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Abstract Book

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3.24. A human exposure system for nanoparticle tracking and oxidative stress biomarker assessment: Developing a novel methodology for future occupational applications

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The lungs are an excellent entry portal for gases and aerosol-transported nanoparticles (NPs) as they present a high surface area with thin epithelial barriers in addition to extensive vasculature. Inhaled NPs can affect health by direct interaction with lung cells and through transfer to other organs. Negative effects are expected from catalytically active NPs that can generate oxidative stress, which can damage cells and launch a cascade of effects, contributing to acute and chronic diseases. The aims of our current study are 1) to better understand the extent inhaled NPs translocate into the circulation and are excreted into urine and 2) the potential of these NPs to induce oxidative stress markers in the lung lining fluid, followed by an increase in such markers in circulation and urine.
We will use an open label, controlled, randomized human volunteer study. Subjects will be assigned to one of two exposure groups, each consisting of 10 healthy non-smoking volunteers. Volunteers will inhale, during 40 minute exposure durations, either biocompatible NPs that will be labeled for tracking purposes, or reactive tobacco-smoke NPs as a positive control for the oxidative stress response. Each volunteer will participate in three experiments; each at a different exposure level. Biological liquids (exhaled breath condensate, blood and urine) will be collected before, immediately after, one hour, three hours and 24 hours after the exposure. Oxidative stress markers will include hydrogen peroxide and malondialdehyde in exhaled breath condensate, blood and urine; 8-hydroxy-2'-deoxyguanosine in urine and total level of anti-oxidants in all biological liquids. To ensure detection of particles in the biological samples, the highest exposure will be at around 500 µg/m3, which is estimated to result in a deposited dose of about $3E^{11}$ particles (estimated mass: 76 µg). Preliminary study results indicate that the current exposure system set up will be suitable for generating a sufficient concentration of particles to meet detection limits in biological samples.
At the conclusion of the study, we will have evaluated the feasibility of this human exposure system for studying the translocation of inhaled NPs. We will also better understand the kinetics of the oxidative stress response from the initial deposition site to other biological fluids. The developed methodology will allow for a non-invasive evaluation of the inhaled NPs target dose. Such information is important for determining substance-oriented human health risk, particularly for occupational and pharmaceutical exposure scenarios.