

 <p>afssaps</p> <p>Agence française de sécurité sanitaire des produits de santé DEDIM / DSM / Cellule nouveaux dispositifs / Valérie Soumet</p>	<p><b>Comments from Afssaps regarding the public consultation about a european report of SCENIHR</b></p>	Date : 08/08/2007
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**Source :** report on “Opinion of 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”, SCENHIR, 29 mars 2007.

## I. Comments :

### 1. **The questions mentioned point 3.6.1. “Methods for the characterisation of nanoparticles” p.28 :**

Comment :

*Within the remains framework of wear generated by the implanted biomaterials (articular prosthesis in particular), the origin, the concentration, the size, the shape of the particles are parameters to be taken into account, as well as the properties of surface.*

*The sampling intended for the tests must thus be representative, which can be a difficulty: for example, on the level of the calibration. The commercial particles can not correspond to the size given by the manufacturer (ex commercial particles of alumina).*

### 2. **The cytological studies mentioned p.32 permit to consider various cellular types, and systems of co-culture more representative of *in vivo* :**

Comment :

***The macrophages must be favored.*** *Certain lines of these ones are easily set going in vitro and can respond by variations of morphology, size, secretion of cytokines, and viability (apoptose). These phagocytic behaviors are worth to be compared with those of other cellular types, like fibroblasts implied in the cicatrisation phenomena, for example. The fibroblasts insource the micro and nanoparticles too and can answer by a loss of viability and/or secretion of cytokines.*

### 4. **It is important to insist on the physicochemical properties of the nanoparticles which can change during the time (p. 33-34) :**

Comment:

*The physiological environment will take part largely in the evolution of the nanoparticles which, according to their properties of surface, will adsorb serum adhesive proteins more or less. This relation surfaces/proteins with a particular conformation will play a major role in the internalisation of the particles by the cells and the activation of these ones. The surface physico-chemical properties of nanoparticles causes very different cellular reactions. In addition, these surface physico-chemical properties can support the aggregation of the particles.*

### 5. ***In vitro* studies must be developed to study the toxic effects of the nanoparticles p. 39 :**

Comment:

*It is an obviousness, but we have to take into consideration that it is difficult to implement these studies because they require many controls.*

### 6. ***In vitro* studies about the mutagenicity, genotoxicity, cancerogenicity p. 42 :**

Comment:

*Genotoxicity studies must always be supplemented by cytotoxicity studies, and tests with fibroblasts would be taken into account.*

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**II –Additional comment :**

The case of articular prosthesis seems to be a good model to study unfavourable effects of the nanoparticles. Actually, fragments (including nanoparticles) resulting from the wear of materials can cause aseptic unsealing of prosthesis.

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