Task ID: **425.023**

***Project title*:**
Environmental Safety and Health (ESH) Impacts of Emerging Nanoparticles and Byproducts from Semiconductor Manufacturing - Toxicity Assessment and Prediction

Deliverable:
Report on the final selection of materials and process conditions for Phase 1 and Phase 2 NPs

Background:

Numerous reports published in recent years indicate a growing concern for the potential toxicity of engineered nanomaterials (Balbus et al. 2007; Nel et al. 2006; Handy & Shaw, 2007). Toxicity research is a high priority for the semiconductor industry due to the fact that some nanoparticles (*e.g.* chemo-mechanical planarization (CMP) slurry particles) are currently used in semiconductor manufacturing, and various new nano-sized materials (nanowires, carbon nanotubes, immersion lithography nanoparticles) are being considered for upcoming manufacturing processes. Predicting the potential toxicity of emerging nanoparticles (NPs) will require hypothesis-driven research that elucidates how physicochemical parameters influence toxic effects on biological systems. Of particular concern are NPs of less than 0.1 μm that would escape normal mechanisms of cellular defense (Gwinn & Vallyathan, 2006; Stern & McNeil, 2008). The intrinsic capacity of NPs to penetrate biological tissue may in itself not be the primary cause of toxicity; rather surface properties of NPs may accentuate (or minimize) toxicity. These include high specific surface area, reactive surfaces, and adsorptive surfaces for other toxic chemicals. Contaminants can also accumulate in NPs via nano-capillary condensation (Kelvin effect) in the particle pores. NPs have very high surface curvatures, engendering high surface tensions and energies that might have unique effects on living cells. Reactive radical species can have prolonged lifetimes when sorbed onto NPs. There is a growing consensus that reactive oxygen species (ROS, composed primarily of hydroxyl radicals, hydrogen peroxide and superoxide) are a major contributing factor of NP toxicity (Gwinn & Vallyathan, 2006; Limbach et al., 2007). ROS are normally produced in and around living tissues; however, overproduction can lead to cell toxicity and loss of cell and tissue function.

Objective and key findings:

The goal of this project is to characterize the potential toxicity of current and future NPs and NP-byproducts of SC manufacturing. The information will be used to develop mechanistic hypotheses that will be applied to developing rapid toxicity assessment protocols applicable in the industrial workplace, as well as to predicting the ESH impacts of NPs based on physicochemical properties.

The objective of this task is to select the nanomaterials that will be investigated in this project and the process conditions to be applied to prepare and modify the nanomaterials with model contaminants.

Method of Approach

Previous studies on the ESH effect of NPs have generally focused on generic feed materials and have not included the effect of processing conditions and interactions with other contaminants. Our preliminary studies (Seed project report, 11th ERC Annual Review, Feb 2008) have revealed that the processing conditions have a significant effect on the properties which determine the ESH impact of NPs. An example is the secondary CMP particles generated from polishing of wafers and attrition of the CMP pad. In most cases, it is anticipated that the changes in the NP during processing are the primary causes of NP toxicity due to the association of contaminants with the NPs. The combination of selective sorption of contaminants on the surfaces (locally high dosage effect), stabilization of process-generated intermediates (exposure time effect), and ability of cell penetration of NP (delivery effect) make NPs effective carriers of other contaminants to cells. These synergistic effects cannot be investigated without process considerations of particular importance to SC manufacturing due to the complexity and the large number of processes and materials used. This task will be the first systematic evaluation of NPs throughout the manufacturing process, considering the potential toxicity (or detoxification) from a wide array of intermediates that arise during production.

Technical Results and Data:

The nanomaterials selected for study have been classified in two categories, namely, Phase I NPs and Phase II NPs. The project will initially focus on hafnium dioxide (HfO_2) NPs used in immersion photolithography, and silicon dioxide (SiO_2) NPs utilized as abrasives in CMP slurries (**Phase 1 NPs)**. Subsequently, the focus will be on other types of CMP-related primary and secondary NPs (*i.e.* cerium dioxide (CeO_2) and alumina (Al_2O_3)) (**Phase 2 NPs**).

The project will investigate the physico-chemical characteristics and toxic effects of the materials selected with and without surface contamination by copper and organics typically present in the CMP and post-CMP cleaning processes. Copper is highly inhibitory to many microorganisms and higher aquatic organisms (Gerhardt et al. 1993; Roesijadi, 1992), but this metal displays low toxicity against human cells. Therefore, arsenic will also be used as a model contaminant of CMP nanoparticles. The selection of arsenic, a well known inhibitor of human cells, as an additional model contaminant is expected to advance work in the project because the PI leading the human toxicity studies has extensive experience with the study of arsenic toxicity. The results will be on interest to SRC companies because gallium arsenic alloys are being considered for introduction in semiconductor manufacturing. Planarization of GaAs should be expected to lead to interactions between arsenic and abrasive NPs in the CMP slurries.

Dispersion of NPs in biological media utilized for toxicity testing is very challenging (Sager et al. 200; Schulze et al. 2008). Testing the impact of material size on toxicity will require effective dispersion of the NP in the aqueous media. This project will investigate various methods to functionalize NP surfaces using biocompatible ligands in order to promote the stability of NP dispersions and prevent aggregation. Initial studies will consider surface modification by poly-acrylates, thiol-terminated polyethylene glycols (PEGs), and amino acids such as lysine.

Some arrangements have been made with industrial partners and Sematech for preparation and selection of samples (*e.g.* immersion lithography Hf-based NPs were supplied in collaboration with Cornell University via a Sematech agreement). SiO_2, CeO_2 and Al_2O_3 NPs in various sizes are commercially available. Fractionation of commercial inorganic oxide samples by ultra-centrifugation will be used to obtain sub-samples of a given material with a narrow particle size distribution.

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