An integrated cellular approach to predict the risk of nanomaterials following occupational exposure

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The areas of nanotechnology involve a wide range of applications spanning from energy, consumer products, electronic components, reconditioning, medicine, cosmetic, textiles to food. However, the growing production of these materials, called nanomaterials (NMs) and their relative potential exposure for an increasing number of workers, may pose risks in both occupational and environmental settings. At occupational level, inhalation results the primary route of NMs exposure and thus lungs become the main target organ for NMs toxicity. In this view, one of the goals of the Italian National Project focusing on Occupational Exposure of NM (NanoKEY) was to develop integrated and standardized methods (e.g., *in vitro* acellular and cellular tests) for quantifying the level of exposure to a NM by workers involved in NMs production to optimize workers protection. As exposure in manufacturing facilities occurs repeatedly over a long-time frame, the potential pulmonary toxicity of NMs should be assessed by chronic repeated studies. In this contribution, we show the results of the NanoKEY project on the suitability of a 3D lung model coupled to a nebulizer system (enables dose deposition monitoring) to simulate a chronic workplace exposure to graphene and silica NMs (the selected case studies). This was achieved by assessing biological parameters (i.e., cytotoxicity, cytokines release and cell membrane damage) that in the adverse outcome pathways (AOPs) relevant to inhalation toxicity are referred as Key Events (KEs). This approach was validated putting in correlation the effective accumulated dose on the lung tissues with the emission level of the NMs experimentally measured in the occupational facility where the selected NMs are weekly produced. This integrated *in vitro* approach, when validated by *in vivo* evidence, is expected to advance the risk management of NMs in workplaces.