessary information about the current burden of disease crucial for making rational decisions about initiatives to prevent these diseases in the future. Moreover, the Tonawanda Environmental Health Center will assist the community to translate these findings into action to reduce the disease burden going forward.

Introduction

The Tonawanda Coke Corporation was convicted of releasing coke oven gas in violation of the Clean Air Act. Coke oven gas is a complex mixture of compounds, including hydrogen, methane, carbon oxides, polycyclic aromatic hydrocarbons, benzene, and heavy metals. The United States Environmental Protection Agency (EPA) classifies coke oven emissions as a Group A, known human carcinogen (<http://www.epa.gov/ttnatw01/hlthef/cokeoven.html>). Similarly, the International Agency for Cancer Research classifies coke production as carcinogenic to humans (Group 1 carcinogen) (1). Epidemiologic studies conclusively demonstrate that coke oven workers engaged in charging the coke ovens have a higher incidence of lung cancer mortality as compared with coke oven workers engaged in other work activities (2, 3). In addition to lung cancer, reproductive effects and cardiopulmonary mortality have also been associated with coal combustion (4) in epidemiologic studies. Given that coke oven emissions are known human health hazards, residents of Tonawanda and Grand Island, New York began expressing concern about adverse health effects due to pollution emanating from the Tonawanda Coke facility.

In 2007, at the urging of the local community, the New York State Department of Environmental Conservation (DEC) measured ambient concentrations of benzene that exceeded acceptable levels in several locations surrounding the Tonawanda Coke facility. Tonawanda residents requested that the New York State Department of Health (DOH) conduct a health study to address concerns that high levels of benzene could be causing adverse health effects because benzene is a known human carcinogen, and constituent of coke oven emissions (5). Subsequently, DOH conducted a registry-based health study to compare the incidence of cancers and the prevalence of birth defects in several communities surrounding the Tonawanda Coke facility (6). The DOH study observed that lung cancer incidence was higher than expected in several of these communities. However, registry-based studies can have important limitations that preclude making strong inferences about whether coke oven emissions released from Tonawanda Coke caused these cancers or birth defects. For instance, authors of the DOH study note that they were unable to control for potential confounding by cigarette smoking, the leading cause of lung cancer in the United States. Consequently, the DOH study is provocative and provides clues that residents in this community are experiencing increased morbidity (i.e., cancers) as compared with other communities, but has important limitations that prevent scientifically rigorous inferences about exposure and the diseases examined.

Given that coke oven emissions are known to be toxic to humans, that the Tonawanda Coke facility released large amounts of coke oven gas into the ambient air, and that the New York State Department of Environmental Conservation has documented ambient concentrations of benzene and formaldehyde to exceed acceptable levels, we propose to conduct a community-based epidemiologic study to determine the disease burden in the Tonawanda and Grand Island communities. Secondly, we propose to investigate associations between adverse health events and proximity to Tonawanda Coke and ambient air pollution to further understand the role of pollution in the etiology of these diseases. The proposed project was designed to achieve three notable benefits for these communities. First, the phase I research activities of the proposed project will identify the constellation of diseases/conditions that are primary contributors to mortality and morbidity in this community. Second, once we have identified the major diseases of concern, the longitudinal phase of the proposed project will also be able to begin elucidating the likely explanations for the increased incidence of these diseases, whether it is environmental exposures or lifestyle factors. Third, the biomonitoring activities of the proposed project will inform the community about their current exposure to benzene, which will be crucial to developing strategies to reduce exposure.

Significance

Coke oven emissions consist of a complex mixture of toxic and carcinogenic constituents including polycyclic aromatic hydrocarbons (e.g., benzo(a)pyrene), benzene, and heavy metals. **Table 1** depicts 50 hazardous compounds identified in coke oven emissions by the US EPA (2). As previously noted, coke oven emissions are known human hazards at occupational exposure levels, which are generally much higher than environmental exposure levels. It is unknown, however, to what extent lower levels of exposure to these

pollutants increase the risk of adverse health effects. Given this uncertainty about the exposure-response relationship it is challenging to provide clear and unequivocal information about the risks posed by coke oven emissions released to the Tonawanda and Grand Island communities.

The NYSDOH conducted a “health outcomes review” because of the communities concerns about industrial pollution (6). Briefly, the health outcomes review conducted by the NYSDOH relied on the New York State Cancer Registry and the New York State Birth Defects Registry. Necessarily, the only health outcomes assessed included cancers (multiple sites) and the prevalence of birth defects. Other important public health outcomes, including cardiovascular, respiratory, and metabolic conditions (e.g., diabetes mellitus) were not evaluated. Moreover, a number of methodological limitations in the NYSDOH health study limit the inferences that can be rendered about the outcomes assessed. As previously mentioned, the cancer sites that had increased incidence in several community sections all have established risk factors that need to be considered. These cancers (e.g., cancer of the lung and bladder), having multiple causes, further complicates clear and concise communication with the public. Smoking tobacco, for instance, is a leading cause of lung cancer in the United States and accounts for nearly 90% of all lung cancer cases diagnosed in the United States. In order to rigorously determine whether exposure to coke oven emissions released from Tonawanda Coke contribute to adverse health effects, it is necessary to assess and control for other known risk factors (e.g., smoking) to remove confounding, a major threat to observational research. Fortunately, confounding by other risk factors has long been known and methods have been developed to mitigate their effect in observational research. The proposed project is designed to directly investigate adverse health effects associated with low level exposure to coke oven emissions, controlling for other known risk factors that may confound associations, a key limitation of the NYSDOH health study.

Table 1. Hazardous Coke Oven Gas Constituents

Benzene soluble organics	Cumene
Benzene	Butadiene
Hydrocyanic acid	Carbonyl sulfide
Toluene	Benzo(e) pyrene
Naphthalene	Benzo(b)fluoranthene
Xylene	Phosphorus
Lead	Hydrochloric acid
Benzo(a)pyrene	Hydrofluoric acid
Acenaphthylene	Chromium
Arsenic	Cadmium
Nickel	Phenol
Fluoranthene	Cobalt
Manganese	Antimony
Pyrene	Dibenzofuran
Selenium	Cresol, p-
Anthracene	Beryllium
Benzo(a)anthracene	Mercury
Acenaphthene	Cresol, o-
Indeno(1,2,3-cd)pyrene	Benzo(k)fluoranthene

In addition to the limited number of health outcomes evaluated, the potential for confounding from smoking and other important risk factors, the NYSDOH study did not assess individual exposure levels and is essentially ecological in nature. The overall approach to exposure classification in the NYSDOH study was to group census blocks into high impact and moderate impact areas based on benzene concentrations measured by the NYSDEC. The use of these impact areas to classify exposure assumes that within each area all individuals were exposed uniformly. Given that the diffusion of air pollutants is highly dynamic and influenced by a number of factors, including, pollutant concentration, particle size, wind direction, and atmospheric turbulence (7), the veracity of this assumption is questionable and further limits the conclusions that can be drawn for the NYSDOH study. The current project proposes to use several exposure assessment modalities that will overcome the limitations inherent in the NYSDOH study. Specifically, we propose to assess current internal dose levels of benzene by measuring urinary benzene metabolites and several geographic information science (GIS) based approaches to reconstruct historical exposure to each participant’s residence.

In summary, the proposed project will provide the residents of Tonawanda and Grand Island with important information regarding the current health status of the community. Such information is a prerequisite for sound decision making and focusing initiatives to reduce the burden of disease in the community. The longitudinal phase of the proposed project will be crucial for the identification of the major determinants of the mortality and morbidity in the community, and again, a prerequisite to public health action intended to reduce the burden of disease. In addition, the biomonitoring study (aim 2) will provide the community with crucial information about ongoing exposure that will be critical to identifying solutions to reduce these exposures.

1. Exposure and Health Study of the Residents of Tonawanda and Grand Island

Specific Aims

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We propose to conduct a multi-phase epidemiologic study to investigate the current health status of residents of the Town of Tonawanda and Grand Island (census tracts 73.02 and 73.04). Broadly, this initial phase of the Tonawanda Health Study will consist of a comprehensive health survey to characterize the prevalence of numerous health conditions, including cardiovascular diseases, diabetes mellitus, cancers, kidney disease, and respiratory diseases. This baseline health survey will be crucial in identifying the major health concerns of the community as well as identifying health conditions to target in the longitudinal phase of the Tonawanda Health Study. In addition to characterizing the current burden of disease in the residents of Town of Tonawanda, we propose to collection biologic specimens (i.e., blood, urine, saliva, and toe nail clippings) to biomonitor and characterize the current body burden to hazardous pollutants in the environment. Finally, we propose to use current and historical air pollution data form this region and Geographic Information Science (GIS) to reconstruct historical exposure to air pollution for the residents of the Town of Tonawanda and Grand Island. This aspect of the phase I studies will be crucial in future phases to estimate the association between exposure to pollutants emanating from the Tonawanda Coke facility and the incidence of adverse health effects.

The second phase of the Tonawanda Health Study is comprised of active and passive follow-up activities and epidemiologic analyses of incident disease. Passive follow-up consists of linking established databases to track the current residential address of all cohort members. The National Change of Address database maintained by the United States Post Office is commonly used for this type of tracking. In addition, the New York State public health law requires that physicians, laboratories, and hospitals that diagnose and treat cancers report to the New York State Cancer Registry. By linking with the Cancer Registry we will identify cohort members who have been diagnosed with any cancer. We will then use these data to conduct epidemiologic analyses of exposure (assessed in phase I) and cancer incidence. In addition, we will link with the National Death Index to identify decedent cohort members and the cause of death and determine whether cause-specific mortality is associated with exposure. In addition to passive follow-up, we will also conduct active follow-up on the cohort to determine the incidence of non-reportable diseases. Active follow-up consists of conducting additional rounds of a health surveys on a two year interval to ascertain recent diagnoses of cardiovascular disease, diabetes mellitus, respiratory disease, and other conditions.

We propose a prospective cohort study of residents in the Town of Tonawanda and Grand Island, consisting of two phases and total of four specific aims.

Phase 1 (years 1 and 2)

- 1) **Determine the current community health status for the Town of Tonawanda and Grand Island by conducting a baseline health survey.** We will quantify the prevalence of all major health conditions (e.g., cardiovascular diseases, cancers, respiratory diseases, diabetes mellitus, and kidney disease). We will also obtain information on known and established risk factors such as smoking, diet, reproductive history and family history of diseases.
- 2) **Characterize the extent of current ongoing exposure to benzene among residents of the Town of Tonawanda and Grand Island.** We will quantify urinary benzene metabolites (i.e., phenol, catechol, hydroquinone, 1,2,4-trihydroxybenzene, *t,t*-muconic acid, and *S*-phenylmercapturic acid) in spot urine specimens to estimate current body burden of benzene.

Phase 2 (years 3 to 10)

- 3) **Reconstruct historical exposure to air pollution using the AirData maintained by the US EPA and Geographic Information Science (GIS).**
- 4) **Initiate 10 years of active and passive surveillance in the cohort residents of the Town of Tonawanda and Grand Island to determine the incidence of chronic diseases and investigate potential associations with exposure to pollutants emanating from the Tonawanda Coke Corp.**

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In summary, we propose to conduct an epidemiologic cohort study to characterize the current health status of the Tonawanda and Grand Island communities and to determine current body burden of benzene, a known human carcinogen and constituent of coke oven emissions. In addition, establishing a large baseline cohort will facilitate the two major research activities (i.e., passive and active follow-up) to further expand our knowledge of the health effects associated with unwitting exposure to coke oven gas and other environmental pollutants. Targeted active follow-up activities will be developed to test novel hypotheses that require the collection of additional information and/or biologic specimens. For example, a subset of cohort members previously determined to be highly exposed to coke oven gas in the baseline cohort assessment and a subset of cohort members with low-exposure could be randomly selected and recruited to investigate whether the incidence of myocardial infarction (MI) is increased among exposed cohort members. This would require active follow-up to identify MI cases because MI is not a reportable condition and treating physicians do not report MI cases to state maintained registries. The baseline cohort will also serve as a sampling frame from which smaller and more expensive molecular epidemiologic studies will be conducted to test important hypotheses regarding environmental exposure to air pollutants and adverse health effects.

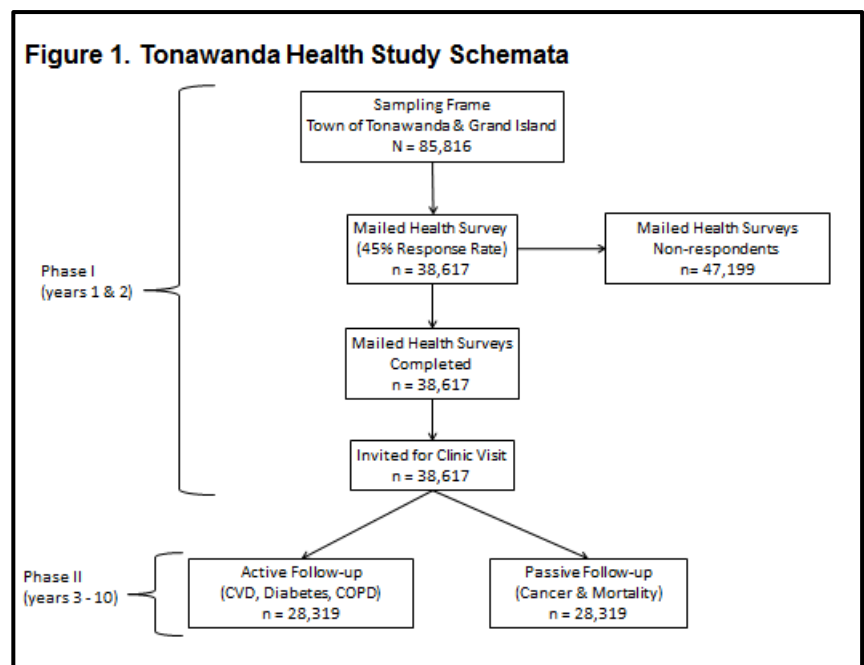
Research Plan

Source Population. The Town of Tonawanda and Grand Island (census tracts 73.02 and 73.04), New York has 85,816 residents (U.S. 2010 Census). Fifty-three percent of the residents are female (n=45,516). All current residents will comprise the source population for the proposed project.

Study Design: Prospective Cohort Study. We propose a prospective observational cohort study design to address the project goals and aims described previously. The overall study plan has been divided into two phases, with phase I (years 1-2) being focused on recruitment and baseline data collection activities that relate to specific aims 1 and 2, while Phase II (years 3-10) activities relate to aims 3 and 4. We

propose ten years of follow-up because of compelling evidence indicating that the latent period between exposure to benzene, and other leukemogenic chemicals is between two and ten years (8).

Recruitment. The Town of Tonawanda and Grand Island (census tracts 73.02 and 73.04), New York has 85,816 residents (U.S. 2010 Census) who will comprise the source population from which we will recruit study participants. Rather than develop a sampling frame, which randomly selects a proportion of the source population, we propose to target the entire source population for recruitment. Broadly, our approach will include advertising to the community through the local newspapers (i.e., Buffalo News and Tonawanda News), local radio, (WBFO), and television (Channels 2, 4, 7). However, our primary approach will be direct mailing of health surveys to residents at their homes. We will purchase a residential list for the Town of Tonawanda and Grand Island from the Polk City Directories. The Polk City Directories lists 86,000 records for the Town of Tonawanda (personal communication). Through advertising and the Polk City Directory, we should successfully contact nearly all households in the Town of Tonawanda and Grand Island. Given the wide spread coverage in the local media of the prosecution of Tonawanda Coke facility, relying on advertisements will likely skew the sample of participants to individuals with pre-existing conditions and under-ascertain those



without such conditions. The use of the Polk City Directories as the primary sampling frame will reduce the potential for selection biases to compromise the internal validity of the study.

We will not exclude any current residents based on age, sex, or ethnicity from participating in the Tonawanda Health Study; however the proposed mechanism of recruitment (the Polk Directories) will be most appropriate to identify households rather than all members of each household. Therefore, once a member of the household responds by returning a baseline questionnaire, we will then inquire about other family members and invite them to participate as well. Although we will not exclude former residents of Tonawanda and Grand Island or individuals who work in the Town of Tonawanda or Grand Island, but do not reside in there, from volunteering to participate, we will not actively pursue such individuals because of the logistic challenges in enumerating those who move out of the study area.

Baseline Questionnaire. A self-administered mail-back questionnaire will be used to obtain a detailed self-reported medical history, health habits (smoking and alcohol intake, physical activity, and diet), occupational history, residential history, socio-demographic information (ethnicity, education and income) and reproductive history for female participants. Data from the baseline questionnaire will be carefully cleaned and coded prior to being keyed into the study database. The primary variables from the questionnaire that will be used for analyses are shown in **Table 2**.

<p>1. <u>DEMOGRAPHICS</u></p> <ul style="list-style-type: none"> • Age • Sex • Household income • Education • Martial Status • Number of children 	<p>3. <u>LIFESTYLE HABITS</u></p> <ul style="list-style-type: none"> • Smoking history • Alcohol intake • Usual diet • Physical activity
<p>2. <u>MEDICAL HISTORY</u></p> <ul style="list-style-type: none"> • Present disease history <ul style="list-style-type: none"> • Cardiovascular Dx • Hypertension • Diabetes mellitus • Cancers • Kidney Dx 	<p>4. <u>RESIDENTIAL HISTORY</u></p> <ul style="list-style-type: none"> • Street number and name • Years at each residence
	<p>5. <u>OCCUPATIONAL HISTORY</u></p> <ul style="list-style-type: none"> • Longest held job • Work place exposure to solvents and other chemicals

The questionnaire will be designed with the assistance of experts in survey methods and epidemiological research. The questionnaires will be pilot-tested and practical problems related to editing,

coding, and electronically storing the questionnaire responses will be identified and addressed. Of the 85,816 residents of the Town of Tonawanda and Grand Island, we anticipate that the survey response rate will be approximately 45% ($n=38,617$). This estimate is based on several previous epidemiologic studies conducted in Western New York in recent years. We will undertake activities to enhance the response rate to this mail-back health survey. Non-response bias is a concern in epidemiological surveillance and we will be able to investigate this issue in the Tonawanda Health Study cohort by comparing the Tonawanda cohort demographics with that of the 2010 Census for the entire Town of Tonawanda and Grand Island.

Lifestyle health habits. As part of the proposed questionnaire, our planned health survey includes lifestyle and health habits that may confound or modify the association between coke oven gas exposure and chronic disease risk. These questions will ascertain detailed information on dietary intake and alcohol consumption, occupational and leisure-time physical activity, occupational toxin exposures, reproductive health issues, family medical history, and medication usage. The specific questions that will be used to survey the above health variables will be selected, when possible, from existing published questionnaires that have been used in other epidemiologic follow-up studies. Dr. Bonner and research staff in the Department of Social and Preventive Medicine are experienced in developing and assessing the psychometric properties of questionnaires aimed at assessing a variety of environmental, lifestyle, and medical exposures.

Survey methods. We will use established and standard methods to enumerate the Tonawanda Health Study cohort. Our standard practice is to pretest the survey questionnaire, including testing the mail survey. The pilot survey will be tested in a sample of 50 (25 men, 25 women) participants and will allow for an evaluation of

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problems that individuals may have in completing the questionnaire, and identify potential problems with the mailing service firm, with our survey management system, and other aspects of the survey.

We have been heavily influenced by the survey methods recommended by Dillman (9). Specific techniques include a personalized approach (1st class postage, individual inside address and salutation, typed addresses instead of mailing labels, and a social utility discussion in the cover letter), use of colored paper, large font sizes, and a systematic mailing schedule that has been successful in many studies (a pre-notification mailing about 2-3 weeks prior to the initial survey mailing, 3 survey mailings with a reminder postcard 1 week after the initial mailing, a second questionnaire and new cover letter to non-respondents 3 weeks after the initial mailing, and a final mailing [certified mail] to non-respondents 4 weeks after the third mailing). We will conduct follow-up telephone calls as a final attempt to contact non-respondents and obtain responses to the follow-up questionnaire. The logistics of the planned survey are formidable, but we have been successful in managing large cohort study surveys and there is no reason that we will be any less successful with the proposed survey.

We propose to work with a local survey firm, Survey Service, Inc. located in Kenmore, NY, to conduct the survey mailings. In our experience, they are reliable and have never missed a scheduled mailing. We have had no major problems with the logistics of conducting the previous surveys and anticipate that the planned work will be accomplished as described. We will generate the pre-notification letter, the cover letter, and the health survey. We then will send electronic versions of these materials along with the names and addresses of survey participants to Survey Service, Inc. They will print the pre-notification letter and the cover letter and then will prepare the packets for mailing. Packets will be mailed on Tuesday to avoid the weekend. The reminder postcards will be produced in advance and mailed on the following Tuesday. Returned questionnaires are received daily at our study office. Questionnaires returned by the postal service because the participant has moved and the forwarding order has expired will be logged into a bad address file. Returned questionnaires will be opened, reviewed for completeness, and logged into the survey management system as received. Incomplete questionnaires will be flagged and study staff will attempt to contact the participant by telephone to complete missing questions. The non-respondent file will be updated daily and is monitored by the mailing service prior to the next scheduled mailing. They will begin to prepare questionnaire packets for the next mailing. Returns during the week that the next mailing is being prepared will continue to be logged in as received, and the day before the next mailing, the mailing list will be updated. Questionnaire packets for participants who provided these late returned questionnaires will be pulled on the day of the next scheduled mailing. This reduces the likelihood that a person who has already returned a questionnaire will get a second one. Research staff will populate and monitor a tracking database throughout the entire survey period and will provide our study team with a final report on respondents and non-respondents. We will attempt a final contact of non-respondents using the telephone, after which the survey period will be closed.

In addition to the above detailed survey techniques, we also will implement in the planned follow-up survey other methods that have been reported to enhance survey response rates (10-12). These include: (1) the use of pre-notification study newsletter to reacquaint participants with the study's objectives, with previous study findings, and to alert participants about the forthcoming health survey, (2) use of a 2 color survey and large font sizes, (3) inclusion of a clever message on the outbound mailing envelop to increase the likelihood of participants opening the survey, (4) use of public service announcements about the study in various local media outlets, (5) mailing the pre-notification newsletter, (6) inclusion of a pen with the study name and logo on it.

In summary, the mail survey will be implemented following the methods that have been successful in published studies. We believe that the proposed research team and associated study staff have demonstrated competence in conducting such surveys and expect to be successful with the survey planned in this application.

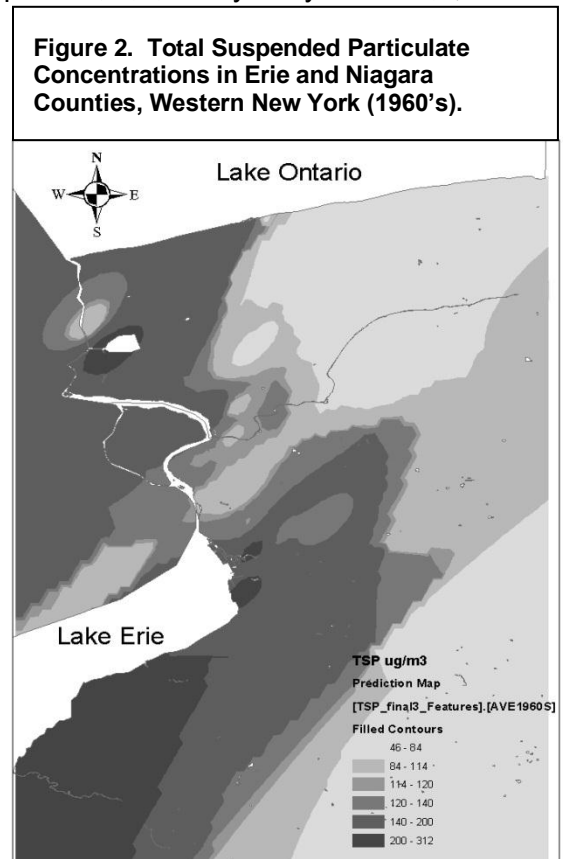
Baseline Clinical Evaluation and Biologic Specimen Collection. After participants agree to participate in the Tonawanda Health Study and return the baseline questionnaire, research staff will telephone respondents to schedule a clinical visit at the School of Public Health and Health Professions Center for Health Research

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(University at Buffalo). At this clinical visit, participants will be asked to complete an additional food frequency questionnaire to assess usual diet, and will be asked to donate, blood, urine, saliva, and toe nail clippings. A urine collection container will be given to each participant prior to the interview with instructions for collecting a clean specimen. Blood will be collected into four 10ml vacutainer tubes (2 EDTA, 1 heparin, and 1 serum) by an experienced phlebotomist to minimize participant discomfort. Saliva will be collected with an Oragene DNA self-collection kit. All samples will be immediately placed into wet ice and transported to our processing laboratory where each specimen will be processed, aliquoted and stored at -80°C at the University at Buffalo's Clinical and Translational Research Center BioBank for future testing. A 0.5ml aliquot of urine will be used by our analytical laboratory to quantitate six urinary benzene metabolites (see Biomonitoring Current Exposure below). Anthropometric measures (weight, height, waist circumference) and blood pressure will be measured by trained research staff.

Coke Oven Gas Exposure Assessment. Given that the primary emission of concern from the Tonawanda Coke Corp. plant was coke oven gas, which is a complex mixture of constituents that are known hazardous air pollutants, we propose several metrics to assess human exposures in the Tonawanda Health Study. These metrics are designed to capture various aspects of exposure that may contribute to adverse health effects in the Town of Tonawanda and Grand Island. Broadly, these metrics can be classified into biomonitoring of current exposures, which are ongoing, and historical exposures, which happened in the past, recent as well as long-term.

Biomonitoring Current Exposure. Biomonitoring has become an important approach to assessing body burden to environmental contaminants in recent decades (13) and can provide important information regarding the types and levels of exposure to pollutants. Given the high ambient concentrations of benzene found in several communities surrounding the Tonawanda Coke Facility by the DEC air sampling study, we propose to quantify urinary benzene metabolites (i.e., phenol, catechol, hydroquinone, 1,2,4-trihydroxybenzene, *t,t*-muconic acid, and *S*-phenylmercapturic acid) in spot urine specimens to estimate current body burden of benzene. The method developed by Waidyanatha et al (2004) will be used to quantify these six main benzene metabolites in participant urine specimens (3). Briefly, 0.5ml of urine is treated with internal standards and extracted with 100 μl of hexane and derivatized with 100 μl Trisil reagent and heated to 70°C for 30 minutes. Derivatized extracts will be analyzed by gas chromatography-electron impact-mass spectrometry (GC-EI-MS)(3). Several limitations need to be considered when interpreting data on urinary benzene metabolites. First, these metabolites are not necessarily specific to benzene exposure and are synthesized in small amounts from normal endogenous metabolic processes. Second, benzene is ubiquitous in the environment, arising from a myriad of sources, including tobacco smoke and automobile emissions. Therefore, urinary levels may not accurately reflect exposure specifically to coke oven gas released from Tonawanda Coke. Third, individual genetic variability in benzene metabolizing enzymes may impact urinary metabolite excretion. Nonetheless, a comparison of levels of urinary benzene metabolites among the Tonawanda Health Study cohort members with other populations will be informative as to whether exposures are high in Tonawanda and Grand Island and whether body burden is correlated with proximity residential to the Tonawanda Coke Facility and/or disease outcomes.



Historical Exposure Assessment. The biologic half-life of benzene metabolites is quite short. Consequently, urinary benzene metabolites are generally poor estimates of long-term exposure and other methods are required to quantify or reconstruct historical exposures. Several historical exposure metrics will be developed to reconstruct historical exposure to coke oven gas emitted from Tonawanda Coke Corp. Residential proximity to Tonawanda Coke Corp. will be the initial metric that will be derived from a GIS approach, and will also serve as a foundation for several other metrics. In the baseline questionnaire, we will ascertain each cohort member's residential history, including all addresses and the duration of residence at each address in the Town of Tonawanda and Grand Island. These data will be used to geocode each participant address and the Tonawanda Coke Corp. address. Geocoding is a standard practice that locates addresses (i.e., latitude and longitude) on a map and a GIS database that can then incorporate other information for that location. For instance, the geocoded addresses will be used to calculate the Euclidean distance between each cohort member's residence and Tonawanda Coke, albeit a crude, but important estimate of potential exposure to hazardous emissions from Tonawanda Coke. In addition, we will integrate duration of residence with proximity to a cumulative estimate of exposure to emission from Tonawanda Coke.

This estimate of cumulative exposure, however, does not incorporate the intensity of exposure (i.e., concentration), and therefore, retains measurement error, which could hamper our ability to identify associations between proximity, duration of proximity, and the integrated metric, cumulative proximity. Fortunately, ambient air monitoring of total suspended particulate (TSP) as well as other criterion air pollutants have been routinely measured in Erie County since the late 1950's and monitoring continues today. The US EPA warehouses these data that will be used to reconstruct historical exposures to total suspended particulates, and particulate matter <10 microns (PM₁₀). We successfully used this same approach to investigate air pollution exposure over the life course and breast cancer risk in a previous study (14). Specifically, we will reconstruct an annual intensity of exposure at each participant's residence using standard geostatistical interpolation methods (e.g., inverse distance interpolation). Using inverse distance interpolation, Figure 2 depicts the annual average concentration of TSP in Erie and Niagara Counties in the 1960's. Once each address has been assigned an annual average concentration of TSP and PM₁₀, we will then integrate cumulative exposure estimate for these two air pollutants. We must recognize that the air monitoring system that has been set in place captures air pollution from sources in addition to the Tonawanda Coke Corp. Nonetheless, coke production is a major contributor to air pollution and the geospatial pattern that emerges from this exposure assessment may add supporting evidence that emissions from the Tonawanda Coke plant contribute to the overall levels of air pollution as well as adverse health events among Tonawanda and Grand Island residents.

In addition to the metrics described above, we will seek to partner with the New York Department of Environmental Conservation to develop dispersion models based on their air monitoring activities relating to the Town of Tonawanda and Grand Island.

Case-finding and verification. The case-finding questions for ascertaining chronic disease occurrence are comparable to the approach taken in other large scale epidemiologic studies that have used mail-back questionnaires for population surveillance. Sensitivity and specificity of questions for the specific diseases that we will survey tend to be quite high in other population samples that use similar case-finding questions (15-18). For example, among a large cohort of women and men prospectively followed in the Aerobics Center Longitudinal Study, a sensitivity of 98% and a specificity of 99% has been seen for reported physician-diagnosed hypertension obtained from responses to a mail-back questionnaire that used the same case-finding question as we will use (15). Using a similar case-finding question as we will use for physician diagnosed type 2 diabetes, investigators in the Nurses' Health Study and the Health Professionals Follow-up Study found >95% agreement between reported cases and diabetes status based on medical record review (16, 17).

Although the case-finding questions that we will use are similar to those that have successfully been used in other large prospective studies, we realize that differences in population characteristics may influence the accuracy of recalled and reported health information. We therefore, will implement a rigorous case verification

system to validate and adjudicate reported study endpoints for specific analysis projects. This will require several standardized activities that will be carefully monitored to protect participant and data confidentiality, to include: obtaining from participants appropriate HIPAA and consent forms to permit obtaining medical records from their healthcare provider; electronic coding and tracking of case follow-up correspondences and medical record information; use of standardized definitions for case validation and adjudication; convening periodic meetings of trained and experienced case adjudicators (e.g., physicians, nurse practitioners, epidemiologists) to review and validate reported case files; and ongoing monitoring and updating study data files and survey response records. The process of case verification is substantial and will progress through the duration of the proposed study.

Statistical Analysis. Standard epidemiologic statistical methods developed for cohort studies (19) will be employed to test the proposed specific aims. Because there are several planned analyses in the proposed project, we begin with an overview of methods and then highlight a general approach to the analysis plan for each hypothesis. Where numbers permit, we will carry out the overall analyses separately in women and in men, and by baseline age group. Statistical analysis of study endpoints will be based on the multiple-logistic regression model for binary outcomes, given that the date of onset of these outcomes is sometimes unknown or uncertain. The loss of efficiency compared with time-to-event analysis will be negligible, and no cases need be omitted due to incomplete event times. The measure of association will be the odds ratio (OR), here a close approximation to the risk ratio, with associated Wald *p*-values and 95% confidence intervals. This is an approach that has been used in other large prospective cohort studies (20). Prevalent cases at baseline will be excluded from analyses. Incident cases will be counted up to the first mail survey on which an endpoint is self-reported; they are then removed from subsequent follow-up. Adjustment of ORs for baseline differences in age, sex, race, and length of follow-up will be standard, with all analyses stratified by survey period. Adjustment for potential confounding between exposure and covariates not intermediate in the causal pathway will be applied as needed. Among these are socioeconomic status, smoking history, body mass index, family history, prevalent disease at baseline (when not used as the outcome) dietary and alcohol intake, physical activity habits, sleep habits, and in some analyses, occupational toxin exposures and reproductive health factors among women. One-*df* tests for trend in cumulative incidence rates or ORs across grouped levels of exposure will use ordinal scoring for categorical exposure variables. Numerical exposure variables first will be centered and then mean scoring will be used as the metric between groups entered in trend analysis as ordinal terms. Additivity (goodness-of-link) and time-dependence of effects will be examined, and residuals will be inspected for model departures and outliers.

2. Tonawanda Coke Corporation Occupational Cohort Study

We recognize that not only were residents unwittingly exposed to coke oven gas, but so were Tonawanda Coke Corporation employees. Therefore, we propose to conduct a retrospective occupational cohort study to investigate all-cause and cause-specific mortality among past and current employees. For this component of the Tonawanda Health Study, we will use employee records to retrospectively reconstruct a cohort of individuals who were or currently are employed by Tonawanda Coke Corp. All employee records, dating back to 1978 when the Tonawanda Coke Corp. started, will be reviewed by trained research staff. Research staff will abstract the employees' names, date of births, date of hire, and date of termination. Job titles and the corresponding starting date and ending date for that job will also be abstracted for each job held. We will work with an industrial hygienist to develop a job exposure matrix (JEM) to assess exposure to coke oven gas based on the job title. Briefly, a JEM ranks the probability and level of exposure to specific industrial chemicals based on specific job titles and the associated job activities.

We will link with the National Death Index (NDI) to determine the vital status of all the employees. For all decedent employees identified through the NDI linkage, we will obtain death certificate to determine the cause of death. The primary analyses will assess mortality among this occupational cohort. First, standardized mortality ratios (SMR) will be calculated using the New York State age and sex specific mortality rates as the comparison group. This comparison with the New York State will provide preliminary information about whether the employees at Tonawanda Coke Corp. have a higher mortality rate than the State. However, this

type of analysis is potentially prone to a selection bias, termed the 'healthy worker effect.' It's been long recognized that employed individuals have lower mortality than the general population because sick individuals tend to drop out of the work force. Nonetheless, SMR analyses are important first steps and not all occupational studies are equally susceptible to the health worker effect. Second, we propose to conduct internal comparisons within the cohort itself. For this set of analyses, we will compare the mortality rates (all-cause and for each cause-specific mortality) among employees with different exposure levels to coke oven gas.

3. Tonawanda Environmental Health Education Center

The University at Buffalo proposes to establish a Tonawanda Environmental Health Education Center to meet the continuing needs of the community to promote health and wellness as part of the Tonawanda Health Study. The Environmental Health Education Center will provide a readily accessible site for meeting community members interested in participating in the Health Study, supporting the activities of the Health Study and providing outreach and educational activities throughout the 10 year duration of the Tonawanda Health Study.

Community members from the Town of Tonawanda and University at Buffalo faculty from The Schools of Public Health and Health Professions, Biomedical Sciences, and Nursing will participate in the planning and development phase of establishing the Center.

It is anticipated that the Environmental Health Education Center will be managed by a Director of Environmental Health Education (RN, MPH) who will be assisted by two Health and Wellness Educators with experience in nursing, public health, and environmental health. The Center space must be designed to provide confidential space for explaining the goals of the Tonawanda Health Study, consenting those that agree to participate, assisting with completion of the study questionnaires, and answering questions from the community related to the Tonawanda Health Study. Three phlebotomists will collect biological specimens from study participants that enroll in the Tonawanda Health Study.

Other functions of the Tonawanda Environmental Health Education Center will include, but are not limited to:

- Providing an Environmental Health and Wellness Resource for Residents of the Town of Tonawanda.
- Providing access to health professionals that can provide a wide range of educational activities to promote health and wellness for members of the community
- Providing access to environmental health professionals that can educate community members and address the concerns of community members
- Providing blood pressure screening, health education regarding hypertension, and when medically necessary assist community members in obtaining medical care from a physician. It is not anticipated that physicians will treat community members in the Center, but the center staff will provide health education and when necessary refer community members to physicians.
- Providing a wide range of printed and electronic resources on environmental health and wellness.
- Provide a site for launching additional new health and wellness initiatives, such as diabetes screening and education, if indicated by the results of the Tonawanda Health Study or if requested by the community.

As data from the Tonawanda Health Study becomes available, health educators will communicate the results to community members. These finds will include the individual data on exposure to critical air pollutants (urine benzene metabolite levels) and population based finding on the state of the health of residents of the Town of Tonawanda.

A critical role for the team of Health Educators will be to help explain the findings of the Health Study, provide strategies for improving the health of the individual and the health of the community, and address the wide range of questions that are expected to be raised by individual community members.

Matthew R. Bonner, Ph.D. *The Tonawanda Health Study*

Advisory Committee and Community Engagement. We propose to establish an advisory committee to oversee and advise the study investigators during the course of the Tonawanda Health Study. The advisory committee will consist of three scientific advisors and three community representatives. The scientific advisors should have diverse, but pertinent scientific expertise in disciplines that will complement the research staff. These disciplines include, but are not limited to exposure assessment, spatial statistics, medicine, and toxicology. Community representatives to the advisory committee will be identified by community leaders. The advisory committee, in cooperation with the study investigators, will develop procedures to ensure that members of the community are active participants in steering the scientific directions of the Tonawanda Health Study. The advisory committee will also provide oversight and work with the study investigators to develop periodic reports to the community on study activities and important results. We will also develop a Tonawanda Health Study website to post periodic updates, electronic copies of reports to the community, and all scientific publications and presentations coming from the Study.

The sustained success of this project will be highly dependent upon the community's participation, in terms of being willing research subjects and in steering the research agenda to increase our knowledge about potential health effects associated with environmental pollution, particularly pollution emanating from Tonawanda Coke.

Future Directions. Given the opportunity to establish a large population-based cohort in the Town of Tonawanda and Grand Island, a unique scientific resource will be established that will facilitate long-term contribution to understanding the role that environmental pollution has in a number of chronic diseases. In fact, one of the primary strengths of a cohort study is that we can investigate many different diseases and their relationship with pollution. It's reasonable to anticipate that the Tonawanda cohort would be under surveillance until that last member dies as has been done with the Framingham MA cohort, which was established in 1948. To achieve such a long-term goal, we have proposed to collect numerous biologic specimens such as blood, urine, saliva, and toenails and to store these specimens in our department's biorepository. While we have not proposed specific research activities for these specimens, other than the urine, they are a critically important resource that will permit study investigators to test new hypotheses using new and novel laboratory assays going forward. For example, the saliva specimens are a good source for participant DNA that will permit investigations of genetic susceptibility and genetic contribution to risk of certain diseases, and the impact of environmental factors on these outcomes. Stored urine samples can be used in the future to measure exposures to other pollutants, such as pesticides or phthalates. Toe nail clipping can be used to assess exposure to heavy metals such as lead cadmium, and arsenic. Blood will be used to assess blood lipids and fasting glucose, which will be important to characterizing baseline cardiovascular disease risk and other health conditions, including diabetes mellitus. All of these resources, including the biologic specimens, the questionnaire and health survey data, the active and passive surveillance of the cohort will offer great opportunities to conduct epidemiologic research and investigate novel and cutting-edge hypotheses. Once the Tonawanda Health Study cohort and all the data for phase I have been collected and the health survey has been analyzed, we will initiate ancillary studies to investigate new scientific hypotheses that emerge. These ancillary studies will be funded through standard grant seeking mechanisms at the National Institutes of Health (NIH) and foundations. For example, aberrant DNA methylation has been etiologically linked with several cancer sites. To investigate DNA methylation in the Tonawanda Health Study, we would seek funding from the NIH to cover the costs of measuring DNA methylation in the stored DNA samples. Finally, in the event that a community based Environmental Health Institute is proposed for this region, the Tonawanda Health Study may serve as the primary research arm of such an Institute.

Institutional Support and Administration of Funds. The University at Buffalo's Sponsored Projects Services in the Office of the Vice President for Research and Economic Development will administer the funds allocated for this proposed project. Oversight of all allocated funds will be conducted in accordance with the University at Buffalo's established research policies, including ethical conduct of research and fiscal administration of sponsored projects. The University at Buffalo is committed to supporting the local community and recognizes the importance of public health research within local communities.

Timeline

Time Table										
AIMS/TASKS	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8	Year 9	Year 10
Develop Protocols & Questionnaires	XX									
Recruit Participants	XX	XX								
Clinic Visits	XX	XX	XX							
Laboratory Assays	XX	XX	XX							
Active Follow-up			XX			XX			XX	
Passive Follow-up			XX			XX			XX	
Exposure Reconstruction		XX	X							
Employee Record Abstraction	XX	XX								
Data Analysis		XX	XX	XX	XX	XX	XX	XX	XX	XX
Report & Manuscript Development		XX	XX	XX	XX	XX	XX	XX	XX	XX
Health Education Center	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX

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Budget Justification

Personnel

Dr. Matthew R. Bonner is requesting 30% effort for years 1 through 10. Dr. Bonner's expertise is in environmental epidemiology. He has extensive experience in conducting large prospective cohort studies with active surveillance, biologic specimen collection and cancer registry linkage. Dr. Bonner's previous research has focused primarily on environmental exposures and several outcomes, including cancer and neurobehavioral deficits. As the principal investigator, he will oversee and have responsibility for all aspects of the project, including supervision of research staff, active surveillance, study design, study protocol development, questionnaire development, active surveillance, clinic visits, data warehouse and web portal development and management, data analysis and interpretation of study results, and manuscript development and publication. In addition to overseeing all aspects of the research studies, Dr. Bonner will oversee all aspects and management of the Tonawanda Environmental Health Center.

Dr. James Olson is requesting 10% of base salary for the 10 year duration of this project. Dr Olson is a UB Distinguished Professor and Director of the Environmental Health Division within the School of Public Health and Health Professions. As a toxicologist and environmental health scientist, Dr. Olson has experience and expertise ranging from basic research on xenobiotic metabolism and global gene expression to assessment of biomarkers of exposure, effect and susceptibility in large, international, population-based studies. Dr. Olson will work with Dr. Bonner and study staff in the conduct of the project, focusing on study protocol development, questionnaire development, collection of biologic specimens, assaying of biologic specimens, data analysis and interpretation of study results and manuscript development.

Co-investigator, To Be Named, is requesting 5% of base salary for the 10 year duration of this project. The co-investigator will work with Drs. Bonner, Olson and study staff in the conduct of the project, with a particular focus on overseeing the laboratory analyses proposed. In addition, the co-investigator will participate in active surveillance study design, study protocol development, questionnaire development, data analysis and interpretation of study results and manuscript development.

Project Coordinator, To Be Named, will assist Dr. Bonner in the day-to-day operations of this research project. The project coordinator will be responsible for database management of tracking the return of completed questionnaires and coordinating with Survey Services, a local survey firm, ensure completing of the questionnaire mailing. Other essential activities include assisting in the development of the questionnaires, cover letter to accompany the questionnaire, newsletter, telephone follow-up with non-responders, event verification activities, routing IRB and HIPPA forms, Database development, and other activities to accomplish the goals of the research project. We are requesting 75% effort for the duration of the project.

Study Manager, To Be Named, Will work closely with the Project Coordinator and Dr. Bonner in the day-to-day operations of this research project. The Study Manager will oversee the clinic visits, have direct supervisory responsible for the research staff (phlebotomists, research associates) and coordinate with the laboratory staff the transfer of biologic specimens to the laboratory. Other essential activities include assisting in the development of the questionnaires, cover letter to accompany the questionnaire, newsletter, telephone follow-up with non-responders, event verification activities, routing IRB and HIPPA forms, Database development, and other activities to accomplish the goals of the research project. We are requesting 75% effort for the duration of the project.

Ms. Mya Swanson, Data Manager, will act as the Data Manager throughout the proposed project. Ms. Swanson, who has 30 year of experience with epidemiologic studies in Western New York, will serve throughout the course of this program as data manager. She will develop necessary study reports and ensure that investigators have a proper understanding of the methods involved and their performance. She will work closely with investigators and supervise the Project Coordinator in developing data collection forms, data entry procedures and data file preparation (extraction) procedures and will participate in the analysis of the data. Ms.

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Swanson's activities on this project will be more concentrated in years 2 through 5; therefore we are requesting 50% of her salary for year 1, 100% for years 2 through 5, and 50% for years 6 through 10.

Phlebotomists (3), To Be Named, will conduct all blood draws during the clinical visit. In addition, the Phlebotomists may also assist the Research Associates in collecting the other biologic specimens (urine, saliva, and toe nail clippings). We are requesting 50% salary for both Phlebotomists in year 1 and 75% salary in years 2 and 3 of the project.

Research Associates (2) to be committed to the Tonawanda Health Study, To Be Named, will assist Ms. Swanson and the Project Coordinator, and the Study Manager in the day-to-operations of the research project. Specifically, the Research Associates will conduct the administration of the food frequency questionnaire and collection of urine, saliva, and toenail clippings. The Research Associates will also assist in event verification activities, telephone follow-up of non-responders, data management and other activities. We are requesting 100% effort for both positions for the duration of the project.

Research Associates (2) to be committed to the Tonawanda Coke Occupational Cohort Study, To Be Named, will assist Ms. Swanson and the Project Coordinator, and the Study Manager in the day-to-operations of the research project. Specifically, the Research Associates will conduct employee record abstraction for job title, years of employment and identifying information to linkage with the National Death Index and New York State Cancer Registry. The Research Associates will also assist data management and other activities. We are requesting 100% effort for both positions for the years 1 through 5 of the project.

Laboratory Technicians (2), To Be Named, will be under the direct supervision of Dr. Olson, will be conduct the urinary benzene metabolite assays planned in years 1, 2 and 3. We are requesting 75% salary for one Laboratory Technician and 50% salary for a second Laboratory Technician for years 1 through 3.

Equipment

Dedicated instrumentation (gas chromatography-electron impact-mass spectrometry (GC-EI-MS)) is needed to complete the analysis under aim 2 during the first phase of the proposed study. Aim 2 will characterize the extent of current ongoing exposure to benzene among residents of the Town of Tonawanda and Grand Island by quantifying urinary benzene metabolites (i.e., phenol, catechol, hydroquinone, 1,2,4-trihydroxybenzene, *t,t*-muconic acid, and *S*-phenylmercapturic acid) in spot urine specimens to estimate current body burden of benzene. The method of Waidyanatha et al., 2004, was chosen since it has been peer reviewed and optimized as a sensitive and rapid method for analysis of six urinary benzene metabolites in human urine.

Using 2 dedicated instruments, the chromatographic method for the analysis of 6 benzene metabolites requires about 45 min of instrument time on each instrument to analyze one urine sample. With the automatic sample injector working 24 hour a day, 5 days a week, it will be possible to analyze 8,320 urine specimens per year. Three years of analysis will allow us to quantify benzene metabolites in urine specimens from 24,960 residents.

The Analytical Toxicology Lab at the University of Buffalo has dedicated laboratory space and small equipment needed for urine sample preparation prior to the chromatographic analysis. However, the laboratory does not have GC-EI-MS instruments which can be dedicated 100% time for the next 3 years to conduct this study. Agilent Technologies provided quotes for GC-EI-MS instruments with an auto injector (providing 24 hr/day analysis capabilities). A total of \$200,000 was budgeted for two instruments.

Supplies for Blood and Urine Collection (\$12 per subject)

Specimen collection supplies, including urine collection cups, vacutainers, alcohol pads, cryovials, latex gloves, butterfly needles, sharps containers

Laboratory Supplies (\$20 per subject)

Supplies for analysis of Urinary Benzene metabolites

(Extraction vials, autosampler vials and caps, inserts, chemical, reagents, GC columns, gas, other glassware, and gloves)

Oragene kits for collection of saliva and isolation of DNA

Biorepository Service & Fees (\$70,000 per year for 10 years)

All biological specimens collected from this project will be banked and maintained at the University at Buffalo's Clinical and Translational Research Center BioBank. Services include sample management, sample processing, aliquotting, and storage in -80 freezers and sample retrieval and shipping to testing laboratories.

Data Warehouse & Web Portal Development (\$120,000 for year 1)

The proposed project will partner with the University at Buffalo's Center for Unified Biometrics and Sensors to develop a state of the art data warehouse to integrate all participant data collected, including health survey data, laboratory test results, and data obtain from linking with the New York State Cancer Registry and the National Death Index). We also develop a secure web portal to collect additional information from study participants via the internet.

Other Expenses

Polk Directory (\$3,000) for the Town of Tonawanda containing the names and addresses of the Tonawanda residents will be purchased to serve as the primary sampling frame for the proposed project.

We are requesting \$10,000 for advertising in local papers, radio, and television.

Survey Service, Inc. (\$1,070,984 total for years 1, 3, 6, and 9) will be contracted for printing and mailing of the 3 waves of questionnaires and pre-notification postcards and newsletter. They will also conduct various activities to correct addresses including a search of the National Change of Address database, and other strategies to up-date cohort member addresses.

Event verification (\$31,800 total; years 3, 6, and 9) contact with participant physician's to confirm self-reported disease events. Our requested \$10,600 per year is to cover costs associated with these activities, including physician office photocopy and mailing and/or medical records charges and other related activities.

Participant incentives are requested to increase participation to the clinic visit. A \$40 incentive will be paid to each participant who completes the clinic visit.

Job exposure matrix development (\$50,000 total for years 1 and 2). We will contract with an industrial hygiene consulting firm to develop a job exposure matrix for employees of the Tonawanda Coke Corporation.

Advisory Committee Activities (\$150,000 total for years 1-10). These activities include honoraria for the scientific advisors (\$1,000 per visit per scientific advisor), travel and lodging for the scientific advisors (\$3,000 per visit per advisor),

Tonawanda Environmental Health Education Center

Personnel

Director of Environmental Health Education, To Be Named, will direct the day-to-day operations of the health center under Dr. Bonner's oversight. The director will supervise the two health educators to provide the services outlined in this proposal. We are requesting 100% effort for the 10 year period of the project at an annual salary and fringe benefits of \$100,000.

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Health Educator with RN/MPH (2), To Be Named, will be supervised by the Director of Environmental Health Education to provide the services outlined in the proposal. We are requesting 100% effort for the 10 year period of the project at an annual salary and fringe benefits of \$80,000

Other annual costs for 10 years of the Center

We propose to rent space in the community to facilitate recruitment into the Tonawanda Health Study and to be a local health education resource for the community. We estimate that an annual lease for 1,500 square foot facility will cost \$18,000.

We also estimate following annual cost for:

Utilities	\$6,000
Phone, internet, and Cable	\$2,000
Office supplies	\$2,000
<u>Lease on photocopier scanner</u>	<u>\$2,500</u>
Sub-total	\$12,500

We estimate that the total annual costs including the personnel, rent, and utilities to be \$290,500

In addition to these annual costs, we estimate a one-time expense for the following:

Office furniture, chairs for community meetings	\$12,000
Computer and printer/photocopy /scanner FAX	\$5,000
Flat screen TV for educational activities	\$1,000
Office supplies	\$2,000
Phlebotomy chairs 3x500 =	\$1,500
Storage cabinets	\$1,500
File cabinets	\$1,000
Lights, carpet, painting	\$7,000
Estimated Remodeling cost	\$25,000
Refrigerator	\$2,000
Freezer	\$2,000
<u>Centrifuge</u>	<u>\$3,000</u>
Sub-total	\$63,000

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Bonner, Matthew R		POSITION TITLE Associate Professor	
eRA COMMONS USER NAME (credential, e.g., agency login) MBONNER			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	MM/YY	FIELD OF STUDY
Ohio University, Athens, OH	B.A.	1989-1991	Anthropology
University of Rochester, Rochester, NY	M.P.H.	1995-1998	Epidemiology
University at Buffalo, Buffalo, NY	Ph.D.	1998-2003	Epidemiology
National Cancer Institute, Bethesda, MD	Postdoc	2003-2005	Epidemiology

A. Personal Statement

Broadly, my background is in occupational/environmental and molecular epidemiology. Much of my research has focused on the cancer risks associated with occupational and environmental exposure to pesticides and ambient air pollution. I am the principal investigator of the New York State Angler Cohort Study, a prospective cohort study of 17,000 anglers and spouses. The primary purpose of this cohort study is to investigate long-term exposure to environmental pollutants, such as organochlorine insecticides, found in the Great Lakes region and cancer risk. In addition, I am a co-investigator on prospective cohort study in Beijing, China to investigate air pollution and perturbations in biomarkers of oxidative stress/damage and immune function. Of particular relevance to the application, I have successfully collaborated with Dr. Olson (Co-I) on a cohort study investigating neurobehavioral deficits in Adult Egyptian cotton workers in the same region of Egypt since 2007. Through these sustained research activities, I have developed extensive expertise in designing and conducting large prospective cohort studies, including recruiting and enrolling participants, developing questionnaires, collecting biologic specimens, tracing participants, developing relational databases that integrate data from various research activities, and analyzing longitudinal data.

B. Positions and Honors**Positions and Employment**

2003-2005 Postdoctoral Fellow, Occupational and Environmental Epidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health, Department of Health and Human Services, Bethesda, MD.

2005-2011 Assistant Professor, Department of Social and Preventive Medicine, University at Buffalo, Buffalo, NY.

2011- Associate Professor, Department of Social and Preventive Medicine, University at Buffalo, Buffalo, NY.

Honors and Awards

National Cancer Institute Predoctoral Training Fellowship, 1999-2003.

Saxon Graham Award for excellence in epidemiology, University at Buffalo, 2003.

National Cancer Institute Postdoctoral Fellowship Award 2003-2005.

University at Buffalo Exceptional Scholars –Young Investigator Award, 2010.

C. Selected Peer-reviewed Publications (14 of 48)

1. Lan Q, Mumford JL, Shen M, Demarini DM, **Bonner MR**, He X, Yeager M, Welch R, Chanock, Tian L, Chapman RS, Zheng T, Keohavong P, Caporaso N, Rothman N. Oxidative damage-related genes ARK1C3 and OGG1 modulate risks for lung cancer due to PAH-rich coal combustion emissions. *Carcinogenesis* 2004 Vol. 25 (1), 2177-2181. PMID: 15284179

2. **Bonner MR**, Han D, Nie J, Rogerson P, Vena JE, Muti P, Trevisan M, Edge SB, Freudenheim JL. Breast Cancer Risk and Exposure in Early Life to Polycyclic Aromatic Hydrocarbons using Total Suspended Particulates as a Proxy Measure. *Cancer Epidemiology, Biomarkers, and Prevention* 2005 Vol. 14 (1), 53-60. PMID: 15668476
3. **Bonner MR**, Lee WJ, Sandler DP, Hoppin JA, Dosemeci M, Alavanja MCR. Occupational Exposure to Carbofuran and the Incidence of Cancer in the Agricultural Health Study. *Environmental Health Perspectives* 2005 Vol. 113 (3) 285-289. PMID:1253753
4. **Bonner MR**, Rothman N, Mumford JL, He X, Shen M, Welch R, Yeager M, Chanock S, Caporaso N, Lan Q. Green tea consumption, genetic susceptibility, PAH-rich smoky coal and the risk of lung cancer. *Mutation Research-Genetic Toxicology and Environmental Mutagenesis* 2005 Vol. 582/1-2, 53-60. PMID: 15668476
5. **Bonner MR** and Alavanja MCR. The Agricultural Health Study Biomarker Workshop on Cancer Etiology, Introduction: Overview of Study Design, Results, and Goals of the Workshop. *Journal of Biochemical and Molecular Toxicology* 2005 Vol.19 (3), 169-171. PMID: 15977198
6. **Bonner MR**, Nie J, Han D, Vena JE, Rogerson P, Freudenheim JL. Secondhand Smoke Exposure in Early Life and the Risk of Breast Cancer among Never Smokers. *Cancer Causes and Control* 2005 Vol. 16, 683-689. PMID: 16049807
7. **Bonner MR**, Bennett WP, Xiong W, Lan Q, Brownson RC, Harris CC, Field RW, Lubin JH, Alavanja MCR. Radon, Secondhand Smoke, Glutathione-S-transferase M1 and Lung Cancer among Women. *International Journal of Cancer* 2006 Vol. 119, 1462-1467. PMID: 16642467
8. **Bonner MR**, Coble J, Beane-Freeman L, Blair A, Sandler D, Hoppin JA, Alavanja MCR. Malathion Exposure and the Incidence of Cancer in the Agricultural Health Study. *American Journal of Epidemiology* 2007, Vol. 166 (9), 1023-1034. PMID: 17720683
9. Farahat FM, Olson J, Fenske RA, Galvin K, **Bonner MR**, Rohlman DS, Lein PJ, Anger WK. Chlorpyrifos Exposures in Egyptian Cotton Field Workers. *Neurotoxicology*, 2010 Vol. 31 (3): 297-304. PMID: 20193710
10. Shen M, Zhang L, **Bonner MR**, Liu CS, Li G, Vermeulen R, Dosemeci M, Yin S, Lan Q. Association between mitochondrial DNA copy number and occupational benzene exposure. *Environ Mol Mutagen*, 2008, Vol.49 (6), 453-7. PMID: 17632764
11. **Bonner MR**, Shen M, Liu CS, DiVita M, He X, Lan Q. Mitochondrial DNA Content and Lung Cancer Risk. *Lung Cancer* 2009, Vol. 63 (3), 331-4. PMID: 18691788
12. Farahat FM, Ellison CA, Olson JR, **Bonner MR**, Crane AL, Fenske RA, Galvin K, Rohlman DS, Anger WK, Lein PJ. Biomarkers of chlorpyrifos exposure and effect in Egyptian cotton field workers. *Environmental Health Perspectives*. 2011 Vol. 119(6): 801-6. PMID:21224175
13. Ellison CA, Crane AL, **Bonner MR**, Knaak JB, Browne RW, Lein PJ and Olson JR. PON1 status does not influence cholinesterase activity in Egyptian agricultural workers exposed to chlorpyrifos. *Toxicology and Applied Pharmacology*. 2012 Dec 15;265(3):308-15
14. Li Y, Nie J, Beyea J, Rudra CB, Browne RW, **Bonner MR**, Mu L, Trevisan M, Freudenheim JL. Exposure to traffic emissions: Associations with biomarkers of antioxidant status and oxidative damage. *Environ Res*. 2013 Feb;121:31-8.
15. Crane AL, Rasoul GA, Ismail AA, Hendy O, **Bonner MR**, Lasarev MR, Al-Batanony M, Singleton ST, Khan K, Olson JR, Rohlman DS. Longitudinal assessment of chlorpyrifos exposure and effect biomarkers in adolescent Egyptian agricultural workers. *J Expo Sci Environ Epidemiol*. 2013 Jul;23(4):356-62.

D. Research Support

Ongoing Research Support

R01 ES022163-01 Rohlman (PI)
NIEHS

3/4/2013 – 11/30/2017

“Assessing Vulnerability of the Adolescent Brain to Organophosphorus Pesticides”

This is a large multidisciplinary, international study (Menoufia University in Egypt) that will evaluate neurobehavioral impacts of organophosphorus pesticides in adolescents, using standardized behavioral tests, biomarkers of exposure, and metabolic genotyping. The longitudinal study will investigate the relationship between sensitive and specific biomarkers of pesticide exposure, effect and susceptibility and multiple measures of neurobehavioral function in this unique cohort over a 5 year period to assess cumulative and potentially reversible effects. Our overarching hypothesis is that the inherent plasticity of the developing adolescent brain will allow recovery from selected neurobehavioral deficits associated with short- and long-term exposures to pesticides.

Role: Co-Investigator

NIH 1R01ES018846-01A1 (Mu)

02/04/2011-12/31/2013

Biological Response to Air Quality Change in Beijing pre-, mid- and post-Olympics

The aims of the proposed study are to examine whether changes in air pollution exposure over the course of the Olympics are related to changes in oxidative damage and antioxidant defense, or related to changes in respiratory and systemic inflammatory response.

Role: Co-Investigator

Completed:

1 R-833454 (Olson)
US EPA STAR Grant

09/01/2007-08/31/2012

CYP-Specific PBPK/PD Models to Interpret Biomarkers for Organophosphate Pesticides

The primary objective of the proposed studies is to improve existing pharmacokinetic /pharmacodynamic (PBPK/PD) models to better estimate exposures, target tissue dose and resulting effects in human populations, utilizing the abundance of urinary metabolite / biomarker data for the organophosphate (OP) pesticides, chlorpyrifos, parathion, methyl parathion, and diazinon. It is hypothesized that more accurate measures of exposure, target tissue dose and subsequent effects will come from existing PBPK/PD models, which incorporate human CYP-specific kinetic parameters (Km and Vmax) for OP metabolism, CYP-specific content in the liver, and the function and content of genetic variants in key enzymes (CYP2B6, CYP2C19, PON1) which regulate OP metabolic activation and detoxification.

Role: Co-investigator

R01 ES016308 (Anger and Lein)
NIEHS

05/15/2008 – 05/14/2012

Biomarkers of Organophosphorus Pesticide-Induced Neurotoxicity

The proposed studies will test the hypotheses that OP-induced neurobehavioral deficits are dose-related and that measures of oxidative stress and inflammation are better predictors of neurobehavioral deficit than cholinesterase inhibition. These hypotheses will be tested by studying a cohort of adult pesticide application workers in Egypt's Menoufia Governorate previously reported to exhibit the broadest range of neurobehavioral deficits in humans following OP exposure. Rat studies will be conducted in parallel to test candidate biomarkers as predictors of OP-induced neurobehavioral deficits. The proposed studies will provide critical data needed to develop effective biomarkers of OP exposure, biological response and genetic susceptibility.

Role: Co-investigator

1R01 TS000077 (Bonner)

09/30/2007-09/29/2011

ATSDR/CDC

New York State Angler Cohort Follow-up Study (NYSACS)

Proposed is follow-up of a cohort of New York State licensed anglers to investigate consumption of contaminated Great Lakes sport fish and selected adult chronic diseases, including endometriosis, cancer and thyroid disease.

Role: Principal Investigator

R21 (Rusiecki)

09/24/2008-08/31/2011

NIH

Pesticide Exposure and DNA Methylation in Pesticide Applicators

Proposed is a study to determine the relationship between lifetime exposure to specific pesticides and altered DNA methylation, including global hypomethylation and gene-specific hypermethylation, in a group of pesticide applicators enrolled in the Agricultural Health Study.

Role: Co-investigator

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME James R. Olson		POSITION TITLE Professor of Pharmacology and Toxicology	
eRA COMMONS USER NAME JROLSON			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Illinois Wesleyan University, Bloomington, IL	BA	1974	Chemistry
Medical College of Wisconsin – Milwaukee, WI	MS	1976	Pharmacology
Medical College of Wisconsin – Milwaukee, WI	PhD	1978	Pharmacol/Toxicology

A. Personal Statement

As a co-investigator for the Tonawanda Health Study, I will work with Dr. Bonner and study staff in conducting all phases of the project, focusing on study protocol development, questionnaire development, collection of biologic specimens, assaying of biologic specimens, data analysis and interpretation of study results and manuscript development. I will also be available to interact with community members on issues related to toxicology and environmental health. As a U.B. Distinguished Professor, with appointments in Social and Preventive Medicine (School of Public Health and Health Professions) and Pharmacology and Toxicology (School of Medicine and Biomedical Sciences), I have maintained an active, productive research program in toxicology and the environmental health sciences. My research experience and expertise ranges from basic research on xenobiotic metabolism and global gene expression to assessment of biomarkers of exposure, effect and susceptibility in large, international, population-based studies. For the past 32 years, I have maintained a consistent, strong record of extramural funding as a Principal Investigator (PI) and Co-Investigator (Co-I) from agencies including NIEHS, U.S. EPA, and CDC/ATSRD. I have extensive experience successfully mentoring junior faculty, postdoctoral fellows, Ph.D., M.D./Ph.D. and M.S. students, including serving as the major professor for 15 Ph.D. students that trained in my lab. My former students and fellows have received an NRSA Predoctoral Fellowship, numerous awards from the Society of Toxicology and currently are enjoying successful research and teaching careers (tenure track faculty, Assistant Dean, and senior research and regulatory positions in industry).

Positions and Honors

1978-1980	Res. Assoc. Vanderbilt University, Nashville, Tennessee, Center in Environ. Toxicology
1980-1986	Assistant Professor, Dept of Pharmacology and Therapeutics, SUNY/Buffalo, NY
1984-present	Associate Director, Toxicology Research Center, SUNY/Buffalo, NY
1986-1994	Associate Professor, Dept of Pharmacology and Toxicology, SUNY/Buffalo, NY
1994-2009	Clinical Professor, Dept. Social & Preventive Medicine, SUNY/Buffalo, NY
1994-present	Professor, Department of Pharmacology and Toxicology, School of Medicine and Biomedical Sciences, SUNY/Buffalo, NY
2010-present	Research Professor and Director, Environmental Health Sciences Division, Dept. Social and Preventive Medicine, School of Public Health and Health Professions, SUNY/Buffalo, NY
2007	Sustained Achievement Award, Exceptional Scholar Program, University at Buffalo
2012	U.B. Distinguished Professor

B. Selected Peer-Reviewed Publications (most recent from over 100)

Farahat, F.M., Ellison*, C.A. Bonner, M.R., McGarrigle, B.P., Crane, A.L*, Fenske, R.A., Lasarev, M.R., Rohlman, D.S., Anger, W.K., Lein, P.J., Olson, J.R. Biomarkers of chlorpyrifos exposure and effect in Egyptian cotton field workers. *Environmental Health Perspectives*, (2011) 119: 801-806. doi:10.1289/ehp.1002873

Yang D, Lauridsen H, Buels K, Chi L-H, La Du J, Bruun DA, Olson JR, Tanguay RL, Lein PJ. Chlorpyrifos-oxon disrupts zebrafish axonal growth and motor behavior. *Toxicol Sci*, (2011) 121(1), 146–159. doi: 10.1093/toxsci/kfr028.

Foxenberg RJ*, Ellison CA*, Knaak JB, Ma, C, and Olson, JR. Cytochrome p450-specific human PBPK/PD models for the organophosphorus pesticides: chlorpyrifos and parathion. *Toxicology*, (2011) 285, 57-66. <http://dx.doi.org/10.1016/j.tox.2011.04.002> .

Ellison, C.A.* , Smith, J.N., Lein, P.J., and Olson, J.R. Pharmacokinetics and pharmacodynamics of chlorpyrifos in adult male Long-Evans rats following repeated subcutaneous exposure to chlorpyrifos. *Toxicology* 287, 137-144, 2011. doi:10.1016/j.tox.2011.06.010 |

Ellison, C.A*., Tian. Y*., Knaak, J.B., Olson, J.R. Human hepatic cytochrome P450-specific metabolism of the organophosphorus pesticides methyl parathion and diazinon, *Drug Metabolism and Disposition* (2012) 40: 1-5. dmd.111.042572

Ellison, C.A*., Abou El-Ella, S.S., Tawfik, M., Lein, P.J., Olson, J.R. Allele and genotype frequencies of CYP2B6 and CYP2C19 polymorphisms in an Egyptian population. *Journal of Toxicology and Environmental Health, Part A*, (2012) 75: 1-10. DOI: 10.1080/15287394.2012.641201

Lein PJ, Bonner MR, Farahat FM, Olson JR, Rohlman DS, Fenske RA, Lattal KM, Lasarev MR, Galvin K, Farahat TM, Anger WK. Experimental strategy for translational studies of organophosphorus pesticide neurotoxicity based on real-world occupational exposures to chlorpyrifos. *Neurotoxicology*. (2012) 33 (4): 660-668. doi:10.1016/j.neuro.2011.12.017

Crane, A.L*., Klein, K., Zanger, U.M., Olson, J.R., Effect of CYP2B6*6 and CYP2C19*2 genotype on chlorpyrifos metabolism. *Toxicology* (2012) 293: 115-122. doi:10.1016/j.tox.2012.01.006

Fenske, R.A., Farahat, F., Galvin, K., Fenske, E.K., Olson J.R., Contributions of Inhalation and Dermal Exposure to Chlorpyrifos Dose in Egyptian Cotton Field Workers, *International Journal of Occupational and Environmental Health*, (2012) 18 (3): 198-209. Doi:10.1179/1077352512z

Crane, A.L*., Klein, K., Olson, J.R., Bioactivation of chlorpyrifos by CYP2B6 variants. *Xenobiotica*, (2012) 42(12): 1255-1262. DOI: 10.3109/00498254.2012.702246

Ellison, C.A.* , Crane, A.L.* , Bonner, M.R., Knaak, J.B., Browne, R.W., Lein, P.J., and Olson, J.R. PON1 status does not influence cholinesterase activity in Egyptian agricultural workers exposed to chlorpyrifos. *Toxicology and Applied Pharmacology* (2012) 265: 308-315. doi.org/10.1016/j.taap.2012.08.031
*Equal contributing first authors

Feo, M.L., Gross, M.S., McGarrigle, B.P., Eljarrat, E., Barceló, D., Aga, D.S., and Olson, J.R. Biotransformation of BDE-47 to Potentially Toxic Metabolites Is Predominantly Mediated by Human CYP2B6. *Environmental Health Perspectives* (2013) 121 (4): 440-446. doi:10.1289/ehp.1205446

Crane, A.L*., Singleton, S.T*., Lasarev, M. R., Ismail, A., Abdel Rasoul, G., Hendy, O., McGarrigle, B.P., Bonner, M.R., Olson, J.R., and Rohlman, D.S. Longitudinal Assessment of Chlorpyrifos Exposure and Effect Biomarkers in Adolescent Egyptian Agricultural Workers. 2013. *Journal of Exposure Science and Environmental Epidemiology*, (2013) 23: 356-362. doi:10.1038/jes.2012.113

Dadson, O.A.* Ellison, C.A.* Singleton, S.T.* Chi, L.H., McGarrigle, B.P., Lein, P.J., Farahat, F.M., Farahat, T., Olson, J.R. Metabolism of profenofos to 4-bromo-2-chlorophenol, a specific and sensitive exposure biomarker. *Toxicology* (2013) 306: 35-39. 10.1016/j.tox.2013.01.023

Tang, X., Wu, X., Dubois, A.* , Sui, G., Wu, B., Lai, G., Gong, Z., Gao, H., Liu, S., Zhong, Z., Lin, Z., Olson, J. and Ren X. Toxicity of Trimethyltin and Dimethyltin in Rats and Mice. *Bull Environ Contam Toxicol* (2013) 90: 626-633. DOI 10.1007/s00128-013-0975-x

Tang, X, Li, N, Kang, L, Dubois, AM, Gong, Z, Wu, B, Lai, G, Yang, A, Ruan, X, Gao, H, Zhu, H, Ge, Y, Zhang, J, Lin, Z, Olson, JR, and Ren, X. Chronic Low Level Trimethyltin Exposure and the Risk of Developing Nephrolithiasis. *Occupational and Environmental Medicine*, (2013) 70 (8): 561-567. doi:10.1136/oemed-2012-101261

Ongoing Research Support

F30 ES020655-01A1 Olson (PI) 2/1/2012 – 1/31/2014
NIEHS

“The Impact of Genetic Variability on Human Susceptibility to Chlorpyrifos”

NRSA Predoctoral Fellowship on behalf of Alice Crane, MD/PhD student.

It is hypothesized that known functional polymorphisms in human CYP2B6 will exhibit variability in the kinetics for the bioactivation of CPF to CPF-O and that the CYP2B6 genotype of an individual will be related to their relative susceptibility to CPF toxicity. This project will determine the key *in vitro* kinetic parameters for CPF metabolism by each CYP2B6 polymorphism of interest. Kinetic data from identified allelic isoforms will be incorporated into a recently developed human physiologically based pharmacokinetic/pharmacodynamic (PBPK/PD) model for CPF in order to investigate the impact of CYP2B6 genotype on modeling simulations which predict BuChE and AChE inhibition using various exposure scenarios.

Role: Mentor for Alice Crane

R21 ES021554 Olson and Aga (PIs) 4/1/12 – 3/31/2014 1.2 calendar
NIEHS

“Bioactivation of PBDEs by Human Cytochrome P-450”

The overall objectives of this application are to characterize the enzyme- and congener-specific metabolism of PBDEs in humans and investigate qualitative and quantitative differences in metabolism which are related to genetic variability in key biotransforming enzymes. The proposed studies will ultimately better inform future mechanistic and epidemiological studies investigating the potential of PBDEs and their metabolites to produce neurobehavioral / neurodevelopmental disorders. In addition, these studies will lead to the identification of potential genetic biomarkers that contribute to interindividual variability in the bioactivation of PBDEs and ultimately the relative susceptibility of individuals to potential adverse effects of these agents.

Role: PI (contact)

R01 ES022163-01 Rohlman (PI) 3/4/2013 – 11/30/2017 1,2 calendar
NIEHS

“Assessing Vulnerability of the Adolescent Brain to Organophosphorus Pesticides”

This is a large multidisciplinary, international study (Menoufia University in Egypt) that will evaluate neurobehavioral impacts of organophosphorus pesticides in adolescents, using standardized behavioral tests, biomarkers of exposure, and metabolic genotyping. The longitudinal study will investigate the relationship between sensitive and specific biomarkers of pesticide exposure, effect and susceptibility and multiple measures of neurobehavioral function in this unique cohort over a 5 year period to assess cumulative and potentially reversible effects. Our overarching hypothesis is that the inherent plasticity of the developing adolescent brain will allow recovery from selected neurobehavioral deficits associated with short- and long-term exposures to pesticides.

Role: Co-Investigator, PI for studies conducted at the University at Buffalo (10% Effort)

OVERLAP: NONE

Recently Completed Research Support

RO1 ES016308 Anger and Lein (PIs) 5/15/08 – 5/14/13 1.2 calendar
NIEHS

“Biomarkers of Organophosphorus Pesticide-Induced Neurotoxicity”

The proposed studies will test the hypotheses that OP-induced neurobehavioral deficits are dose-related and that measures of oxidative stress and inflammation are better predictors of neurobehavioral deficit than cholinesterase inhibition. These hypotheses will be tested by studying a cohort of adult pesticide application workers in Egypt’s Menoufia Governorate previously reported to exhibit the broadest range of neurobehavioral deficits in humans following OP exposure. Rat studies will be conducted in parallel to test candidate biomarkers as predictors of OP-induced neurobehavioral deficits. The proposed studies will provide critical data needed to develop effective biomarkers of OP exposure, biological response and genetic susceptibility.

Role: Co-investigator; PI for studies conducted at the University at Buffalo

R-833454 Olson (PI) 9/1/07-8/31/12

US EPA STAR Grant

“CYP-Specific PBPK/PD Models to Interpret Biomarkers for Organophosphate Pesticides”

The primary objective of the proposed studies is to improve existing pharmacokinetic /pharmacodynamics (PBPK/PD) models to better estimate exposures, target tissue dose and resulting effects in human populations, utilizing the abundance of urinary metabolite / biomarker data for the organophosphate (OP) pesticides, chlorpyrifos, parathion, methyl parathion, and diazinon. It is hypothesized that more accurate measures of exposure, target tissue dose and subsequent effects will come from existing PBPK/PD models, which incorporate human CYP-specific kinetic parameters (Km and Vmax) for OP metabolism, CYP-specific content in the liver, and the function and content of genetic variants in key enzymes (CYP2B6, CYP2C19, PON1) which regulate OP metabolic activation and detoxification.

Role: PI

RO1 ES016308-02S Anger and Lein (PIs) 5/1/09 – 4/30/2012

NIEHS

“Biomarkers of Organophosphorus Pesticide-Induced Neurotoxicity”

Research Supplement to Promote Diversity in Health-Related Research on behalf of

Corie Ellison, Ph.D. Candidate, University at Buffalo, James Olson, Major Advisor. Role: PI and major professor

R21 ES017223 01 Rohlman (PI) 7/1/09 – 6/30/2012

NIEHS

“Assessing Vulnerability of the Adolescent Brain to Organophosphorus Pesticides”

The goal of this application is to examine the dose-related response of the adolescent brain to OP pesticides, to determine if repeated exposures produce a progressive deficit and to determine if this deficit is reversible.

Role: Co-Investigator, PI for studies conducted at the University at Buffalo

CURRICULUM VITAE

Name: Matthew R. Bonner

Work Address: Department of Social and Preventive Medicine
School of Public Health and Health Professions
University at Buffalo
The State University at New York
270 Farber Hall
3435 Main Street
Buffalo, New York, 14214
Phone #: (716) 829-5385
Fax #: (716) 829-2979
Email: mrbonner@buffalo.edu

Citizenship: United States

Education:

Ph.D. University at Buffalo, 2003
Epidemiology and Community Health
Dissertation Title: Environmental Exposures in Early Life and the Risk of Breast Cancer

M.P.H. University of Rochester, 1998

B.A. Ohio University, 1991
Major: Anthropology

Employment History:

8/11-present Associate Professor (tenure), Department of Social and Preventive Medicine, School of Public Health and Health Professions, University at Buffalo, The State University of New York, Buffalo, New York.

6/08-present Adjunct Assistant Professor, Division of Cancer Prevention and Population Sciences, Roswell Park Cancer Institute, Buffalo, New York.

8/05-8/11 Assistant Professor, Department of Social and Preventive Medicine, School of Public Health and Health Professions, University at Buffalo, The State University of New York, Buffalo, New York.

- 8/05-present Adjunct Investigator, Occupational and Environmental Epidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health, Department of Health and Human Services, Bethesda, Maryland.
- 8/03-8/05 Postdoctoral Fellow, Occupational and Environmental Epidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health, Department of Health and Human Services, Bethesda, Maryland.
- 4/99-6/03 Predoctoral Fellow, Cancer Training Fellowship, Department of Social and Preventive Medicine, University at Buffalo, The State University of New York, Buffalo, New York.
- 9/98-5/99 Graduate Assistant, Department of Social and Preventive Medicine, University at Buffalo, The State University of New York, Buffalo, New York.
- 1/96-5/98 Teaching Assistant, Department of Community and Preventive Medicine, University of Rochester School of Medicine and Dentistry, Rochester, New York.
- 4/94-7/95 Deferred Donor Registry Investigator, American Red Cross Blood Services, Rochester, New York.
- 3/94-4/94 Sample Management Supervisor, American Red Cross Blood Services, Consolidated Testing Laboratory, Rochester, New York.
- 1/93-3/94 Laboratory Assistant, American Red Cross Blood Services, Consolidated Testing Laboratory, Rochester, New York.

Honors and Awards:

University at Buffalo Exceptional Scholars –Young Investigator Award, 2010.

National Cancer Institute Postdoctoral Fellowship, 2003-2005.

Saxon Graham Award for Outstanding Research in Epidemiology, School of Public Health and Health Professions, University at Buffalo, 2003.

National Cancer Institute Predoctoral Training Fellowship, 1999-2003.

Outstanding Teaching Assistant Award, University of Rochester School of Medicine and Dentistry, 1997.

Professional Affiliations:

American Association for the Advancement of Science
American Association for Cancer Research
American College of Epidemiology
International Society for Environmental Epidemiology
Society for Epidemiologic Research

Departmental Service:

- 2009-2012 Member, Education Committee, Department of Social and Preventive Medicine, School of Public Health and Health Professions, University at Buffalo.
- 2008-2009 Chair, Environmental Health Program Advisory Committee, Department of Social and Preventive Medicine, School of Public Health and Health Professions, University at Buffalo.
- 2008-2009 Member, Admissions Committee, Department of Social and Preventive Medicine, School of Public Health and Health Professions, University at Buffalo.
- 2007-current Member, Recruitment Committee, Department of Social and Preventive Medicine, School of Public Health and Health Professions, University at Buffalo.
- 2006-present Member, Preliminary Exam Committee, Department of Social and Preventive Medicine, School of Public Health and Health Professions, University at Buffalo.
- 2005-2007 Member, Education Committee, Department of Social and Preventive Medicine, School of Public Health and Health Professions, University at Buffalo.
- 1999-2003 Student Member, Education Committee, Department of Social and Preventive Medicine, School of Public Health and Health Professions, University at Buffalo.

School of Public Health and Health Professions Service:

- 2012-present Member, Department of Social and Preventive Medicine Chair Search Committee, School of Public Health and Health Professions, University at Buffalo.

- 2009-2012 Director, Environmental Health MPH Program, Department of Social and Preventive Medicine, School of Public Health and Health Professions, University at Buffalo, The State University of New York, Buffalo, New York.
- 2009-2012 Member, MPH Program Committee, School of Public Health and Health Professions, University at Buffalo.
- 2009-2010 Member, Environmental Health Scientist Search Committee, School of Public Health and Health Professions, University at Buffalo.
- 2009-2011 Member, Academic Affairs Committee, School of Public Health and Health Professions, University at Buffalo.
- 2006-2008 President, Faculty Council, School of Public Health and Health Professions, University at Buffalo.

University Service:

- 2010 Member, Proposition Exam Committee, Department of Pharmacology and Toxicology, School of Medicine and Biomedical Sciences, University at Buffalo.

Other Professional Service:

- 2011-present Committee Member, New York State Great Lakes Biomonitoring Project Advisory Committee. New York State Department of Health.
- 2008 Program Committee Member, American College of Epidemiology Annual Scientific Sessions, Tucson, Az.
- 2004-2005 Co-chair, Mentoring Sub-Committee, NIH Fellows Committee, National Institutes of Health, National Institutes of Health.
- 2004-2005 Basic Science Representative, NIH Fellows Committee, National Cancer Institute, National Institutes of Health.
- 2004 Member, Organizing Committee, Agricultural Health Study Cancer Biomarker Workshop, National Cancer Institute, National Institutes of Health.

Grant Review:

- 2013 Panel member, Susan G. Komen for the Cure, Challenge Grants-Investigator Initiated Research: New Exposure Assessment Tools. Grapevine, Texas. (3/6/2013-3/8/2013).
- 2011 Ad hoc panel member, National Institutes of Health, Infectious Diseases, Reproductive Health, Asthma and Pulmonary Conditions Study Section. Washington, D.C. (10/13/2011-10/14/2011).
- 2011 Cancer Care Ontario Applied Cancer Research Units Review Panel. Toronto, Ontario, Canada.
- 2010 National Institute of Environmental Health Sciences Special Emphasis Panel, Breast Cancer and the Environment Review Committee (ZES1 LKB-V 02).
- 2008 National Cancer Institute Special Emphasis Panel, Small Grants for Behavioral Research in Cancer Control (ZCA1 SRLB-H (M1); ZCA1 SRBL-H (O2); and ZCA1 SRRB-K (O1).

Teaching:

Courses

- 2013 Advanced Methodology (SPM 502) Department of Social and Preventive Medicine, School of Public Health and Health Professions, University at Buffalo.
- 2008 Applications of Epidemiology to Environmental Health (SPM 551) Department of Social and Preventive Medicine, School of Public Health and Health Professions, University at Buffalo.
- 2006-present Molecular Epidemiology (SPM 614) Department of Social and Preventive Medicine, School of Public Health and Health Professions, University at Buffalo.

Guest Lectures

- 2007-present Environmental Epidemiology. In: Toxicology Principles and Practice (PMY 626) Department of Pharmacology and Toxicology, School of Medicine and Biomedical Sciences, University at Buffalo.
- 2006-present Analysis of Cohort Studies and Exposure Response Analyses. In: Analysis of Health Related Data (PTR 502) Department of Cancer Pathology and Prevention, Roswell Park Cancer Institute.

Theses and Dissertations:

Ph.D.

- 2007 Antara Majumdar: Maximum Likelihood Estimation of Measurement Error Models Based on the Monte Carlo EM Algorithm. Department of Biostatistics, School of Public Health and Health Professions, University at Buffalo. Committee Member.
- 2008 Mary Platek: Alcohol Consumption and Risk of Breast Cancer: Possible Mechanisms. Department of Social and Preventive Medicine, School of Public Health and Health Professions, University at Buffalo. Committee Member.
- 2009 Theodore Brasky: Non-steroidal Anti-inflammatory Drugs, Cyclooxygenase-2 Variation, and Breast Cancer Risk. Department of Social and Preventive Medicine, School of Public Health and Health Professions, University at Buffalo. Committee Member.
- 2011 Corie Ellison: Refining human physiologically based pharmacokinetic/ pharmacodynamic (PBPK/PD) models for organophosphate exposure: inclusion of cytochrome P-450 (CYP) specific metabolism. Department of Pharmacology and Toxicology, School of Medicine and Biomedical Sciences, University at Buffalo. Committee Member.
- 2012 Alice Crane: The Impact of Genetic Variability of Target Enzymes on Human Susceptibility to Chlorpyrifos. Department of Pharmacology and Toxicology, School of Medicine and Biomedical Sciences, University at Buffalo. Committee Member.

M.S.

- 2009 Melanie Ruszczyk: DNA Repair Genes and Ovarian Cancer Prognosis. Department of Social and Preventive Medicine, School of Public Health and Health Professions, University at Buffalo. Committee Member.
- 2010 Miriam Silverberg: Retrospective Review of Allopurinol Dose and Renal Function in Gout Patients With and Without Allopurinol Reactions. Committee Member
- 2012 Oswald Dadson: Human Exposure to Propenfos in Egypt. Department of Pharmacology and Toxicology, School of Medicine and Biomedical Sciences, University at Buffalo. Committee Member.
- 2013 John Heberger: A case-case comparison of ergonomic exposures associated with musculoskeletal injuries in maintenance workers of mineral processing mills and coal preparation plants. Committee Chair

M.P.H.

- 2008 Carleen Pope: PCBs and Thyroid Conditions in Anniston Alabama. Department of Social and Preventive Medicine, School of Public Health and Health Professions, University at Buffalo. Committee Chair.
- 2008 Rajprakash Chennamaneni: Determinants of PCB serum concentrations in Anniston Alabama. Department of Social and Preventive Medicine, School of Public Health and Health Professions, University at Buffalo. Committee Chair.
- 2009 Krista Trivieri: Organochlorine Pesticide serum concentration in Anniston Alabama. Department of Social and Preventive Medicine, School of Public Health and Health Professions, University at Buffalo. Committee Chair
- 2012 Joel Merriman: Use of Cellphone-Based Time-Activity Data for Air Pollution Estimation. Committee Member.

Current Ph.D. Student Mentees

Joseph Green
Catherine Callahan

Reviewer for Professional Journals:

American Journal of Epidemiology
Cancer
Cancer Causes and Control
Cancer Epidemiology, Biomarkers & Prevention
Epidemiology
Environmental Health Perspectives
Environmental Research
International Journal of Cancer
Journal of Occupational and Environmental Medicine
Lancet-Oncology
Preventive Medicine
Pulmonary Medicine
Respiratory Medicine

Invited Presentations:

Secondhand Smoke, Radon, *GSTM1*, and Lung Cancer in Women. Department of Social and Preventive Medicine, School of Public Health and Health Professions, University at Buffalo, State University of New York, Buffalo, NY. October 22, 2004.

Environmental and Occupational Exposures, Genetic Susceptibility, and Lung Cancer. Graduate School of Public Health, University of Pittsburgh, Pittsburgh, PA. December 6, 2004.

Radon, glutathione-s-transferase M1 and lung cancer in US women. Society for Epidemiologic Research. Salt Lake City, Utah. 2004.

The Agricultural Health Study: An Update. American Association of Pesticide Control Officers Spring Meeting, Arlington, VA., March 16, 2005.

Pesticides and the Cancer Risk. Roswell Park Cancer Institute, Buffalo, NY. December 16, 2006.

U.S. Atomic Energy Commission Sites and the Risk of Breast Cancer. Department of Geography. University at Buffalo. Buffalo, NY. October 19, 2007

Organophosphate Insecticides and the Incidence of Cancer. Center for Research on Occupational and Environmental Toxicology. Oregon Health Sciences University, Portland, OR. October 29, 2007.

Epidemiologic Methods. Department of Family Medicine. Menofia University. Shibin El-Kom, Egypt. July 2, 2009

Halogenated Hydrocarbons, Fish Consumption and the Incidence of Cancer. Department of Epidemiology. Brown University. February 22, 2012.

Consumption of L. Ontario Sport Fish and the Incidence of Colorectal, Lung, and Prostate Cancer in the New York State Angler Cohort Study. International Society for Environmental Epidemiology, Columbia, South Carolina. August 27, 2012

Chlorpyrifos Exposure and Respiratory Health among Adolescent Pesticide Applicators. Society of Neuroscientists of Africa. Rabat Morocco. June 16, 2013

Peer Reviewed Publications:

(1) **Bonner MR**, McCann SE, Moysich KB. Dietary Factors and the Risk of Testicular Cancer. *Nutrition & Cancer*, 2002 Vol. 44(1): 35-43.

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- (6) **Bonner MR**, Han D, Nie J, Rogerson P, Vena JE, Muti P, Trevisan M, Edge SB, Freudenheim JL. Breast Cancer Risk and Exposure in Early Life to Polycyclic Aromatic Hydrocarbons using Total Suspended Particulates as a Proxy Measure. *Cancer Epidemiology, Biomarkers, and Prevention*, 2005 Vol. 14 (1): 53-60.
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†This abstract was awarded “Best Abstract” by the Occupational and Public Health Specialty Section.

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^{*}Presentations by students under the supervision of Dr. Bonner.

Research Support:

COMPLETED

R01 CA92040 (Freudenheim) 3/01/2006-5/31/2006 5%
NIH/NCI \$2,463,093 (Total Costs)

Methylation and Oxidation in Breast Cancer Epidemiology

Proposed is an analysis of an existing case-control study to examine two etiological mechanisms, one-carbon metabolism and/or oxidative stress and breast cancer.

Role: Co-Investigator

R01 TS000077 (Bonner) 9/30/2007-9/29/2011 30%
ATSDR/CDC \$599,637 (Total Costs)

New York State Angler Cohort Follow-up Study

Proposed is follow-up of a cohort of New York State licensed anglers to investigate consumption of contaminated Great Lakes sport fish and selected adult chronic diseases, including endometriosis, cancer and thyroid disease.

Role: Principal Investigator

R21 CA131934 (Rusiecki) 9/24/2008-8/31/2011 5%
NIH/NCI \$366,120 (Total Costs)

Pesticide Exposure and DNA Methylation in Pesticide Applicators

Proposed is a study to determine the relationship between lifetime exposure to specific pesticides and altered DNA methylation, including global hypomethylation and gene-specific hypermethylation, in a group of pesticide applicators enrolled in the Agricultural Health Study.

Role: Co-investigator

1 R-833454 (Olson) 9/1/2007-8/31/2012 2%
US EPA STAR Grant \$749,612 (Total Costs)

CYP-Specific PBPK/PD Models to Interpret Biomarkers for Organophosphate Pesticides

The primary objective of the proposed studies is to improve existing pharmacokinetic /pharmacodynamic (PBPK/PD) models to better estimate exposures, target tissue dose and resulting effects in human populations, utilizing urinary metabolite / biomarker data for organophosphate (OP) pesticides, chlorpyrifos, parathion, methyl parathion, and diazinon.

Role: Co-Investigator

Contract No: HHSN268201100001C (Wactawski-Wende) 10/1/2010-9/30/2011 5%
NIH/NHLBI \$8,172,692 (Total Costs)

Women's Health Initiative Extension 2010-2015

This study is aimed at extending further the WHI resource by continuing to collect additional health outcomes as a part of a five year extension study 2010-2015.

Role: Co-Investigator

R01 ES016308 (Anger) 6/1/2008-4/30/2012 10%
 NIH/NIEHS \$ 2,417,854 (Total Costs)

Biomarkers of Organophosphorus-Induced Neurotoxicity

Proposed is a study to determine the relationship between chlorpyrifos exposure and neurobehavioral deficits among Egyptian cotton workers occupationally exposed to chlorpyrifos

Role: Co-Investigator

CURRENT

R01 (Freudenheim) 6/11/2007-5/30/2012 2.5%
 NIH/NCI \$1,399,788 (Total Costs)

Interdisciplinary Training in Cancer Epidemiology at UB

Proposed is a training program for pre-doctoral candidates in cancer epidemiology with an interdisciplinary component including an understanding of cancer biology.

Role: Co-Investigator

1R01ES018846-01A1 (Mu) 02/04/2011-12/31/2013 10%
 NIH/NIEHS \$1,305,615 (Total Costs)

Biological Response to Change in Air Quality in Beijing pre-, mid- and post- the Olympics

Proposed is a study to take advantage of the improved air quality corresponding to the 2008 Beijing Olympics to investigate early biologic perturbations in oxidative and immunologic markers to better understand the early physiologic effects of air pollution.

Role: Co-investigator

R01 (Rohlman) 10%
 NIH/Fogarty International Center \$3,231,244 (Total Costs)

Vulnerability of the Adolescent Brain to Organophosphorus Pesticides

Proposed is a longitudinal study of 200 adolescent Egyptian pesticide applicators and non-applicators to investigate associations between exposure to organophosphorus insecticides (OP) and neurobehavioral function. A comprehensive biologically-based exposure assessment, incorporating levels of urinary pesticide metabolites and key enzymes in OP metabolism, will be used to estimate internal dose and determine dose-response relationships with neurobehavioral functioning. In addition, research capacity at Menoufia University will be increased by: (a) building epidemiologic research capacity, (b) teaching grant writing and research skills in short courses held locally and through videoconferences, and (c) provide mentoring and international education experiences.

Role: Co-Investigator

PENDING

None

CURRICULUM VITAE

James Raymond Olson

Office

Department of Pharmacology
 and Toxicology
 School of Medicine and Biomedical Sciences
 University at Buffalo
 102 Farber Hall
 Buffalo, New York 14214
 Phone: (716) 829-2319
 Fax: (716) 829-2801
 jolson@buffalo.edu

Home

97 Troy View Lane
 Williamsville, NY 14221
 (716) 631-8415

EDUCATION

<u>Degree</u>	<u>University</u>	<u>Field of Study</u>	<u>Year</u>
Ph.D.	Medical College of Wisconsin Milwaukee, Wisconsin	Pharmacology-Toxicology	1978
M.S.	Medical College of Wisconsin Milwaukee, Wisconsin	Pharmacology	1976
B.A.	Illinois Wesleyan University Bloomington, Illinois	Chemistry	1974

POSTDOCTORAL TRAINING

1978-1980	Vanderbilt University Nashville, Tennessee	Center in Environmental Toxicology
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PRESENT POSITION

UB Distinguished Professor
 Dept. Pharmacology and Toxicology, School of Medicine and Biomedical Sciences
 Director, Environmental Health Sciences Division, Dept. Social and Preventive Medicine, School of Public Health and Health Professions, University at Buffalo

PROFESSIONAL EMPLOYMENT HISTORY:

2010-present	Research Professor and Director, Environmental Health Sciences Division, Dept. Social and Preventive Medicine, School of Public Health and Health Professions, University at Buffalo
1994-present	Professor, Dept. Pharmacology & Toxicology, University at Buffalo State University of New York, Buffalo, New York
1994-2009	Clinical Professor, Dept. Social & Preventive Medicine, State University of New York, Buffalo, New York
1994-2002	Director, Environmental Health Sciences Graduate Group State University of New York, Buffalo, New York
1986-1994	Associate Professor, Department of Pharmacology and Therapeutics,

State University of New York, Buffalo, New York
1984-present Associate Director, Toxicology Research Center
State University of New York, Buffalo, New York
1980-1986 Assistant Professor, Department of Pharmacology and Therapeutics
State University of New York, Buffalo, New York.
1979-1980 Postdoctoral Fellow, NIEHS Individual National Research Service Award, Center in
Environmental Toxicology, School of Medicine, Vanderbilt University, Nashville, TN
1978-1979 NIEHS Postdoctoral Toxicology Trainee, Center in Environmental Toxicology,
School of Medicine, Vanderbilt University, Nashville, Tennessee

FELLOWSHIPS, AWARDS, HONORS:

2012 University at Buffalo, Distinguished Professor
2007 Sustained Achievement Award, Exceptional Scholar Program, University at Buffalo
2005 Visionary Innovator, UB Office of Science Technology Transfer and Economic Outreach
1981 Pharmaceutical Manufacturers Association Foundation Starter Grant
1979 NIEHS National Research Service Award for Individual Postdoctoral Fellows,
Center in Environmental Toxicology Vanderbilt School of Medicine, Nashville,
Tennessee.
1973 NSF Research Fellowship, Department of Chemistry, Illinois Wesleyan University,
Bloomington, Illinois.
1971 Phi Eta Sigma, National Scholastic Honorary, Illinois Wesleyan University,
Bloomington, Illinois.

PROFESSIONAL MEMBERSHIPS AND ACTIVITIES:

Society of Toxicology
American Society for Pharmacology and Experimental Therapeutics

Reviewer for Toxicological Sciences, Toxicology and Applied Pharmacology, Fundamental and Applied Toxicology, Journal of Pharmacology and Experimental Therapeutics, Environmental Health Perspectives, Cancer Research, Carcinogenesis, Regulatory Toxicology, Pharmacology & Toxicology, Archives of Biochemistry and Biophysics, Life Sciences, Biology of Reproduction, Preparative Biochemistry, Biochemical Pharmacology, Drug Development Research, Environmental Science and Technology, New England Journal of Medicine, Occupational and Environmental Medicine, Environmental Toxicology and Pharmacology, Toxicology In Vitro, Toxicology, Drug Metabolism and Disposition, Chemico-Biological Interactions, Chemosphere, Cancer Epidemiology Biomarkers and Prevention, Journal of Toxicology and Environmental Health

Reviewer for grant proposals submitted to the National Institute of Environmental Health Sciences (NIEHS), RCMI Program of NIH, U.S. EPA, Veterans Administration, the March of Dimes Birth Defects Foundation, The Great Lakes Research Consortium, Syracuse, NY, the Michigan Great Lakes Protection Fund, Wisconsin Sea Grant College Program, Air Force Office of Scientific Research, Research Council of Canada, Manitoba Health Research Council

Served as special ad hoc peer reviewer for "Research Proposals Dealing with the Effects of Agent Orange and Agent Blue with Emphasis on Delayed Effects." Veterans Administration, Washington, D.C., May 1982.

"International Peer Review Workshop on Dioxins", Environmental Criteria and Assessment Office, U.S. EPA, Cincinnati, OH, July 27-29, 1983.

U.S. Environmental Protection Agency. Peer review and Revision of Criteria Documents on 2,3,7,8-tetrachloro-, 1,2,3,7,8-pentachloro-, 1,2,3,7,8,9-hexachloro- and 1,2,3,6,7,8-hexachloro-dibenzo-p-dioxin. 1983-1986.

Served as a special expert consultant for the U.S. EPA Science Advisory Board Meeting in Washington, D.C. on November 28-29, 1984. (Regarding Health Assessment Documents for Polychlorinated dibenzo-p-dioxins).

Served as a special ad hoc peer reviewer for RFP NIH-ES-85-1, "Methods Development to Assess Human Metabolism of Chemical Xenobiotics", NIEHS, Research Triangle Park, NC, February 20, 1985.

U.S. Environmental Protection Agency. Review and Revision of Drinking Water Criteria Document for Polychlorinated Biphenyls (PCBs), 1986-1987.

U.S. Environmental Protection Agency. Review and Revision of Document on Interim Procedure for estimating risks associated with exposures to mixtures of chlorinated dibenzo-p-dioxins and -Dibenzofurans (CDDs and CDFs). 1986-1987.

Member of Peer Review Panel for Toxicological Profiles for:

"Selected PCBs (Aroclor -1260, -1254, -1248, -1242, -1232, -1221, and -1016)"

"2,3,7,8-Tetrachlorodibenzo-p-dioxin"

Documents developed by the Agency for Toxic Substances and Disease Registry (ATSDR), U.S. Public Health Service, August, 1987.

Served as special consultant for the U.S. EPA Science Advisory Board Meeting in Washington, D.C. on November 19, 1987. (Regarding Drinking Water Document for Polychlorinated Biphenyls).

Member of U.S. EPA Review Panel on "The Toxicity Potential of Brominated Dibenzofurans (BrDFs)". Washington, D.C., May 11, 1988.

U.S. Environmental Protection Agency. Revision and Update of Drinking Water Criteria Document for 2,3,7,8-tetrachlorodibenzo-p-dioxin. August and September, 1988.

External Reviewer for NATO/CCMS Report 178 Scientific Basis for the development of the International Toxicity Equivalency Factor (I-TEF) Method of risk assessment for complex mixtures of dioxins and related compounds in US EPA, Interim Procedures for Estimating risks associated with exposure to mixtures of chlorinated dibenzo-p-dioxins and -dibenzofurans (CDDs and CDFs) and 1989 Update. EPA/625/3-89/016, March 1989.

Invited to participate in Disciplinary Workshop to Evaluate Risks to Human Health Associated with Exposure to Toxic Chemicals in the Great Lakes Basin Ecosystem (served as facilitator for Toxicology/Environmental Chemistry Group). Niagara-on-the-Lake, Ontario, April 15-18, 1989.

Invited to participate in International Working Conference to Evaluate Risks to Human Health Associated with Exposure to Toxic Chemicals in the Great Lakes Basin Ecosystem. Buffalo, NY, Sept. 30-Oct. 3, 1989.

Ad hoc peer reviewer for RFP NIH-ES 90-06, "In vitro Methods to Assess Human Metabolism of Chemical Xenobiotics". NIEHS, June 14, 1990.

U.S. Environmental Protection Agency. Invited to participate as a Contributing Author for The Health Assessment for 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) and Related Compounds. June 1991 - Present.

Peer Reviewer for the Agency for Toxic Substances and Disease Registry (ATSDR) Toxicological Profile for Chlorinated Dibenzo-p-dioxins, February, 1992.

Reviewer for Reverse Site Visit of Environmental Health Sciences Programs of Research Centers in Minority Institutions (RCMI) Program, NIH, Bethesda, Maryland, May 3-6, 1992.

Author and reviewer at U.S. EPA Dioxin Peer Review Workshop: Health Assessment Document, Vienna, VA, Sept. 22-23, 1992.

Invited Reviewer/Participant for "Technical Review Workshop on the Reference Dose (RfD) for Aroclor 1016" U.S. EPA Washington, DC, May 24-25, 1994.

Invited Reviewer/Participant for "Science Panel Meeting on Chlorinated Dibenzo-p-dioxins" ATSDR, Atlanta, GA, August 10, 1994.

Workshop Facilitator for Human Health Effects Session of "Chlorine Conference" Buffalo, NY, May 3-4, 1995.

Peer Reviewer for U.S. EPA Research Grants Program "Reducing Uncertainty in Risk Assessment and Improving Risk Reduction Approaches in Health and Air Quality", Research Triangle Park, NC, Aug. 20-21, 1995.

US Environmental Protection Agency, Human Health Peer Review Panel, Alexandria, VA, July 9-10, 1996.

Peer Reviewer for The Agency for Toxic Substances and Disease Registry (ATSDR), "Toxicological Profile for Chlorinated Dibenzo-p-dioxins", January 1997.

USEPA, Health Effects and Exposures to Particulate Matter and Associated Air Pollutants. Grant Peer Review Panel, Alexandria, VA, June 3-4, 1997.

Peer Review Panel for Experimental Toxicology Division of the National Health & Environmental Effects Research Laboratory, USEPA, Research Triangle Park, NC, September 22-24, 1997.

Peer Reviewer for The Agency for Toxic Substances and Disease Registry (ATSDR), "Toxicological Profile for Chlorinated Dibenzo-p-dioxins", October, 1998.

NIEHS Program Project Grant Review Panel. March 25, 1999

U.S. EPA September 2000 Draft Final. Exposure and Human Health Reassessment of 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) and Related Compounds. Part II: Health Assessment for 2,3,7,8-TCDD and Related Compounds. Author for Chapter 1, Disposition and Pharmacokinetics (EPA/600/P-00/001Be)

Author of Review Chapter on the “Pharmacokinetics of PCBs” for the U.S. EPA, 2000.

US EPA Workshop on PCB non-cancer assessment, focusing on congener specific data. Washington D.C. April 5, 2001.

2001-2003 Editorial Board of the *Buffalo Physician and Biomedical Scientist*

Member of Steering Committee for the “Anniston Community Health Research Consortium” 2003-present

NIEHS Program Project Review. “Endocrine Disruption: Epidemiology, Genetics and Toxicology” Research Triangle Park, NC October 18-19,2004

Invited Seminar. “Hepatic Gene Expression Profiling from the NTP Dioxin Toxic Equivalency Factor Studies” NIEHS. October 18, 2004.

Invited Presentation. “Biomarkers of Human Exposure to Pesticides Utilizing a New PBPK/PD Model and Kinetic Data on Pesticide Metabolism” US EPA 2004 Science to Achieve Results (STAR) Progress Review Workshop—Human Health Symposium. Philadelphia, PA. October 28-29,2004.

NIGMS Special Emphasis Panel for the review of grants on Predictive ADME-Toxicology. Bethesda, MD, June 30 – July, 1, 2005

Invited presentation, “Toxicology of Dioxin and Related Chemicals” for a symposium entitled, "Where Toxicology Meets the Law-Focus on Dioxin". American Chemical Society National Meeting Washington DC, August 31, 2005.

Invited Presentation. “CYP-Specific Metabolism of Organophosphate Pesticides and the Development of CYP-Specific PBPK/PD Models to Assess Human Exposure and Risk”. Center for Research in Occupational and Environmental Toxicology (CROET), Oregon Health Sciences University, December 11-12, 2006.

Invited Speaker “PCB Exposure Assessment Anniston, AL” Community Presentation, CDC/ATSRD sponsored meeting, Anniston, AL April 1, 2008

Invited Speaker “Assessment of Human Exposure to PCBs and Determinants of Exposure in Anniston, AL” Fifth PCB workshop, New Knowledge Gained from Old Pollutants. Iowa City Iowa, May 18-22, 2008

Author and Peer Reviewer for the formal EPA response the National Academy of Sciences (NAS) Review of the Dioxin Reassessment (starting 11/2008 and continuing for approximately the next 3 years)

Panelist for US EPA / NAS Workshop on the Dioxin Reassessment, Cincinnati, OH , February 18-20, 2009

Member of the Institute of Medicine’s (IOM) Committee for Review of the Health Effects in Vietnam

Veterans to Herbicides- *8th Biennial Update* 2010-2012

Genotyping Research and Training Related to Biomarkers of Susceptibility to OP Pesticides. Menoufia University, Shebin El-kom, Egypt. January 3-13, 2011.

Member of External Advisory Committee, Pharmacology and Toxicology B.S. program, University of Wisconsin, Madison, Oct 6-7, 2011.

Member of the Institute of Medicine's (IOM) Committee to Review the Health Effects in Vietnam Veterans of Exposure to Herbicides- *9th Biennial Update* 2012-2013

COMMUNITY SERVICE

Great Lakes Laboratory Advisory Board. State Univ. College at Buffalo

Scientific and Technical Advisory Board of the Ecumenical Task Force of the Niagara Frontier. (Provide expertise on persistent environmental contaminants, including dioxin).

Member of Instructional Committee, Amherst Central School District, Amherst, NY. 1991-1992.

Guest Lecturer for Graduate Toxicology Course, State University College at Buffalo (4 hr every other year)

Member of Church Council, St John Lutheran Church, Williamsville, NY (2010-2014)

SERVICE TO THE UNIVERSITY, SCHOOL OF MEDICINE AND BIOMEDICAL SCIENCES and SCHOOL OF PUBLIC HEALTH AND HEALTH PROFESSIONS

1982-1987 Alternate representative to the Faculty Council, School of Medicine
1982-Present Pre-clinical Academic Advisor for First and second year Medical students, And MSTP students
1983-1987 Member of the Faculty Council Committee on Promotion and Tenure
1984-1996 Member of the First Year Selective Program Committee (Chairman, 1985-1989)
1984-1986 Alternate Pre-clinical representative to the Executive Committee, School of Medicine 1985-1989 Member of the Year One Committee, School of Medicine
1986-1993 Departmental Representative to Health Sciences Divisional Committee (Chair, 1990-92)
1986-Present Associate Director, Toxicology Research Center
1986-2005 MSTP Steering Committee
1989-1993 Biomedical Sciences Graduate Education Committee (chairman)
1989-1994 Graduate School Executive Committee
1991-1992 Member of Search Committee for new Chair of Dept. of Social and Preventive Medicine
1993-1996 Educational Programs and Policy Committee of the Faculty Senate
1995-1998 Appointment and Promotions Committee to Research Rank, School of Medicine and Biomedical Sciences
1994-1997 Member of Search Committee for New Chair of Dept. Physiology & Biophysics
1994-2002 Director, Graduate Group in Environmental Health Sciences
1995-Present Steering Committee, Environmental Institute Task Force/Environment and Society Institute
1995-2000 Graduate School Subcommittee on Graduate Faculty Membership

1996-2006 Institutional Animal Care and Use Committee (IACUC), Chair (1997-2006)
 1997-1998 Interdisciplinary Graduate Program Admissions Committee
 1997- 1998 Search Committee for new Director of the Laboratory Animal Facilities
 1999 Member WNY IAIMS Research Information Resources planning team
 1999 Member of Planning Committee for Proposed Merger of the Departments of
 Pharmacology and Toxicology and Biochemical Pharmacology
 1999 Member of Search Committee for new Clinical Veterinarian
 1999-2002 Member of the ad hoc Committee on Promotions to Unqualified (Tenure) Ranks, School of
 Medicine and biomedical Sciences
 2000 Member of Search Committee for new Chair of Dept. Pharmaceutics
 2001-2003 Editorial Board of the *Buffalo Physician and Biomedical Scientist*
 2003-2006 Member of the ad hoc Committee on Promotions to Unqualified (Tenure) Ranks, School of
 Medicine and biomedical Sciences
 2003-present Associate Director Environment and Society Institute, University at Buffalo
 2004-2005 Chair of the Search Committee for the Director or Laboratory Animal Facilities and
 Resources at the University at Buffalo and RPCI
 2005-present Member of Steering Committee of the Interdisciplinary Graduate Program in Biomedical
 Sciences (IGPBS)
 2006-2007 Member of Search Committee for Director of Div of Environmental Health, School of
 Public Health
 2006-2008 Member of Search Committee for Audiology Faculty, Dept of Communicative Disorders
 and Sciences, University at Buffalo
 2007 Member of Search Committee for Chair, Dept of Pharmacology and Toxicology, University
 at Buffalo
 2007-2008 Member of Search Committee for Animal Research Compliance Administrator
 2007-2008 Member of Search Committee for Environmental Epidemiology Faculty, School of Public
 Health
 2008 Member of Interdisciplinary Graduate Program in Biomedical Sciences Admissions
 Assessment Committee
 2008-2009 Member of Distinguished Scientist Seminar Series
 2008-2011 Member of the ad hoc Committee on Promotions to Unqualified (Tenure) Ranks, School of
 Medicine and biomedical Sciences (Chair, 2009-2010)
 2008-present Member of the Faculty Council Standing Committee for Facilities Planning and Budget
 2008-2011 Member of the Faculty Council Standing Committee for Biomedical Research Affairs
 2008-2009 Member of the Faculty Search Committee for Pharmacology and Toxicology
 2009-2010 Co-Chair of Search Committee for Environmental Health Sciences Faculty, School of Public
 Health and Health Professions

DEPARTMENTAL SERVICE

1981-2010 Coordinator for Departmental Controlled Substances License
 1981-1984 Coordinator for Departmental Seminar Program
 1982-2003 Member of the Curriculum Committee (Chair, 1994-2003)
 1982-1983 Member of the Search Committee for New Faculty
 1986-1993 Director of Graduate Studies
 1986-2003 Admissions Committee
 1997-present Member of Departmental IFR Committee
 1998-1999 Proposition Exam Committee (Chair, 1999)

2006-present Director, Undergraduate Program in Pharmacology & Toxicology
 2008 Chair, Proposition Exam Committee
 2008-2009 Member of Search Committee for Pharmacology and Toxicology Faculty
 2009-present Chair of Undergraduate Education Committee
 2009-present Member Education Committee
 2009-present Chair of Appointment, Promotion, and Tenure Committee
 2010-present Director, Environmental Health Sciences Division, Dept. Social and Preventive Medicine,
 School of Public Health and Health Professions

COURSES TAUGHT 1996-present

PMY 601	Fundamentals of Pharmacology	5 hrs, Lecture
PMY 831	Principles of Pharmacology (Dental)	4 hrs, Lecture
PMY 501	General Principles of Pharmacology I	3 hrs, Lecture
PMY 626&627	Toxicology Principles & Practice Toxicology at Target Organs (course coordinator)	14 hrs, Lecture
PMY 525	Advanced Pharmacology	3 hrs, Lecture
PMY 502	Mechanisms of Drug Action	3 hrs, Lecture
PMY 504	Special Techniques	
PMY 409	Experimental Pharmacology (undergraduate teaching lab course director)	
PMY 756	Environmental Toxicology Research	
BCP 302	Introduction to Pharmacology	3 hr, Lecture
PT 503	Pharmacology	2 hr, Lecture
PHC 630	Drug Metabolism and Disposition	4 hrs, Lecture
SPM 614	Molecular Epidemiology	5 hrs, Lecture
ICM 504	Foundations II: Principles of Disease and therapy	4 hrs, Lecture
NTR 600	Pathophysiology of Nutrition Related Diseases	2 hrs, Lecture
LAW937	Science and Environmental Law	6 hr lecture and discussion
BMS 511	Techniques Seminar	1 hr lecture
SPM 649	Advanced Environmental Health Science	6 hrs
SPM 650	Environmental Toxicology and Risk Assessment	8 hrs
UE141	Climate change: past, present, and future	2 hrs

Research Supervision:

Postdoctoral: 1995-1999 Frank D. Stephen, Ph.D.
Current Position: Assistant Professor, Biological Sciences,
 D'Youville College, Buffalo, NY

Postdoctoral: 1997-2001 Adam Drahushuk, Ph.D.
Current Position: Pharmacy Director, Mercy Suburban Hospital, PA

Postdoctoral: 2011 Corie Ellison, Ph.D.
Accepted offer: Toxicologist, The Procter & Gamble Co.

Major Advisor for Graduate Students:

Sistine M. Chen, M.S. (1985). "The Metabolism and Disposition of 2,3,7,8-

tetrachlorodibenzo-p-dioxin (TCDD) in Freshwater Fish".

Victor J. Wroblewski, Ph.D. (1987). "Interspecies differences in the hepatic metabolism of 2,3,7,8-tetrachlorodibenzo-p-dioxin: Role in toxicity."

Current Position: Senior Research Fellow in Drug Disposition, Eli Lilly (manages a group of 20 scientists dedicated to the development of biologic therapeutics)

Emily S. Shen, Ph.D. (1987). "The relationship between the murine Ah locus and 2,3,7,8-tetrachlorodibenzo-p-dioxin hepatic metabolism, enzyme induction and toxicity".

Current Position: Principal Scientist, Wyeth Research

David A. Tonucci (Ph.D. 1994). "The Effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) on Vitamin A Homeostasis and Its Relationship to Developmental Toxicity in the Holtzman Rat."

Current Position: Head, NOAM Regulatory Assurance Givaudan Flavors

Hung-Liang Tai (Ph.D. 1994). "Characterization of the Role of Cytochrome P450-1A1 and 1A2 in the Metabolism and Disposition of Polychlorinated Dibenzofurans in the Rat and Human."

Current Position: Senior Scientist XenoPort, Inc.

Gilda Pelosi (M.A., 1996) "Characterization of Rat Hepatic Cytochrome P450 Activities Following Inhalation Exposure to p-Chlorobenzotrifluoride (PCBTF)"

Adam Draushuk (Ph.D., 1997) "Expression and Induction of Cytochrome P-450 1A1 and 1A2 in Rat and Human Liver"

Current Position: Pharmacy Director, Mercy Suburban Hospital, PA

Brain P. Slezak (Ph.D., 1997) "Comparative Expression of Cytochrome P450 1A1 in Extrahepatic Tissues from Rats and Humans: the Effects of 2,3,7,8-Tetrachlorodibenzo-p-dioxin"

Current Position: Principal Research Toxicologist, DuPont Haskell Global Centers for Health and Environmental Sciences

Jason R. Catania (MS, 2000) "Precision Cut Rat Liver Slices in Dynamic Organ Culture as an In Vitro Model to Assess Drug Induced Modulation of Cytochrome P-450s"

Jeanine A. Hand (Ph.D., 2001) "*In Vivo* and *In Vitro* Comparison of Cytochrome P-450 Expression and DNA Adduct Formation in Rat Liver and Lung Treated with Benzo(a)pyrene"

Current Position: Research Scientist, Cambridge University United Kingdom

David Shubert (Ph.D., 2002) "Effect of Subchronic and Chronic Exposure to Halogenated Aromatic Hydrocarbons on Cytochrome P4501 Enzymes and 17 β -Estradiol Metabolism"

Current Position: Assistant Dean Undergraduate Education, School of Medicine and Biomedical Sciences, University at Buffalo

Chad Vezina (Ph.D., 2003) "A Toxicogenetic and Toxicogenomic Approach Towards Understanding the Mechanism of Dioxin Toxicity"

Current Position: Assistant Professor, Department of Comparative Biosciences, School of Veterinary Medicine, University of Wisconsin Madison

Robert Foxenberg (Ph.D., 2007) “Improving PBPK/PD Modeling for Two Model Organophosphorous Pesticides, Parathion and Chlorpyrifos”
Current Position: Toxicologist, NACP Global Product Safety, Kimberly-Clark Corp

Bladimir J. Ovando (Ph.D., 2007) “Toxicogenomic Analysis of Hepatic Gene Expression Following Exposure to Persistent Organic Pollutants”
Current Position: Human Safety Toxicologist, The Procter & Gamble Co.

Adam Manzella (M.A., 2007) “Structure Dependent Characterization of Polychlorinated Biphenyls (PCBs) and Polybrominated Diphenyl Ethers (PBDEs) as inhibitors of the Breast Cancer Resistance Protein (ABCG2) Transporter”
Current Position: Scientist, Frontier Science and Technology Research Foundation, Amherst, NY

Kevin M. Kransler (Ph.D., 2008) “Gestational Exposure to 2,3,7,8-Tetrachlorodibenzo-p-dioxin Adversely Affects Lung Development”
Current Position: Senior Toxicologist, ExxonMobil Biomedical Sciences, Inc.

Kevin Christie (BS/MS, 2009) “Polychlorinated Biphenyls (PCBs) and Polybrominated Diphenyl Ethers (PBDEs) are Inhibitors of the Breast Cancer Resistance Protein (ABCG2) Transporter”
Current Position: Production Scientist, Life Technologies, Grand Island, NY

Corie Ellison (Ph.D., 2011) “Assessing the human health risks of exposure to organophosphorus pesticides”
Awards presented at the annual meeting of the Society of Toxicology:
The Occupational and Public Health Specialty Section "Best Student Abstract" Award
The Risk Assessment Specialty Section “Perry J. Gehring Best Graduate Student Abstract Award”
The Regulatory and Safety Evaluation Specialty Section Graduate Student Travel Award
Current Position: Toxicologist, The Procter & Gamble Co.

Yuan Tian (M.A., 2011) “Human Cytochrome P-450 Specific Metabolism of Diazinon”
Current Position: Research Technician with Tartis, a subsidiary of Cleveland BioLabs, Inc

Oswald Dadson (BS/MS, 2012) “Profenophos Metabolism and Estimates of Profenofos Exposure in Egyptian Cotton Field Workers”
Current Position: Laboratory Data Manager, Frontier Science and Technology Research Foundation, Amherst, NY

Alice Cane, MD/PhD student, defended PhD dissertation May, 2012. “Assessment of Human Exposure and Susceptibility to Chlorpyrifos” **Current Position:** Medical Student
Women in Toxicology SIG Vera W. Hudson and Elizabeth K. Weisburger Scholarship Fund Student Award for outstanding record of achievement in academics, leadership, and service.
Society of Toxicology Annual Meeting, March, 2012
John Doull Graduate Student Award from the Risk Assessment Specialty Section, Society of Toxicology Annual Meeting, March 2012
The Occupational and Public Health Specialty Section "Best Student Abstract" Award. Society of Toxicology Annual Meeting, March 2012

Amber Dubois (M.S., 2013) “Identifying Human Susceptibility Genes and Potentially Novel Mechanisms of Chlorpyrifos-Induced Toxicity” (jointly mentored with Xuefeng Ren, SPM)

Currently Serving as Major Advisor for:

Steve Singleton, PhD student

Major Advisor for Undergraduate Research

David Manns 2001-02
Matilda Afful, Summer 2002 McNair Research Internship Program
Jackie Thomas Fall 2006 Collegiate Science & Technology Entry Program (CSTEP)
Corie Ellison Fall 2006 Collegiate Science & Technology Entry Program (CSTEP)
Jessica Klapa, spring 2008
Yuan Tian, fall 2008
Courtney Smith, Fall 2009
Amber Dubois, spring 2010
Oswald Dadson Summer 2010, McNair Research Internship Program

Major Advisor for CLIMB UP and Institute for Strategic Enhancement of Educational Diversity (iSEED) summer undergraduate research programs

2013- Carmen Marable, North Carolina A&T State University
2012- Danielle Forde-Riddick: Medgar Evers College (CUNY)
2011-Denise Yancey- Jackson State University
2010-Oswald Dadson- UB

Served as a member of the Ph.D. Committee for:

Andrew Soiefer, Ph.D. 1983
Kathleen Mulder, Ph.D. 1985
Michael Aleo, Ph.D. 1988
Pei Hui, Ph.D. 1994
Alka Patel, M.D./Ph.D. 2000
Karen Drahushuk, Ph.D. 2002
Michael Bloom, PhD, Social and Preventive Medicine 2004
Sara Lupton, PhD, Chemistry 2010
Suresh Pendem, PhD student, Nutrition Science 2011
Chao Tong, PhD student, Pharmacology and Toxicology 2011
HoeHun Ha (Bryan), PhD, Geography 2011
Joeseph Green PhD, SPM , present

Served as a member of the M.A./M.S. Committee for:

Karen Lintz, M.A. 1992
Chik On Choy, M.S. 1992, Dept. of Medical Technology

Anjmun Sharma, M.A. 1995
Casey Stinson, M.A. 1996
Lai-Har Chi, M.A. 1997, Dept. Clinical Laboratory Sciences
Li Feng M.S. 1998, Dept. Clinical Laboratory Sciences
Debra Ketch M.S. 2000, Biotechnical and Clinical Laboratory Sciences
Smitha R. James M.S. 2002, Biotechnical and Clinical Laboratory Sciences
Jennifer Helferich MS 2004
Neva Alles MS 2006, Biotechnical and Clinical Laboratory Sciences
Michelle Lum MS 2006, Biotechnical and Clinical Laboratory Sciences
Mitan Jain MS 2008, Biotechnical and Clinical Laboratory Sciences
Padmini Sahoo 2009, Biotechnical and Clinical Laboratory Sciences
Anand S Devasthanam MS 2010, Biotechnical and Clinical Laboratory Sciences
Geraldine Raja MS 2010, Biotechnical and Clinical Laboratory Sciences
Shipra MS 2011, Biotechnical and Clinical Laboratory Sciences

Served as member of MPH Committee

Alyssa Irla, MPH 2011
Joel Merriman, MPH 2012

Served as Outside Reader for:

Norikazu Terao, Ph.D. 1983, Dept. Pharmaceutics
Bradley K. Wong, Ph.D. 1987, Dept. Pharmaceutics
Paul Koser, Ph.D. 1987, Dept. Pharmacol., Roswell Park
Ronald P. Dahms, Ph.D. 1989, Dept. Pharmacol., Roswell Park
Suk-Jae Chung, Ph.D. 1991, Dept. Pharmaceutics
Paul Fiorella, Ph.D., 1994, Dept. Biochemistry
Shyanher Wang, Ph.D., 1997, Dept. Physiology
Keke Hu, Ph.D., 1998, Dept. Chemistry & Biochemistry, Univ. of Guelph
Gabriela Popescu, Ph.D., 1999, Dept. Biochemistry

Past Grant Support

Principal Investigator: James R. Olson, Ph.D.
Co-investigator: James McReynolds, Ph.D., Dept. Biophysical Sciences, SUNY at Buffalo
Title: Mechanism(s) for Toxicity of Chlorinated Dibenzodioxins
Source: NIEHS, 2 RO1 ESO2693
Total Project Period: 7/1/81 - 6/30/88
Total Support: \$245,437 (direct costs)

Principal Investigator: Jerome A. Roth, Ph.D.,
Co-investigators: James Olson, Ph.D. and Paul Kostyniak, Ph.D.
Title: Biochemical Indices of Cell-specific Neurotoxicity
Source: NIEHS, 1 RO1 ES03655
Total Project Period: 5/1/85 - 4/30/88
Total Support: \$210,183 (direct costs)

Principal Investigator: Paul J. Kostyniak, Co-investigators: James R. Olson, Mary Taub
 Title: Primary Cultures of Renal Proximal Tubules: A New In Vitro Model for Assessing Drug and Chemical Induced Nephrotoxicity.
 Source: The John Hopkins Center for Alternatives to Animal Testing
 Project Period & Support: 2/1/86-1/31/89 \$18,000

Principal Investigator: James R. Olson, Ph.D.
 Co-investigators: Drs. R.E. Hruska, F.L. Bellino, S. Sobel
 Title: Interspecies Variability in the Embryotoxic and Teratogenic Potential of Polychlorinated Dibenzo-p-dioxins.
 Source: March of Dimes Birth Defects Foundation (No. 15-127).
 Total Project Period: 12/1/87-12/31/89
 Support: \$52,083

Principal Investigator: James R. Olson, Ph.D.
 Title: Developmental Toxicity of Polychlorinated Dibenzo-p-dioxins
 Source: Research Development Funds, SUNY/Buffalo
 Total Project Period: 3/1/88-6/30/90
 Support: \$20,512

Principal Investigator: James R. Olson
 Title: Assessing the Hazard of Trifluoromethyl Polychlorinated Biphenyls, A New Class of Persistent Environmental Contaminants
 Source: N.Y. Great Lakes Research Consortium
 Project Period: 8/91-7/92
 Support: \$22,385

Principal Investigator: James R. Olson
 Title: Assessing Dioxin-like Activity of Halogenated Thianthrenes
 Source: Occidental Chemical Corp.
 Project Period: 7/1/90-12/31/92
 Support: \$9,469

Principal Investigator: John E. Vena (Social & Preventive Medicine)
 Co-Investigator: James R. Olson (5%)
 Title: Risk Perception, Reproductive Health Risk and Consumption of Contaminated Fish in a Cohort of New York State Anglers
 Source: Great Lakes Protection Fund RM 791-3021
 Project Period: March 1992 - March 1993
 Support: \$205,000

Principal Investigator: James R. Olson, Ph.D.
 Co-Investigators: Subodh Kumar, Ph.D., James McReynolds, Ph.D.
 Title: Metabolism of Polychlorinated Dioxins and Dibenzofurans in the Rat and Human.
 Source: U.S. EPA Grant R815915
 Total Project Period: 4/15/90-4/14/94
 Support: \$494,706 total

Principal Investigator: Joseph L. Napoli (Biochemistry)
 Co-Investigator: James R. Olson (10%)
 Title: Xenobiotics and Retinoids
 Source: NIEHS, ESO5 9505-01
 Project Period: 3/1/92-2/29/96
 Support: \$107,641 direct cost/year

Principal Investigator: James R. Olson, Ph.D.
 Title: Characterization of Cytochrome p-450 Induction and In Vitro Metabolism of PCBTF in PCBTF Exposed Rats
 Source: Occidental Chemical Corp.
 Project Period: 1/1/95 - 12/31/96
 Support: \$19,980 total costs (TRC services account)

Principal Investigator: James R. Olson, Ph.D.
 Title: Induction of Cytochrome p-450 in Precision Cut Human Liver Slices in Dynamic Organ Culture
 Source: Pfizer Pharmaceuticals, Inc.
 Project Period: 11/5/94 - 12/31/97
 Support: \$51,384 total costs (TRC services account, UBF)

Principal Investigator: James R. Olson, Ph.D.
 Co-Investigator: John E. Vena, Ph.D., (5%, Social & Preventive Medicine)
 Thomas Gasiewicz, Ph.D., (5%, University of Rochester)
 Title: Biomarkers of Dioxin-like Compounds
 Source: NIEHS ROI ESO6556
 Project Period: 9/1/93 - 8/31/98
 Support: \$142,648 direct costs for year 4

Principal Investigator: Diane Bofinger
 Co-Investigator: James R. Olson, Ph.D.
 Title: Dioxin Biomarkers and Endometriosis
 Source: NIEHS RO3 ES 08539
 Project Period: 9/1/96 - 8/31/98
 Support: \$50,000 direct costs

Principal Investigator: James R. Olson, Ph.D.
 Title: Partition Coefficients for Halogenated Organics
 Source: Occidental Chemical Corp.
 Project Period: 4/1/97 - 9/30/99
 Support: \$19,980 (TRC services account, UBF)

Principal Investigator: James R. Olson, Ph.D.
 Title: Induction of CYP-450s by Dioxins in Rats and Humans
 Source: NIEHS 1 R03 ES 09440-01
 Project Period: 2/9/98-2/8/00
 Support: \$76,500

Principal Investigator: James R. Olson, Ph.D.
 Title: Assessment of Cytochrome P-450 Induction in Precision Cut Slices of Rat Liver
 Source: Pfizer Inc., Central Research
 Project Period: 12/1/97-11/30/00
 Support: \$67,455

Principal Investigator: Adam Drahusuk
 Co-Investigators: Stephen Koury and James Olson
 Title: Function of Polymorphisms in Human CYP1A1, 1A2, and 1B1
 Source: Multidisciplinary Research Pilot Program, SUNY/Buffalo
 Project Period: 6/1/99 - 5/30/01
 Support: \$20,000

Principal Investigator: James R. Olson
 Co-Investigator: Paul J. Kostyniak
 Title: Uptake and Activity of Holagenated Aromatic Hydrocarbons in Rat and Human Liver
 Source: U.S. EPA grant R 825808-01
 Project Period: 10/1/97-9/30/01
 Support: \$293,260/year one; \$905,529/project period

Principal Investigator: James R. Olson
 Co-Investigators: Patrick O'Keefe, NYS Dept. of Health, Lawrence Skinner, NYS DEC
 Title: Use of a Reporter Gene Bioassay to Screen for Dioxin-Like Compounds in Fish from Lake Ontario and the St. Lawrence River
 Source: New York Great Lakes Research Consortium
 Project Period: 9/1/00- 12/31/01
 Support: \$19,699 direct costs

Principal Investigator: Diane P. Bofinger, Ph.D.
 Co-Investigator: James R. Olson, Ph.D.
 Title: Effect of Dioxin Exposure on Liver Metabolism of Steroid Hormones and Dioxin-Like PCBs in Rhesus Monkeys with and without Endometriosis
 Source: Endometriosis Association
 Project Period: 9/1/00- 8/31/02
 Amount: \$50,000 direct costs

Principal Investigator: John E. Vena (Social and Preventive Medicine)
 Co-Investigator: James R. Olson (10%)
 Title: The New York State Angler Cohort Study - Exposure Characterization and Reproductive Developmental Health
 Source: ATSDR/CDC PN92594
 Project Period: 10/1/92 - 9/30/02
 Support: \$369,923 direct costs/year

Principal Investigator: James R. Olson, Ph.D.

Title: Graduate Group for Environmental Health Sciences
 Source: Graduate School, University at Buffalo
 Project Period: 7/1/95 - 6/30/03
 Support: \$2,500 / year

Principal Investigator: James R. Olson, Ph.D.
 Co-Investigator: Patrick O'Keefe, PhD, NYS Dept. of Health, Lawrence Skinner, NYS DEC
 Title: Use of a Reporter Gene Bioassay to Screen for Dioxin-Like Compounds in the Great Lakes
 Source: New York State Great Lakes Protection Fund
 Project Period: 10/1/00- 3/31/03
 Support: \$84,961

Principal Investigator: James R. Olson, Ph.D.
 Title: "Applications of Gene Microarrays in Environmental Health Research"
 Source: Environment and Society Institute University at Buffalo
 Project Period: 2/1/02-1/31/04
 Support: \$18,400

Principal Investigator: James R. Olson, Ph.D.
 Title: "Alterations in Gene Expression Following Exposure to Chemical Carcinogens"
 Source: IRCAF Program University at Buffalo
 Project Period: 4/10/02-2/28/03
 Support: \$27,400

Principal Investigator: Harish C. Sikka, Ph.D., Subodh Kumar Ph.D., SUNY College at Buffalo
 Co-Investigator: James R. Olson, Ph.D.
 Title: Effect of the Postnatal Development on the Metabolism of PAHs and the Repair of PAH-induced DNA Damage
 Source: Philip Morris External Research Program \$862,820 (total costs)
 Project Period: 7/1/02-6/30/06
 Support: \$93,336 (total costs to UB)

Principal Investigator: Minoti Sharma, Ph.D.
 Co-Investigator: James R. Olson, Ph.D. (10% effort)
 Title: "Chemoprevention of Uterine Cancer Risk by Antioxidants"
 Source: NCI R01 CA86875
 Project Period: 4/01/01 – 3/31/06
 Support: \$114,289 total costs to UB in years 3 and 4

Principal Investigator: Susan Schantz, Ph.D. (University of Illinois)
 Co-Investigators: Paul Kostiyaniak, James Olson (University at Buffalo)
 Title: "Children's Environmental Health Center"
 Source: NIEHS&U.S. EPA
 Project Period: 10/1/01 – 9/30/06
 Support: \$1,330,300 total costs to UB over 5 years (\$5,568,988 total project)

Principal Investigator: James R. Olson, Ph.D.
 Co-Investigators: James B. Knaak, Ph.D. and Paul Kostyniak, Ph.D.
 Title: "Biomarkers of Human Exposure to Pesticides Utilizing a New PBPK/PD Model and Kinetic Data on Pesticide Metabolism in Humans"
 Source: U.S. EPA STAR grant R-830683
 Project Period: 2/15/03 – 12/17/06
 Support: \$479,319 direct costs (\$747,704 total costs)

Principal Investigator: James R. Olson
 Title: "University-Community Consortium for Anniston Environmental Health Research"
 Source: ATSDR/CDC award # U50/ATU473215 (\$3,200,000 total costs)
 Subcontract from Jacksonville State University
 Project Period: 10/1/03- 12/15/07
 Support: \$243,697 total costs to University at Buffalo

Principal Investigator: James R. Olson
 Co-investigator: Kate Rittenhouse-Olson
 Title: "Identification of functional peptide ligands for the AhR"
 Source: NIEHS 1 R03 ES12911-01
 Project Period: 6/4/04-3/31/07
 Support: \$100,000 direct costs (\$149,018 total costs)

Principal Investigator: Marilyn Morris
 Co-investigator: James R. Olson
 Title: "Dietary Isothiocyanates in Cancer Prevention: Effects on Estrogen Metabolism"
 Source: NCI 1R03CA121404-01A1
 Project Period: 12/1/06-11/30/08
 Support: \$100,000 direct costs (\$156,516 total costs)

Principal Investigator: Richard Browne
 Co-investigators: KR Olson and JR Olson (10% effort)
 Title: Research Reagents for Human Serum Paraoxonase 1
 Source: NYSTAR Technology Transfer Incentive Program.
 Project Period: 3/1/07 – 8/31/08
 Support: \$162,263 (total costs)

Principal Investigator at UB: James Olson
 Principal Investigator: Diane Rohlman, OHSU
 Co-investigators: Gaafar Mohamed Abdel-Rasoul Hasan Ismail and Ahmed AbdelGawad, Menoufia University, Shebin El-Kom, Egypt
 Title: "Assessing Vulnerability of the Adolescent Brain to Organophosphorus Pesticides"
 Source: NIEHS R21 ES017223 01
 Project Period: 7/1/09 – 3/31/2012
 Total Costs to UB: \$64,040

Principal Investigator at UB: James Olson

Principal Investigators: Kent Anger and Pamela Lein, OHSU
 Title: "Biomarkers of Organophosphorus Pesticide-Induced Neurotoxicity"
 Research Supplement to Promote Diversity in Health-Related Research on behalf of Corie Ellison, Ph.D. Candidate, University at Buffalo, James Olson, Major Advisor.
 Source: NIEHS RO1 ES016308-02S
 Project Period: 5/1/09 – 4/30/12
 Total Costs to UB: \$174,780

Principal Investigator: James R. Olson
 Co-investigators: Richard Browne, Matthew Bonner, James Knaak, Paul Kostyniak, Aiming Yu
 Title: CYP-Specific PBPK/PD Models to Interpret Biomarkers for Organophosphate Pesticides
 Source: US EPA STAR Grant R833454
 Project Period: 9/1/07 – 8/31/12
 Support: \$749,612

Principal Investigator at UB: James Olson
 Principal Investigators: Kent Anger and Pamela Lein, OHSU
 Co-investigators: Matthew Bonner, UB, James Knaak, UB, Richard Fenske and Kit Galvin, WU, and Diane Rohlman, OHSU; Fayssal Farahat, Taghreed Farahat, Ahmed Raia, Menoufia University, Shebin El-Kom, Egypt
 Title: "Biomarkers of Organophosphorus Pesticide-Induced Neurotoxicity"
 Source: NIEHS RO1 ES016308
 Project Period: 6/1/08 – 4/30/2013
 Total Costs for Project: \$2,417,854
 Total Costs to UB: \$777,129

Current Grant Support

Principal Investigators: James Olson (contact) and Diana Aga, Chemistry
 Title: "Bioactivation of PBDEs by Human Cytochrome P-450"
 Source: NIEHS 1R21 ES021554
 Project Period: 4/1/2012 – 3/31/2014
 Total Costs: \$433,483

Principal Investigator: James Olson
 Title: "The Impact of Genetic Variability on Human Susceptibility to Chlorpyrifos"
 NRSA Predoctoral Fellowship on behalf of Alice Crane, MD/PhD student
 Source: NIEHS F30 ES020655-01A1
 Project Period: 2/1/2012 – 1/31/2014
 Total Costs: \$64,438

Principal Investigator: Diane Rohlman, University of Iowa
 Co-investigators: James Olson (Principal Investigator at UB), Matthew Bonner, UB, Gaafar Mohamed Abdel-Rasoul Hasan Ismail and Ahmed AbdelGawad,

Title: Menoufia University, Shebin El-Kom, Egypt
"Assessing Vulnerability of the Adolescent Brain to Organophosphorus Pesticides"
Source: NIEHS 1R01ES022163-01
Project Period: 3/4/2013 to 11/30/2017
Total Costs to UB: \$872,699

PUBLICATIONS

Peterson, R.E., Olson, J.R. and Fujimoto, J.M. Measurement and alteration of the capacity of the distended biliary tree in the rat. *Toxicology and Applied Pharmacology* 36:353-368, 1976.

Olson, J.R., Fujimoto, J.M. and Peterson, R.E. Three methods for measuring the increase in the capacity of the distended biliary tree in the rat produced by alpha-naphthylisothiocyanate treatment. *Toxicology and Applied Pharmacology* 42: 33-43, 1977.

Olson, J.R., Hosko, M.J. and Fujimoto, J.M. Alterations in the liver cell transmembrane potential following CCl₄ and bile salt treatment of rats *Life Sciences* 25:2043-2050, 1979.

Olson, J.R. and Fujimoto, J.M. Evaluation of hepatobiliary function in the rat by the Segmented Retrograde Intrabiliary Injection (SRII) technique. *Biochemical Pharmacology* 29:205-211, 1980.

Olson, J.R. and Fujimoto, J.M. Demonstration of a D-glucose transport system in the biliary tree of the rat by use of the Segmented Retrograde Intrabiliary Injection (SRII) technique. *Biochemical Pharmacology* 29:213-219, 1980.

Jansen, M.A., Olson, J.R. and Fujimoto, J.M. Taurolithocholate-induced increase in the intrabiliary pressure generated during retrograde intrabiliary infusion of saline in rats: antagonism by taurocholate and glycocholate. *Toxicology and Applied Pharmacology* 54:9-19, 1980.

Olson, J.R., Holscher, M.A. and Neal, R.A. Toxicity of 2,3,7,8-tetrachloro- dibenzo-p-dioxin (TCDD) in the golden syrian hamster. *Toxicology and Applied Pharmacology* 55:67-78, 1980.

Olson, J.R., Gasiewicz, T.A. and Neal, R.A. Tissue distribution, excretion and metabolism of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in the golden syrian hamster. *Toxicology and Applied Pharmacology* 56:78-85, 1980.

Neal, R.A., Olson, J.R., Gasiewicz, T.A. and Geiger, L.E. The Toxicokinetics of 2,3,7,8-tetrachlorodibenzo-p-dioxin in mammalian systems. *Drug Metabolism Reviews* 13:355-385, 1982. (Contains original, previously unpublished data).

Sawahata, T., Olson, J.R., and Neal, R.A. Identification of metabolites of 2,3,7,8-tetrachlorobenzo-p-dioxin (TCDD) formed on incubation with isolated rat hepatocytes. *Biochem. Biophys. Res. Commun.* 105:341-346, 1982.

Olson, J.R. and Wroblewski, V.J.* Metabolism of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in isolated

hepatocytes from guinea pigs and rats. *Chemosphere*, 14:979-982, 1985.

Wroblewski, V.J.* and Olson, J.R. Hepatic metabolism of 2,3,7,8- tetrachlorodibenzo-p-dioxin (TCDD) in the guinea pig and rat. *Toxicol. Appl. Pharmacol.* 81:231-240, 1985.

Kleeman, J.M., Olson, J.R., Chen, S.M. and Peterson, R.E. Metabolism and disposition of 2,3,7,8-tetrachlorodibenzo-p-dioxin in rainbow trout. *Toxicol. Appl. Pharmacol.* 83:391-401, 1986.

Kleeman, J.M., Olson, J.R., Chen, S.M. and Peterson, R.E. 2,3,7,8,- tetrachlorodibenzo-p-dioxin metabolism and disposition in yellow perch. *Toxicol. Appl. Pharmacol.* 83:402-411, 1986.

Olson, J.R. Metabolism and Disposition of 2,3,7,8-tetrachlorodibenzo-p-dioxin in guinea pigs. *Toxicol. Appl. Pharmacol.* 85:263-273, 1986.

Kung, M.P., Kostyniak, P.J., Olson, J., Malone, M. and Roth, J.A.: Studies on the *in vitro* effect of methylmercury chloride on rat brain neurotransmitter enzymes. *J. Appl. Toxicol.* 7:119-121, 1987.

Shen, E.S.* and Olson, J.R. The relationship between murine Ah phenotype and the hepatic uptake and metabolism of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Drug Metab. and Dispos.* 15:653-660, 1987.

Wroblewski, V.J.* and Olson, J.R. The effect of inducers and inhibitors of monooxygenase activity on the hepatic metabolism of 2,3,7,8-tetrachlorodibenzo-p-dioxin by the rat and hamster. *Drug Metab. and Dispos.* 16:43-51, 1988.

Wroblewski, V.J.*, Gessner, T. and Olson, J.R. Qualitative and quantitative differences in the induction and inhibition of hepatic benzo(a)pyrene metabolism in the rat and hamster. *Biochem. Pharmacol.* 37:1509-1517, 1988.

Kleeman, J.M., Olson, J.R., and Peterson, R.E. Toxicity and biotransformation of 2,3,7,8-tetrachlorodibenzo-p-dioxin in six species of Freshwater fish. *Fund. Appl. Toxicol.* 10:206-213, 1988.

Kung, M.P., Nickerson, P.A., Sansone, F.M., Olson, J.R., Kostyniak, P.J., Adolf, M.A., Lein, P.J. and Roth, J.A. Effect of short term exposure to hexachlorophene on rat brain cell specific marker enzymes. *Fund. Appl. Toxicol.* 11:519-527, 1988.

Kung, M.P., Kostyniak, P.J., Olson, J.R., Sansone, F.M., Nickerson, P.A., Adolf, M.A., Ziembiec, N. and Roth, J.A. Cell specific enzyme markers as indicators of neurotoxicity: Effects of acute exposure to methylmercury. *Neurotoxicology* 10:41-52, 1989.

Olson, J.R., Gutman, S.I., and Shen, E.S*. Reexamination of the dose-response relationship for induction of the hepatic monooxygenase system by 2,3,7,8-TCDD. *Chemosphere* 18:363-370, 1989.

Olson, J.R., Bellin, J.S., and Barnes, D.G. Reexamination of data used for establishing Toxicity Equivalence Factors (TEFs) for Chlorinated Dibenzop-dioxins and dibenzofurans (CDDs and CDFs). *Chemosphere* 18:371-381, 1989.

Shen, E.S.* , Guengerich, F.P. and Olson, J.R. Biphasic response for hepatic microsomal enzyme induction by 2,3,7,8-tetrachlorodibenzo-p-dioxin in C57BL/6J and DBA/2J mice. *Biochem. Pharmacol.*

38:4075-4084, 1989.

Hruska, R.E. and Olson, J.R. Species differences in estrogen receptors and in the response to 2,3,7,8-tetrachlorodibenzo-p-dioxin exposure. *Toxicol. Lett.* 48:289-299, 1989.

Kung, M.P., Nickerson, P.A., Sansone, F.M., Olson, J.R., Kostyniak, P.J., Adolf, M. and Roth, J.A. Effect of Chronic Exposure to Hexachlorophene on Rat Brain Cell Specific Marker Enzymes. *Neurotoxicol.* 10:201-210, 1989.

Olson, J.R., McGarrigle, B.P., Tonucci, D.A.*, Schechter, A. and Eichelberger, H. Developmental Toxicity of 2,3,7,8-TCDD in the rat and hamster. *Chemosphere.* 20:1117-1123, 1990.

Aleo, M.D., Taub, M.L., Olson, J.R. and Kostyniak, P.J. Primary cultures of rabbit renal tubule cells: II. Selected phase I and phase II metabolic capacities. *Toxicol. In Vitro* 4:727-733, 1990.

Shen, E.S. *, Gutman, S.I. and Olson, J.R. Comparison of 2,3,7,8-tetrachlorodibenzo-p-dioxin-mediated hepatotoxicity in C57BL/6J and DBA/2J mice. *J. Toxicol. Environ. Health* 32:367-381, 1991.

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Olson, J.R. and McGarrigle, B.P. Comparative Developmental Toxicity of 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD). *Chemosphere* 25: 71-74, 1992.

Tai, H.L. *, McReynolds, J.H., Goldstein, J.A., Eugster, H.P., Sengstag, C., Alworth, W.L., and Olson, J.R., Cytochrome P-4501A1 Mediates the Metabolism of 2,3,7,8-Tetrachlorodibenzofuran (TCDF) in the Rat and Human. *Toxicology and Applied Pharmacology.* 123:34-42, 1993.

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Olson, J.R., McGarrigle, B.P., Gigliotti, P.J., Kumar, S. and McReynolds, J. Hepatic Uptake and Metabolism of 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) and 2,3,7,8-Tetrachlorodibenzo furan (TCDF). *Fundamental and Applied Toxicology* 22:631-640, 1994.

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J. R. Olson, M. S. Gross, M. L. Feo, S. T. Singleton, A. L. Crane, B. P. McGarrigle¹, E. Eljarrat, D. Barcelo and D. S. Aga Biotransformation of BDE-47 to Potentially Toxic Metabolites Is Predominantly Mediated by Human CYP2B6: Implications for Interindividual Variability in Metabolism and Retention of BDEs. Annual Meeting Society of Toxicology, San Antonio, TX 2013

S. T. Singleton, J. B. Knaak, L. Chi, B. P. McGarrigle, F. M. Farahat and J. R. Olson. Alpha-Cypermethrin Metabolism and Exposure Assessment in Egyptian Agricultural Workers. Annual Meeting Society of Toxicology, San Antonio, TX 2013

F. D. Stephen, L. A. Georger¹, M. R. Bonner, P. J. Kostyniak, J. R. Olson, M. S. Bloom and J. E. Vena. Serum Great Lakes Pollutant Levels in Lake Ontario Fish and Wildlife Consumers. Annual Meeting Society of Toxicology, San Antonio, TX 2013

A. Dubois, J. R. Olson and X. Ren. Use of a Human Haploid Cell-Based Loss of Functional Genetic Screening Model to Identify Human Susceptibility Genes for Chlorpyrifos Toxicity. Annual Meeting Society of Toxicology, San Antonio, TX 2013

W. K. Anger, F. M. Farahat, P. J. Lein, J. R. Olson, M. Lasarev and D. Rohlman. Dose-Dependent Behavioral Deficits in Egyptian Agricultural Workers with Chronic Organophosphorus Pesticide (OP) Exposures. Annual Meeting Society of Toxicology, San Antonio, TX 2013

D. Rohlman, K. Khan, A. A. Ismail, G. Abdel Rasoul, M. R. Bonner, M. R. Lasarev, A. L. Crane, S. T. Singleton and J. R. Olson. Chlorpyrifos Exposure and Self-Reported Neurological Symptoms in Adolescent Pesticide Applicators. Annual Meeting Society of Toxicology, San Antonio, TX 2013

Invited National and International Presentations (more recent years)

“Biomarkers of Dioxin-Like Compounds” Dept. of Biology, University of Waterloo, Waterloo, ON, Canada, March 22, 2001.

“Exposure to Halogenated Aromatic Hydrocarbons (HAHs) and Expression of CYP1A1 in Consumers of Lake Ontario Fish and Wildlife” International Conference on Chemical Mixtures. Atlanta, GA, September 10-12, 2002.

“Hepatic Gene Expression Profiling from the NTP Dioxin Toxic Equivalency Factor Studies” NIEHS, Research Triangle Park, N.C., October 18, 2004.

“Biomarkers of Human Exposure to Pesticides Utilizing a New PBPK/PD Model and Kinetic Data on Pesticide Metabolism” US EPA 2004 Science to Achieve Results (STAR) Workshop—Human Health Symposium. Philadelphia, PA. October 28-29, 2004.

“Toxicology of Dioxin and Related Chemicals” American Chemical Society Symposium on Where Toxicology Meets the Law-Focus on Dioxin, Washington DC, August 31, 2005.

“CYP-Specific Metabolism of Organophosphate Pesticides and the Development of CYP-Specific PBPK/PD Models to Assess Human Exposure and Risk”. Center for Research in Occupational and Environmental Toxicology (CROET), Oregon Health Sciences University, December 11-12, 2006.

“PCB Exposure Assessment Anniston, AL” Community Presentation, CDC/ATSRD sponsored meeting, Anniston, AL April 1, 2008

“Assessment of Human Exposure to PCBs and Determinants of Exposure in Anniston, AL” Fifth PCB workshop, New Knowledge Gained from Old Pollutants. Iowa City Iowa, May 18-22, 2008.

“Biomarkers of Exposure, Effect and Susceptibility to Organophosphate Pesticides in Egyptian Cotton Field Workers” Girl's University in Riyadh, Saudi Arabia, Nov. 3, 2009.

“Biomarkers of Organophosphorus Pesticide-Induced Neurotoxicity” School of Public Health, University of Puerto Rico, San Juan, PR Dec. 2, 2009.

“Biomarkers of Exposure, Effect, and Susceptibility to Organophosphorus (OP) Pesticides”. Menoufia University, Shebin El-kom, Egypt. January 5, 2011.

“Use of CYP-specific parameters and human biomarker data to develop a human PBPK/PD model for dermal chlorpyrifos exposure” American Chemical Society , AGRO Division, Symposium on Parameters for Pesticide QSAR and PBPK/PD Models. Denver, CO. August 28 - September 1, 2011.

"Metabolic Activation by Cytochrome P-450 2B6 : Implications for Human Susceptibility to the Toxic Effects of Pesticides and Brominated Diphenylether Flame Retardants" Hobart and William Smith Colleges, Geneva, NY. November 8, 2012.

“Biomarkers of Human Exposure, Effect and Susceptibility to Pesticides used in the Nile Delta” Department of Occupational and Environmental Health, School of Public Health, University of Iowa. Iowa City, Iowa. April 12, 2013

Invited Local Presentations (more recent years)

“Tissue Slices in Organ Culture: A New Experimental Model to Assess the Human Risks of Persistent Great Lakes Contaminants” Dept. of Civil, Structural and Environmental Engineering, University at Buffalo, October 17, 1997.

“Tales of an Academic Toxicologist in the Halls of Environmental Law” Colloquium on Current Issues in Environmental Law and Policy, School of Law, University at Buffalo. Feb. 23, 1998.

“Use of Liver and Lung Slices in Dynamic Organ Culture to Assess the Expression of Dioxin-Responsive Genes“ Dept. of Biology, Canisius College, Buffalo, NY. February 5, 1999.

“Use of Liver and Lung Slices in Dynamic Organ Culture to Assess DNA Adduct Formation and the Expression of Dioxin-Responsive Genes” Dept. Biophysics, Roswell Park Cancer Institute, Buffalo, NY. May 10, 1999.

“Expression of Dioxin-Responsive CYPs in Rats and Humans” Dept of Pharmaceutical Sciences, November 29, 2001.

“Comparative Gene Expression Profiling Following Chronic Exposure to Environmentally Relevant Halogenated Aromatic Hydrocarbons” Buffalo Excellence in Biological Sciences Seminar Series, UB Center of Excellence in Bioinformatics. June 19, 2003.

“Kinetic Data on Organophosphate Pesticide Metabolism in Humans to Allow PBPK/PD Models to Assess Risk” Dept of Pharmaceutical Sciences, University at Buffalo, November 17, 2005.

“Biomarkers of Organophosphorus Pesticide-Induced Neurotoxicity” Dept. Pharmacology and Toxicology, University at Buffalo, June 29, 2009.

“Biomarkers of Organophosphorus Pesticide-Induced Neurotoxicity” Dept of Social and Preventive Medicine, University at Buffalo. Oct. 16, 2009.

“Biomarkers of Organophosphorus Pesticide-Induced Neurotoxicity” Dept. of Chemistry, University at Buffalo, March 3, 2010.

“Biomarkers of Exposure, Effect and Susceptibility to Organophosphate Pesticides in Egyptian Cotton Field Workers” Global Health Day, School of Public Health and Health Professions, University at Buffalo, April 15, 2011.



University at Buffalo
The State University of New York

Office of the Provost

September 13, 2013

Aaron J. Mango
Assistant United States Attorney
Western District of New York
138 Delaware Avenue
Buffalo, NY 14202

Dear Mr. Mango:

The University at Buffalo is honored to be given the opportunity to apply its significant research expertise to the implementation of a multi-phase epidemiologic study investigating the current health status of residents of the Town of Tonawanda and Grand Island after being exposed to emissions from the Tonawanda Coke facility. We realize this is a significant statement of trust from the judicial system, and are truly honored to be considered as an honest broker for this important study. The project proposed by Professors Mathew Bonner and James Olson will clearly benefit the residents of Tonawanda and Grand Island by providing important information regarding the current health status of the community. Such information will provide the tools for sound decision-making and focused initiatives that will reduce the burden of disease in the community. The longitudinal phase of the proposed project will be crucial for the identification of the major determinants of the mortality and morbidity in the community, and again, a prerequisite to public health action intended to reduce the burden of disease. In addition, the biomonitoring study will provide the community with crucial information about ongoing exposure that will be critical to identifying solutions to reduce these exposures.

UB will commit significant resources in support of this project which demonstrates our commitment to productive community engagement. There are two key principles that inform our plans to engage partners locally and around the world. The first principle is that engagement is essential to our ability to achieve the overall purpose of the university. The university, within the broader social system, has the fundamental responsibility to fuel knowledge creation and application to enhance societal purposes. The second principle is that improving the life of our communities will lead to excellence in the core missions of our institution – research, teaching and service – and, at the same time, enhance the quality of life in the communities we engage. As an engaged university we cultivate reciprocal relationships with our surrounding publics through shared tasks that help faculty and students learn and the community grow stronger. These efforts support and promote a more extensive engagement culture on our campus, create curricular opportunities and develop our students' civic competencies and habits. Engaging our community provides students exposure to new ways of learning, including involvement in faculty-led research that is relevant, grounded in community problems and rigorous in method. And, of course, our engagement will directly and positively impact health outcomes of our neighbors – this is why this is so important for us a university to effectively engage in this project.

Mr. Aaron Mango
September 13, 2013

2

The University at Buffalo recognizes the importance of public health research within our local communities, and we are firmly committed to engaging and supporting the local community in this important project. The project also firmly aligns with UB's strategic planning which includes the launching of a new institute engaged in research at the intersection of water, energy and the environment, including effects on human health. This new institute – UB RENEW (UB Research and Education in eEnergy, Environment and Water) – will pull together existing faculty strength at UB and will attract and recruit additional new faculty expertise, thus adding depth and breadth to research across the disciplines. The vision of UB RENEW is to build a comprehensive program of research, education and engagement that focuses on the environment, and impacts on health from environmental conditions will be a critical component of UB RENEW's focus. Over the next ten years, the university will invest over \$30 million to launch and support UB RENEW. The project outlined by Professors Bonner and Olson could be a lead project for UB RENEW.

The University at Buffalo will administer the funds allocated for this proposed project, and all of the funds awarded by the court for this project will be used to directly support this study. We note that if this project was funded by the U.S. federal agencies that fund research of this nature (e.g., the National Institutes of Health, the Environmental Protection Agency or the Department of Energy), the university would be reimbursed with an additional \$6.8 million to partially compensate for actual costs incurred by the university to support its facilities and administrative costs. We assure that even without these additional dollars, the university is fully committed to the project's scope and to ensure its completion as outlined in the proposal. Oversight of all allocated funds will be conducted in accordance with UB's established research policies, including ethical conduct of research and fiscal administration of sponsored projects.

Should this proposal result in an award, it will be a great opportunity for our university to impact the health of the citizens of our region. With this award, we are committed to providing the necessary support to this project in order to ensure its successful completion.

Sincerely,



Charles F. Zukoski

Provost and Executive Vice President for Academic Affairs



Tonawanda Community Fund

An affiliate of "The Wellness Institute of Greater Buffalo"

Hon. William Skretny
Chief United States District Judge for the Western District of New York
2 Niagara Square
Buffalo, N.Y. 14202
August 2, 2013

Dear Honorable Skretny,

I am pleased to submit two community service project ideas for your review and consideration when sentencing the defendants in the *Tonawanda Coke Corp v United States of America* lawsuit and verdict. I am grateful for the opportunity to submit these ideas and appreciate any feedback from you and the Department of Justice, as I am truly committed, along with my project collaborators, to seeing each of these projects funded and come to fruition. I have also included a copy of my impact statement because both project ideas were conceptualized from my personal experiences and working as a community activist/citizen scientist for the last ten years.

The first project idea with an estimated budget of approximately \$700,000 and entitled "Determining the Environmental Impact of Coke Oven Emissions Originating from Tonawanda Coke Corp." was written as a result of the citizen science work a few of my neighbors and I started last year. We decided to test our soil after learning that a similar community's soil in N. Birmingham, Al, where two foundry coke plants reside, was contaminated with dangerous chemicals. We found the same dangerous chemicals in the Tonawanda neighborhood we tested. Additionally, we have continued our efforts in other impacted neighborhoods to some extent this summer, but are unable to complete a comprehensive investigation due to lack of funding.

The second project idea entitled "Niagara Riverfront Community Wellness and Resource Center" and "Cherry Farm Project" with an estimated budget of \$7.8 million, was also submitted to you by the Town of Tonawanda, but as two separate projects. . The purpose as to why I am submitting these ideas together and in greater detail is to provide you with a vision of how a few of the proposed project ideas "fit" together. Also note, with the later project idea, I have incorporated the first project into the "citizen science" section.

I decided not to pursue letters of support for these ideas from elected official's as I was not sure if it appropriate and necessary. I am hoping that whatever decisions you make are not swayed by politics and that my sincere efforts, track record, as well as the phenomenal reputation of the collaborators on these projects will speak for themselves.

Lastly, and once again, I want to acknowledge the collaborators I was so fortunate to work with in crafting these project proposals. Even though I conceptualized both ideas, the top-notch reputation of each collaborator and commitment in our shared vision is what made these project ideas possible.

Please feel free to contact me, if you have any questions.

Sincerely,

Jackie James Creedon
Tonawanda Community Fund
716-873-6191

Determining the Environmental Impact of Coke Oven Emissions Originating from Tonawanda Coke Corp. on Surrounding Residential Community

Description:

- A comprehensive environmental air and soil investigation to examine the impact of Tonawanda Coke's (TCC) foundry coke emissions, specifically particulate organic material (POM) in the immediate surrounding environment.
- A scientific investigation and collaboration between University at Buffalo, SUNY Department of Chemistry, State University of New York at Fredonia Department of Chemistry, and the local community group, Tonawanda Community Fund, an affiliate of Analytical Solutions, Inc.

Goals:

- To characterize and measure the POM originating from Tonawanda Coke Corp. via air sampling and chemical analysis and determine what chemicals are specific to TCC.
- To determine what chemicals are present in the surrounding residential community (Tonawanda, NY) via soil and air analysis, potential source(s), and if levels pose a potential health risk and warrant remediation.
- To determine if further facility reductions are warranted and if TCC facility needs additional controls.

Background:

- Particulate Organic Material (POM), a significant portion of Coke Oven Emissions, are identified in the 1990 Clean Air Act Amendments as a hazardous air pollutant (HAP) and are classified by the USEPA as a known human carcinogen.
- There are many sources of POM in Tonawanda: Tonawanda Coke Corporation (TCC) is one source. TCC is the sole source of Coke Oven Emissions in Tonawanda, NY.
- Coke Oven Emissions, also a HAP and human carcinogen, are characterized as consisting of a mixture of POM, organic chemicals and metals. The semi-volatile organic constituents of Coke Oven Emissions are often termed as benzene soluble organics (BSO), which is considered an appropriate surrogate for quantifying the cancer risk associated with Coke Oven Emissions. BSO's adhere on the surface of POM. Both BSO's and POM will be examined by specific methods at University at Buffalo and SUNY Fredonia.
- Two HAPs (BSO and benzene) were responsible for the elevated cancer risk estimate in the surrounding residential communities around Tonawanda Coke Corporation.
- In 2011, Benzene (gas phase) emissions from TCC were drastically reduced due to significant process modifications and environmental controls. Reductions were further verified and quantified by NYS DEC/EPA community monitors located in Tonawanda. To date, POM emissions from the TCC facility appear to have been reduced due to installation of particulate reduction apparatus called baffles; however, there has been no community monitoring verifying potential reductions. This proposed study would monitor, measure and characterize such emissions.
- In Nov. 2012, the local community group, Tonawanda Community Fund (TCF), conducted a preliminary soil investigation and found elevated levels of polycyclic aromatic hydrocarbons (PAH),

a class of chemicals including some which are carcinogens, that are associated with foundry coke production and POM.

- Tonawanda and surrounding communities have a long history of community complaints of POM interfering with quality of life.

Steps and Timeline:

1. Develop sampling plan for air analysis.
 - Jan.-March 2014
2. Community Communication: input, permissions, etc.
 - Feb- April 2014
3. Equipment set up and implementation
 - May-June 2014
4. Collect and analyze air samples.
 - July - Nov 2014
5. Evaluate data from air samples.
 - Nov 2014-Jan. 2015
6. Generate air sample reports and develop plan for soil testing
 - Jan-March 2015
7. Report air results to community and get community input for soil testing.
 - March-April 2015
8. Finalize soil testing/sampling plan, get permissions
 - April-May 2015
9. Collect and analyze soil samples
 - June-Aug 2015
10. Evaluate Data and Generate Reports- share with community people
 - July-Sept 2015
11. Final Report and Final Community Meeting
 - Develop next step(s): dependent on sample results.
 - Nov.-Dec 2015

Deliverables:

- Research report determining TCC POM characterization and environmental impact via soil and air exposure routes.
- Educate community on:
 - Soil and Air Test Data and Results: chemicals present, possible sources, TCC chemicals present and corresponding levels.
 - Adverse effects of chemicals originating from TCC.
 - Other possible chemicals present.
 - Precautions to minimize exposure
- Community Engagement: Initiate discussions with area elected officials and government agencies (DEC and EPA) regarding next steps and possible “clean-up” scenarios.

Roles and Responsibilities:**Professor Joseph A. Gardella, Jr., John and Frances Larkin Professor of Chemistry, University at Buffalo, SUNY**

Professor Gardella and his graduate assistants will be responsible for air sample collection and analysis of POM via solid state mass spectrometry methods such as Time of Flight Secondary Ion Mass Spectrometry. Professor Gardella's group has developed new specific sample extraction methods to solubilize BSO's more efficiently for analysis. Further, Professor Gardella will provide Geographic Information Analysis of the neighborhoods to develop a geospatial sampling plan within the neighborhood for soil samples and work on training of residents on sample collection.

Professor Michael Milligan, Department of Chemistry, SUNY College at Fredonia

Dr. Michael Milligan is a professor of chemistry at the State University of New York at Fredonia, where he has been a faculty member for 20 years. Dr. Milligan is a chemical engineer and environmental chemist, and has almost 30 years experience in gas chromatographic/mass spectrometric (GC/MS) techniques. He will be responsible for the following aspects of this project:

- Sample cleanup, GC/MS analysis, and data processing for the quantification of polycyclic aromatic hydrocarbons (PAHs) in all collected air samples;
- Comprehensive 2-dimensional gas chromatographic/time-of-flight mass spectrometric (GCxGC-TOF) analysis of a subset of soil and air samples to identify unique chemical markers associated with the coking process;
- Supervision of an undergraduate research student (chemistry or environmental sciences major) who will work full time during the summer months and part time during the academic year on this project, and;
- Assist with the other PIs on this project with data analysis, data interpretation, publication, and public notification of the conclusions of this work.

Jackie James Creedon: Tonawanda Community Fund, An Affiliate of Analytical Solutions, Inc.

Ms. James-Creedon was one of the founding members and first executive director of the Clean Air Coalition of WNY. James-Creedon has made it her personal mission to find out why she and so many people in her community are sick: and in 2011 created the Tonawanda Community Fund to continue this mission. She holds a B.S. in Chemistry, is owner of Analytical Solutions, Inc. and today continues empowering and helping her community through citizen science.

Ms. James-Creedon and her volunteers and staff will be responsible for the following tasks:

- Assist researchers and solicit input from community developing a sampling plan for air and soil analysis.
- Obtain general health information and permissions from air and soil sampling locations.
- Generate community soil and air testing reports.
- Collaborate with other industry experts regarding data result interpretations.
- Act as facilitator between researchers and community. Services provided to the community include: Share and interpret data results, educate community on adverse health affects and precautions pertaining to toxins present, develop possible next step(s).

Proposed Budget

PI: Dr. Joseph Gardella

Sponsor: TBD

Start Date: 01/01/2014

	Year 1				Year 2				Total
	Effort in months	Salary	Monthly salary	Total	Effort in months	Salary	Monthly salary	Total	
Summer									
Gardella, Joseph (PI)	0.50	161,242	\$53,747	\$26,874	0.50	164,466	\$54,822	\$27,411	\$54,285
Salaries Total				\$26,874				\$27,411	\$54,285
Fringe Total Summer 17%				\$4,569				\$4,660	\$9,228
Total				\$31,442				\$32,071	\$63,513
Research									
Milillo, Tammy	2.00	40,800	\$3,400	\$6,800	2.00	41,616	\$3,468	\$6,936	\$13,736
Salaries Total				\$6,800				\$6,936	\$13,736
Fringe Total 42.5, 43%				\$2,890				\$2,982	\$5,872
Total				\$9,690				\$9,918	\$19,608
Grad Student									
TBD	6.00	25,000	\$2,083	\$12,500	6.00	25,500	\$2,125	\$12,750	\$25,250
Fringe Total 16%				\$2,000				\$2,040	\$4,040
Total				\$14,500				\$14,790	\$29,290
All Salary				\$46,174				\$47,097	\$93,271
All Fringe				\$9,459				\$9,682	\$19,141
All Total				\$55,632				\$56,779	\$112,412
OTPS:									
Purchased service (Test America)				\$193,900				\$0	\$193,900
Supplies				\$1,000				\$1,000	\$2,000
Subaward - SUNY Fredonia				\$43,830				\$43,830	\$87,660
Subaward - Analytical Solutions				\$53,540				\$52,540	\$106,080
Other - NMR time				\$1,000				\$1,000	\$2,000
Equipment				\$7,000				\$0	\$7,000
Tuition - \$472, \$519/ch, 1ch/sem				\$944				\$1,038	\$1,982
Total Other Costs				\$301,214				\$99,408	\$400,622
Total Direct Costs				\$356,846				\$156,187	\$513,034
Total IDC Base				\$276,532				\$58,779	\$335,312
Indirect Costs (59% Y1, 59.5% Y2 MTDC)				\$163,154				\$34,974	\$198,128
Total Costs				\$520,000				\$191,161	\$711,161