Columbia University Superfund Research Program: "Health Effects and Geochemistry of Arsenic and Manganese
PI: Joseph Graziano, PhD
2012 Annual Progress Report (Submitted 1 February 2013)

Center Executive Summary

A. Center Highlights: Below we provide five highlights of our research accomplishments in the past year.

Highlight- Project 1: Health Effects of Arsenic Longitudinal Study
PI: Habibul Ahsan

Highlight Title: Arsenic exposure from drinking water, arsenic methylation capacity, and carotid intima-media thickness in Bangladesh

Background: Arsenic exposure from drinking water has been related to cardiovascular disease (CVD). The primary metabolic pathway of inorganic arsenic (InAs) in humans is one-carbon methylation. Once ingested, InAs is methylated to monomethylarsonic acid (MMA) and dimethylarsinic acid (DMA). Mechanistic studies have shown that MMA^{III} is more toxic than InAs or any of the pentavalent metabolites. The relative distribution of total MMA and DMA in urine reflects arsenic methylation capacity. High levels of urinary MMA%, an indicator of incomplete methylation, has been positively related to an array of arsenic-related health effects including skin lesions, skin cancer, urothelial carcinoma, bladder cancer, and lung cancer. However, the relationship between urinary MMA% and preclinical or clinical endpoints of CVD is unknown.

Carotid intima-media thickness (cIMT) is an ultrasound measure of early atherosclerosis and a validated surrogate marker for clinical endpoints. The evaluation of inter-relationships between arsenic exposure, biomarkers specific for susceptibility to arsenic exposure, and cIMT may help identify arsenic exposure – a worldwide environmental problem - as an emerging risk factor for CVD.

Advances: As part of project 1 of the Columbia SRP, we conducted a study of 959 subjects randomly selected from the Health Effects of Arsenic Longitudinal Study, a population-based, prospective cohort study in Araihazar, Bangladesh, with participants enrolled since 2000. cIMT was measured during 2010-2011, on average 7.2 years after baseline. Arsenic exposure was measured in baseline well water and urine samples collected at baseline and two subsequent biennial follow-up visits prior to cIMT measurement. We found positive associations between baseline urinary arsenic and well arsenic with cIMT. Every one standard deviation increase in urinary arsenic (357.9 µg/g creatinine) and well arsenic (102.0 µg/L) was related to a 11.7 µm (95% confidence interval: 1.8, 21.6) and 5.1 µm (95% confidence interval: -0.2, 10.3) increase in cIMT, respectively. There was a positive relationship between MMA% in baseline urine and cIMT. For every 10% increase in MMA%, there was an increase of 12.1 µm (95% confidence interval: 0.4, 23.8) in cIMT. Among participants with higher urinary MMA%, a higher ratio of urinary MMA to InAs, and a lower ratio of DMA to MMA, the association between well arsenic and cIMT was stronger.

Significance: To the best of our knowledge, the present study is the first that reports a positive association between arsenic exposure and cIMT using urinary arsenic as a biomarker for the exposure, and the first that reports a positive association between incomplete arsenic methylation capacity, indicated as a higher level of urinary MMA%, and cIMT. The findings indicate an effect of past long-term arsenic exposure on cIMT, which may be potentiated by suboptimal or incomplete arsenic methylation capacity. Future prospective studies are needed to confirm the association between arsenic methylation capacity and atherosclerosis-related outcomes.

For more information contact:
Habibul Ahsan
Yu Chen
Joseph Graziano

Reference:

Chen Y, Wu F, Graziano JH, et al. Arsenic exposure from drinking water, arsenic methylation capacity, and carotid intima-media thickness in Bangladesh. *Am J Epidemiol*. In press.

Highlight- Project 2: Consequences of Arsenic and Manganese Exposures on Children
PI: Joseph Graziano

Highlight Title: Exposure to arsenic from household wells and intelligence of schoolchildren in Maine

Background: Arsenic (As) exposure is known to be associated with an increased risk for various cancers as well as cardiovascular, pulmonary, neurologic and other diseases in adults. In recent studies of children in Bangladesh and elsewhere in the developing world, exposure to As via drinking water was negatively associated with certain domains of child intelligence and working memory, even after adjustment for social factors. However, generalizing these findings to children in the US is problematic since the tests utilized to assess child intelligence have not been standardized in Bangladesh and elsewhere, and poor nutrition might influence both arsenic metabolism and child intelligence. We therefore carried out a study to examine the relationship between water As exposure and child intelligence (using the WISC-IV) in 272 children in grades 3-5 in Maine, where almost one-third of these children's homes had water As levels greater than the US EPA's maximum contaminant level of 10 µg/L. Aside from child intelligence, we also assessed factors known to influence intelligence, including the home rearing environment (HOME), the number of children in the home, and maternal IQ.

Advances:
On average, the children were nearly 10 years of age and their mean household water As (WAs) was 9.88 µg/L. When we examined the simple association between WAs and child intelligence, WAs was associated with decreased scores on most WISC-IV subscales. After statistical adjustment for the HOME environment and number of siblings, WAs remained significantly negatively associated with Full Scale IQ, Perceptual Reasoning and Working Memory scores. Compared to those with WAs<10 µg/L, exposure to WAs $\geq$ 10 µg/L was associated with reductions of 2.68 points in Full Scale IQ ($p < .10$) and 3.94 points in Perceptual Reasoning scores ($p=.02$), while exposure to WAs $\geq$ 20 µg/L was associated with a 5.08 point reduction in Working Memory scores ($p <.05$). To our surprise, WAs was also associated with both maternal IQ and education; mothers with higher IQ were more likely to have reported having their well tested and having a filtration system in place. Thus, not surprisingly, when statistical models examining the relationship between WAs and child IQ also considered the impact of maternal IQ, the size of the effect on child IQ decreased to 2.76 points for Perceptual Reasoning, 4.05 points for Working Memory and 1.30 points for Full Scale IQ.

Significance: Our findings of an adverse association between WAs and child IQ are consistent with our own similar findings in 10 and 6 year old children in Bangladesh, and with those of others in India, Bangladesh and Mexico. They are also consistent with results of a small pilot study of children in Oklahoma, where hair As was adversely associated with IQ. Collectively, these studies emphasize the need for families relying on household wells for drinking water to arrange for well testing, and, if necessary, for the installation of appropriate filtering systems. Arsenic should be added to the list of environmental exposures that can lead to reduced intelligence and potentially the need for special education.

For more information contact:

Joseph Graziano
Gail Wasserman

Reference
Wasserman G, Liu X, Kline J, Factor-Litvak P, LoIacono N, van Geen A, Mey J, Levy D, Abramson R, Schwartz, A, Graziano, JH.Exposure to arsenic from household wells and intelligence, in Maine schoolchildren. *Environ Health Perspect*, in review, 2013.

Highlight Project 3: Impact of Nutrition on Arsenic-Induced Epigenetic Dysregulation
PI: Mary Gamble

Highlight Title: Blood glutathione redox status and global methylation of peripheral blood mononuclear cell DNA in Bangladeshi adults

Background: Global DNA hypomethylation is believed to play a role in carcinogenesis and is commonly found in tumor tissue and transformed cells. Although oxidative stress and DNA hypomethylation often co-occur in carcinogenesis, possible modulating effects of oxidative stress on DNA methylation have not been extensively studied in humans. Many enzymes involved in DNA methylation, including DNA methyltransferases and histone deacetylases, may show altered activity under oxidized intracellular conditions. Additionally, depletion of the body's primary antioxidant, glutathione (GSH), may lead to global DNA hypomethylation through depletion of *S*-adenosylmethionine (SAM), the universal methyl donor for transmethylation reactions. Thus, we tested the hypothesis that increased oxidative stress is associated with decreased global DNA methylation by examining associations between blood GSH concentrations and blood GSH redox state with global methylation of peripheral blood mononuclear cell (PBMC) DNA in Bangladeshi adults, and we also examined whether these associations may be explained by changes in blood SAM.

Advances: We calculated the blood GSH redox state using the Nernst equation, which takes into account the concentrations of both GSH and its oxidized form, glutathione disulfide (GSSG); increased GSSG relative to GSH is indicative of an oxidized state. In models adjusting for gender, age, and water arsenic exposure, we found that a more oxidized blood GSH redox state was associated with decreased global DNA methylation ($P = 0.009$). The concentration of blood GSH was positively associated with global DNA methylation, but it did not reach statistical significance ($P = 0.11$). Furthermore, we did not find that the blood GSH redox state was significantly associated with blood SAM ($P = 0.23$), which suggests that oxidative stress does not influence global DNA methylation through SAM depletion.

Significance: Our findings suggest that a more oxidized blood GSH redox state is associated with a decrease in global DNA methylation, but these associations did not appear to be mediated by changes in SAM. Alteration of GSH redox may be a mechanism through which environmental exposures and other factors influence DNA methylation. It may also be of interest to examine whether redox therapies might help to prevent progressive loss of global DNA methylation in cancer and other diseases.

For more information contact:

Mary Gamble

Reference:

Niedzwiecki M, Hall MN, Liu X, Oka J, Harper KN, Slavkovich V, Ilievski V, Levy D, van Geen A, Mey JL, Alam S, Siddique S, Parvez F, Graziano JH, and Gamble MV. Blood glutathione redox status and global methylation of peripheral blood mononuclear cell DNA in Bangladeshi adults. (2013; manuscript in review).

Highlight- Project 4: Arsenic, Iron, Sulfur and Organic Carbon Speciation and their Impact on Groundwater Arsenic
PI: Ben Bostick

Highlight Title: Radiocarbon Dating Microbial DNA from Aquifers to Understand Carbon Cycling

Background:
Over 100 million people are exposed to unsafe levels of arsenic (As) by drinking shallow groundwater in South and Southeast Asia. The health effects are numerous and include increased risk of multiple cancers and mortality and numerous non-cancer outcomes. The arsenic occurs naturally in the sediment and is released from the sediment to the water during microbial respiration. The release of As to groundwater has been linked to the reductive dissolution of iron oxides coupled to the microbial respiration of organic carbon. As microbes

utilize organic carbon and iron oxides, they release arsenic sorbed onto the iron oxide minerals into the groundwater.

The source of organic carbon fueling this microbial reduction is unknown. There are two major hypotheses for the source of organic carbon. Either organic carbon is deposited with the sediments or exogenous organic is transported into the aquifer by groundwater flow. Furthermore, it is often assumed that the exogenous organic carbon is of recent anthropogenic origin. However, all conclusions pertaining to the source of organic carbon have been based on indirect data. Differentiating these possibilities is critical in that they impart unique limits on the sustainable use of water supplies, and the management of these precious water resources.

Advances:
To directly determine the source of OC fueling the microbial reduction we developed a new method to determine the radiocarbon (^{14}C) signature of microbial DNA isolated from groundwater samples. The method consists of filtering at least 3000 liters of groundwater and preferably over 20,000 liters. The filters are returned to the lab where the DNA is extracted and purified and then radiocarbon dated. Purification is a multistep process to remove environmental contaminants such as humic acids and laboratory contaminants such as surfactants required for DNA extraction. A present day radiocarbon date would indicate human contamination as the primary source of organic carbon whereas older dates would indicate a natural geologic source.

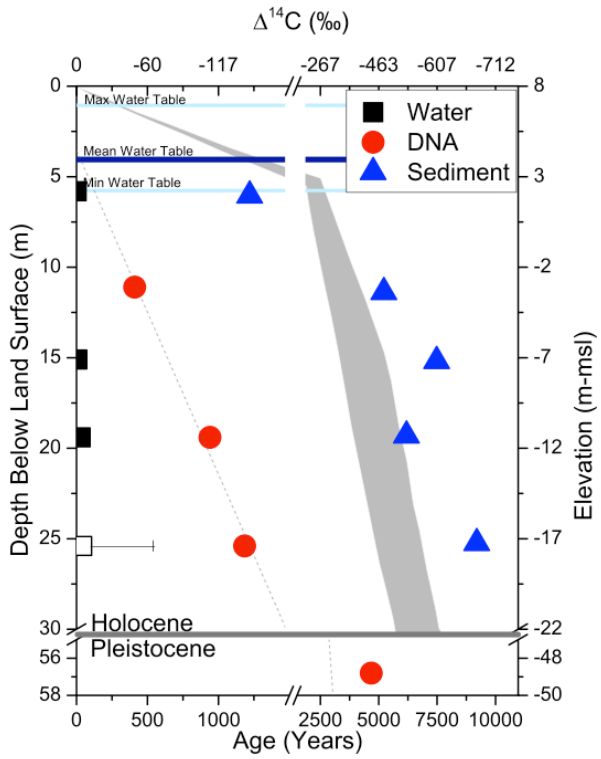

Figure 1. Vertical profiles comparing water ages, DNA ages, and sediment ages from the Site F well nest in Bangladesh. Note that there is a break in the depths from 30-55m and the scale on the ages changes at 1500 years. The data clearly shows that the DNA ages are older than the water and younger than the sediment. This indicates that the slow advection of organic carbon from the surface is fueling microbial reduction and arsenic release within the aquifer.

This study consisted of 4 samples collected from the Site F well nest in Araihazar, Bangladesh. This site has been monitored for many years, and has geological properties well suited for an initial study. The area is sandy and has high recharge rates indicating that if humans are impacting an aquifer it would occur the quickest in this location. Three DNA samples were collected and analyzed from the shallow, high-As aquifer and one sample from the underlying, low-As aquifer. The microbial DNA was consistently older than the groundwater and also younger than the total sediment carbon, by as much as several thousand years. Metagenomic analysis indicated that heterotrophic microorganisms dominated the microbial community. These results imply that surface-derived organic carbon is advected within the aquifer, albeit more slowly than groundwater, and represents a critical pool of organic carbon for aquifer microbial communities. In summary, the organic carbon utilized by the aquifer microbes is recharged at the surface and then slowly moves into and through the aquifer over 100's to 1000's of years.

Significance: Microbes are ubiquitous in the subsurface and numerous organic carbon sources are present. Utilizing this method we can now begin to constrain the sources of organic carbon utilized by microbes to fuel microbial respiration and arsenic release. This work shows that advection of organic carbon into the subsurface is a critical process. This method will be widely applicable to understand organic carbon sources in the subsurface.

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For More Information Contact:
Brian Mailloux
Benjamin Bostick
Alexander van Geen

Reference:
Mailloux BJ, Trembath-Reichert E, Cheung J, Watson M, Stute M, Freyer GA, Ferguson A, Ahmed KM, Alam Md J, Buchholz BA, Zheng Y, Bostick BC, van Geen A. Advection of Surface-Derived Organic Carbon Fuels Microbial Reduction in Bangladesh Groundwater. *Proc. Nat. Acad. Sci. USA*, 2013;In Press.

Highlight- Project 5: Application of Enhanced Mitigation Methods for Groundwater Arsenic at US Superfund Sites
PI: Steve Chillrud

Highlight Title: Using Direct Observations of Geological Processes to Assess Remediation Options at Superfund Sites

Background:
The Vineland Chemical Company, located in southern New Jersey, manufactured arsenic-based herbicides from 1950 to 1994, resulting in considerable soil, sediment and groundwater arsenic contamination. The contaminated aquifer has undergone remediation since 2001 using a pump-and-treat approach that controls groundwater flow direction and slowly removes arsenic from the aquifer. This approach is common at sites affected by arsenic and other contaminants, but often must be sustained for long periods of time in part because arsenic desorption is slow and unfavorable under typical soil conditions. Prior work has shown that oxalic acid, a natural organic acid, can greatly increase the efficiency of soil As extractions, and thus enhance pump-and-treat and reduce the time period of remediation by decades.

To better understand the oxalic acid amendment approach, we need to understand how much of the arsenic is removed, what causes residual arsenic to remain in the soil, and to what extent persistent arsenic can contaminate groundwater in the future. This research combined laboratory experiments performed within an X-ray beam and hydrological modeling to answer these questions at the microscopic scale, and to relate it to the field scale.

Advances:
We set up a column experiment of contaminated Vineland aquifer sediments inside the synchrotron beam to enable us to peer into the sediments as water and oxalic acid flows through it. This method provides a movie of the microscopic processes as they occur, including that of oxalate displacing iron and arsenic from mineral substrates. Because this technique is capable of imaging distinct mineral grains, it can examine the potential effect of different mineral substrates on both the rate and extent of arsenic desorption (release into the solution phase). In doing so, it provides a window to directly observe the effect of heterogeneous mineralogy in complex environmental samples, and to help engineer remediation strategies to account for this inherent complexity.

During the course of the column experiment, about 80% of the arsenic was extracted from the sediments, and most of the extracted arsenic was associated with reactive iron oxides. The rate of desorption depended on the sediment iron mineralogy . Furthermore, the recalcitrant arsenic appeared to be structurally bound—it essentially was stable in specific mineral grains—rather than being associated with stagnant pore waters that do not interact with the oxalate solution. Importantly, the mean rate determined with this technique was scalable to the column scale and field scale, indicating that the processes at the micron scale are representative of the larger system.

Significance:

The oxalic acid amendment approach has potential to greatly increase the effectiveness of pump and treat operations. However, the environment is inherently complex, and understanding this complexity and then accounting for it is necessary to properly assess how to protect human and environmental health. The methods used provide quantitative chemical information about the rate and extent of chemical processes critical to water quality, and a visual image of their heterogeneity. This real-time method can be applied to study myriad environmental processes, and to obtain fundamental chemical constants from those observations.

For More Information Contact:
Benjamin Bostick
Steven Chillrud
Brian Mailloux

References:
Wovkulich K, Mailloux BJ, Bostick BC, Dong H, Bishop M, Chillrud S. Use of microfocused X-ray techniques to investigate the mobilization of arsenic by oxalic acid. *Geochim. Cosmochim. Acta* 2012:91:254-70. PMCID: PMC3501129

Wovkulich, K, Mailloux BJ, Lacko A, Keimowitz AR, Stute M, Simpson HJ, Chillrud SN, 2010. Chemical Treatments for Mobilizing Arsenic from Contaminated Aquifer Solids to Accelerate Remediation. Applied Geochemistry, 25: 1500–1509. PMCID: PMC2976553. doi:10.1016/j.apgeochem.2010.08.001

B. Personnel Updates: There have been no changes in the key personnel listed in the Notice of Grant Award.

C. SRP Trainee Highlights:

Maria Argos, Dr. Ahsan's former PhD student (currently a Research Associate (Assistant Professor)) worked on analyses for Dr. Ahsan's SRP Project. She focused on arsenic exposure in relation to mortality and skin lesions as well as diet in relation to urinary arsenic concentrations. Dr. Argos was recognized with an award in international health at the Congress of Epidemiology in 2011 for her publication on arsenic in relation to mortality. Dr. Argos has presented her work at a Workshop on Arsenic and Epigenetics in AZ in September, 2012, as well as to a joint meeting of NIEHS SRP and ATSDR in GA in August 2012. Dr. Argos has also been involved in the statistical analyses for Dr. Ahsan's current SRP project.

Christine George, one of Dr. Graziano's minority PhD students, spent 15 months in Bangladesh with support of a Fulbright scholarship. She derived five first author papers from her work on arsenic in Bangladesh. She defended her PhD dissertation in 2012 and is now an Assistant Professor at Johns Hopkins University.

Megan Hall, Dr. Gamble's former post-doctoral research fellow (currently an Assistant Professor) worked on statistical analyses for Dr. Gambles previous SRP Project. She focused on the effects of arsenic exposure on glutathione concentrations. Her work was also selected for oral presentation at the 2011 SRP Meeting in Kentucky. Dr. Hall now has a K99/R00 award from NIEHS to study nutritional influences, particularly of choline and betaine, on arsenic methylation. Dr. Hall has also been involved in the statistical analyses for Dr. Gamble's current SRP Project.

Kristin Harper, Dr. Gamble's post-doctoral research fellow, worked on Aims 1 and 3 of our previous SRP Project. She is working on analyses of differentially methylated CpGs by arsenic exposure using Illumina's new 450K array and was instrumental in generating preliminary data for aim 3 of our new SRP Project 3. Dr. Harper presented her work at a Workshop on Arsenic and Epigenetics in AZ in September, 2012 (described above and manuscript in preparation).

Caitlin Howe is a PhD student in Dr. Gamble's laboratory. She has been working on analyses related to aim 2 of our previous SRP Project in which we are analyzing associations between s-adenosylhomocysteine and s-

adenosylmethionine and arsenic methylation. She is currently working on analyzing histone modifications for all aims of the current SRP Project 3. Caitlin presented her work as a poster at the 2012 Annual SRP Meeting; her poster was selected for first prize in the category of biomedical posters.

Stephanie Melkonian is a fifth-year PhD student in Dr. Ahsan's research group. She has been working on analyses related to Aim 1 of Dr. Ahsan's SRP project examining factors that modify the association between arsenic exposure and skin lesion risk. She completed several publications in relation to this work.

Ivan Mihajlov, a PhD candidate in Earth & Environmental Sciences who works on Project 6 and is co-advised by Dr. van Geen, is expected to defend his PhD by the end of summer 2013.

Megan Niedzwiecki, Dr. Gamble's PhD student, worked on laboratory and data analyses for the folate and oxidative stress (FOX) study from Aim 3 of Project 4 of Dr. Gamble's previous SRP Project. She studied the effects of redox status on methylation of arsenic and DNA which will be a focus of her thesis. Her work was selected for oral presentation at the 2011 SRP Meeting in Kentucky. Her work was also selected for an oral presentation at the 2012 FASEB Summer Research Conference (described above).

Brandilyn Peters, Dr. Gamble's PhD student is also working on analyses of differentially methylated CpGs by arsenic exposure and was, along with Kristin (above), instrumental in generating preliminary data for our new SRP Project 3. She also analyzed all of the homocysteine data for aim 2. Brandi presented her work as a poster at the 2012 Annual SRP Meeting.

Brandon Pierce, Dr. Ahsan's former post-doctoral research fellow (currently an Assistant Professor)) worked on analyses for Dr. Ahsan's SRP Project. He primarily has focused on dietary modifiers of the association between arsenic and skin lesion risk. Dr. Pierce now has a R01 award from NIEHS ONES program to examine arsenic exposure in relation to telomere length.

Jing Sun, a third year PhD student in Earth and Environmental Engineering who is working on Project 5, gave a platform presentation at the 22nd V.M. Goldschmidt 2012 conference entitled "Arsenic Mobilization from Contaminated Aquifer Sediments by Chemical Amendments for Accelerated Remediation."

D. Publication/Patent Consolidated List

2012 Publications:

Argos M, **Ahsan H**, **Graziano JH**. Arsenic and human health: epidemiologic progress and public health implications. *Rev Environ Health*. 2012;doi:10.1515/reveh-2012-0021. PMCID: In progress.

Arita A, Shamy MY, Chervona Y, Clancy HA, Sun H, Hall MN, Qu Q, **Gamble MV**, **Costa M**. The effect of exposure to carcinogenic metals on histone tail modifications and gene expression in human subjects. *J Trace Elem Med Biol* 2012;26:174-8. PMID: 22633395 doi: 10.1016/j.jtemb.2012.03.012

Bennear L, Tarozzi A, Pfaff A, Soumya HB, Ahmed KM, **van Geen A**. Impacts of a randomized controlled trial in arsenic risk communication on household water supply choices in Bangladesh, *J Environ Econ Manage*, 2012; in press.

Clancy HA, Sun H, Passantino L, Kluz T, Muñoz A, Zavadil J and **Costa M**. Gene expression changes in human lung cells exposed to arsenic, chromium, nickel or vanadium indicate the first steps in cancer. *Metallomics* 2012;4(8):784-93. PMID: 22714537 doi: 10.1039/c2mt20074k

Chen Y, McClintock TR, Segers S, Parvez F, Islam T, Ahmed A, Rakibuz-Zaman M, Hasan R, Sarwar G, **Ahsan H**. Prospective investigation of major dietary patterns and risk of cardiovascular mortality in Bangladesh. *Int J Cardiol*. 2012;doi.org/10.1016/j.ijcard.2012.04.041. PMCID: In progress.

*Chervona Y, Hall MN, Arita A, Wu F, Sun H, Tseng HC, Ali E, Uddin MN, Liu X, Zoroddu MA, **Gamble MV***, **Costa M**. Association Between Arsenic Exposure and Global Post-translational Histone Modifications Among Adults in Bangladesh. *Cancer Epidemiol Biomarkers Prev*. 2012;12:2252-60. doi: 10.1158/1055-9965. PMCID: PMC3518638

Chervona Y, **Costa M**. The control of histone methylation and gene expression by oxidative stress, hypoxia and metals. *Free Radic Biol Med* 2012;53(5):1041-7. PMCID: PMC3432141

*Ferguson AS, Layton AC, **Mailloux BJ**, Culligan PJ, Williams DE, Smartt AE, Feighery J, McKay L, Knappett P, Alexandrova E, Arbit T, Emch M, Escamilla V, Ahmed KM, Alam MJ, Streatfield PK, Yunus M, **van Geen A**. Comparison of fecal indicators with pathogenic bacteria and rotavirus in groundwater, *Sci Total Environ*, 2012;431:314–22. PMID: 22705866 NIHMS387725

Gamble MV and Hall MN. Relationship of nutrition and urinary creatinine with arsenic metabolism. Commentary. *Environ Health Perspect*. 2012;120(4):A145-6. PMCID: PMC3339472

*George CM, **Zheng Y**, **Graziano JH**, Rasul SB, Mey JL, **van Geen A**. Evaluation of an arsenic test kit for rapid well screening in Bangladesh, *Environ Sci Technol* 2012;46:11213–9. PMID: 22866936

*George CM, Khan K, Islam T, Singha A, Moon-Howard J, **Factor-Litvak P**, **van Geen A**, **Graziano JH**. Approaches to increase arsenic awareness in Bangladesh: An evaluation of an arsenic education program. *Health Educ Behav*. 2012;Sep 14. [Epub ahead of print] doi: 10.1177/1090198112454735, PMID: 22984214

*George CM, **van Geen A**, **Slavkovich V**, Singha A, **Levy D**, Islam T, Ahmed KM, Moon-Howard J, Tarozzi A, **Liu X**, **Factor-Litvak P**, **Graziano JH**. A cluster-based randomized controlled trial promoting community participation in arsenic mitigation efforts in Bangladesh. *Environ Health.* 2012;11:41. doi: 10.1186/1476-069X-11-41. PMCID: PMC3506475

*George CM, **Graziano JH**, Mey JL, **van Geen A**. Impact on arsenic exposure of a growing proportion of untested wells in Bangladesh, *Environ Health* 2012;11:7. doi: 10.1186/1476-069X-11-7. PMCID: PMC3334680

Hall MN, **Gamble MV**. Nutritional manipulation of one-carbon metabolism: effects on arsenic methylation and toxicity. *J Toxicol* 2012;2012:595307. PMCID: PMC3317163

*Khan K, **Wasserman GA**, **Liu X**, Ahmed E, **Parvez F**, **Slavkovich V**, **Levy D**, Mey J, **van Geen A**, **Graziano JH**, **Factor-Litvak P**. Manganese exposure from drinking water and children's academic achievement, *NeuroToxicology* 2012;33:91-7. PMCID: PMC3282923

*Knappett PSK, LD McKay, A Layton, DE Williams, MJ Alam, MR Huq, J Mey, JE Feighery, PJ Culligan, **BJ Mailloux**, J Zhuang, V Escamilla, M Emch, E Perfect, GS Sayler, KM Ahmed, **A van Geen**, Implications of fecal bacteria input from latrine-polluted ponds for wells in sandy aquifers, *Environ Sci Technology* 2012;46: 1361–70. PMID: 22191430 NIHMS349773 doi: 10.1021/es202773w

*Knappett P, McKay LD, Layton A, Williams DE, Alam MJ, **Mailloux BJ**, Ferguson AS, Culligan PJ, Serre ML, Emch M, Ahmed KM, Sayler GS, **van Geen A**. Unsealed tubewells lead to increased fecal contamination of drinking water. *J Water Health* 2012;10(4):565-78. doi: 10.2166/wh.2012.102. PMID: 23165714

***Mailloux BJ**, Trembath-Reichert E, Cheung J, Watson M, **Stute M**, Freyer GA, Ferguson AS, Ahmed KM, Alam MJ, Buchholz BA, Thomas J, Layton AC, **Zheng Y**, **Bostick BC**, **van Geen A**. Advection of surface-derived organic carbon fuels microbial reduction in Bangladesh groundwater. *PNAS*, 2013; in press.

Melkonian S, Argos M, **Chen Y**, **Parvez F**, Pierce B, Ahmed A, Islam T, **Ahsan H**. Intakes of several nutrients are associated with incidence of arsenic-related keratotic skin lesions in Bangladesh. *J Nutr*. 2012;142(12):2128-34. PMCID: PMC3497963.

Pesola GR, **Parvez F**, **Chen Y**, Ahmed A, Hasan R, **Ahsan H**. Arsenic exposure from drinking water and dyspnoea risk in Araihazar, Bangladesh: a population-based study. *Eur Respir J*. 2012;39(5):1076-83. PMCID: In progress.

Pierce BL, Kibriya MG, Tong L, Jasmine F, Argos M, Roy S, Paul-Brutus R, Rahaman R, Rakibuz-Zaman M, **Parvez F**, Ahmed A, Quasem I, Hore SK, Alam S, Islam T, **Slavkovich V**, **Gamble MV**, Yunus M, Rahman M, Baron JA, **Graziano JH, Ahsan H**. Genome-wide association study identifies chromosome 10q24.32 variants associated with arsenic metabolism and toxicity phenotypes in Bangladesh. *PLoS Genet* 2012;8:e1002522. PMCID: PMC3285587

Pilsner JR, Hall MN, **Liu X**, Ilievski V, **Slavkovich V**, **Levy D**, **Factor-Litvak P**, Yunus M, Rahman M, **Graziano JH**, **Gamble MV**. Influence of prenatal arsenic exposure and newborn sex on global methylation of cord blood DNA. *PLoS One* 2012;7:e37147. PMCID: PMC3360698

Syed EH, Melkonian S, Poudel KC, Yasuoka J, Otsuka K, Ahmed A, Islam T, **Parvez F**, **Slavkovich V**, **Graziano JH**, **Ahsan H**, Jimba M. Arsenic Exposure and Oral Cavity Lesions in Bangladesh. *J Occup Environ Med*. 2013;55(1):59-66. PMCID: In progress.

Wovkulich, K, **Mailloux BJ**, **Bostick BC**, Dong H, Bishop ME, **Chillrud SN**. Use of Microfocused X-ray Techniques to Investigate Mobilization of Arsenic by Oxalic Acid. *Geochim Cosmo Acta*, 2012;91:254-70. PMCID: PMC3501129

*Wu F, Jasmine, F, Kibriya MG, Liu ML, Wojcik O, **Parvez F**, Rahaman R, Roy S, Paul-Brutus R, Segers S, **Slavkovich V**, Islam T, **Levy D**, Mey JL, **van Geen A**, **Graziano JH**, **Ahsan H**, **Chen Y**. Association between arsenic exposure from drinking water and plasma levels of cardiovascular markers, *Am J Epidemiol* 2012;175(12):1252-61. PMCID: PMC3372314

2012 Patents: None

Progress Reports of Individual Projects and Core Operations

Project 1: A Cohort Study of Health Effects of Arsenic Exposure in Bangladesh
PI: Habibul Ahsan

A. Specific Aims

There are no deviations in the specific aims from those that have already been reported.

B. Studies and Results

This prospective cohort study recruited 11,746 men and women in Araihazar, Bangladesh, during 2000-2002 to investigate the health effects of arsenic exposure, with an initial focus on skin lesions and skin cancers. Between 2006 and 2011, the cohort was expanded to 30,033 individuals. Expansion participants were enrolled into the cohort through in-person interviews and had blood and urine samples collected in the same manner as the original cohort. The design of this multidisciplinary project and cohort description has been published (Ahsan et al., 2005). We have numerous publications utilizing the baseline cross-sectional data on arsenic exposure and adverse health effects, including prevalent skin lesion cases, as well as longitudinal analyses of mortality, incident skin lesions, diabetes, cardiovascular disease, and respiratory disease with the prospective data.

In-person interviews and clinical examinations of the cohort participants are conducted every 2 years. The twelve-year follow-up visit of the original cohort and six-year follow-up visit of the expansion cohort is currently being planned and will be underway soon. To date, the Trace Metals Core Laboratory has completed measurements of urinary total arsenic concentration in all baseline, two-year follow-up, and four-year follow-up samples from the original HEALS cohort and all baseline and two-year follow-up samples of the expansion cohort.

Utilizing the data collected from the first three follow-up visits (2-, 4-, and 6-year visits) of the original cohort, our prospective analyses based on individual-level data clearly suggest dose-dependent association between arsenic exposure and skin lesion risk, even at low exposure levels (water arsenic concentration <100 µg/L) (Argos et al. 2011). Additionally, we showed that low intake of vitamin E and C significantly increased risk of keratotic arsenical skin lesion development (Melkonian et al. 2012). Using cross-sectional data, we also observed an increased prevalence of oral cavity lesions among individuals with higher arsenic exposure (Syed et al. 2013). We showed that arsenic exposure was clearly associated with heart disease mortality, particularly among smokers (Chen et al. 2011). We also have a manuscript under review, in which we observed an increased risk of respiratory disease mortality in relation to increases in arsenic exposure (Argos et al. Under review). Furthermore, we showed that arsenic exposure was associate with dyspnoea, which is a characteristic manifested by cardiac or pulmonary diseases (Pesola et al. 2012). We also showed that chronic arsenic exposure from drinking water is related to cardiovascular-related biomarkers of vascular inflammation and endothelial dysfunction (Wu et al. 2012).

The objectives of our current analyses and follow-up interviews are to specifically examine the aims stated in the renewal of this project, have not been modified since the last progress report. Several other manuscripts are being drafted for publication reporting results of our prospective cohort analyses of modification of the effects of arsenic on mortality and incidence of skin lesions.

In addition to the above-mentioned components, resources from this prospective cohort study have also yielded many other ancillary studies and publications including three additional R01 grants from NIH to investigate the genetic and nutritional aspects as well as chemoprevention of arsenic health effects.

C. Significance

The association between individual-level arsenic exposure and dermatological, pulmonary, and cardiovascular health outcomes has not been well established in the scientific literature, particularly at low-to-moderate exposure levels. Our overall goal is to prospectively evaluate the effects of various measures of

arsenic exposure and metabolism on: i) incidence of skin lesions and skin cancer, ii) incidence and mortality from chronic lung disorders and mortality from lung cancers, iii) incidence and mortality from cardiovascular disease (CVD), and iv) a number of biological and preclinical markers potentially involved in skin and lung disorders/cancers and CVD. The information derived from this study will have direct public health impact on arsenic-exposed populations and can be incorporated in future prevention and mitigation measures for reducing arsenic-induced health effects in this population.

D. Plans

We will continue to actively follow-up participants biennially as well as through our chronic disease surveillance mechanism between follow-up visits for the successful achievement of the aims of this project.

E. Publications

Syed EH, Melkonian S, Poudel KC, Yasuoka J, Otsuka K, Ahmed A, Islam T, Parvez F, Slavkovich V, Graziano JH, Ahsan H, Jimba M. Arsenic Exposure and Oral Cavity Lesions in Bangladesh. *J Occup Environ Med*. 2013;55(1):59-66. PMCID: In progress.

Melkonian S, Argos M, Chen Y, Parvez F, Pierce B, Ahmed A, Islam T, Ahsan H. Intakes of several nutrients are associated with incidence of arsenic-related keratotic skin lesions in Bangladesh. *J Nutr*. 2012;142(12):2128-34. PMCID: PMC3497963.

Argos M, Ahsan H, Graziano JH. Arsenic and human health: epidemiologic progress and public health implications. *Rev Environ Health*. 2012;doi:10.1515/reveh-2012-0021. PMCID: In progress.

Chen Y, McClintock TR, Segers S, Parvez F, Islam T, Ahmed A, Rakibuz-Zaman M, Hasan R, Sarwar G, Ahsan H. Prospective investigation of major dietary patterns and risk of cardiovascular mortality in Bangladesh. *Int J Cardiol*. 2012;doi.org/10.1016/j.ijcard.2012.04.041. PMCID: In progress.

Wu F, Jasmine F, Kibriya MG, Liu M, Wójcik O, Parvez F, Rahaman R, Roy S, Paul-Brutus R, Segers S, Slavkovich V, Islam T, Levy D, Mey JL, van Geen A, Graziano JH, Ahsan H, Chen Y. Association between arsenic exposure from drinking water and plasma levels of cardiovascular markers. *Am J Epidemiol*. 2012;175(12):1252-61. PMCID: PMC3372314.

Pierce BL, Kibriya MG, Tong L, Jasmine F, Argos M, Roy S, Paul-Brutus R, Rahaman R, Rakibuz-Zaman M, Parvez F, Ahmed A, Quasem I, Hore SK, Alam S, Islam T, Slavkovich V, Gamble MV, Yunus M, Rahman M, Baron JA, Graziano JH, Ahsan H. Genome-wide association study identifies chromosome 10q24.32 variants associated with arsenic metabolism and toxicity phenotypes in Bangladesh. *PLoS Genet*. 2012;8(2):e1002522. PMCID: PMC3285587.

Pesola GR, Parvez F, Chen Y, Ahmed A, Hasan R, Ahsan H. Arsenic exposure from drinking water and dyspnoea risk in Araihazar, Bangladesh: a population-based study. *Eur Respir J*. 2012;39(5):1076-83. PMCID: In progress.

Argos M, Parvez F, Rahman M, Rakibuz-Zaman M, Ahmed A, Hore SK, Islam T, Chen Y, Pierce BL, Slavkovich V, Olopade C, Yunus M, Baron JA, Graziano JH, Ahsan H. A Prospective Cohort Study of Urinary Total Arsenic Concentration and Lung Disease Mortality in Bangladeshi Adults. 2012; Under review.

F. Project-Generated Resources

The research supported by this grant has not currently resulted in data, research materials, protocols, software, or other information to be shared with other investigators.

Project 2: *Consequences of Arsenic and Manganese Exposure on Children*
PI: Joseph Graziano

A. Specific Aims: The specific aims of this project have not changed.

B. Studies and Results: This project builds upon our discovery that exposure to arsenic (As) and manganese (Mn) in drinking water has adverse effects on intelligence in children. The research under project 2 falls into three categories:

1) A recently completed study of As and child intelligence in school children in Maine, which has been described above in Highlight #2;

2) Statistical analysis of a follow-up study of 300 children involved in a 2 x 2 design, i.e., high/low (<10 ppb) drinking water As and high/low (< 400 ppb) water Mn, with 75 children in each cell. We previously described the adverse associations between these exposures and child intelligence (Wasserman et al, 2011). All children were subsequently provided with access to deep, low As wells at school and at their village and intellectual functioning was assessed one year later.

3) We have successfully launched a new study whose specific aims were the topic of our 2011 competitive renewal application. The study first asks whether the As-induced respiratory disease observed in adults also manifests itself in adolescents, and what are possible physiologic mechanisms? Second, to what extent do associations between WAs and both lung function brain function reflect the effects of exposure in utero and in infancy, periods of dramatic development for these systems? Third, are WAs and WMn associated with specific cognitive functions in addition to intelligence?

This third study draws on an existing sample of 780 adolescents (15-17 years old) whose mothers are participants in the HEALS Study (Project #1). Based on mothers' well As, measured five times from 2000 until the present, we were able to define four groups of adolescents with varying levels and patterns of exposure to As. Defined on the basis of WAs levels, four groups include adolescents with exposures that are: Group 1) consistently low (mean WAs = 3 ppb); Group 2) consistently moderate (mean WAs = 26 ppb); Group 3) consistently high (mean WAs = 146 ppb); and Group 4) high from conception through roughly age one (mean WAs = 201 ppb) but much lower thereafter (mean WAs =13 ppb). Within each group, there is wide variation in WMn concentrations. Three specific aims target As exposure and pulmonary function (FEV1 and FVC) as well as biomarkers of lung dysfunction in exhaled breath condensate.

Three additional aims expand our earlier work on As, Mn and neuropsychologic outcomes by considering components of Executive Function (planning, sustained attention, working memory) that have been mapped to brain regions thought to be affected by exposure to these elements. Components of Executive Function will be measured with the Cambridge Neuropsychological Test Automated Battery (CANTAB), a computerized and well validated set of tests; intelligence will also be assessed. We will examine adolescents, an understudied age group, because certain components of Executive Function and lung development do not mature until this age; studies with younger children would miss these health effects.

During the past year all supplies and equipment for the study were purchased and delivered to the field site in Bangladesh. In addition, Drs. Graziano and Wasserman and PhD student Tiffany Sanchez visited Bangladesh twice to carry out training regarding the measurements of intelligence, the CANTAB, pulmonary function testing and the collection of exhaled breath. Our field staff are also now completing a preliminary survey to locate as many of the 780 potential participants as possible; the vast majority are available for study. To date we have completed the complete assessment of 26 children and many others have been successfully recruited and are scheduled for evaluation.

C. Significance: Collectively, the work conducted in this project has contributed to the growing body of knowledge concerning the adverse health effects of both As and Mn on children's health. We believe that knowledge of these adverse health effects on children will increase the rate at which families will alter their behavior – both in the United States and abroad – to test their wells and pursue remediation when necessary

D. Plans: In the coming year we will complete the analysis of study #2 (above). In addition, we will continue to pursue the field work of study #3 (above).

Student Involvement:

One doctoral student is currently involved in this project. **Tiffany Sanchez**, a minority PhD student, will ultimately derive her PhD dissertation from the pulmonary aims of this project.

Christine George, another of Dr. Graziano's minority PhD students, spent one year in Bangladesh with support of a Fulbright scholarship. She defended her PhD dissertation in 2012 and is now an Assistant Professor at Johns Hopkins University.

E. Publications:

Wasserman G, Liu X, Kline J, Factor-Litvak P, LoIacono N, van Geen A, Mey J, Levy D, Abramson R, Schwartz, A, Graziano' JH.Exposure to arsenic from household wells and intelligence, in Maine schoolchildren. *Environ Health Perspect*, in review, 2013.

Wasserman GA, Liu X, Kline J, Factor-Litvak P, LoIacono N, van Geen A, Mey J, Levy D, Graziano' JH: Water arsenic, manganese and motor function in young adults in Bangladesh, in preparation.

F. Project-Generated Resources: n/a

Project 3: Impact of nutrition on arsenic-induced epigenetic dysregulation
PI: Mary Gamble

A. Aims. No modifications have been made to the aims.

B. Studies and Results:

An emerging body of evidence suggests that As exposure leads to epigenetic dysregulation. We have previously demonstrated that chronic As exposure is associated with increased global DNA methylation. We hypothesize that the mechanism underlying this relates to As-induced alterations in post-translational histone modifications (PTHM). This work involves a cross-disciplinary collaboration with Max Costa at NYU that will take advantage of samples collected from our folate trial (FACT) to carry out a set of aims related to nutrition/environment/epigenetic interactions. We plan to characterize the influence of As exposure on histone modifications, relate changes in histone modifications to changes in DNA methylation, and characterize the impact of folic acid supplementation on these marks. Finally, using the Infinium Human Methylation450 array, we will identify a set of genes that are differentially methylated by As exposure and determine gene-specific histone modifications at these loci. Collectively, these aims will begin to elucidate the molecular events that underlie the effects of As and folate on DNA methylation.

We have made significant progress on aims 1a to 1d that have been published (Chervona et al, 2012) and aim 3 (manuscript in preparation). In this preliminary study of N=40 FACT study participants, we have found that total urinary As (uAs) was positively correlated with H3K9me2 ($r = 0.36$, $P = 0.02$) and inversely with H3K9ac ($r = -0.47$, $P = 0.002$). The associations between As and other PTHMs differed in a gender dependent manner. These findings are summarized in a Figure (below).

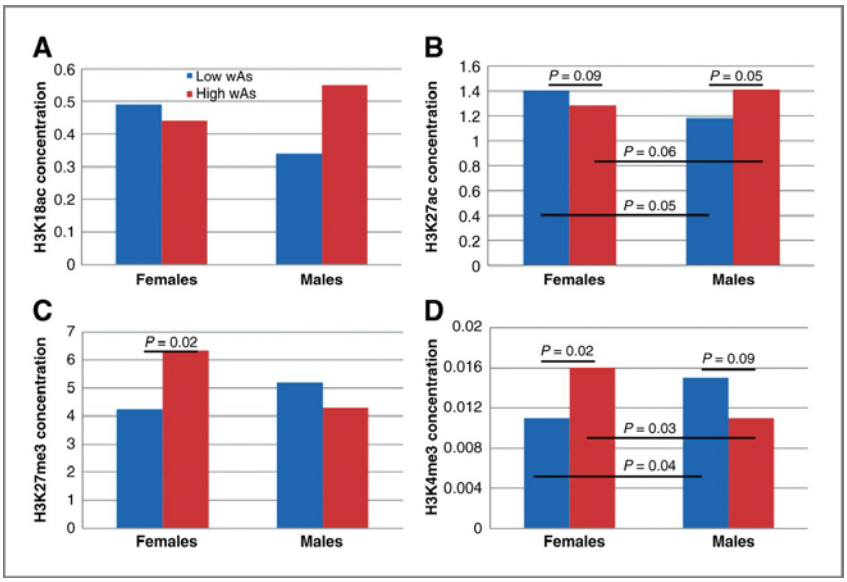

Figure Legend. Median concentrations of histone marks by sex and wAs categorya for (A) H3K18ac, (B) H3K27ac, (C) H3K27me3, and (D) H3K4me3b. A, low wAs range = 50 to 81 μg/L, high wAs range = 150 to 500 μg/L. B, on the basis of a Kruskal–Wallis test, there is a statistically significant overall difference among the 4 groups for H3K27Ac (P = 0.049), H3K27me3 (P = 0.048), and H3K4me3 (P = 0.02). Using Wilcoxon rank-sum tests, we also tested for (i) differences in histone marks by high/low wAs within gender and (ii) differences in histone marks by gender within wAs category (high/low)—P values less than 0.10 are indicated. Chervona Y et al. Cancer Epidemiol Biomarkers Prev 2012;21:2252-2260

Exposure to As is associated with alterations of global PTHMs. We were somewhat surprised to observe that several of the patterns of association thus far observed between As exposure and several histone marks differ by gender.

C. Significance: These findings contribute to the growing body of evidence linking As exposure to epigenetic dysregulation, which may play a role in the pathogenesis of As toxicity. Improving our scientific knowledge in the field of As-induced epigenetic dysregulation has tremendous implications for both preventive- and treatment-based approaches to reducing the burden of As-induced diseases. First, methyl donor status is readily amenable to manipulation by nutritional interventions. While it is generally accepted that folate influences DNA methylation, it is not known if this effect is direct, or if it is mediated by an upstream effect on histone modifications which may be more dynamic than changes in DNA methylation. Thus, folate and other modifiers of the methyl donor pool may represent simple, low cost, low-risk interventions for prevention of As-induced disease. Furthermore, gaining mechanistic insights of As-induced epigenetic dysregulation may lead to additional therapeutic approaches for As toxicity, as multiple components of the epigenetic machinery are targets for existing and emerging drug development. Currently, there are no proven effective interventions -- preventive or therapeutic -- that specifically target intermediates in the underlying pathways that may be common to As-induced disease. Such interventions are critically needed.

D. Plans: In the next funding cycle, we plan to continue to analyze PTHMs in a much larger number of study participants from samples collected at multiple time points from our folic acid supplementation trial and to analyze plasma folate and B12 levels in these same participants. We will also study changes in gene expression in peripheral blood mononuclear cells from a subset of the FACT study participants as a function of As exposure. Gene expression will be assessed using Affymetrix gene chips and RT PCR. We will also study the persistence of gene expression following removal of As exposure using cell culture systems. If gene expression alterations persist after removal of the As we will study epigenetic histone marks in the promoter of genes using CHIP.

Finally, we have also initiated bi-monthly joint lab meetings between the Costa lab at NYU and the Gamble lab at Columbia University to further foster our continued collaboration. The first such joint lab meeting was on December 20th and our next is planned for mid-February 2013.

E. Publications from the current funding cycle:

Hall MN, **Gamble MV**. Nutritional manipulation of one-carbon metabolism: effects on arsenic methylation and toxicity. *J Toxicol* 2012;2012:595307. PMCID: PMC3317163

Pilsner JR, Hall MN, Liu X, Ilievski V, Slavkovich V, Levy D, Factor-Litvak P, Yunus M, Rahman M, Graziano JH, **Gamble MV**. Influence of prenatal arsenic exposure and newborn sex on global methylation of cord blood DNA. *PLoS One* 2012;7:e37147. PMCID: PMC3360698

Pierce BL, Kibriya MG, Tong L, Jasmine F, Argos M, Roy S, Paul-Brutus R, Rahaman R, Rakibuz-Zaman M, Parvez F, Ahmed A, Quasem I, Hore SK, Alam S, Islam T, Slavkovich V, **Gamble MV**, Yunus M, Rahman M, Baron JA, Graziano JH, Ahsan H. Genome-wide association study identifies chromosome 10q24.32 variants associated with arsenic metabolism and toxicity phenotypes in Bangladesh. *PLoS Genet* 2012;8:e1002522. PMCID: PMC3285587

Arita A, Shamy MY, Chervona Y, Clancy HA, Sun H, Hall MN, Qu Q, **Gamble MV**, Costa M. The effect of exposure to carcinogenic metals on histone tail modifications and gene expression in human subjects. *J Trace Elem Med Biol* 2012;26:174-8. PMID: 22633395 doi: 10.1016/j.jtemb.2012.03.012

Chervona Y, Hall MN, Arita A, Wu F, Sun H, Tseng HC, Ali E, Uddin MN, Liu X, Zoroddu MA, **Gamble MV***, Costa M*. Association Between Arsenic Exposure and Global Post-translational Histone Modifications Among Adults in Bangladesh. *Cancer Epidemiol Biomarkers Prev*. 2012;12:2252-60. doi: 10.1158/1055-9965. PMCID: PMC3518638

Gamble MV and Hall MN. Relationship of nutrition and urinary creatinine with arsenic metabolism. Commentary. *Environ Health Perspect*. 2012;120(4):A145-6. PMCID: PMC3339472

Clancy, HA, Sun H, Passantino L, Kluz T, Muñoz A, Zavadil J and Costa M. Gene expression changes in human lung cells exposed to arsenic, chromium, nickel or vanadium indicate the first steps in cancer. *Metallomics* 2012;4(8):784-93. PMID: 22714537 doi: 10.1039/c2mt20074k

Chervona Y, Costa M. The control of histone methylation and gene expression by oxidative stress, hypoxia and metals. *Free Radic Biol Med* 2012;53(5):1041-7. PMCID: PMC3432141

Hall MN, Niedzwiecki M, Liu X, Harper KN, Alam S, Slavkovich V, Ilievski V, Levy D, Siddique S, Parvez F, Mey JL, van Geen L, Graziano JH and **Gamble MV**. (2013). Chronic arsenic exposure and blood glutathione and glutathione disulfide concentrations in Bangladeshi adults. *Environ Health Perspect* (accepted with minor revisions).

Harper KN, Hall MN, Liu X, Ilievski V, Oka J, Calancie L, Slavkovich V, Levy D, Mey JL, van Geen L, Graziano JH and **Gamble MV**. (2013) Arsenic and oxidative damage: A dose-response study of drinking water arsenic exposure in humans. *Amer J Occup and Env Med* (in review).

Niedzwiecki M, Hall MN, Liu X, Oka J, Harper KN, Slavkovich V, Ilievski V, Levy D, van Geen A, Mey JL, Alam S, Siddique S, Parvez F, Graziano JH and **Gamble MV**. A dose-response study of arsenic exposure and global methylation of peripheral blood mononuclear cells in Bangladeshi adults. *Environ Health Perspect* (in review).

Harper KN, Peters B, Gamble MV. Batch Eefects and pathway analysis: Two potential perils in cancer studies involving DNA methylation array analysis. (manuscript in preparation)

Niedzwiecki M, Hall MN, Liu X, Oka J, Harper KN, Slavkovich V, Ilievski V, Levy D, van Geen A, Mey JL, Alam S, Siddique S, Parvez F, Graziano JH, and Gamble MV. Blood glutathione redox status and global methylation of peripheral blood mononuclear cell DNA in Bangladeshi adults. (2013; manuscript in review).

Oral/Poster Presentations in 2012

September 22, 2012. Presentation at a workshop on Arsenic and Epigenetics sponsored by the University of AZ SRP Program entitled, "Batch Effects and Pathway Analysis: Two Potential Perils in Cancer Studies Involving DNA Methylation Array Analysis." Presented by Dr. Gamble's post-doctoral Research Scientist, Kristin Harper.

On October 8, 2012, Dr. Gamble gave a seminar to the Graduate Center for Toxicology at the University of Kentucky entitled, "Influence of nutritional status on arsenic methylation and toxicity."

October 17 to 19, 2012. Served as a Member of the University of AZ SRP Program's External Advisory Board.

October 21 to 23, 2012. Attended the SRP's 25th Annual Meeting in Raleigh, NC. Dr. Gamble's lab was represented by poster presentations by two PhD students. Brandilyn Peters' poster was entitled, "Creatinine, arsenic metabolism, and renal function in an arsenic-exposed population in Bangladesh" and Caitlin Howe's poster was entitled, "Associations between s-adenosylmethionine, s-adenosylhomocysteine and arsenic methylation." The latter was awarded best poster for biomedical sciences.

July 22 to 27, 2012. Attended the FASEB Summer Research Conference entitled, "Folic Acid, Vitamin B12 and One-Carbon Metabolism" in Crete, Greece. Dr. Gamble's lab was represented by three presentations. Two oral presentations: Megan Niedzwiecki presented a talk entitled," Whole blood glutathione redox status is associated with lower plasma homocysteine concentrations in folate‐deficient Bangladeshi adults". Meg Hall presented a talk entitled, "Associations of Plasma Choline and Betaine with Homocysteine and Arsenic Methylation". In addition, Brandilyn Peters presented a poster entitled, "Effects of folic acid and creatine supplementation on plasma homocysteine in Bangladeshi adults."

May 30 to June 1, 2012, Attended a Conference sponsored by the Children's Environmental Health Network entitled, "The Contribution of Epigenetics in Pediatric Environmental Health" at which Dr. Gamble gave an oral presentation entitled, "Influence of prenatal arsenic exposure and newborn sex on global methylation of cord blood DNA."

F. Project Generated Resources: This project has generated genome wide DNA methylation data using the 450K HumanMethylation Array from Illumina. The first manuscript utilizing this data is in preparation (Harper et al, see above) and another is forthcoming. In accordance with our data sharing plan, once this data has been published, we will make it publicly available.

Student Involvement in Project 4 (Gamble, PI)

Yana Chervona is a PhD student in Max Costa's lab at NYU. She ran all of the laboratory assays of histone modifications for our pilot study for aims 1a to 1d and aim 2b. This work was recently published (see Chervona et al CEBP 2012 above).

Megan Niedzwiecki, Dr. Gamble's PhD student worked on laboratory and data analyses for the folate and oxidative stress (FOX) study from Aim 3 of Project 4 of Dr. Gamble's previous SRP Project. She studied the effects of redox status on methylation of arsenic and DNA which will be a focus of her thesis. Her work was selected for oral presentation at the 2011 SRP Meeting in Kentucky. Her work was also selected for an oral presentation at the 2012 FASEB Summer Research Conference (described above).

Megan Hall, Dr. Gamble's former post-doctoral research fellow (currently an Assistant Professor) worked on statistical analyses for Dr. Gambles previous SRP Project. She focused on the effects of arsenic exposure on glutathione concentrations. Her work was also selected for oral presentation at the 2011 SRP Meeting in Kentucky. Dr. Hall now has a K99/R00 award from NIEHS to study nutritional influences, particularly of choline and betaine, on arsenic methylation. Dr. Hall has also been involved in the statistical analyses for Dr. Gamble's current SRP Project.

Kristin Harper, Dr. Gamble's post-doctoral research fellow, worked on Aims 1 and 3 of our previous SRP Project. She is working on analyses of differentially methylated CpGs by arsenic exposure using Illumina's new 450K array and was instrumental in generating preliminary data for aim 3 of our new SRP Project 3. Dr. Harper presented her work at a Workshop on Arsenic and Epigenetics in AZ in September, 2012 (described above and manuscript in preparation).

Brandilyn Peters, Dr. Gamble's PhD student is also working on analyses of differentially methylated CpGs by arsenic exposure and was, along with Kristin (above), instrumental in generating preliminary data for our new SRP Project 3. She also analyzed all of the homocysteine data for aim 2. Brandi presented her work as a poster at the 2012 Annual SRP Meeting.

Caitlin Howe is a PhD student in Dr. Gamble's laboratory. She has been working on analyses related to aim 2 of our previous SRP Project in which we are analyzing associations between s-adenosylhomocysteine and s-adenosylmethionine and arsenic methylation. She is currently working on analyzing histone modifications for all aims of the current SRP Project 3. Caitlin presented her work as a poster at the 2012 Annual SRP Meeting; her poster was selected for first prize in the category of biomedical posters.

Project 4: Arsenic, Iron, Sulfur and Organic Carbon Speciation
PI: Benjamín Bostick
Co-Investigators: Brian J. Mailloux, Steve Chillrud, Lex van Geen

A. Specific Aims

The specific aims of Project 4 address the role of mineralogy and organic matter source and properties on the expression of dissimilatory iron and sulfur reduction, and how such properties affect arsenic solid solution partitioning in a wide range of environments. These processes are intimately linked to the location of groundwater arsenic contamination and thus the location and extent of human and environmental risk, yet we do not understand these processes. Our overall goal is to understand the fundamental connection between sediment properties, biogeochemical processes, and arsenic fate and transport. We make use of samples from field environments at both existing Superfund sites (in collaboration with Project 5) and Bangladesh (in collaboration with Project 6).

B. Studies and Results

This project examined both the connection between (a) sediment mineralogy and (b) organic matter source on biogeochemical processes in arsenic-contaminated aquifers. Many (but not all) iron minerals strongly retain arsenic strongly, minimizing its solubility and thus limiting its transport, and bioavailability/toxicity. Despite their importance, it is quite difficult to accurately quantify these phases, or to study their properties.

Role of Ferrihydrite in Regulating the Fate of Arsenic. In 2012, we developed a number of methods that are ideal to characterize these phases, and to measure changes in these phases that occur in sediments, and how those phases and changes affect arsenic partitioning. These studies used a number of sediments collected from our field sites, and found that metastable ferrihydrite is a critical phase in As retention, and that its facile formation (under oxidizing conditions) and dissolution (under reducing conditions, or when dissolved using an extractant like oxalate) is predictive of arsenic bioavailability and transport. Other minerals, notably magnetite, also have the ability to strongly retain arsenic. Remediation strategies based on inducing magnetite formation

are currently being developed in collaboration with Project 5 to enhance *in situ* magnetite formation as a method of immobilization-based remediation strategies.

Molecular-Scale Studies within Complex Environments. To properly remediate contaminated sites, or to understand the long term risks of arsenic contamination, we need to be able to predict arsenic adsorption and transport properties. To do so, we need a molecular/mineral scale view of how these processes occur, and a method of scaling these molecular-scale studies to larger scales. Molecular-scale views of adsorption and mineralogy are difficult in heterogeneous sediments, and it is often very difficult to relate to environmental scales. We made major advances in both of these areas in 2012, many of which are the basis for the conclusions regarding ferrihydrite and magnetite that are presented above. In particular, we developed new synchrotron-based methods of monitoring the rates of both adsorption/desorption and mineral dissolution/transformations on arsenic transport at the mineral grain scale for the first time. Among the studies that were performed, desorption rates were measured in laboratory studies from the Vineland Chemical Superfund site that are capable of determining the fundamental chemical properties (both the thermodynamics and kinetics of specific molecular processes) on the efficacy of pump and treat remediation. Moreover, the kinetics of these microscopic processes were predictive of macroscopic (column-scale) arsenic transport. This study was highlighted by the Geochemical Society. We also used similar methods to show that the distribution of reactive iron phases was important to arsenic sorption when contaminated groundwater flows into uncontaminated aquifers. This scenario is relevant to Bangladesh (the experiments used sediments from at-risk aquifers in Bangladesh obtained in collaboration with Project 4) and at Superfund sites susceptible to plume migration. These studies found that the sediments contain a number of reactive sites that effectively retard arsenic, and that arsenic transport can be effectively modeled by the saturation of the most reactive sites.

Mineral Reactivity in Model Systems. Often, it is beneficial to use model systems to fully understand the mechanisms of environmental processes. In 2012, we used model systems containing both chromium and nickel substituted ferrihydrite and/or goethite and arsenic to study how oxalate extracts arsenic from sediments. In column studies, it was determined that minimal iron minerals were extracted from sediments by oxalate, and that disproportionately more arsenic was released from sediments than minerals were dissolved. Thus, oxalate appears to extract arsenic by competitive adsorption of protonated forms of oxalate. This observation is important because it implies that the enhanced pump-and-treat remediation strategies should be engineered to maintain high enough oxalate activities, and also low pH. High-pH environments experience decreased extraction efficiency and can result in the precipitation of oxalate.

Reactive Organic Matter in Reducing Sediments. The microbes that reduce reactive iron phases like ferrihydrite require a reactive organic matter source. In 2012, we collected DNA from a series of arsenic-contaminated aquifers in Bangladesh to ascertain the source of organic matter that drives this reduction. These data indicate somewhat surprisingly that organic matter from the source is efficiently transported to depth within aquifers, and that this advected organic matter is disproportionately responsible for reduction. At sites where there is little or no hydrological connection between near-surface groundwater and shallow, high-arsenic groundwater, surface-derived organic matter is less important but still appears to contribute to reduction. Efficient lateral transport of organic matter from distal shallow sources is probably critical in these sites.

C. Significance

The chemical parameters that describe arsenic transport are needed to understand the distribution of arsenic in the environment, and to predict how this spatial distribution will evolve over time. The physical-chemical parameters derived from these studies, and the underlying importance of specific mineral phase concentrations on these parameters, should be useful both to characterize contamination, and to develop effective remediation strategies for arsenic. In these studies, we have found that reactive phases such as ferrihydrite affect arsenic fate. Since these phases are found in limited concentrations in many natural systems, there is a limited capacity of natural aquifer sediments to retard arsenic. The reduction of these phases can release arsenic into solution, but can in some cases form magnetite, which can immobilize arsenic. Much of our future plans revolve around understanding how to enhance magnetite formation to improve remediation technologies.

D. Plans

In collaboration with Project 5. We have data that suggest that oxidative pathways are most effective to produce magnetite in contaminated sediments and are highly effective at remediating arsenic, but we have not optimized. We are beginning a series of column experiments designed to optimize magnetite formation through the oxidation of ferrous iron by nitrate. In environmental systems, we also need to be able to monitor and quantify the spatial and temporal evolution of these mineral transformations. In collaboration with Lee Slater and Demitris Ntarlagiannis (Rutgers-Newark), we are developing biogeophysical monitoring methods of doing so, first in columns, and eventually will be extended to field trials of various remediation technologies. We will also continue other column and batch studies with both model systems and Superfund site sediments, to determine how geochemical processes occur. We have begun to work at the Dover Municipal Landfill Superfund site, and we will begin to characterize both the arsenic and iron speciation in those sediments, and the potential remediation of that site using both the oxalate- and magnetite-based remediation strategies. We hope that these remediation options can be used at this site as part of its long term management strategy.

In collaboration with Project 6. In project 6, we have begun the critical process of understanding the distribution of iron minerals and reactive organic matter sources within the site M and B areas of Bangladesh, where we are trying to characterize how surface water can be advected to depth either through or laterally to contaminate intermediate and deep aquifers often tapped as alternative water supplies, and to understand the mineralogy of sediments in deep, low-arsenic aquifers. We also will examine the source of reactive organic carbon in deep aquifers that are low in arsenic but that appear to contain atomic bomb tritium (and thus young groundwater that implies there is effective advection from the surface). These sites could be particularly vulnerable to arsenic contamination in the future as a consequence of anthropogenic forcing (i.e., extensive groundwater pumping).

E. Publications, Patents, Other supported by Project 4

Wovkulich, K, B.J. Mailloux, B.C. Bostick, H. Dong, M.E. Bishop, S.N. Chillrud. Use of Microfocused X-ray Techniques to Investigate Mobilization of Arsenic by Oxalic Acid. *Geochim Cosmo Acta*, 2012;91:254-70. PMCID: PMC3501129

Nielsen, L. N. and B. C. Bostick. Integrating Variable Aquifer Geochemistry and Sediment Properties into Models of Contaminant Retention. Appl. Geochem. Submitted 2012.

Quicksall A.N. and B. C. Bostick. 2012. Variable Rates of Microbially-Mediated Iron and Sulfate Reduction: Impact on Aqueous Arsenic Levels. Geochim. Cosmochim. Acta. Submitted.

B. J. Mailloux, E. Trembath-Reichert, J. Cheung, M. Watson, M. Stute, G. A. Freyer, A. Ferguson, K. M. Ahmed, Md, J. Alam, B. A. Buchholz, Y. Zheng, B. C. Bostick, A. van Geen. 2012. Advection of Surface-Derived Organic Carbon Fuels Microbial Reduction in Bangladesh Groundwater. Proc. Nat. Acad. Sci. USA, 2013; in press.

Sun, J., S.N. Chillrud, B.J. Mailloux, M. Stute, B.C. Bostick. Magnetite Formation under Acidic Conditions in Arsenic Contaminated Aquifer Sediments. *Environ. Sci. Technol*., Submitted, 2012.

Sun, J., S.N. Chillrud, B.J. Mailloux and B.C. Bostick. Arsenic Mobilization from Contaminated Aquifer Sediments by Chemical Amendments for Accelerated Remediation. Talk at the 22nd V.M. Goldschmidt 2012 Conference.

Bostick BC. Geochemical Approaches to Remediating Arsenic at Superfund Sites. Columbia University Superfund Research Program Monthly Seminar/Webinar, Oct. 15, 2012.

Students and Post-docs whose research is supported completely or in part by Project 4:

Jing Sun, 3rd yr PhD student, Earth and Environmental Sciences, Columbia University. Advised by PI.
Ivan Mihajlov, 5th year PhD student, Earth and Environmental Sciences, Columbia University

Louis Smith (undergraduate, Columbia University). _Role: to examine iron mineralogy in contaminated sediments and study how those transformations affect arsenic retention in batch system.
Rajib Momzuder, 1st year PhD student, Earth and Environmental Sciences, Columbia University
Rachel F. Silvern Undergraduate Barnard College
Sarah M. Lyon Undergraduate Barnard College
Aleq Abdullah Undergraduate Barnard College
Asia Carter Undergraduate Barnard College
Carol Kim Undergraduate Barnard College
Colleen Mulvihill Undergraduate Barnard College

PI Initiated Research Translation
To determine how to minimize arsenic exposure in contaminated areas, it is necessary to identify low-arsenic groundwater sources, and other potential problems with those groundwater sources. PI Bostick is actively doing this through a World Bank supported project in Cambodia, where a significant population is exposed to high-As groundwater. This alternatives analysis suggests that centralized water treatment may in fact be much more cost-effective than previously recognized. PI Bostick is also working with both consultants and EPA officials in Region 2 to identify areas where natural arsenic is being released at landfill sites that have been classified as Superfund sites, and where in situ magnetite formation may be particularly effective to contain the extent and spread of this groundwater contamination.

In working with EPA region 2, PI Bostick presented our data on both oxalate-based and reductive transformations of sediments at the Vineland site, and how they could be improve pump and treat remediation at the site. A number of staff in EPA region 1 (including Darryl Luce) have been working with PI Bostick to examine how these approaches might be used at arsenic-contaminated sites in New England. PI Bostick also consulted with EPA and NIEHS staff regarding the potential for redox processes in shallow estuarine sediments in Region 10 to control mollusk arsenic concentrations and the potential risk to indigenous groups that depend on these species as a food source. We also are collaborating as a group with Michael Webster of GeoInsight to pilot in situ immobilization approaches at the Dover Municipal Landfill site, and to implement technologies that are developed from this research.

The analytical techniques that are used in this project represent cutting-edge technologies that are uniquely possible at synchrotron. PI Bostick is a leader in using these technologies, and has been appointed by the Stanford Synchrotron Radiation laboratory (SSRL) at Stanford University as a representative to the National User Facility Organization (NUFO), which working closely with the Association of American Universities (AAU) and government relation experts to develop plans and compile material for outreach purposes. This position spans the sciences and engineering.

Project 5: Application of enhanced mitigation methods for groundwater arsenic at US Superfund sites

PI: Steven Chillrud
Co-Investigators: Ben Bostick, Brian J. Mailloux, Martin Stute

A. Specific Aims

Our overall goal has not changed and is to investigate enhanced remediation options for groundwater contaminated with arsenic; specifically on two separate approaches including oxalic acid injections to improve the efficiency of pump and treat at removing arsenic and the potential of immobilization of arsenic onto the target mineral magnetite. Our multi-scale approach of carrying out investigations at the micron scale to bench scale to field scale includes efforts and samples at two sites- the Vineland Superfund Site in Southern NJ and the Dover Municipal Superfund Site in Dover New Hampshire. We have changed the emphasis of the field portion of our project, with much more emphasis being placed at the Dover site where the local managers are

enthusiastic about the work we plan on doing there and much less emphasis at the Vineland site where our field efforts have been suspended.

B. Studies and Results

In 2012, we have focused on laboratory experiments on samples from the Dover Municipal Landfill Site and from the Vineland Chemical Company Site, data analyses and manuscript preparations, and a series of meetings with the geophysicists from Rutgers University-Newark and Dover Site Managers to plan future activities. These generally resulted in two activities: first was test our oxalic acid accelerated pump-and-treat (P&T) approach at the Dover site; second was explore *in situ* As immobilization approach with magnetite as the target.

Oxalic acid introduction and arsenic mobilization: Our past work at the Vineland site suggests that introduction of oxalic acid can substantially enhance the release of As from sediments and potentially dramatically lower the pump-and-treat (P&T) remediation time-scale. Continued work investigated this mobilization showed that we observed similar behavior in iron and arsenic mobilization at the micron scale as at much larger scales through use of column experiments being analyzed in real time by synchrotron methods (Wovkulich et al. 2012). The Dover site also uses traditional P&T. This site is quite different from Vineland since its aquifer sediments have much lower As concentrations and the As contamination is thought to be natural As mobilized by reducing conditions imparted by the landfill. We have been testing whether the addition of oxalic acid can work at this site. In laboratory batch extraction and column experiments, oxalic acid effectively mobilized As from Dover sediments. We also have analyzed and compared a series of reducing condition batch incubations with original Dover and Vineland sediments and sediments after oxalic acid extraction. Our data suggest that oxalic acid introduction in the subsurface can improve the P&T operation efficiency at different As-contaminated sites with a range of pHs and redox potentials, and that the As left in Dover sediments after oxalic acid extraction is much less mobile. In addition we are identifing the most amenable areas and determine optimal amendments for improving P&T, and how oxalic acid impacts specific Fe minerals including ferrihydrite and goethite.

Magnetite formation and arsenic immobilization: Magnetite adsorbs As(III) and As(V) on its surface, and can incorporate As(V) into its structure. Unlike many other minerals, magnetite is stable across typical groundwater redox zones found at contaminated Superfund sties. Accordingly, magnetite is a potentially attractive Fe mineral in which to immobilize As in the solid phase in many contaminated environments. We have been investigating the concept of *in situ* amendment injections to promote the production of magnetite as a long-term As sink. Our initial results indicated that simultaneous addition of Fe(II) and nitrate could achieve magnetite formation and this could be a promising As remedial method while additions to form sulfides was not able to maintain dissolved As at low levels (Cai et al, submitted). Over the past year, we have performed additional laboratory microcosm experiments on samples from Vineland, with various amounts of Fe(II) and nitrate, to further improve the magnetite strategy. The results of solution chemistry in these microcosms targeted to produce magnetite matched previous experiments; dissolved As concentrations decreased to low levels. The solid-phase speciation analysis with synchrotron-based X-ray Absorption Spectroscopy (XAS) will be conducted soon. We also had a series of meetings to plan a series of column experiments with colleagues from Rutgers University-Newark, who specialize in the application of geophysical (indirect) methods, to monitor the rates of magnetite production and As removal and evaluate the potential hydrodynamic effects. These experiments have just begun.

C. Significance

With the exception of lead, more National Priority Sites have arsenic as an issue than any other contaminant of concern. Yet, there are very limited remediation strategies for groundwater systems contaminated with dissolved As that are efficient and time effective. As such more methods are needed. Our work focuses on developing two enhanced remediation strategies which could potentially save time and money at Superfund sites contaminated with arsenic.

D. Plans

Over the next year we will continue working on our aims. In collaboration with Project 4 and Cores C and D, we will carry out a series of column experiments to optimize conditions for production of magnetite and determine whether geophysical parameters can be used to monitor the progress of mineral production. Using the reducing groundwater at the site, we will also carry out a series of column experiments at the Dover Municipal Landfill Site investigating both methods (the efficacy of oxalic acid at mobilizing arsenic from Dover sediments and whether oxidizing reagents can be used to stimulate magnetite production and lowering of arsenic concentrations in the effluent). Finally, together we will also carry out additional baseline field site characterization in preparation for in situ pilot experiments.

E. Publications, Patents, Other supported by Project 5

Wovkulich, K, Mailloux BJ, Bostick BC, Dong H, Bishop ME, Chillrud SN. Use of Microfocused X-ray Techniques to Investigate Mobilization of Arsenic by Oxalic Acid. *Geochim Cosmo Acta*, 2012;91:254-70. PMCID: PMC3501129

Sun, J., S.N. Chillrud, B.J. Mailloux, M. Stute and B.C. Bostick. Magnetite Formation under Acidic Conditions in Arsenic Contaminated Aquifer Sediments. *Environ. Sci. & Technol*., Submitted, 2012.

Sun, J., S.N. Chillrud, B.J. Mailloux and B.C. Bostick. Arsenic Mobilization from Contaminated Aquifer Sediments by Chemical Amendments for Accelerated Remediation. Talk at the 22nd V.M. Goldschmidt 2012 Conference.

Bostick. B.C. Geochemical Approaches to Remediating Arsenic at Superfund Sites. Columbia University Superfund Research Program Monthly Seminar/Webinar, Oct. 15, 2012.

Students and Post-docs who worked on Project 5:

Jing Sun, 3rd yr PhD student, Earth and Environmental Sciences, Columbia University
Dr. Peter Knappett is a post-doctoral investigator with expertise in hydrogeology appointed in 2012.

PI Initiated Research Translation

Most of project 5 is focused on developing and understanding enhanced remediation approaches and if successful transfer them to Superfund sites. As such much of these projects can be said to be directly related to technology transfer effort. Additional efforts include:

Dr. Steven Chillrud, PI
- a. Project 5 is focused on developing and understanding enhanced remediation approaches and if successful transfer them to Superfund sites. As such almost entire project can be said to be a big technology transfer effort.
- b. Feb. 21, 2012: Conference call with EPA Region 10 to discuss the RARE proposal to control mollusk arsenic concentrations and the potential risk to indigenous groups that depend on these species as a food source. (EPA names = Duncan Bruce, Roseanne Iorenzana) (Joe Graziano, Ben Bostick, Steve Chillrud, Meredith Golden.
- c. Jan. 12, 2012 Met with EPA Region 2 managers of Vineland (Michael Sivak, Nica Klaber, Diane Cutt) Ben Bostick, Steve Chillrud, Brian Mailloux, Martin Stute
- d. Oct. 6, 2012: Open house at LDEO, As Issues, Hand Pump Water Race, and Rockland County water issues,.

Dr. Mailloux
- a. Jan. 12, 2012 Met with EPA Region 2 managers of Vineland (Michael Sivak, Nica Klaber, Diane Cutt)
- b. Feburary 2012: spoke to high school students on multiple Saturdays as part of Science Saturday Seminars at Barnard College.

Dr. Stute
- a. June 2012: Presentation to a middle school class of Columbia's Secondary School of Math, Science and Engineering on groundwater contamination using sand tanks

b. Oct. 6, 2012: Open house at LDEO: Arsenic Issues, Hand Pump Water Race, and Rockland County water issues
c. 2012: Developed You-Tube instructional videos on contaminated aquifer using sand tanks: http://www.youtube.com/watch?v=wTq6-ipjUD0 Bangladesh Groundwater System http://www.youtube.com/watch?v=pyevjRiz1UI- Arsenic Contamination in Bangladesh
d. 2012: Organized workshop/class on sustainable development that developed videos on arsenic testing and treatment for the Hunterdon County Department of Health and New Jersey Department of Environmental Protection Office of Science.

Project 6: *Defining the Sustainable Uses of Low-Arsenic Aquifers in Bangladesh*
PI: Alexander van Geen
Outside Collaborator: Kazi Matin Ahmed

A. Specific Aims

The aims of this applied environmental science project have not changed, and are (1) to lower the exposure to arsenic (As) in the cohort of >30,000 participants in the Health Effects of Arsenic Longitudinal Study (HEALS) in Araihazar and (2) to improve our understanding of the processes that threaten the quality of groundwater in low-As aquifers of Bangladesh.

B. Studies and Results

(1) Over 28,000 tube-wells were tested for As with the ITS Econo-Quick field-kit in 2012 by a team of 10 village health workers. Results were posted by attaching a blue (As $\leq$10 ug/L), green (10<As$\leq$50 ug/L), or red (As>50 ug/L) metal placard to each pumphead. Results are also entered directly on hand-held GPS units in the field. The quality of the data is monitored on Google Earth by connecting each GPS unit to the laptop of our field supervisor, by random re-testing of 5% of the tubewells in the field, and by laboratory measurements. Results for 491 quality-control samples indicate that not a single well that did not meet the Bangladesh standard of 50 ug/L for As was incorrectly labeled with a blue placard and, vice-versa, that not a single well labeled with blue placard actually contained >50 ug/L As. A small proportion (4% of the total) of wells labeled with a green placard actually contained 50-100 ug/L As. A surprisingly high proportion of households (58%) did not know the status of their well and approximately half the affected households are anticipated to switch to a neighboring low-As well.

(2) The Araihazar field-kit survey identified almost 500 wells in the 400-1000 ft depth range that, with a handful of exceptions, are low in As. A subset of ~100 these deep community wells were installed by us in the early phases of the study but most were installed by the government. There are also many private wells in the 150-300 ft depth range that meet the WHO guideline for As. Our current field work focuses on the vulnerability of these intermediate aquifers in those areas where downward flow of shallower high-As groundwater could lead to contamination. Time series data collected over more than a decade in Araihazar and elsewhere show that this process is rare and, if it occurs, is typically gradual and can be monitored. The exception, documented to date only twice in Araihazar, is the failure of the PVC well pipe allowing shallow high-As groundwater to be drawn in. We have found surprising evidence that an impermeable silt/clay layer is not necessarily protective of an intermediate low-As aquifer and that the downward leaching of dissolved organic carbon content from such a layer might actually promote reductive dissolution of iron oxyhydroxides and an increase in groundwater As. We have shifted our focus away from shallow low-As wells because they are often very high in manganese (Mn) and have been associated with increased diarrheal disease in children due to contamination with human waste. We are conducting instead field experiments to lower the uptake of As in rice grains, which is an emerging source of concern.

C. Significance

Beyond the ethical motivation, lowering exposure will help define exposure estimates of the study population in Araihazar and, therefore, the dose-response relationships for various end-points studied under Projects 1, 2, and 3. Our work on the vulnerability of intermediate and deeper aquifers to contamination with As in South Asia is yielding an improved understanding of the impact of groundwater flow on transport of both reactive carbon and As transport and retardation that is applicable elsewhere, including US Superfund sites.

D. Plans

The field-kit testing of an additional 10-15,000 tubewells within Araihazar upazilla is expected to be completed by June 2012. Additional testing for As outside Araihazar in support of a HEALS cohort expansion is likely. A random subset of households will be revisited in order to quantify the impact of testing. The cause of elevated As levels in the few wells in the 300-1000 ft depth range within Araihazar will be explored. Field investigation will continue in the area where gradual increases in As concentrations have been detected over the past decade.

E. Publications, Patents, Other under Project 6 in 2012

*van Geen, BC Bostick, PTK Trang, VM Lan, NN Mai, PD Man, PH Viet, K Radloff, Z Aziz, JL Mey, MO Stahl, CF Harvey, P Oates, B Weinman, C Stengel, F Frei, R Kipfer, M Berg, Delayed contamination of an aquifer with high-arsenic groundwater drawn by the municipal supply of Hanoi, Vietnam, *Nature*, submitted December 2012.

*Mailloux BJ, Trembath-Reichert E, Cheung J, Watson M, Stute M, Freyer GA, Ferguson AS, Ahmed KM, Alam MJ, Buchholz BA, Thomas J, Layton AC, Zheng Y, Bostick BC, van Geen A. Advection of surface-derived organic carbon fuels microbial reduction in Bangladesh groundwater. *PNAS*, 2013; in press.

*Feighery J, BJ Mailloux, AS Ferguson, KM Ahmed, A van Geen, PJ Culligan, Transport of E. coli in aquifer sediments of Bangladesh: Implications for widespread microbial contamination of groundwater. *Water Resources Res*, under revision January 2012.

Bennear L, Tarozzi A, Pfaff A, Soumya HB, Ahmed KM, van Geen A. Impacts of a randomized controlled trial in arsenic risk communication on household water supply choices in Bangladesh, *J Environ Econ Manage*, 2012;in press.

*Knappett P, McKay LD, Layton A, Williams DE, Alam MJ, Mailloux BJ, Ferguson AS, Culligan PJ, Serre ML, Emch M, Ahmed KM, Sayler GS, van Geen A. Unsealed tubewells lead to increased fecal contamination of drinking water. *J Water Health* 2012;10(4):565-78. doi: 10.2166/wh.2012.102. PMID: 23165714

*George CM, Zheng Y, Graziano JH, Rasul SB, Mey JL, van Geen A. Evaluation of an arsenic test kit for rapid well screening in Bangladesh, *Environ Sci Technol* 2012;46:11213–9. PMID: 22866936

*George CM, Khan K, Islam T, Singha A, Moon-Howard J, Factor-Litvak P, van Geen A, Graziano JH. Approaches to increase arsenic awareness in Bangladesh: An evaluation of an arsenic education program. *Health Educ Behav*. 2012;Sep 14. [Epub ahead of print] doi: 10.1177/1090198112454735, PMID: 22984214

*George CM, van Geen A, Slavkovich V, Singha A, Levy D, Islam T, Ahmed KM, Moon-Howard J, Tarozzi A, Liu X, Factor-Litvak P, Graziano A cluster-based randomized controlled trial promoting community participation in arsenic mitigation efforts in Bangladesh. *Environ Health.* 2012;11:41. doi: 10.1186/1476-069X-11-41. PMCID: PMC3506475

*Ferguson AS, AC Layton, BJ Mailloux, PJ Culligan, DE Williams, AE Smartt, J Feighery, L McKay, P Knappett, E Alexandrova, T Arbit, M Emch, V Escamilla, KM Ahmed, MJ Alam, PK Streatfield, M Yunus, A van Geen, Comparison of fecal indicators with pathogenic bacteria and rotavirus in groundwater, *Sci Total Environ*, 2012;431:314–22. PMID: 22705866 NIHMS387725

*Wu F, Jasmine F, Kibriya MG, Liu ML, Wojcik O, Parvez F, Rahaman R, Roy S, Paul-Brutus R, Segers S, Slavkovich V, Islam T, Levy D, Mey JL, van Geen A, Graziano JH, Ahsan H, Chen Y. Association between arsenic exposure from drinking water and plasma levels of cardiovascular markers, *Am J Epidemiol* 2012;175:1252-61. PMCID: PMC3372314

*George CM, Graziano JH, Mey JL, van Geen A, Impact on arsenic exposure of a growing proportion of untested wells in Bangladesh, *Environ Health* 2012;11:7. doi: 10.1186/1476-069X-11-7. PMCID: PMC3334680

*Khan K, Wasserman GA, Liu X, Ahmed E, Parvez F, Slavkovich V, Levy D, Mey J, van Geen A, Graziano JH, Factor-Litvak P. Manganese exposure from drinking water and children's academic achievement, *NeuroToxicology* 2012;33:91-7. PMCID: PMC3282923

*Knappett PSK, LD McKay, A Layton, DE Williams, MJ Alam, MR Huq, J Mey, JE Feighery, PJ Culligan, **BJ Mailloux**, J Zhuang, V Escamilla, M Emch, E Perfect, GS Sayler, KM Ahmed, **A van Geen**, Implications of fecal bacteria input from latrine-polluted ponds for wells in sandy aquifers, *Environ Sci Technology* 2012;46: 1361–70. PMID: 22191430 NIHMS349773 doi: 10.1021/es202773w

Patents- N/A

Student and post-doc involvement under Project 6

Ivan Mihajlov, a PhD candidate in Earth & Environmental Sciences co-advised by the PI, is expected to defend his PhD by the end of summer 2013.
Christine Marie George, co-advised by the PI, defended her PhD dissertation at the Mailman School of Public Health in February 2012 and has been appointed to the faculty of the Bloomberg School of Public Health at Johns Hopkins University.
Md. Rajib Mozumder, a geology graduate from the University of Dhaka, entered the PhD program in Earth & Environmental Sciences in September 2012 is advised by the PI.
Fiona Kinniburgh is a senior majoring in Sustainable Development at Columbia College.
Dr. Peter Knappett is a post-doctoral investigator with expertise in hydrogeology appointed in 2012.

PI initiated Research Translation under Project 6 in 2012

Dr. Lex van Geen, PI

a. July 16-17, 2012 Dhaka: Invited presentation on need to test millions of tubewells in Bangladesh with field-kits. Proposed subsidized fee-based testing with data entry directly on hand-held GPS to facilitate quality control. UK DFID-supported International Growth conference of mostly development economists, attended by Finance Minister and other government, international organization, and NGO representatives. Reported in the local press.
b. January 15-16, 2013 Dhaka : Invited presentation on resilience of deep low-As aquifers based on 10-year time series for community wells in our study area of Bangladesh and more past year's field-kit survey of over 28,000 tubewells. University College London-supported workshop attended by international group of hydrogeologists and government, international organization,and NGO representatives responsible for arsenic mitigation - including government Policy Support Unit.
c. Goldschmidt Conference 2013, sponsored by the Geochemical Society and the European Association of Geochemistry: Proposed to convene session entitled "Impact of air, soil, and water geochemistry on human health". Accepted by the scientific committee for Aug 25-30, 2013 conference in Florence, Italy.

F. Project-Generated Resources- n/a

Administrative Core

Director: Joseph Graziano

Associate Director: Alexander van Geen

General Activities: The Administrative Core continues to function smoothly. Dr. Graziano, the Program Director, and Dr. van Geen, the Associate Director, have been working together to provide leadership to SRP investigators to achieve the goals of the Administrative Core, which include the facilitation of interaction and communication among investigators leading the Research Projects, Support Cores, RTC and CEC; to provide fiscal management and planning; to coordinate SRP activities including seminars, retreats, symposia, and preparation of the annual progress report; to coordinate the reviews of our SRP activities by the External Advisory Committee; and to supervise the utilization of the Research Support Core Laboratories. We communicate continuously with regard to the integration of our biomedical and non-biomedical research programs, and hold joint monthly meetings of all participating faculty to maximize the interactions across biomedical and non-biomedical projects. This communication is evidenced by the number of truly multi-disciplinary publications that have come from our program, involving close collaboration between biomedical, earth, and social scientists.

The Director and Deputy Director also provide mentorship to the many PhD students involved in our research projects, and work with them to guide their preparation of abstracts and presentations at the annual SRP meeting. Indeed, on of our students, Caitlin Howe, won first prize for best poster at the 2012 SRP meeting. The Administrative Core also played a central role in the preparation of our competitive renewal application that was successfully renewed in April, 2012. The Core itself was given a score of 11 by the grant reviewers.

A meeting of our External Advisory Committee has been planned for February 25, 2013. Our External Advisory Committee continues to provide valuable input to our program. The composition of the committee includes: a) Chien-Jen Chen, Committee Chair, and Chairman of the Graduate Institute of Taiwan; b) Andrew Gelman, Professor of Statistics at Columbia University; c) Zoltan Szabo, Research Hydrologist, USGS; d) Margaret Karagas, Chair, Section of Biostatistics and Epidemiology, Dartmouth University; e) X. Chris Le, Professor of Public Health Sciences, University of Alberta; f) Peggy O'Day, Associate Professor of Natural Sciences, University of California, Merced; and g) Robert Wright, Professor of Preventive Medicine and Pediatrics at the Mount Sinai School of Medicine.

All of our scientific team has assembled monthly for a joint two hour meeting which rotates between the Health Sciences Campus and the Lamont-Doherty Earth Observatory Campus; the two campuses are separated by a 20 minute University bus ride. Our monthly meetings include two hours of seminars, typically one hour for biomedical and one for non-biomedical presentations. During the past year we have begun to offer our seminars as a webinar, one that is now attended by many outsiders from EPA, NIH and academia. The seminar series includes a mix of internal and external speakers and has evolved into a world class set of events.

Seminars that have occurred during 2012 include:

February 27
Dr. Yan Zheng, City University of New York Queens College and Columbia University's Lamont-Doherty Earth Observatory: "**Challenges and Opportunities to Mitigate Arsenic Risks in Health, Water Supply and Agricultural Sector**"

March 19th
Akram Alshawabkeh, Co-Director of Northeastern University SRP, George A. Snell Professor of Engineering, and Professor of Civil & Environmental Engineering, Northeastern University: **Puerto Rico Testsite for Exploring Contamination Threats (PROTECT)**

Ivan Mihajlov, Graduate Research Fellow, Columbia University Department of Earth and Environmental Sciences: "**Contamination of a community well in Bangladesh: Where did the arsenic come from**"

April 23
David C. Christiani, Co-Principal Investigator of Harvard's SRP and Elkan Blout Professor of Environmental Genetics, Harvard Medical School and School of Public Health: "**Arsenic exposure, genetic susceptibility and Type 2 Diabetes Mellitus**"

Michael Berg, Research Group Leader with Eawag, Swiss Federal Institute of Aquatic Science and Technology: "**Arsenic in Vietnam's drinking water resources, exposure levels and mitigation**"

May 14
Khalid Khan, Postdoctoral Researcher at Center for Research on Occupational and Environmental Toxicology at Oregon Health and Science University: **Evaluation of a School-Based Intervention for Reducing Arsenic Exposure in Rural Bangladesh**

Alexander van Geen, Lamont Research Professor at Lamont-Doherty Earth Observatory of Columbia University: **The new blanket survey of arsenic in tubewells of Araihazar: a step towards commercial testing throughout Bangladesh?**

September 17
Mark Rosenzweig, Frank Altschul Professor of International Economics and Director of the Economic Growth Center at Yale University: **“Identifying the Hidden Costs of a Public Health Success: Arsenic Well Water Contamination and Productivity in Bangladesh”**

October 15
Dr. Benjamin Bostick, CU SRP scientist at Columbia's Lamont-Doherty Earth Observatory: **"Geochemical Approaches to Remediating Arsenic at Superfund Sites"**

November 19
Dr. Habibul Ahsan, CU SRP Health Effects of As Longitudinal Study (HEALS) project and Director of the Center for Cancer Epidemiology and Prevention at University of Chicago: **“Recent findings and progress of HEALS”**

Dr. Kazi Matin Ahmed, CU SRP scientist and professor at the University of Dhaka's Department of Geology: **“Towards Sustainable Arsenic Mitigation in Bangladesh: Achievements and Challenges”**

December 17
Dr. Peter Knappett, Postdoctoral Research Scientist at Columbia's Lamont-Doherty Earth Observatory: **"Investigating Hydraulic Connections Between Shallow, High Arsenic Aquifers and Deeper, Low Arsenic Aquifers in Bangladesh"**

Dr. Frederick Domann, University of Iowa Carver College of Medicine: **"Redox Regulation of Epigenetic Processes: A Role for Arsenic"**

Core A: *Data Management Core*
PI: Diane Levy

1. Project 1:
    a. The customized data entry system in Bangladesh is currently being utilized to enter follow up data for HEALS:
        i. Follow up 4 for 11,746 original participants
        ii. Follow up 2 for 8,267 new participants (ACE: Arsenic Cohort Expansion)

All data are periodically automatically transferred to Columbia University SQL database located in NY.

    b. A new Access database is currently being programmed to accommodate data entry for the approximately 10,000 newest participants (ACE-2) who have been interviewed in Bangladesh. When the programming and testing are complete the database will be sent to Bangladesh where it will be installed on their secure network. When data entry is complete, the data will be transferred to our NY SQL database.
2. Project 2:
    a. Questionnaires have been reviewed.
    b. Procedures have been programmed to download data from the CANTAB equipment to interim data files. These files will be imported into our SQL database.
3. Project 3:
    a. Periodic uploads of laboratory data to Microsoft SQL server database have taken place and continue to occur.
    b. Data sets have been distributed to the PI and biostatistician for analyses
    c. Close collaboration occurs with students who work with the PI. Students are introduced by the data manager to the data structure that exists; they are oriented to the codebooks. This orientation helps them design and request appropriate datasets for analysis.
4. Security
    a. Note: all data capture and transfer are done according to security protocols established at Columbia University. Data are stored on secure servers; electronic transfers are done over encrypted connections; data are physically moved using encrypted peripheral devices.
5. Additional efforts:
    a. Community Core Engagement
        i. Consulted with Sara Flanagan to help guide her in her programming of a secure database to hold household survey data being collected in Maine
    b. Health Education of School Children in Bangladesh: (Khan, PI)
        i. Final data loads of water data
        ii. Final preparation of datasets
    c. Young Adult Manganese Study: (Graziano, PI)
        i. Final creation of data sets for analysis
    d. Created/taught data management workshop for NIEHS and Superfund investigators, staff and students.
    e. Continued support for undergraduate and graduate students working with PIs on Arsenic related projects.
    f. Continued maintenance of secure database and web servers. Projects detailed above are direct beneficiaries of these services.
    g. Management of data flow continues using the Issue Tracking System and the Query Tracking Systems.
    h. Attending weekly project team meetings to provide data management consultation as projects move forward.

Data Management Core-Supported Publications:

Every publication involving participant data has relied on the Data Management Core for datasets used for analyses.

Core B: *Trace Metals Core Laboratory*

PI: Joseph Graziano
Laboratory Director: Vesna Slavkovich

A. Specific Aims: The primary purpose of the Trace Metals Core Laboratory, which is jointly funded by SRP and our P30 Center, is to provide Center investigators with the capability to obtain analyses of biological samples for a broad array of metals. In addition, the facility provides method development for these analyses, standardization, and quality control. The Trace Metals Core provides analytical support to projects #1, #2 and #3. The Core Laboratories performance in several quality control programs has been outstanding during the past year.

B. Studies and Results:
Collectively, during the past five years, the lab has performed more than 140,000 measurements of metals in urine, blood, nail and other tissue samples, using either atomic absorption spectrophotometry or inductively coupled plasma mass spectrophotometry (ICP-MS), as needed. During the past year, this Core Lab conducted more than 30,000"routine" analyses of biological samples, primarily from projects 1 and 2. A main focus of the Core's activities has been analytical support for As and creatinine measurements for the HEALS Cohort Study (Project #1), which has now completed its fourth biannual follow-up visit. The Trace Metals Core has completed about the analysis of roughly 8,000 urine samples from the first follow-up of the first expansion of the cohort, and roughly 7,000 samples from the baseline of the second cohort expansion. In addition, we have analyzed 8,000 samples from our NCI RO1-funded Bangladesh Vitamin E and Selenium Trial (BEST), of which Dr. Ahsan is the PI. In addition to urine samples from the BEST study we continue to measure blood As and Se for the study. A portion of ICP-MS running time was devoted to Dr. Gamble's NIEHS funded RO1 study entitled "Folate and Creatine Supplementation as Therapeutic Approaches to Lowering Blood Arsenic" (FACT study), mainly measuring As and Se in 4,200 bloods from 600 subjects, i.e., seven time points for each of the 600 subjects. Finally, the lab finished analyses blood, urine and nail arsenic from 300 children in the Bangladesh Child Study follow up (Project #2).

This laboratory is jointly funded by our NIEHS P30 Center, which supports roughly one-third of the laboratories total budget. Support for the FACT and BEST studies, both R01 grants, is derived in part from the P30 Center's support of the lab.

C. Significance: The biomedical projects of this Superfund Research Program have made an enormous contribution to the overall knowledge concerning the health effects of – in particular – arsenic on human health and the factors that increase the risk of developing arsenic related disease outcomes. The Trace Metals Core Laboratory has given each of these biomedical projects the capacity to test their various hypotheses and to have biological samples analyzed with precision and quality control. A very practical use of these findings will be their utility in assisting the US EPA with their ongoing reassessment of the toxicity of inorganic arsenic in the IRIS database.

D. Plans: We plan to continue to support the three biomedical projects with analyses of trace elements in biological samples.

Students involved with this work:

Tiffany Sanchez, a PhD student has worked preparing the field supplies and pilot studies for her thesis dissertation project (Project #2). In addition, several undergraduate students were employed or volunteered as lab personnel for the summer of 2012 and/or throughout the entire year. Yukari Sumizu, a Columbia College student, worked throughout the whole year, part time; Teodora Odzakovic, a New Jersy high school student, volunteered during the summer .

E. Publications: Every publication listed for Projects 2, 3 and 4 has relied on the Trace Metal Core.

F. Project-Generated Resources: n/a

Core C: *Biogeochemistry Core Laboratory*
PI: Alexander van Geen

Co-Investigators: Steven Chillrud, Beizhan Yan

A. Specific Aims

The specific aims of this core have not changed. The Biogeochemical analytical core laboratory is housed at Lamont-Doherty Earth Observatory (LDEO) and provides analyses in support of projects 1, 2, 4, 5, 6 , the Community Engagement Core (CEC), and the Research Translation Core (RTC). Analyses have been carried out by high-resolution inductively coupled plasma mass spectrometry (HR ICP-MS), partly on a newly installed Thermo Element 2 instrument purchased with NSF funds, for up to 33 elements for water, soil, sediment, and sediment leachate. Other analyses carried out include dissolved organic carbon content, x-ray fluorescence (XRF) analyses of sediments, and diffuse spectral reflectance to estimate iron speciation. Finally, this core also analyses exhaled breath condensate for isoprostanes and urea by liquid chromatography mass spectrometry (LC-MS).

B. Studies and Results

In support of the Bangladesh related projects (1,2,3, 4, 6), over 1,850 groundwater and leachate samples were analyzed by HR-ICP-MS. In support of the CEC, over 200 water samples were analyzed by HR-ICP-MS. In support of projects 4 and 5 efforts at Superfund sites, over 900 samples from incubation and column experiments were analyzed by HR-ICP-MS and 10 sediment samples were analyzed by XRF. In addition the core has learned how to carry out As speciation analyses using the new HR-ICP-MS that was recently installed. This ability will allowing projects 4 and 5 to test different hypotheses about mechanisms for mobilization and immobilization. Cuttings from five drill sites X, A, B, C, E and F that were collected in 2008, were analyzed by XRF, in all 243 samples.

The dissolved organic carbon content of groundwater samples of several hundred samples of groundwater from Bangladesh was also measured.

The redox state of iron oxyhydroxides in several hundred samples of fresh drill cuttings was measured in Bangladesh by diffuse spectral reflectance. The elemental composition of the same set of drill cuttings for As, Fe, and Ca, among other elements, was determined with a hand-held X-ray fluorescence instrument. The same instrument was used in 2012 to analyze ~50 intervals in rock core from the Newark basin in support of the government partnership with NJGS to better understand the distribution of As in groundwater in NJ.

In support of project 2, efforts have been made in Dr. Yan's lab to improve the reliability in measuring 8-isoprostane, a biomarker of oxidative stress, in exhaled breath condensate. Though the method we previously developed had a good sensitivity, the peak shape was not ideal. In addition, because the method needed to run samples at a high pH (~10.5) condition, column bleeding was quite substantial and columns had to be replaced often. We modified the method by using a lower pH solvent (~5) and a different internal standard that did not co-elute with the target ompound. Preliminary results showed that the modified method not only kept the high sensitivity but also obtained a better peak shape, with negligible column bleeding and preliminary results suggest the column has extended lifetime. 275 analyses were run by LC-MS in support of this effort.

C. Significance

The significance of the analytical support provided under the Biogeochemistry Core extend beyond the aims of HEALS cohort study (Project 1). The children's health study (Project 2) also relies on the groundwater measurements of As and Mn to investigate neurodevelopmental issues. Mn exposure is a confounding factor for studies of children's mental health and there is no alternative to measuring Mn concentrations in groundwater because no biological sample, urine or blood, has been shown to reflect exposure. In addition, Core C supports Project 2 by making measurements of exhaled breath condensate to investigate respiratory issues and their relationship to As groundwater exposure. In order to understand the processes regulating As concentrations in groundwater, the accurate determination of additional groundwater constituents is essential. The multi-element capability based on high-resolution plasma mass spectrometry (HR ICP-MS) that was developed under a previous funding cycle of the Core has been and will continue to be applied also to a large

numbers of groundwater samples and sediment leachates in support of the proposed studies of Superfund sites and in Bangladesh. Effective remediation strategies for Superfund sites with As contaminated aquifers and offsite transport issues are still lacking.

D. Plans

We will continue to support the analytical needs of the different projects and the Research Translation and Community Engagement Cores. Project 1 is expected to start shipping exhaled breath condensate samples for analysis and the other projects will continue to have analytical needs for water, soil, sediment, and sediment leachate.

E. Publications, Patents, Other supported by Core C

*George CM, Zheng Y, Graziano JH, Rasul SB, Mey JL, van Geen A. Evaluation of an arsenic test kit for rapid well screening in Bangladesh. *Environ Sci Technol* 2012;46:11213–9. PMID: 22866936

*George CM, Graziano JH, Mey JL, van Geen A, Impact on arsenic exposure of a growing proportion of untested wells in Bangladesh, *Environ Health* 2012;11:7. doi: 10.1186/1476-069X-11-7. PMCID: PMC3334680

*Khan K, Wasserman GA, Liu X, Ahmed E, Parvez F, Slavkovich V, Levy D, Mey J, van Geen A, Graziano JH, Factor-Litvak P. Manganese exposure from drinking water and children's academic achievement, *NeuroToxicology* 2012;33:91-7. PMCID: PMC3282923

*van Geen, BC Bostick, PTK Trang, VM Lan, NN Mai, PD Man, PH Viet, K Radloff, Z Aziz, JL Mey, MO Stahl, CF Harvey, P Oates, B Weinman, C Stengel, F Frei, R Kipfer, M Berg, Delayed contamination of an aquifer with high-arsenic groundwater drawn by the municipal supply of Hanoi, Vietnam, *Nature*, sent out for review December 2012.

Wovkulich, K, Mailloux BJ, Bostick BC, Chillrud SN. Use of microfocused x-ray techniques to investigate mobilization of Arsenic by Oxalic Acid. *Geochim. Cosmo. Acta*, 2012;91:254-70. PMCID: PMC3501129

*Wu F, Jasmine, F, Kibriya MG, Liu ML, Wojcik O, Parvez F, Rahaman R, Roy S, Paul-Brutus R, Segers S, Slavkovich V, Islam T, Levy D, Mey JL, van Geen A, Graziano JH, Ahsan H, Chen Y. Association between arsenic exposure from drinking water and plasma levels of cardiovascular markers, *Am J Epidemiol* 2012;175:1252-61. PMCID: PMC3372314

F. Project-Generated Resources- n/a

Core D: *Hydrogeology Support Laboratory*
PI: Peter Schlosser
Outside Collaborators: Dimitrios Ntarlagiannis, Lee Slater, Charles Harvey, Holly Michael

A. Specific Aims:

The overall goal of the Hydrogeology Support Core remains the same, to support our projects by providing information on the groundwater and surface water flow and transport regime at our field sites in Bangladesh and the US.

B. Studies and Results

In 2012, Core D analyzed 135 samples for stable isotopes in support of Project 6. This number included samples from community wells, and samples from the area of detailed study of intermediate-depth aquifer. These analyses allowed to differentiate groundwater samples from community wells at a range of depths and provided insight into the conditions at time of recharge. In other cases, within intermediate-depth aquifers that are vulnerable to As contamination, stable isotope analyses allowed tracing groundwater to recent recharge. In

Bangladesh, the focus is on quantifying groundwater flow from the shallow high-As aquifer to intermediate and deeper aquifers that are low in As. Detailed lithological information was collected and monitoring wells installed at 6 locations within a radius of ~600 m of two sites where As concentrations increased above 50 ug/L over the past decade at 40-50 depth. Atomic bomb-produced tritium (^{3}H) concentrations measured in a subset of the intermediate monitoring wells show a complex pattern of recent recharge associated with low-As concentrations at intermediate depth contrasting with higher-As levels in a shallower but more isolated zone relative to recharge.

In addition, a differential GPS survey of 160 community wells and Columbia-installed monitoring wells was carried out in 2012 to determine their elevations and allow water levels to be compared across the region. Well construction details that impact the suitability of the wells for water level measurements and downhole logging were recorded. A total of 60 pressure loggers were deployed in low-As community wells and monitoring wells in 40 to 220 m depth range across the study region. Three pressure loggers were also deployed in local rivers in determine to their importance for aquifer recharge. In order to assess aquifer continuity and vulnerability, the distribution of major clay layers was mapped across six transects extending to approximately 80 m depth using Electrical Resistivity Tomography (ERT). In addition, the vertical distribution of clay layers was determined by downhole logging using a a combined electromagnetic induction and natural gamma radiation tool. On the basis of our observations and a preliminary model, the location of a new nest of monitoring wells roughly mid-way between Araihazar and Dhaka has been selected. This nest of wells, combined with a more refined model, will help determine whether lower groundwater levels in intermediate and deep wells of Araihazar reflects local withdrawals or more distant pumping for the municipal water supply of Dhaka.

Related to our work at Superfund sites, we have had a series of meetings with our Core D collaborators, Drs. Ntarlagiannis and Slater, at the Rutgers-Newark campus who specialize in the use of geophysical methods for environmental purposes. Both Ntarlagiannis and Slater have long experience with hydro-geophysical experiments and microbial mediated mineral transformations, both in the laboratory and in field applications. . In these meetings we planned out a series of column experiments using the column setup designed by the Rutgers-Newark group, to improve methods of magnetite synthesis and link geophysical parameters to mineral transformation processes and porous media transport properties. These experiments build on the experience gained from previous research on hydro-geophysics and mineral transformations, but adapted to meet the needs of the current project. The Rutgers-Newark geophysical approach is complementary to the traditional geochemical approaches in that it offers a potential tool to quantitatively transfer common geophysical signatures into real-time information about the amount and location of magnetite precipitation at desired spatial scales. By means of this study, we hope to find out how best to form magnetite *in situ* within sediments, and determine the mineral phases and sorption mechanisms (adsorption and/or co-precipitation) that are responsible for As retention. These specific experiments will help evaluate the potential of magnetite for *in situ* As immobilization. Future collaborative investigations using geophysical methods could also probe other alternative remediation options, most notably potential methods of enhancing the effectiveness of traditional pump-and-treat systems. In particular, we have been working to enhance As extraction using *in situ* injection of oxalic acid within groundwater. Geophysical methods may also be useful to trace plume injection and migration, to characterize changes in mineral substrate properties, and to detect the precipitation of calcium oxalate or other solids.

C. Significance

Detailed knowledge of groundwater flow is essential for understanding geochemical processes in the subsurface. Identification of recharge and discharge areas and mechanisms, as well as flow lines are essential for delineating trends in geochemical evolution, including changes in As concentrations, and to quantify reaction rates. Hydrogeology Core D will provide the tools and expertise for collection and analysis of a broad range of hydrogeological data in the US and in Bangladesh under Projects 4, 5, and 6 and the Research Translation Core.

D. Plans:

We will continue to support the laboratory, field and modeling needs of projects 5 and 6.

E. Publications, Patents, Other supported by Core D

*Knappett P, LD McKay, A Layton, DE Williams, MJ Alam, BJ Mailloux, AS Ferguson, PJ Culligan, ML Serre, M Emch, KM Ahmed, GS Sayler, A van Geen, Unsealed tubewells lead to increased fecal contamination of drinking water, *J Water Health* 2012;10(4):565-78. PMID: 23165714

*Knappett PSK, LD McKay, A Layton, DE Williams, MJ Alam, MR Huq, J Mey, JE Feighery, PJ Culligan, BJ Mailloux, J Zhuang, V Escamilla, M Emch, E Perfect, GS Sayler, KM Ahmed, A van Geen, Implications of fecal bacteria input from latrine-polluted ponds for wells in sandy aquifers, *Environ Sci Technol* 2012;46:1361–70. PMID: 22191430 NIHMS349773

*van Geen, BC Bostick, PTK Trang, VM Lan, NN Mai, PD Man, PH Viet, K Radloff, Z Aziz, JL Mey, MO Stahl, CF Harvey, P Oates, B Weinman, C Stengel, F Frei, R Kipfer, M Berg, Delayed contamination of an aquifer with high-arsenic groundwater drawn by the municipal supply of Hanoi, Vietnam, *Nature*, sent out for review December 2012.

Student and Post-doc involvement under Core D

Dr. Peter Knappett is a post-doctoral investigator with expertise in hydrogeology appointed in 2012.

Ashley Samuel, PhD student at Rutgers- Newark.

F. Project-Generated Resources- n/a

Core E: Community Engagement Core

A. Specific Aims
To determine and reduce barriers for testing and treatment of well water arsenic, doubling the rates of both testing and treatment in the central Maine community area by year 5 compared to baseline.

B. Studies and Results
The strategy to reduce barriers to testing and treatment is to develop community interventions based on improved understanding of key behavior influencing factors, implement them on a pilot basis and evaluate. Tools employed will depend on the results of a baseline community survey that is designed to uncover barriers to testing and treatment. A large portion of the survey instrument has been designed to identify key behavioral factors using an integrated model of health and social psychology theories based on the RANAS (Risk, Attitude, Norm, Ability, Self-Regulation) blocks of factors that have to be favorable in order for the new behavior to take root. For example, a survey pretest of 10 Maine well owners found that the self-regulation factor of commitment to monitoring water quality was the most significant difference between those that have tested their well in the past five years as recommended and those that have not, and the majority of households still do not use any type of water treatment. This well water testing and treatment survey instrument was developed with input from Maine CDC and the Maine Geological Survey and was mailed to 1350 households in the greater-Augusta area in early January 2013. A similar survey was also sent in January to 460 households in the area that participated in a Columbia SRP well-testing program between 2006-2010 and were found to have higher than recommended levels of arsenic. This follow-up survey is designed to determine barriers to treatment specifically among households that have already had their well water tested and know their arsenic status.

C. Significance
Within the 17-town greater-Augusta project area it is estimated that at least 13,000 people are at risk of elevated arsenic in their drinking water, based on the rates of well water supply and arsenic testing results. Maine CDC estimates that the rate of well water testing for As was 42% in 2009. Among the estimated 17,600 households relying on private wells for drinking water in the project area, a doubling of the testing rate would

result in about 7400 additional households, more than 18,000 people, knowing their well arsenic status, the first step to reducing exposure and lifetime risks for cancer and excess fatality.

D. Plans
The community baseline and follow-up surveys will provide insight into the barriers and psychological factors behind well water testing and treatment. These results will be developed for publication. Community interventions to promote arsenic testing and treatment will then be developed based on the results of this baseline household survey, will be implemented over the next 2-3 years in the greater-Augusta project area, and then evaluated through an endline survey. The innovative methods for behavior change developed through this project can be used for outreach to residents of other priority areas of Maine and beyond.

E. Publications, Patents, Other
Zheng Y, Flanagan SV, Yang Q, Marvinney RG. (2012, October). *Promoting Arsenic Testing and Treatment to Reduce Health Risks for Residents with Private Wells in Maine.* Poster presented at the 25th Annual Meeting of the Superfund Research Program, Raleigh, NC

Flanagan SV, Marvinney RG, Zheng Y. (2013, March) *Mitigating Arsenic Exposure from Maine's Private Drinking Water Wells by Targeting Behavioral Factors through Community Engagement*. Oral presentation accepted for The Geological Society of America Northeastern Section – 48th Annual Meeting, Bretton Woods, NH

F. Project-Generated Resources: n/a

Research Translation Core
Project co-PIs: Meredith Golden and Steven Chillrud
Co-Investigators: Joseph Graziano, Stuart Braman, Paul Olsen, James Ross, Tricia Chai-Onn

A. Specific Aims:
Our specific aims have not changed and we have made progress on all of them in this last year. However, due to the significant cuts in budget we probably will have to scale back efforts on some of the aims. For example, only selected, easily accessible and transferable layers of the Superfund Footprint Mapper will be updated.

B. Studies and Results:
We present progress over the last year organized into categories of partnering with government agencies, communicating with NIEHS SRP staff and broad audiences, technology transfer, and assisting and/or recording investigator initiated research translation.
Partnering with government agencies: We have several on-going government partnerships related directly to research translation activities. First, in connection with a Barnard College Workshop Project and in collaboration with the NJ DEP Office of Science and the NJ Geological Survey, three short videos for homeowners who may have arsenic in their drinking water been developed along with an accompanying arsenic awareness website. The goal is to encourage well testing, to demystify the testing process and help homeowners understand test results. The videos will undergo final editing this spring in preparation for distribution on YouTube and via links on state and local websites. Second, working closely with the NJ Geological Survey we have sampled cores from the Newark Basin and made arsenic measurements using X-ray diffraction to help advance hypotheses about arsenic distribution related to stratigraphy. The goal is to help improve their risk based risk-based maps for homeowners to guide well drilling location decisions. Third, following up on earlier work with the Rockland County Dept. of Health we worked with a Columbia University Sustainable Development Workshop to provide the Rockland County Legislature with research supporting its efforts to increase the efficiency of outdoor water use.
In addition, the RTC reached out during the development and beta-testing of the NPL Superfund Footprint Mapper to our partners at EPA (Michael Adam, David Parrish, Michael Gill, Freya Margand, Ronald Landy, Helen DuTeau, Melissa Dreyfus, Robert Shewack, Sally Perreault Darney, and Suzanne Wells), CDC/ATSDR (Andrew Dent, Brian Kaplan, Racquel Stephenson, and Tarah Somers), USGS (Zoltan Szabo and Paul Heisig), NIEHS (William Suk, Beth Anderson, Heather Henry, Danielle Carlin, Larry Reed, Liam OFallon, Liz

Ruben, Maureen Avakian, Rebecca Wilson, Mary Gant, and Symma Finn) and staff from other government agencies such as NYS DEC (Steve Parisio). Feedback from these partners as well as conversations with colleagues from other SRP Centers contributed to enhancing the Mapper's content and functionality. Discussions have been initiated with ATSDR to draw the actual boundaries for new NPL sites and those that are only located by points. Future updates to the Mapper; however, will depend on resources available. Participation in a variety of meetings and workshops with representatives from different government agencies has provided opportunities to share expertise and explore areas for collaboration. These included: the NIEHS Data Sharing Strategies Workshop (February, Durham), New York City's Office of Emergency Management (OEM)'s Emergency Operations Center (OEC) (February, Brooklyn), PEPH conference on Strengthening a Dynamic Environmental Public Health Network for Tomorrow: Advancing science through critical reflection (Bethesda, March); Northeast Superfund Research Program Regional Consortium Chemical Mixtures Meeting (Woods Hole, April); Connecting Research and Practice: A Dialogue between ATSDR and the NIEHS SRP (Atlanta, August); Arsenic and Epigenetics Workshop hosted by University of Arizona SRP (Tucson, September); SRP Annual Meeting: 25 Years of Transdisciplinary Research and Training to Protect Human and Environmental Health (Raleigh, October); and throughout the year several Rockland County Legislature open meetings related to water and Brownfields.
Furthermore, several scientists from EPA Region 1 (W.Brandon, J. Chow, D. Golden, R. Hull, A. Loughlin, D. Luce, G. Lombardo, S. Mangion, G. Millan-Ramos, I. Mojica, D. Newton), Region 2 (M. Maddaloni, K. Flynn, D. Cutt), Region 6 (T. Burnton), Region 8 (C. Partridge), Region 9 (M. Gill), and Region 10 (B. Duncan, K. Lynch, M. Stifelman,), NYSDEC (P. John), NH (K. McAllister, M. Gant, C. Kasten), and Rockland County Department of Health (C. Quinn) have tuned-in to participate in our monthly seminar/webinar series. In turn, EPA Region 10 reached out to the Columbia SRP to discuss the potential for collaborating on a research project proposal for EPA Regional Applied Research Effort (RARE) in February 2012 (EPA staff scientists Bruce Duncan, and Roseanne Iorenzana).

Communicating with SRP/NIEHS staff and broad audiences: The redesigned and updated Columbia SRP website (superfund.ciesin.columbia.edu) includes: in depth descriptions of the projects and cores, contact information for all our scientists and staff, archives of progress reports and publications, upcoming events and announcements, interactive maps, and photo galleries for projects and cores. In addition, the website provides direct links to many SRP and Superfund-related resources, including agency websites, mapping tools, news links, all SRP center websites, and key NIEHS SRP forms and documents. The enhanced website provides easy access to updated information about SRP research and events for many audiences, including our own scientists, colleagues at other SRPs, the NIEHS staff, other government agencies, and the public as well. Columbia scientists make their research findings available through a wide-variety of peer-reviewed publications. Project PIs notify NIEHS either directly or via RTC staff of accepted high profile publications, such as the article on Genome-Wide Association Study Identifies Chromosome 10q24.32 Variants Associated with Arsenic Metabolism and Toxicity Phenotypes in Bangladesh published in PLoS Genetics.
RTC continues to help design and participate in innovative bi-directional communications with NIEHS, government agencies, academics, community partners, and the general public. Our activities go beyond simple communications to active participation and leadership in these partnerships. Our SRP Director and RTC co-investigator Joe Graziano is chairing the National Research Council (NRC) committee to evaluate critical scientific issues to assess effects from oral exposure to inorganic arsenic. The committee also includes CU SRP Principal Investigator Habibul Ahsan. Three of our scientists gave presentations as part of the PEPH Program May Webinar series: Mapping and Environmental Public Health: Visualizing Health Disparities. In addition, NIEHS and EPA partners are tuning-in to our monthly multidisciplinary webinars on our bio-medical and geoscience research. As part of the SRP Risk e-Learning webinars hosted by EPA's CLUE-IN, Columbia Director Joe Graziano moderated in October 3 talks that highlighted the SRP's accomplishments in the area of arsenic research and presented his talk on "Emerging Issues: Arsenic Exposure" an overview of the Columbia SRP research and successes related to global human health issues from exposures to arsenic in drinking water. At the Lamont Open House (Palisades NY, October), the RTC gave interactive guided "tours" of the NPL Superfund Footprint: Site, Population, and Environmental Characteristics Mapper for educators, students, EPA Region 2 officials, and the general public. At the Open House demonstration introductions were made with the new EPA Science Technology Liaison, Diane Cutt and led to more discussions at the Annual Meeting which she and her other EPA colleagues attended.

Conducting technology transfer: Much of projects 4, 5 are focused on developing and understanding enhanced remediation approaches and if successful transfer them to Superfund sites. Furthermore, much of project 6 is focused on interventions in Bangladesh and understanding their long-term implications. As such much of these projects can be said to be directly related to technology transfer effort.
Investigator-initiated research translation (summarized by project):

Project 1: Dr. Habibul Ahsan, PI

a. April 2012, *Low-dose Arsenic Exposure in Bangladesh: Findings from the Health Effects of Arsenic Longitudinal Study*, Oral presentation by Dr. Maria Argos at the 2012 Joint International Conference of the Pacific Basin Consortium and Society for Environmental Geochemistry and Health. Gwangju, South Korea.
b. August 2012, *Arsenic Exposure and Mortality in Bangladesh: Findings from the Health Effects of Arsenic Longitudinal Study*. Oral Presentation by Dr. Maria Argos at the 2012 Joint Meeting of ATSDR and the NIEHS Superfund Research Program; Atlanta, GA; 8/2012.
c. September 2012, *Differential DNA methylation related to arsenic exposure in Bangladeshi adults.* Oral Presentation by Dr. Maria Argos at the NIEHS Superfund Research Program Workshop: Epigenetic Actions of Environmental Arsenicals; Tucson, AZ.
d. See Project 2a below.

Project 2: Dr. Joseph Graziano, PI

a. Columbia SRP Director Dr. Joseph Graziano has carried out a wide range of research translation efforts in both the USA and Bangladesh, but here we highlight the fact that he has been selected to chair the National Research Council (NRC) committee to evaluate critical scientific issues to assess effects from oral exposure to inorganic arsenic. The committee also includes CU SRP Principal Investigator Habibul Ahsan and as well as SRP grantees Maragaret Karagas, Rebecca Fry, and Robert Wright. The committee will plan and conduct a public workshop to gather a variety of perspectives from key stakeholders and the public. It will then prepare an interim report providing recommendations on how to address these issues in EPA's Integrated Risk Information System (IRIS) assessment of inorganic arsenic. After the IRIS assessment is revised by EPA, the committee will then review the assessment to determine whether dose-response relationships between inorganic arsenic and cancer and noncancer effects are appropriately estimated and characterized. The committee will also determine whether the arsenic document implements the recommendations made in Chapter 7 of the 2011 NRC report on formaldehyde for improving descriptions of methods and criteria for selecting studies, approaches to evaluating critical studies, weight-of-evidence analyses, and justification of modeling approaches in IRIS assessments. A final report will be published when the project is completed at the end of 2015.
b. Feb 21, 2012: Conference call with EPA Region 10 to discuss RARE proposal to control mollusk arsenic concentrations and the potential risk to indigenous groups that depend on these species as a food source. (EPA names = Duncan Bruce, Roseanne Iorenzana). Based on these discussions, Columbia suggested that EPA reach out to our colleagues at the Dartmouth SRP center to include their expertise on the subject.

Project 3:
Dr. Mary V. Gamble, PI

a. May 30 to June 1, 2012, Attended a Conference sponsored by the Children's Environmental Health Network entitled, "The Contribution of Epigenetics in Pediatric Environmental Health" at which Dr. Gamble gave an oral presentation entitled, "Influence of prenatal arsenic exposure and newborn sex on global methylation of cord blood DNA."
b. July 22 to 27, 2012. Attended the FASEB Summer Research Conference entitled, "Folic Acid, Vitamin B12 and One-Carbon Metabolism" in Crete, Greece. Dr. Gamble's lab was represented by three presentations. Two oral presentations: Megan Niedzwiecki presented a talk entitled, "Whole blood glutathione redox status is associated with lower plasma homocysteine concentrations in folate-deficient Bangladeshi adults." Meg Hall presented a talk entitled, "Associations of Plasma Choline and Betaine with Homocysteine and Arsenic Methylation." In addition, Brandilyn Peters

presented a poster entitled, “Effects of folic acid and creatine supplementation on plasma homocysteine in Bangladeshi adults.”

c. September 22, 2012. Presentation at a workshop on Arsenic and Epigenetics sponsored by the University of AZ SRP Program entitled, “Batch Effects and Pathway Analysis: Two Potential Perils in Cancer Studies Involving DNA Methylation Array Analysis.” Presented by Dr. Gamble’s post-doctoral Research Scientist, Kristin Harper.
d. On October 8, 2012, Dr. Gamble gave a seminar to the Graduate Center for Toxicology at the University of Kentucky entitled, Influence of nutritional status on arsenic methylation and toxicity."
e. October 17 to 19, 2012. Served as a Member of the University of AZ SRP Program’s External Advisory Board.
f. October 21 to 23, 2012. Attended the SRP’s 25th Annual Meeting in Raleigh, NC. Dr. Gamble’s lab was represented by one oral presentation and one poster presentation by two PhD students. Brandilyn Peters’ talk was entitled, “Creatinine, arsenic metabolism, and renal function in an arsenic-exposed population in Bangladesh,” and Caitlin Howe’s poster was entitled, “Associations between s-adenosylmethionine, s-adenosylhomocysteine and arsenic methylation.” The latter was awarded best poster for biomedical sciences
g. 12 publications from the current funding cycle (see Project 3 summary).

Project 4: Dr. Benjamin Bostick, PI

a. Jan. 12, 2012 Met with EPA Region 2 managers of Vineland (Michael Sivak, Nica Klaber, Diane Cutt)
b. Feb. 21, 2012: Conference call with EPA Region 10 to discuss RARE proposal to control mollusk arsenic concentrations and the potential risk to indigenous groups that depend on these species as a food source. (EPA names = Duncan Bruce, Roseanne Iorenzana) (Joe Graziano, Ben Bostick, Steve Chillrud, Meredith Golden.
c. March, 2012. Completed and filed World Bank Report on Alternatives Analysis for Arsenic Contaminated Groundwater in Kandal, Cambodia.
d. Oct. 15, 2012: Bostick. B.C. Geochemical Approaches to Remediating Arsenic at Superfund Sites. Columbia University Superfund Research Program Monthly Seminar/Webinar.
e. December, 2012. Named representative to the National User Facility Organization (NUFO), which working closely with the Association of American Universities (AAU) and government relation experts to develop plans and compile material for outreach purposes. This position spans the sciences and engineering.

Project 5:

Dr. Steven Chillrud, PI

a. Project 5 is focused on developing and understanding enhanced remediation approaches and if successful transfer them to Superfund sites. As such almost entire project can be said to be a big technology transfer effort.
b. Feb. 21, 2012: Conference call with EPA Region 10 to discuss RARE proposal to control mollusk arsenic concentrations and the potential risk to indigenous groups that depend on these species as a food source. (EPA names = Duncan Bruce, Roseanne Iorenzana) (Joe Graziano, Ben Bostick, Steve Chillrud, Meredith Golden.
c. Jan. 12, 2012 Met with EPA Region 2 managers of Vineland (Michael Sivak, Nica Klaber, Diane Cutt) Ben Bostick, Steve Chillrud, Brian Mailloux, Martin Stute
d. Oct. 6, 2012: Open house at LDEO, As Issues, Hand Pump Water Race, and Rockland County water issues,.

Dr. Mailloux

a. Jan. 12, 2012 Met with EPA Region 2 managers of Vineland (Michael Sivak, Nica Klaber, Diane Cutt)
b. Feburary 2012: spoke to high school students on multiple Saturdays as part of Science Saturday Seminars at Barnard College.

Dr. Stute

a. June 2012: Presentation to a middle school class of Columbia's Secondary School of Math, Science and Engineering on groundwater contamination using sand tanks
b. Oct. 6, 2012: Open house at LDEO: Arsenic Issues, Hand Pump Water Race, and Rockland County water issues

c. 2012: Developed You-Tube instructional videos on contaminated aquifer using sand tanks: http://www.youtube.com/watch?v=wTq6-ipjUD0 Bangladesh Groundwater System http://www.youtube.com/watch?v=pyevjRiz1UI- Arsenic Contamination in Bangladesh
d. 2012: Organized workshop/class on sustainable development that developed videos on arsenic testing and treatment for the Hunterdon County Department of Health and New Jersey Department of Environmental Protection Office of Science

Project 6:
Dr. Lex van Geen, PI

a. July 16-17, 2012 Dhaka: Invited presentation on need to test millions of tubewells in Bangladesh with field-kits. Proposed subsidized fee-based testing with data entry directly on hand-held GPS to facilitate quality control. UK DFID-supported International Growth conference of mostly development economists, attended by Finance Minister and other government, international organization, and NGO representatives. Reported in the local press.
b. January 15-16, 2013 Dhaka : Invited presentation on resilience of deep low-As aquifers based on 10-year time series for community wells in our study area of Bangladesh and more past year's field-kit survey of over 28,000 tubewells. University College London-supported workshop attended by international group of hydrogeologists and government, international organization,and NGO representatives responsible for arsenic mitigation - including government Policy Support Unit.
c. Goldschmidt Conference 2013, sponsored by the Geochemical Society and the European Association of Geochemistry: Proposed to convene session entitled "Impact of air, soil, and water geochemistry on human health". Accepted by the scientific committee for Aug 25-30, 2013 conference in Florence, Italy.

C. Significance:
The CU SRP studies of Arsenic (As) and Manganese (Mn) have contributed to a better understanding of the health consequences of exposure, molecular mechanisms, dose-response relationships, range of impacts, exposure pathways, hydrogeologic environments, and vulnerability of specific populations. In addition, partnerships with government agencies in the US and Bangladesh have helped promote effective policies and develop and test remediation strategies. Specific information regarding the geographical range and subterranean hydrogeology of As concentrations in the Ganges-Brahmaputra delta area of Bangladesh. The knowledge generated by our research projects and cores has been guided by and shared with diverse stakeholders.

D. Plans:
We plan on continuing our efforts on all of our aims. However, due to significant cuts in our budget, we most likely will have to scale-back on the extent of our research translation activities. For example, it will not be possible to update all of the content and expand the functionality of the Superfund Footprint Mapper as part of the RTC scope. We may also have to scale back on the number of videos to be produced for NJ and other government partnerships. We plan to work with CEC following analysis of their survey results, both for possible use in designing further efforts in NJ and to assist CEC in the potential use of modified versions of the RTC generated NJ arsenic awareness videos for Maine

D. Publications from RTC

Braman, Stuart and Simon Gruber (2012), Water Conservation and Long-term Water Supply Planning in the Hudson Valley: A Rockland Case Study (CRREO Discussion Brief 7, Summer 2012). New Paltz, NY: State University of New York at New Paltz Center for Research, Regional Education and Outreach.
Morain, SA and AM Budge,eds. International Society for Photogrammetry and Remote Sensing (ISPRS) Book Series: *Environmental Tracking For Public Health Surveillance*, *Chapter 6 Data discovery, access and retrieval* contributions by ML Golden on “Populatioins near Superfund Sites”. 2012. London: CRC Press,Taylor & Francis Group. Print ISBN: 978-0-415-58471-5. eBook *ISBN*: *978-0-203-09327*-6. http://dx.doi.org/10.1201/b12680

F. Project-Generated Resources:
The NPL Superfund Footprint: Site, Population, and Environmental Characteristics Mapper:
This interactive mapping tool created by the CU SRP Research Translation Core permits users to visualize

critical data about inhabitants and areas near Superfund sites. The Mapper is unique compared to other environmental mapping services. It focuses specifically on NPL Superfund sites and provides key demographic information on communities living within one and four miles of the actual site footprint for most NPL Superfund sites. It is easy to use and does not require familiarity with geographic information systems. Novices may easily view the maps, generate data and new maps, and save or print their results.
2012: You-tube video on Contaminated Aquifers using sand tanks (http://www.youtube.com/watch?v=wTq6-ipjUD0)
2012: Organized workshop/class on sustainable development that developed videos on arsenic testing and treatment for the Hunterdon County Dep of Health and New Jersey Department of Environmental Protection Office of Science. Videos entitled: Operation Clean Water: an arsenic awareness video for schoolchildren, What's in your Well Water?: an arsenic awareness video for adults, and Well Water: Keeping NJ Water Contaminant Fee: a video on helping NJ residents understand private well testing and for which contaminants should they test.