

Nanotechnology in medical applications: Risk management issues for emerging technologies.

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Nanotechnology is an enabling technology which in some way will have an impact on many of the currently emerging medical technologies. The potential impact of novel nanotechnology applications on disease diagnosis, therapy, and prevention is foreseen to change health care in a fundamental way. In particular, relevant nanomedical applications are reported in surgery, cancer diagnosis and therapy, biodetection of disease markers, molecular imaging, implant technology, tissue engineering, and devices for drug, protein, and gene delivery. An increasing number of products are currently under clinical investigation and some products are already commercially available [1]. While product development is progressing rapidly, sufficient knowledge on the associated toxicological risks is still lacking. Reducing the size of structures to nanolevel may result in distinctly different properties. For medical applications utilising free nanoparticles or nanostructures, the specific toxicological properties have to be investigated [2]. Also for the toxicokinetic properties (absorption, distribution, metabolism, excretion) of nanoparticles there is an important knowledge gap. It is insufficient to rely on knowledge of the classical toxicity testing of bulk chemical(s) and materials when the risks of nanoparticles and/or nanostructures have to be assessed. RIVM has published two reports [1-2] on nanotechnology in medical applications addressing these topics and is currently carrying out further research. A study in rats has shown that gold nanoparticles exhibit an organ distribution after intravenous administration which is dependent on particle size [3]. The New & Emerging Technologies in Medical Devices Working Group of the European Commission has discussed risk management issues for medical devices utilising nanotechnology and is considering the adequacy of the existing medical devices regulatory regime to deal with these issues. The conclusion of the working group is that, in general, the medical devices directives are adequate to deal with medical devices manufactured utilising nanotechnology. However, because of the specific aspects of nanotechnology

and the existing knowledge gaps, recommendations have been formulated for implementation aspects of the directives and for regulatory guidance. A specific recommendation is the introduction of a new classification rule for products utilising free nanoparticles, to the effect that "All devices incorporating or consisting of particles, components or devices at the nanoscale are in the highest risk Class III unless they are encapsulated or bound in such a manner that they cannot be released to the patient's organs, tissues, cells or molecules". Furthermore, development of regulatory guidance, new mandates for standardization and consideration of the risks of disposal into the environment are recommended. A key starting point for any discussions regarding risks and regulations for medical technology based on nanotechnology is that there should always be a balance: patient safety should be protected without hampering innovation.

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