W **808** **Pulmonary Toxicity of Graphene Nanomaterials: An Emerging Concern in Manufacturing and Applications?**

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Graphene, a one-atom-thick monolayer of carbon, is an engineered nanomaterial (ENM) with physical and chemical properties that may offer application advantages over other carbonaceous ENMs, such as carbon nanotubes (CNT). As use of graphene nanomaterials (GNMs) in a variety of industries and manufacturing increases, the potential for respiratory exposure, particularly in the workplace, also rises. Unlike CNT, toxicity of GNMs has not been well defined. In addition, GNMs can vary in dimension, surface chemistry, number of layers, and other physico-chemical parameters, which in turn may affect toxicological potency of the material. The goal of this workshop is to present the most recent toxicological research findings in the field of GNMs and gain an understanding of the hazard and risk for exposure. The workshop will cover the physico-chemical characteristics and applications of a variety of GNMs, potential exposure in occupational settings, toxicity related to size and composition following various methods of pulmonary exposure in animal models, and comparative toxicity to well-defined carbonaceous ENMs. The outcome for the session is to establish whether GNM exposure poses a potential health hazard by providing an understanding of GNMs and conveying the most recent material science expertise and toxicological research related to respiratory exposure to various forms of GNMs.

W **809** **Physical and Chemical Properties of a Variety of Graphene Nanomaterials—Engineering Materials for Specific Applications**

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Graphene-based materials are a new family of carbon products that hold significant promise because of their unique combination of electrical, mechanical, and optical properties. These materials may lead to ground-breaking new applications in electronics and displays. They may also find uses in many of the legacy applications of carbon additives by enhancing functionality such as reinforcement of elastomers, electrical and thermal conductivity in polymers, among many others. The performance characteristics of graphene-based materials in these applications will be driven largely by their morphology and surface chemistry as well as the quality of their dispersion in the host matrix. There are over a dozen different routes for the synthesis of graphene-based materials relating to the diversity of the potential applications of graphenes in order to meet all performance requirements. These routes produce materials with very different physicochemical characteristics that are quantified through certain key analyticals such as their surface area, thickness, lateral size, and surface chemistry. Some of these characteristics can vary over several orders of magnitude for many of these materials. This presentation will provide an overview of the major synthetic routes and the relevant physicochemical properties of the intermediates and materials produced by these routes. Properties relevant to specific commercial applications will be explored. Understanding how these characteristics relate to the toxicology of these materials via different exposure routes will be an important factor in engineering safer graphene products.

W **810** **Occupational Exposures along the Graphene Product Value Chain: Production, Formulation, and Use**

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Graphene is a two-dimensional crystalline allotrope of carbon with atoms in a densely-packed regular hexagonal lattice. It displays high strength and curability for current density, high surface area/weight ratio, and high light transparency. These characteristics make graphene appealing to industry sectors such as electronics, energy, transportation, and building materials. Because of this unique physical structure, various industries are driven to use graphene and potentially replace carbon nanotubes in the composite sector. Although production of this unique material is expected to double by 2016, the market segmentation is unlikely to change. The incorporation of graphene and its products in technologies and consumer goods is a relatively new and rapidly emerging area. The impact on worker safety is still surrounded with uncertainty. This presentation highlights the production, formulation, use, and disposal processes commonly used along the product life cycle; and by extension serves a beneficial tool for determining the potential exposures, hazards, and risks to occupational workers. Specifically, this talk illustrates market penetration, product families, and future trends while relating to the dose-metrics and toxicological data collected thus far. To date, manufacturers of graphene are dominated by small businesses that produce less than 10 tons per year. Those companies who manufacturer this unique material generally distribute graphene to formulators (who form mixtures and composites for specific applications) and end users (who sell finished products directly into commerce). Because of this, there is a cohort of occupational workers towards the end of the product value chain who may be exposed to multiple engineered materials (e.g. graphene and polymeric mixtures) and whose exposure conditions may vary greatly when compared to workers present in the early in the products life-cycle. Because of these reasons, more research is needed to determine the most accurate worker exposure conditions as well as material form factors that ultimately inform toxicology studies and risk assessments.

W **811** **Particle Characterization and Toxicological Evaluation of Pulmonary Exposure to Graphenes of Different Sizes**

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Manufacturing of graphenes (Gr) may increase the risk of respiratory exposure to workers. The goal of this study was to assess toxicity of three non-oxidized Gr of different sizes [20 μm lateral x 7-10 nm thick (Gr20), 5 μm lateral x 7-10 nm thick (Gr5), and <2 μm lateral x 1-2 nm thick (Gr1)] following respiratory exposure. Carbon black (CB, 15 nm diameter), was used as a particle control. Particles were characterized for surface area (SA), structure, zeta potential, surface reactivity, and agglomeration in vehicle (dispersion medium; DM). Gr samples were found to be similarly composed of two graphite structures, were not surface-reactive, and consisted of 64-72, 75-84, and 28-30 layers for Gr20, Gr5, and Gr1, respectively. Gr1 had the greatest SA followed by CB, then Gr20 and Gr5. Agglomeration in DM ranged from ~5-300 and 0.5-60 μm, for Gr20 and Gr5, respectively, and from ~0.2-5 μm for both Gr1 and CB, with no differences in zeta potential. *In vivo*, male C57BL/6J mice received 4 or 40 μg of Gr1, Gr5, or Gr20, or 40 μg of CB, or DM by pharyngeal aspiration. At 4 hr (0 d), 1d, 7d, 1m, and 2m post-exposure, pulmonary and systemic inflammation and oxidative stress, distribution, clearance, and histopathology were evaluated. Gr deposition in airways vs alveoli, and lung clearance, were size-dependent. No toxicity was observed in any of the low doses. Gr20 and Gr5 increased indices of lung inflammation and injury in lavage fluid and tissue gene expression to a greater degree and duration than Gr1 and CB. Gr5 and Gr20 also showed no to minimal lung epithelial hypertrophy and hyperplasia with resolution over time. In addition, the aorta and liver inflammatory and acute phase genes were transiently elevated in Gr5 and Gr20. When compared to similar doses of carbon nanotubes in the literature, non-oxidized Gr were less potent inducers of toxicity.

W **812** **A Five-Day Repeated Inhalation and 28-Day Post-Exposure Study of Graphene**

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Recently, graphene has received increased attention in many applications such as semiconductor, energy storage, flexible electronics, biosensors and medical imaging due to its unique electronic and chemical properties. Currently, little is known about the potential toxicity associated following an inhalation exposure. A 5-day repeated inhalation toxicity study for graphene was conducted using a nose-only inhalation system for rats. A total of three groups (20 rats per group) were compared: (1) control (ambient air), (2) low-dose (0.68 ± 0.14 mg/m^3 graphene) and (3) high-dose (3.86 ± 0.94 mg/m^3 graphene). Rats were exposed to graphene for 6 h/day for 5 days, followed by recovery for 3, 7 and 28 days. Bioaccumulation and macrophage ingestion of graphene were evaluated in the rat lungs. Exposure of graphene did not change body weight or organ weight of rats after the 5-day exposure and during the recovery period. Graphene was readily ingested by alveolar macrophages in the exposed groups. There was, however, no statistically significant difference in the level of lactate dehydrogenase, protein and albumin between the exposed groups and the control group, indicating very little lung injury following exposure. These results suggest that a 5-day repeated exposure of graphene produce a minimal toxic effect at the concentrations and time points selected in this study.

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