WHAT NEW EU REGULATION MEANS FOR NANOMATERIALS DEVELOPMENT DEDICATED FOR MEDICAL DEVICES UTILISATION

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[ENGINEERING OF BIOMATERIALS 163 (2021) 36]

Introduction

New Medical Devices Regulation (MDR) applies from May 26, 2021 [1]. The new legal regulations point out that in the design and manufacture of medical devices, special care should be taken when using nanoparticles for which there is a high or medium potential for internal exposure. Such devices should be subject to the most stringent conformity assessment procedures.

Nanomaterials have been widely used in medicine and pharmaceuticals because of their specific mechanical, optical and electrical behaviours. They are applied for the detection of biological molecules, imaging of diseased tissues and innovative therapeutics [2].

The detailed review of defined requirements was carried out, in the aspect of research, properties, and manufacturing of biomaterials for use in medical devices, with particular emphasis on the safety of nanomaterials.

Materials and Methods

According to the definition of a medical device, the material itself may be a medical device, e.g. tissue adhesives, tissue prosthesis: vascular grafts, tissue patch, bone restoration, as well as cellular vehicles, etc. The following new aspects of regulations, having a huge impact of nanomaterials development, were analysed:

- definition of a nanomaterial, which appears in the regulations for the first time,
- special classification rule implemented for medical devices incorporating or consisting of nanomaterial,
- risks of particles which are or can be released into the patient's or user's body,
- general safety and performance requirements such as chemical, physical and biological properties,
- new standards regarding material and nanomaterial biocompatibility assessment.

Results and Discussion

Nanomaterial, in the aspect of medical devices, means "a natural, incidental or manufactured material containing particles in an unbound state or as an aggregate or as an agglomerate, and where for 50% or more of the particles in the number size distribution, one or more external dimensions is in the size range 1-100 nm". Moreover, fullerenes, graphene flakes and single-wall carbon nanotubes with one or more external dimensions below 1 nm are also deemed to be nanomaterials. [1]

Due to the risk, all devices incorporating or consisting of nanomaterial are classified as class III, IIb or IIa depending on the internal exposure potential.

Special attention shall be given to nanomaterials during medical devices design and manufacturing, in such a way as to reduce as far as possible the risks linked to the size and the properties of particles which are or can be released into the patient's or user's body, unless they come into contact with intact skin only. The risk analysis according to EN-ISO 14971:2019 standard should be done in the beginning of the medical device design process.

Devices shall be designed and manufactured in such a way as to ensure the general safety and performance requirements are fulfilled. The following biomaterial properties should be considered:

- the choice of materials and substances used in medical device, particularly as regards toxicity as well as all others biocompatibility aspects, in accordance to ISO 10993 standard;
- the compatibility between the materials and substances used with biological tissues, cells as well as body fluids, taking account of the intended purpose of the device and, absorption, distribution, metabolism and excretion where relevant;
- the impact of processes on material properties (manufacturing processes like mould injection, dipping, additive manufacturing, etc; surface engineering; cleaning, disinfection and sterilisation; etc.);
- the mechanical properties of the materials used, reflecting, where appropriate, matters such as strength, ductility, fracture resistance, wear resistance, and fatigue resistance, regarding materials after all technological processes applied in the medical device manufacturing;
- surface properties (topography, roughness, wettability etc.).

ISO/TR 10993-22:2017 standard provides a general framework and highlights important aspects which need to be considered when assessing the safety of medical devices composed of, containing and/or generating nano-objects.

For medical device's producer, the confirmation that the device meets any defined chemical and/or physical specifications is crucial and should be supported by technical data sheets delivered by biomaterial/ nanomaterial manufacturer.

Safely utilisation of medical devices with the materials and substances, including gases, with which the devices enter into contact during their intended use, should be also evaluated, especially, if the device is intended to administer medicinal products.

Devices shall be designed and manufactured in such a way as to reduce as far as possible the risks posed by substances or particles, including wear debris, degradation products and processing residues, that may be released from the device.

The risks associated with the use of the device when it comes into contact with materials, liquids, and substances, including gases, to which it is exposed during normal conditions of use, should be also taken into account.

Conclusions

There is scientific uncertainty about the risks and benefits of nanomaterials used for medical devices. In order to ensure a high level of health protection, special attention risk management process, including risk analysis should be implemented in the very beginning of nanomaterials development in the aspect of medical devices utilisation. In the light of technical and scientific progress the definition of nanomaterial can be changed. If the new nanomaterials development process is performed in accordance with all the regulation requirements, the long time to the market of medical device composed of, containing or generating nanomaterials is reduced. For new nanomaterials the more biocompatibility properties of raw material is confirmed by the material developer, the biggest commercial potential is available in the aspect of medical device market.

References

[1] Regulation (EU) 2017/745.
[2] J. Damodharan, Nanomaterials in medicine – An overview, Materials Today Proceedings, V. 37, Part 2, 2021, 383-385.