

Bioaccumulation, Biopersistence, and Toxicity of CMP Nanoparticles (NPs) in Mammalian and Aquatic Models

University of Texas at Dallas

Task Number: 425.048

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- Dakota Deutsch and Karina Kinghorn, Department of Biological Sciences

Other Researchers:

- Carole Mikoryak, Senior Scientist, Department of Biological Sciences

Cost Share (other than core ERC funding):

- \$235,288 over the life of the award from UT Dallas that includes instrument purchases, graduate student stipends, and faculty salaries.

SRC Engineering Research Center for Environmentally Benign Semiconductor Manufacturing

Objectives

- **Toxicity:** Perform acute and chronic toxicity assays with model organisms based on external CMP-NP doses; relate results to previously reported values for pristine metal oxide NPs and EPA reference toxicants.
- **Bioaccumulation:** Determine the amounts of CMP NPs accumulated by model organisms; correlate findings to toxicity results.
- **Biopersistence:** Determine the time required for model organisms to eliminate accumulated CMP NPs; relate results to previously reported values for pristine metal oxide NPs and EPA reference toxicants.

ESH Metrics and Impact

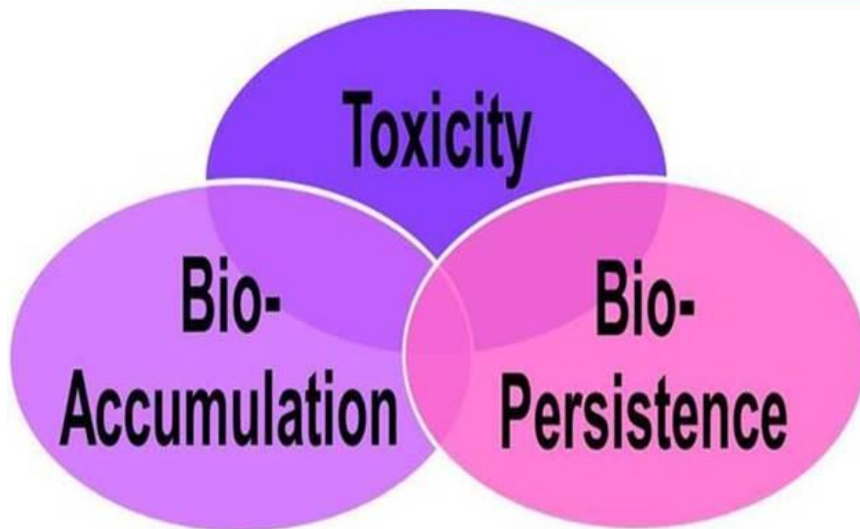
- 1. Reduction in the use or replacement of ESH-problematic materials**
 - Identification of problematic materials requires accurate toxicity tests.
 - The toxicity, bioaccumulation, and biopersistence of pristine and used CMP slurries, including slurries used to polish III/V-containing films, will be assessed to determine whether reduction in their use or replacement is necessary.
- 2. Reduction in emission of ESH-problematic material to environment**
- 3. Reduction in the use of natural resources (water and energy)**
- 4. Reduction in the use of chemicals**

Overview

Model CMP Slurries

- Colloidal Silica
- Fumed Silica
- Ceria
- Alumina

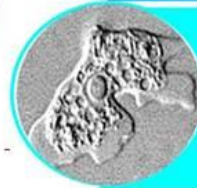
Pristine Slurries and Slurries Used to Polish Conventional Wafers and InGaAs Blanket Films



Mouse Macrophage
(RAW 264.7 cells)



Freshwater Flea
(*Daphnia magna*)

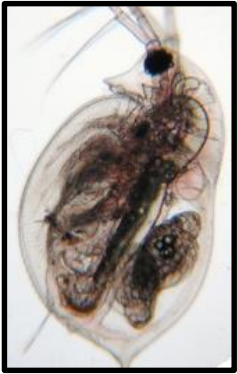


Amoeba
(*Amoeba proteus*)

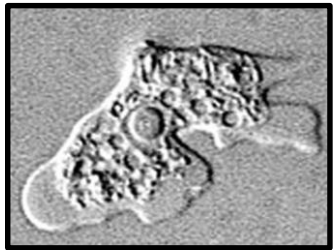
Overview (Test Organisms)



- **RAW 264.7 Macrophage Cells**: The primary responders to foreign particles that initiate proinflammatory responses that can lead to health problems.



- **Freshwater Flea (*Daphnia magna*)**: An established organism recommended by the EPA for ecotoxicity testing.



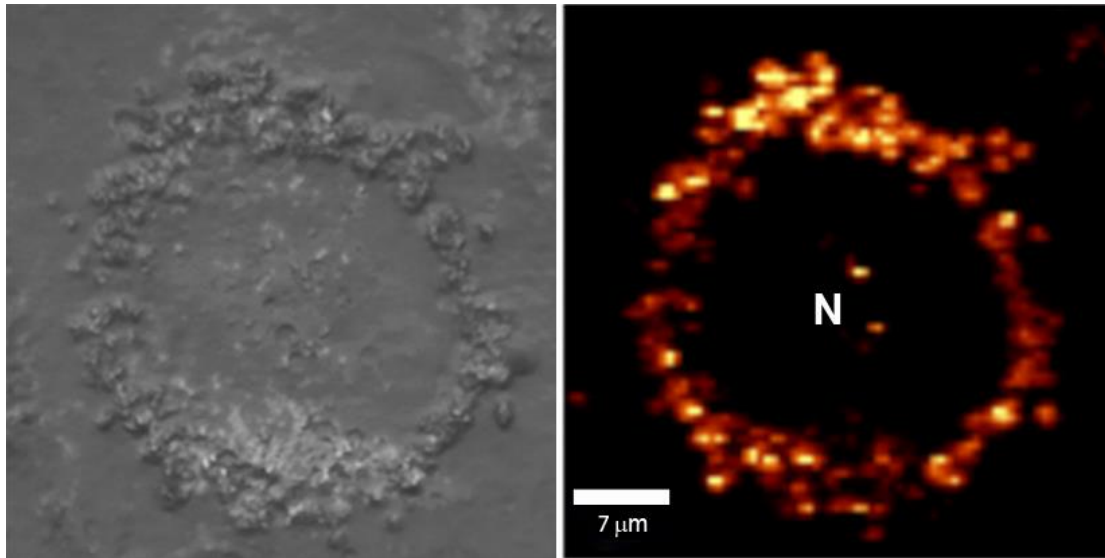
- **Amoeba (*Amoeba proteus*)**: A unicellular organism that resides on the surfaces of plants and sediments in natural waters.

Overview (Toxicity)

- Mammalian Macrophage (RAW 264.7 cells):
 - Acute and chronic IC-50 data based on external CMP-NP doses
 - Acute and chronic IC-50 data based on accumulated CMP-NP amounts
 - Quantify secretion of proinflammatory cytokines
 - Relate toxicity and cytokine responses to those previously reported in predictive models with mice
- Amoeba (*Amoeba proteus*):
 - Acute and chronic IC-50 data based on external CMP-NP doses
 - Acute and chronic IC-50 data based on accumulated CMP-NP amounts
 - Not frequently used in nanotoxicity studies, new insights into the potentially toxic effects of CMP NPs may result
- Freshwater Flea (*Daphnia magna*):
 - Acute and chronic LC-50 data based on external CMP-NP doses
 - Acute and chronic LC-50 data based on accumulated CMP-NP amounts
 - Relate toxicity responses to previously reported values for pristine metal oxide NPs and EPA reference toxicants

Overview (Bioaccumulation)

- **Confocal Raman images of RAW 264.7 cells exposed to the pristine ceria slurry indicate the accumulation of ceria NPs in punctate spots around the nucleus, suggesting that the ceria is in phagolysosomes.**

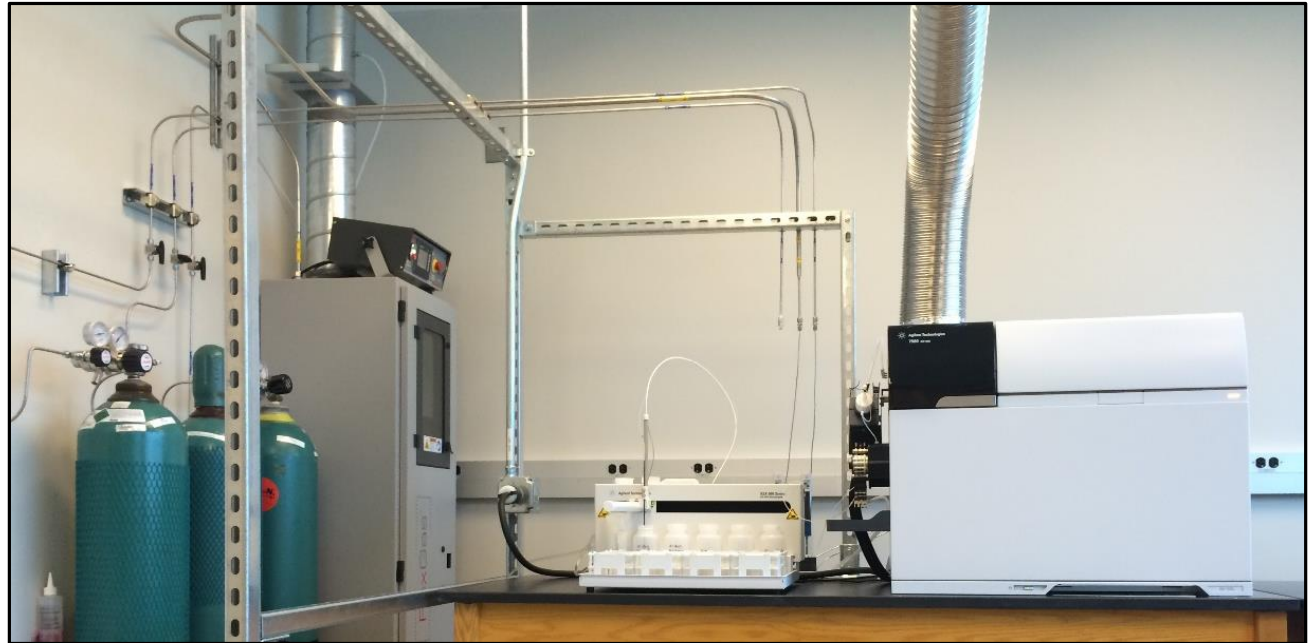


Left, bright field image of a single RAW 264.7 cell exposed to 50 $\mu\text{g}/\text{mL}$ of ceria CMP slurry for 48 h. **Right**, Raman image of the same cell showing the location of ceria on a heat scale where yellow is the most intense signal. **N** marks the center of the cell that is the nucleus.

- **The accumulation and chronic persistence of non-biodegradable material within phagolysosomes may interfere with the normal and essential functions of this organelle in cells.**

Methods: Bioaccumulation & Biopersistence

- The bioaccumulation of metal oxide NPs (and III/V-elements) by test organisms upon chronic exposure to pristine and used CMP slurries will be measured by inductively coupled plasma – mass spectroscopy (ICP-MS).

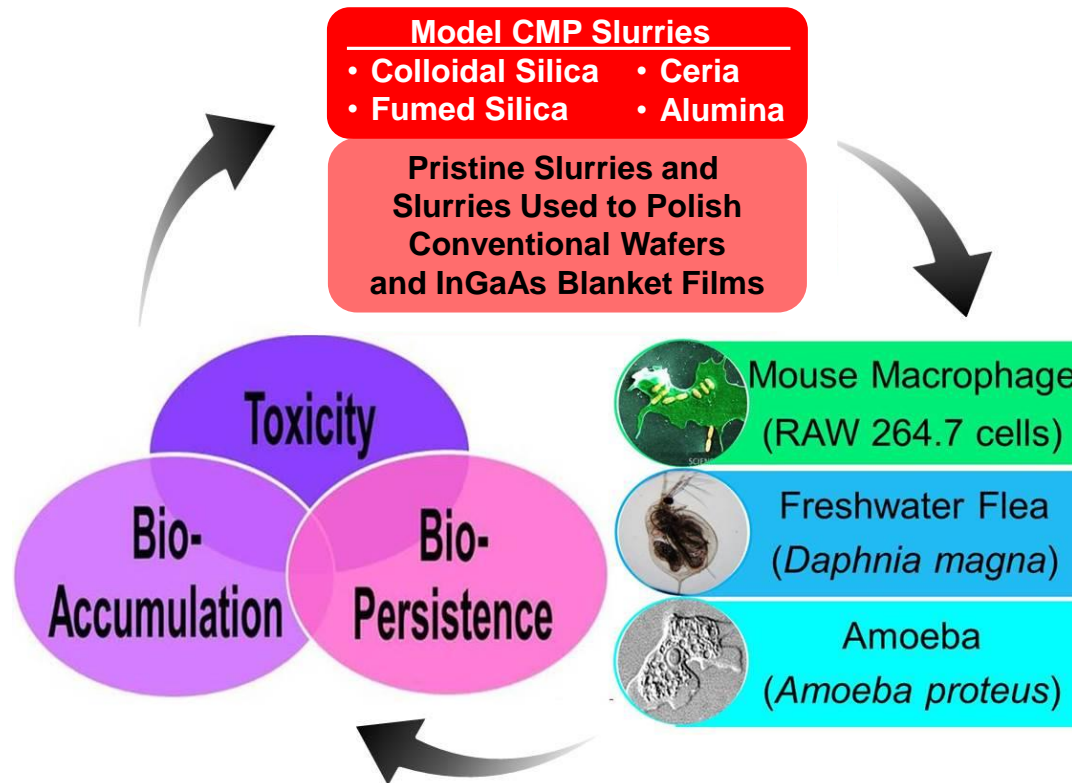


- The biopersistence of metal oxide NPs (and III/V-elements) from model organisms will also be monitored by ICP-MS after the organisms are loaded with pristine or used CMP NP slurries and then placed in a NP-free environment.

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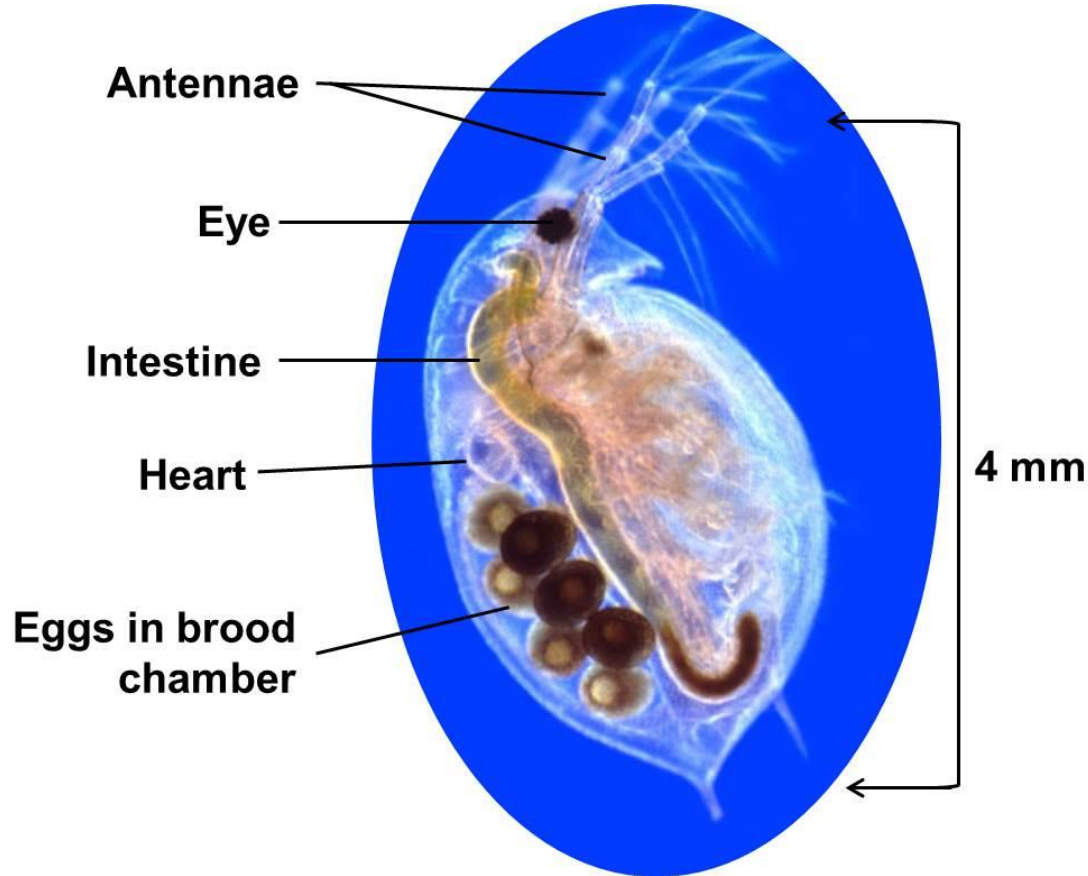
The combined results should provide quantitative data on the effects of CMP NPs with model test organisms that can guide EHS decisions on CMP NP and III/V-element risk.



Introduction to Daphnia



Daphnia magna is a freshwater flea found in ponds and lakes.



These water fleas are very small, usually 2-5 mm long, with an overall shape similar to a kidney bean.

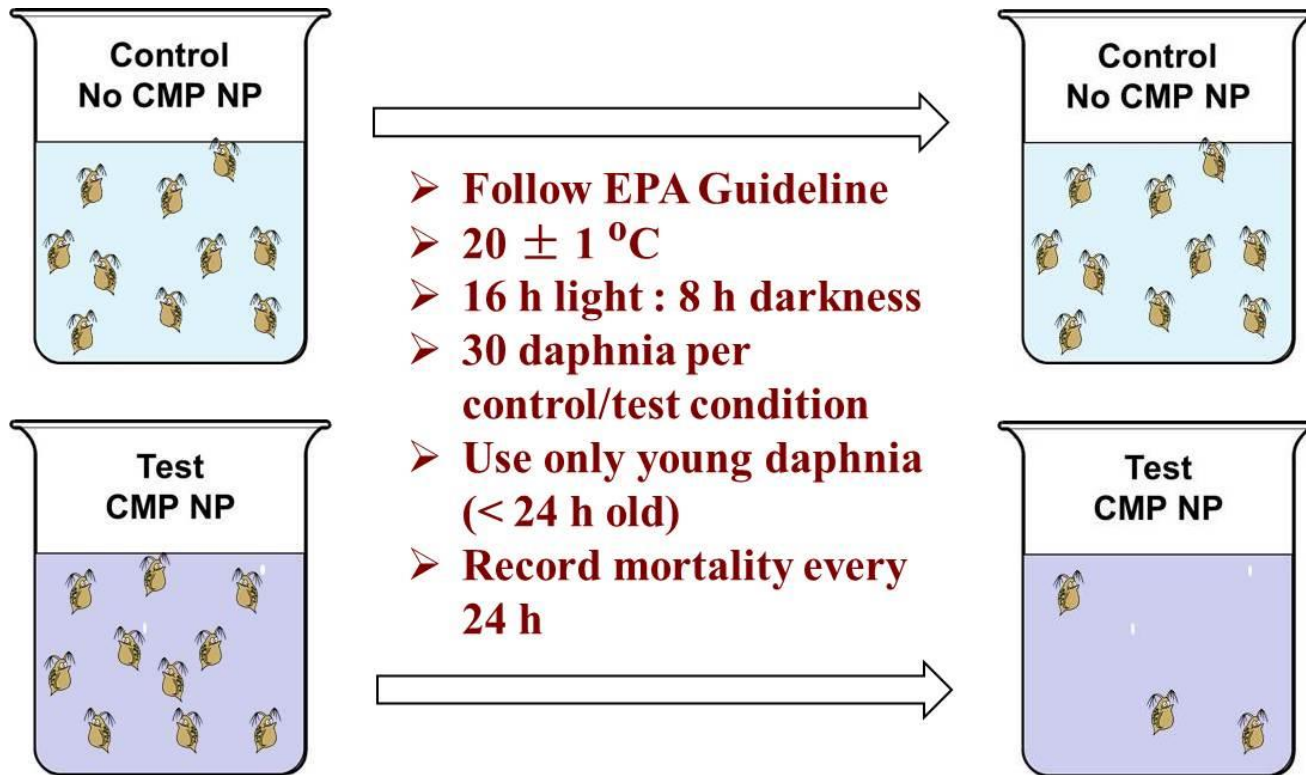
Introduction to Daphnia (continued)



The normal life span of Daphnia is about 40 days.

Assessment of Toxicity and Exposure Times

- Three independent experiments will be performed for each of the four CMP NP slurries at various concentrations.
- LC-50 values will be determined for acute (4 days exposure) and chronic (21 days exposure) toxicity.

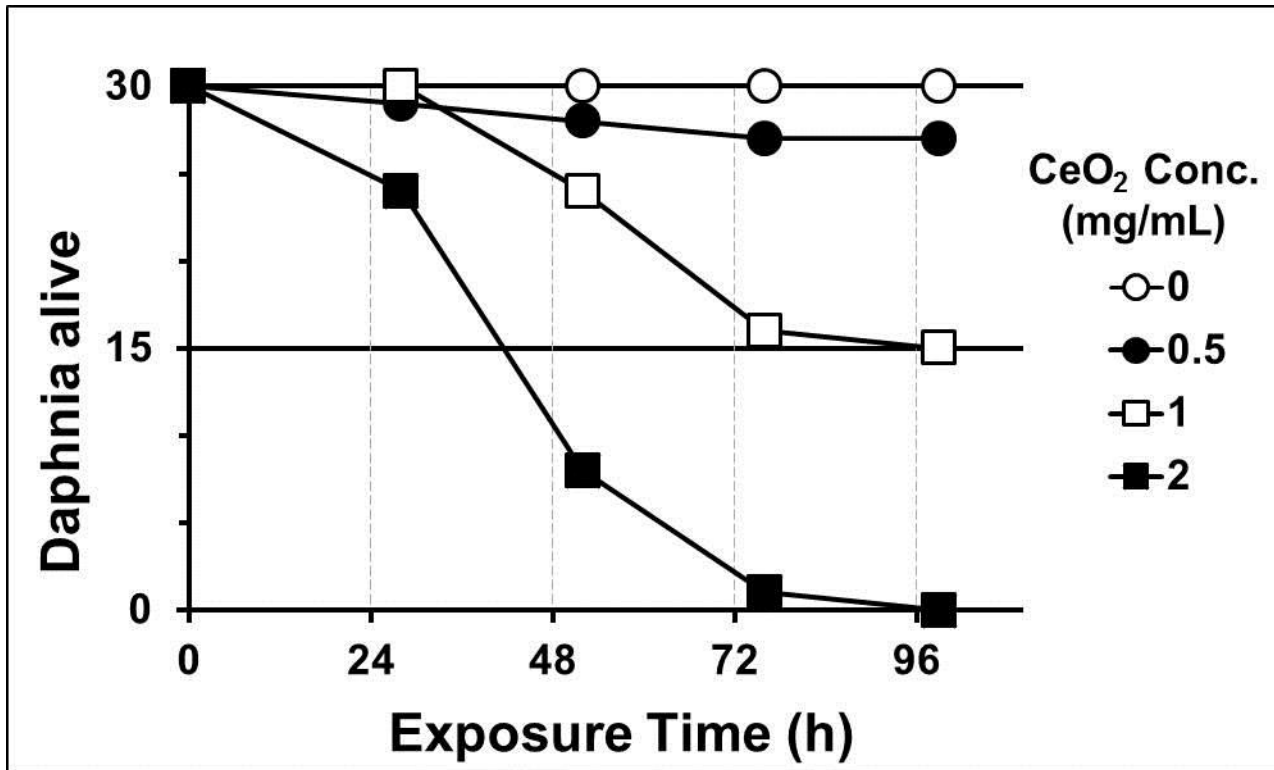


- Details provided on the poster

Properties of Pristine CMP Slurries

Pristine Slurry	Colloidal Silica (<i>c</i>-SiO₂)	Fumed Silica (<i>f</i>-SiO₂)	Ceria (CeO₂)	Alumina (Al₂O₃)
Concentration (mg/mL)	30	50	10	30
pH	2.5 - 4.5	10.0	3.0 - 4.0	4.5 - 5.0
pH adjusting agent	Acetic acid	KOH	-	HNO₃
Particle size (nm)	50 - 60	120 - 140	60 - 100	80 - 100

Daphnia Toxicity Test Results with Ceria



Exposure Time (h)	LC-50 (mg/mL)
24	≥ 2.0
48	~ 1.7
72	~ 1.2
96	~ 1.0

Conclusion: The toxicity of ceria is concentration and exposure time dependent.

Future Work

- **Complete acute and chronic toxicity assessments on pristine CMP slurries.**
- **Conduct acute and chronic toxicity assessments on used CMP slurries.**
- **Quantify the actual amounts of CMP NPs (and III/V-elements) accumulated by Daphnia using ICP-MS.**
- **Similar Toxicity, Bioaccumulation, and Biopersistence studies will also be performed with macrophage cells and amoeba.**

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Questions?

Industrial Interactions and Technology Transfer

Industry Liaisons:

- **David Speed, IBM**
- **Brian Raley, Global Foundries**
- **Reed Content, Global Foundries**

Technology Transfer (Task Deliverables):

- **Year 1**
Acute and chronic data on toxicity tests and IC-50 values with test organisms based on external CMP-NP amounts.
- **Year 2**
Acute and Chronic data on amounts of CMP NPs accumulated by test organisms.
- **Year 3**
Data on time required to eliminate the accumulated CMP NPs from test organisms.

Publications, Presentations, and Recognitions/Awards

- **To be added as project progress**