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**Are physical/chemical Properties of Nanoparticles relevant
for Biological Effects?**

Can Ultrafine Particles Deposited in the Lungs Initiate Pathobiological Responses?

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Current knowledge is not sufficient to answer the question raised in the title. The outcome of a number of epidemiological and toxicological studies suggested the hypothesis that the inhalation of ultrafine ambient particles (particles smaller than 100 nm in diameter) initiates, in susceptible individuals, acute pathobiological responses of the respiratory and cardiovascular system. Properties other than the particle size (i.e. chemical or surface properties of ultrafine ambient particles) are not considered.

Ultrafine particles contribute very little to the mass concentration of ambient particles. It is therefore unlikely that their mass concentration is the appropriate dose metric associated with their suggested biological effectiveness, and responses should occur regardless of the chemical composition of the particles. On the other hand, the vast majority of ambient particles is ultrafine so that it is more likely that the appropriate dose metric is their number concentration. In other words, ultrafine ambient particles will cause biological responses because of their generic nature as particles. This working hypothesis was recently tested in this laboratory.

96 healthy rats were daily exposed for 6 hours to 20 - 30 nm particles composed of elemental carbon, elemental silver or iron oxide at concentrations of 10^6 cm^{-3} over periods up to 10 days. None of the exposures altered the alveolar-capillary permeability, the number and function of cells recovered from the lungs by lavage, and the structure of the lungs or generated proinflammatory reactions. The working hypothesis had therefore to be rejected as far as acute responses are concerned.

Nevertheless it is possible that healthy lungs are susceptible to prolonged exposures to ultrafine particles. It is also possible that compromised lungs are susceptible. When these open questions are answered it seems appropriate to simulate adsorption of chemicals on the huge surface area of ultrafine particles in the open atmosphere and to expose animals to these particles with manipulated surface properties. When pathobiological responses occur, it is necessary to establish dose-response relationships and thus identify the appropriate dose metric of ultrafine particles (number, surface area or mass) associated with

respiratory responses. And finally, a similar series of exposure studies have to be performed to look into cardiovascular and other systemic responses and to identify the appropriate dose metric associated with these responses.

Up to now, it is not plausible that ultrafine particles are able to cause pathobiological reactions. Therefore, the series of exposure experiments discussed above have to be accompanied by appropriate in vitro studies. All these in vivo and in vitro studies are required before the hypothesis that ultrafine particles have to be considered a health risk can be confirmed or rejected and before the biological mechanisms by which these particles might interact with the lungs can be identified.