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**Ultrafine Dust and Nanoparticles: Hazard Identification in vitro**

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Ambient fine and ultrafine particles (UFP) are unintentionally released into the atmosphere mainly by combustion of fossil fuel. Epidemiological studies demonstrated that increased levels of UFP (less than 100 nm in aerodynamic diameter) are associated with increased respiratory and cardiovascular mortality and morbidity. These effects were observed in particular in susceptible persons, in very young and older people and those with compromised respiratory and cardiovascular systems.

Engineered nanoparticles come into contact with biological systems not only through their use in drug delivery systems or for gene transfer. They are also produced for food and cosmetic chemistry and many other technical applications. The increasing production, particularly of metal oxide nanoparticles and new carbon materials, will enhance the possible exposure at work places, packing stations and during application of the products. In addition, waste treatment and containment at the end of a products life cycle must be considered. Because of all these reasons, it is of great interest to determine how these materials, when coming in contact with living organisms, are taken up, transported in or through cell layers, and affecting biological functions. Metal oxides are actually the most prominent produced variants of nanoparticles and new carbon modifications are the most promising ones, thus these two types are interesting with respect to their cellular uptake and possible influence on important cellular mechanisms in vitro.

Inhaled particles in the nanometer range are deposited by diffusion in all regions of the respiratory tract. From exposure to ambient particles or occupational exposure to mineral dust particles (e.g. quartz) it is known that particles are taken up by lung cells and induce local effects by oxidative injury and pulmonary inflammation. This can lead to long-term consequences such as chronic bronchitis (COPD), fibrosis and possibly to cancer. Very small particles are even able to translocate through the air/blood barrier in the lung and get access to the blood circulation and to distal organs. This, together with the release of mediators from lung target cells possibly causes the systemic effects on the cardiovascular system, which can lead to arrhythmia or myocardial infarction.

In vitro cell culture studies support the physiological response observed in animals and humans. Particles with the ability to generate reactive oxygen species due to their surface properties and/or adsorbed transition metals or organic components are most critical since induction of intracellular oxidative stress seems to be a key event of the biological effects of combustion generated particles. Intracellular oxidative stress may induce damage by disturbing the balance between oxidant and anti-oxidant processes, leading to activation of transcription factors via different signalling cascades, translocation of transcription factors into the nucleus, gene activation, synthesis of anti-oxidant enzymes and/or inflammatory mediators. Exceeding oxidative stress may also modify proteins, lipids and nucleic acids, which further stimulates the anti-oxidant defence system or even leads to cell death.

A large number of studies provided evidence that the smaller the particle size, the higher is the tendency for an increase of pulmonary toxicity, even if the same material is relatively inert in bulkier form (e.g., carbon black and TiO<sub>2</sub>).

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