**Developments in the regulatory framework for nanostructured medical devices and applications**

*Giuseppe D'Avenio*
*National Institute of Health*

Background - Nanomaterials (NMs) are becoming popular also in the domain of medical devices (MDs). The peculiar characteristics of such materials are gaining much interest in the biomedical area, in view of enhancing the biocompatibility of the medical device obtained with them. Of primary importance, their physico-chemical properties can be tuned as a function of their size. Besides the theoretical advantages, though, also the associated risks must be carefully considered.

Aim - This study is aimed at illustrating the current regulatory oversight for nanostructured medical devices, referring both to the Medical Device Directive (MDD) 93/42/EEC and to the new Regulation for MD (2017/745), which will replace the former in the forthcoming years.

Methods - The European regulatory framework was examined to consider the provided guidance for dealing with the risks associated to NMs.
Experimental activities were also carried out with different techniques (e.g., MTT, electric cell-substrate impedance sensing (ECIS), SEM), in order to evaluate the cell damage potential of some relevant NMs (ZnO, silver), already used in the fabrication of MDs

Results - The comparison of the MD Directive with the new Regulation reflects the increased concerns about safety of NMs, as used in medical devices, especially considering the implantable types, which are permanently in contact with the recipient's body. In particular the new Regulation on MDs states that MDs incorporating or consisting of NM are in class III (i.e., the highest class of risk) unless the NM is encapsulated or bound in such a manner that it cannot be released into the patient's or user's body when the device is used within its intended purpose (Rule 19).
The experimental activity at the ISS confirmed that, as it is generally agreed upon, that the ISO 10993 series must be revised in order to consider the specificity of NMs, as for biocompatibility and toxicity.
In general, the results were very sensitive to NM concentration, showing the necessity of defining a clear threshold for each NM-contact type combination.

Conclusion -The progress of nanotechnology is impacting the field of medical devices, enabling to obtain unprecedented performance. Nevertheless, as recognized by the new EU regulatory framework, many problems are still open about the biocompatibility and toxicity of NM-containing MDs, requiring both methodological improvements and extensive testing, before NMs can be used in MDs with appropriate safety margins.