

## Scientific Committee on Emerging and Newly Identified Risks (SCENIHR)

### Request for a scientific opinion:

#### Guidance on the Determination of Potential Health Effects of Nanomaterials Used in Medical Devices

### BACKGROUND

Today, a more widespread application of nanotechnologies and nanomaterials is imminent or already occurring in many areas, including health care. For nanomedicine, the three largest areas of application are diagnostics, drug delivery and regenerative medicine (ETP Nanomedicine 2009). In addition there are applications in surgery and thermotherapy (Vauthier et al. 2011).

In the field of medical devices, the following cases of alleged use of nanomaterials have been identified by Notified Bodies:

- Carbon nanotubes in bone cements;
- Nanopaste hydroxyapatite powder for bone void filling;
- Polymer setting material with nanoparticles in dental cements;
- Polycrystalline nanoceramics in dental restorative materials;
- Nanosilver or other nanomaterials used as coatings on implants and catheters;
- Nanosilver used as an antibacterial agent, for example in wound dressings (see also Wijnhoven et al. 2009).

Furthermore, there are reports on iron-oxide nanoparticles injected into tumour cells to be heated-up by radiation or an external magnetic field<sup>1</sup>. This type of use has not yet been clearly attributed to the legislation on medicines or to the legislation on medical devices. On one hand, the immediate effect is mechanical as the tumour cells burst. On the other hand, one might regard the legislation on medicines applicable as the burst cells are metabolised at a later point in time.

Although the general risk assessment requirements applicable for materials used in medical devices and previous scientific opinions on risk assessment of nanomaterials (see e.g. SCENIHR 2006, 2007 and 2009) are useful when assessing nanomaterials for medical applications, there is a need for further clarification in the risk assessment of such products. Especially for medical devices there is such a need in view of the decentralised regulatory system ("New Approach"). The risk assessor, be it the manufacturer, the Notified Body or the authority, should be aware of the specific characteristics of nanomaterials in order to obtain appropriate information to be able to do the risk assessment of the application of nanomaterials in a medical technology.

The European Commission has published two proposals for a revision of the medical devices legislation: a Proposal on medical devices (COM(2012)542) and a Proposal on in vitro diagnostic medical devices (COM(2012)541). These proposals include a definition of nanomaterial taken from Commission Recommendation 2011/969/EU on the definition of

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<sup>1</sup> See as an example for the latter the product description of MagForce at: <http://www.magforce.de/english/home1.html>

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nanomaterial and provisions on the risk classification, the labelling and the instructions for use of medical devices containing nanomaterial. In addition, the general safety and performance requirements now contain a specific requirement to design and manufacture medical devices in such a way as to reduce to minimum the risks linked to the size and the properties of particles used. Special care shall be applied when devices contain or consist of nanomaterial that can be released into the patient's or user's body. The risk classification influences the stringency of the applicable conformity assessment procedure.

## **1. TERMS OF REFERENCE**

In light of the expected increase in the application of nanotechnologies to medical devices, the SCENIHR is requested to provide guidance on the risk assessment of medical devices containing nanomaterials. This guidance should enable the classification of different categories of medical devices containing nanomaterials according to their level of risk.

This guidance shall take into account different categories of medical devices such as:

- a. Non-invasive medical devices, e.g. devices coming into contact with the intact skin,
- b. Invasive devices (surgical or not), e.g.:
  - o woundcare materials,
  - o implantable medical devices,
  - o dental and bone fillings and cements,
  - o injectable nanomaterials.

In this assessment, where relevant, the SCENIHR is invited to differentiate between free, fixed, and embedded nanomaterials.

The guidance should also differentiate the cases where the nanomaterial can be released into the patient's or user's body and the cases where the nanomaterial is deliberately intended to be released into the human body.

Deadline: December 2013

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Supporting documents:

Afssaps (Agence française de sécurité sanitaire des produits de santé), Biological assessment of medical devices containing nanomaterials – Scientific Report (19.8.2011).<sup>2</sup>

ETP Nanomedicine (2009). Roadmaps in nanomedicine towards 2020. Downloadable from <http://www.etp-nanomedicine.eu/public/press-documents/publications/etpn-publications>

Mercanzini, S.T. Reddy, D. Velluto, Ph. Colin, A. Maillard, J.-C. Bensadoun, J.A. Hubbell, Ph. Renaud, Controlled release nanoparticle-embedded coatings reduce the tissue reaction to neuroprostheses, *J. Control. Release* 145 (2010) 196–202.

SCENIHR (Scientific Committee on Emerging and Newly Identified Health Risks), Risk assessment of products of nanotechnologies, 19 January 2009.

SCENIHR (Scientific Committee on Emerging and Newly-Identified Health Risks), The appropriateness of the risk assessment methodology in accordance with the Technical Guidance Documents for new and existing substances for assessing the risks of nanomaterials, 21-22 June 2007.

SCENIHR (Scientific Committee on Emerging and Newly-Identified Health Risks). The appropriateness of existing methodologies to assess the potential risks associated with engineered and adventitious products of nanotechnologies, 10 March 2006.

Skotland T, Iversen T-G, Sandvig K. New metal based nanoparticles for intravenous use: requirements for clinical success with focus on medical imaging. *Nanomedicine: Nanotechnology, Biology and Medicine* 6, 730-737, 2010

Thalhammer et al. *Biomaterials* 31, 2097-2104, 2010 The use of nanodiamond monolayer coatings to promote the formation of functional neuronal networks

Van Der Zande M, Walboomers, Brannvall M, Olalde B, Jurado MJ, Alava JI, Jansen JA. Genetic profiling of osteoblast like cells cultured on a novel bone reconstructive material consisting of poly-L-lactide, carbon nanotubes, and microhydroxyapatite in the presence of bone morphogenic protein-2. *Acta Biomater.* 6, 4352-4360, 2010.

Vauthier C, Tsapis N, Couvreur P. Nanoparticles: heating tumors to death? *Nanomedicine* 2011, 6(1): 99-109.

Wijnhoven SWP, Peijnenburg WJGM, Herberts CA, Hagens WI, Oomen AG, Heugens EHW, Roszek B, Bisschops J, Gosens I, Van de Meent D, Dekkers S, De Jong WH, Van Zijverden M, Sips AJAM, and Geertsma RE. Nano-silver - A review of available data and knowledge gaps in human and environmental risk assessment. *Nanotoxicology* 2009, 3(2): 109-138.

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<sup>2</sup> <http://www.afssaps.fr/Activites/Surveillance-du-marche-des-dispositifs-medicaux-et-dispositifs-medicaux-de-diagnostic-in-vitro-DM-DMDIV/Dispositifs-medicaux-Operations-d-evaluation-et-de-controle-du-marche/Dispositifs-medicaux-Operations-d-evaluation-et-de-controle/Evaluation-biologique-des-dispositifs-medicaux-contenant-des-nanomateriaux>