

## FY06-LIV(54)-142

# “Investigating the Importance of the Mercury–Selenium Interaction”

Submitted by: Energy & Environmental Research Center  
Request for: \$55,000; Total Project Costs: \$ 260,000  
Principal Investigator: Nicholas V.C. Ralston

### PARTICIPANTS

<u>Sponsor</u>	<u>Cost Share</u>
US Tuna Foundation	\$ 150,000
Coteau Properties Company	\$ 5,000
Falkirk Mining Company	\$ 5,000
National Fisheries Institute	\$ 40,000
Great River Energy	\$ 5,000
NDIC	<u>\$ 55,000</u>
Total Cost	\$ 260,000

### Project Schedule - 24 Months

Contract Date – 12/09/05

Start Date – 12/09/05

Completion Date – ~~3/31/07~~

– ~~9/30/07~~

– 12/31/07

### Project Deliverables

Contract Signed: 12/09/05

Quarterly Reports:

12/31/05(✓); 3/31/06(✓);

6/31/06 (✓); 9/30/06 (✓); 12/31/06 (✓)

Final Report: ~~3/31/07(–)~~

~~9/30/07(–)~~

12/31/07 (✓)

### OBJECTIVE / STATEMENT OF WORK:

The primary objective is to clarify the biochemical mechanism for dietary selenium’s protective effect against methylmercury toxicity. The project will determine the interactions between mercury and selenium in animal models comparing results to an on-going Seychelles Study (by others). The three proposed studies will examine the effects of dietary intakes of methylmercury and the protective effects of dietary selenium in order to resolve important questions regarding the significance of mercury–selenium interactions in human health

### STATUS

July 1 – December 31, 2005. The selenium-dependent protection study began November 21-2005 and is planned to continue until late March. The health of selenium-deficient rats exposed to methylmercury has degraded more swiftly than expected. The protection against mercury toxicity conferred by adequate or enriched dietary selenium is dramatically different from what has been observed in rats fed selenium-deficient diets.

January 1 – March 31, 2006. There was continued testing of mercury-selenium ratios in rat diets and data reporting.

April 1 – June 30, 2006. Results of the this project’s studies were shared in two presentations (*Selenium’s Protective Effects Against Methylmercury Bioaccumulation and Toxicity* and *Selenium as a Bioindicator of Susceptibility to Methylmercury Bioaccumulation and Toxicity*) at the 14<sup>th</sup> International Conference on Environmental Bioindicators in Baltimore, Maryland in April.

July 1 – September 30, 2006. Five presentations describing aspects of this project were made at the Eighth International Conference on Mercury as a Global Pollutant in Madison in August. Two presentations of this work were made at the Twenty-Third International Neurotoxicology Conference in Little Rock, Arkansas, in September.

October 1 – December 31, 2006. Elemental analysis of the brain, kidney, and liver from the animals in the study is nearly complete. Enzyme analysis was delayed because of difficulties obtaining necessary calibration equipment. This has been resolved and enzyme analysis is underway. Statistical analysis of mercury and selenium treatment effects on food consumption and growth of rats has been completed, and analysis of interactions between diet and elemental distributions in tissues is being completed.

January 1 – March 31, 2007. Diets reflecting the range of dietary selenium (Se) intakes at low, normal, or rich levels were fed to rats. These diets were supplemented with methylmercury at either negligible or high dietary concentrations. The results of the analyses were documented.

April 1 – June 30, 2007. Elemental analysis of Hg and Se in the brain, kidney, liver, testes, pituitary, and blood has been completed. Results from this project coincide with other studies in confirming that mercury sequesters selenium, and this is the proximal cause of mercury toxicity. The results of this study demonstrate that Hg:Se ratios are more appropriate reference criteria for risk assessment than tissue Hg concentrations alone.

July 1 – September 30, 2007. Other than ongoing analysis of enzyme activities, all tasks for this project are completed. Results from this project were presented and discussed at the Air Quality VI Conference in Arlington, Virginia. The draft final report and manuscripts for publication are in progress.

Final Report. Two animal studies were performed to examine the role of dietary Se in preventing and treating methylmercury (MeHg) toxicity. Selenium contents of blood samples from mothers and children participating in the current Seychelles study that had been analyzed in a previous project were statistically evaluated and prepared for publication in coordination with results of mathematical models developed in this project. The results of these tasks have been presented in numerous national and international meetings and have been submitted for publication in prestigious journals.

Among animals that were exposed to diets with high MeHg concentrations (~10 ppm; 50  $\mu\text{mol/kg}$ ), toxic effects were entirely dependent on the amount of Se present in the diet. Rats that were fed low-Se (0.1  $\mu\text{mol/kg}$ ), high-MeHg diets showed compromised growth after 2 weeks, started to lose weight and develop motor function disabilities that progressively worsened after 10 weeks, and started to die of Hg toxicity after 18 weeks. Rats that were fed diets with adequate Se (1.0  $\mu\text{mol/kg}$ ) also showed growth impairments after 2 weeks, but the effects were not as severe as in the low-Se group, and they did not have motor function impairments or other health consequences. In contrast, no adverse effects from MeHg exposure were noted among rats that were fed rich-Se (10  $\mu\text{mol/kg}$ ) diets. Low-Se rats that had developed symptoms of Hg toxicity after 10 weeks were rescued by switching them to rich-Se diets. The Se-rescued rats resumed normal growth and their motor function symptoms stabilized, regardless of whether or not their diets contained high MeHg.

Statistical analysis of these animal studies and consideration of data from the major human studies

indicate maternal MeHg exposure is not directly related to risk of adverse effects in their children, but the Hg:Se molar ratio in the seafoods they consumed is directly proportional to the effects that were observed. Similarly, the amount of Hg in blood and brains of animals exposed to high dietary MeHg was not associated with Hg toxicity, but Hg:Se molar ratios were directly related. Amounts of dietary Se reflecting the amounts in ocean fish prevented and reversed toxic effects from exposure to MeHg at levels many times higher than those that typically occur in ocean fish.

There have been contrasting and conflicting findings in the major human studies designed to test the hypothesis that “Maternal exposure to MeHg is directly associated with adverse child development outcomes.” This appears to be because the conventional hypothesis is incomplete. However, the findings of the human studies are entirely consistent and mutually supportive if the hypothesis is updated to the more comprehensive form: “Maternal exposure to MeHg in excess of dietary Se intake is directly associated with adverse child development outcomes.” Based on this new paradigm, future risk assessments regarding effects of MeHg exposure will need to establish Hg:Se molar ratios in fish that are being eaten and in blood samples of populations exposed to Hg from fish consumption. Failure to properly consider the Hg:Se molar ratio results in the mistaken impression that Hg exposure is directly associated with risk.