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TITLE: SURFACE AREA OF PARTICLE ADMINISTERED VERSUS MASS IN DETERMINING THE PULMONARY TOXICITY OF ULTRAFINE AND FINE CARBON BLACK: COMPARISON TO ULTRAFINE TITANIUM DIOXIDE

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ABSTRACT: Nanoparticles are characterized by having a high surface area per mass. Particulate surface area has been reported to play an important role in determining the biological activity of nanoparticles. However, recent reports have questioned this relationship. This study was conducted to determine whether mass of particles or surface area of particles is the more appropriate dose metric for pulmonary toxicity studies. In this study, rats were exposed by intratracheal instillation to various doses of ultrafine and fine carbon black. At 1, 7, or 42 days post-exposure, inflammatory and cytotoxic potential of each particle type was compared on both a mass dosage (mg/rat) as well as an equal surface area dosage (cm2 of particles per cm2 of alveolar epithelium). In an additional study, the pulmonary responses to instillation of ultrafine carbon black were compared to equivalent particle surface area doses of ultrafine titanium dioxide. Results Ultrafine carbon black particles caused a dose dependent but transient inflammatory and cytotoxic response. On a mass basis, these responses were significantly (65 fold) greater than those for fine sized carbon black. However, when doses were equalized based on surface area of particles given, the ultrafine carbon black particles were only slightly (non-significantly) more inflammogenic and cytotoxic compared to the fine sized carbon black. At one day post-exposure, inflammatory potencies of the ultrafine carbon black and ultrafine titanium dioxide particles were similar. However, while the pulmonary reaction to ultrafine carbon black resolved with time, the inflammatory effects of ultrafine titanium dioxide were more persistent over a 42 day post-exposure period. Conclusion These results indicate that for low toxicity low solubility materials, surface area of particles administered rather than mass burden of particles may be a more appropriate dose metric for pulmonary toxicity studies. In addition, ultrafine titanium dioxide appears to be more bioactive than ultrafine carbon black on an equivalent surface area of particles delivered basis.