POTENTIAL STERILIZATION METHODS FOR IMPLANTABLE DEVICE FOR THERAPEUTIC DELIVERY

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Introduction

Surgical implants intended to deliver therapeutics should fulfil essential requirements, such as mechanical and chemical stability in physiological environment during treatment of a disease or during their lifespan, and then be explanted or gradually degraded. In order to guarantee proper functioning of such system, especially in the case of complex configuration or multifunctional tasks of the implant, e.g. active medical devices, besides selection of biomaterials and involved manufacturing processes, the designer should also consider potential sterilization method. Academia scientist involved in early stage development of a system delivering therapeutics often ignore possible detrimental effect of sterilization on material properties or functioning of the device. Though the sterilization by a validated method is critically needed when it comes to commercialization of the new device.

Validation of selected sterilization technique in terms of its effectiveness, reliability and reproducibility is the prerequisite the manufacturer is requested to demonstrate to the notifying authorities in order to prove microbiological safety of the new device.[1]

The manufacturer intended to distribute medical products within EU should follow regulations specified in directives of 90/385/EEC, 93/42/EEC, 98/79/EC, updated with Regulation (EU) 2017/745 of April 5th 2017, with regards to sterilization, and further, may follow the guidance provided in ISO standards. Reduction of the bioburden on and in the device to Sterility Assurance Level (SAL) 10^{-6} is required.

Materials and Methods

The theoretical approach to selection of potentially applicable sterilization methods is based on the knowledge of properties of the polymeric materials composed the device of bio-electronic implant intended for delivering therapeutics from genetically engineered cells stimulated by light, the complexity of its design and presence of sensitive components or subsystems, FIG. 1.[2] The device should be provided sterile for cells loading, therefore terminal sterilization of manufactured implant or aseptic processing of pre-sterilized components may be applied.

Results and Discussion

Approach to selection of a sterilization technique should begin on screening materials, components or systems included in the implant device. If all of these can withstand high temperature, a dry hot air (160-200°C) or moisturised air (steam, 121 or 134°C) methods may be the first choice. The methods are very reliable and easy to control. The complex shapes and inner elements are also heated, thus the device is entirely sterilized. The method is in principle restricted for thermoplastics, and unsuitable for biodegradable polymers. However, high degree of crystallinity of polymeric materials with high melting temperature may reduce potential negative effects of thermal treatment. Encompassed electronics as well as the presence of optically functional polymers – opacity may occur, eliminate thermal methods of sterilization.

As only low-temperature methods are acceptable, radiation may be considered – its reliable and relatively inexpensive. Either electron beam or gamma rays are highly penetrable and provide sterility of the entire implant, not only its surface, which is especially appropriate for complicated shapes or highly porous materials. Many polymers may be sterilized by radiation, even some biodegradable ones.[3] Nevertheless, the delivered energy may cause polymer degradation, which (if not compensated by crosslinking) reduces applicability of this method. Besides, radiation induces severe deterioration of electronics (one should note that thermal annealing may restore its operation).

Plasma - hydrogen peroxide may be considered, and applied as effective surface sterilization method. One should take under consideration rise of the temperature (40-60°C) and pressure changes during the process. Surfaces not resistant to highly oxidative environment may be altered; this may influence optical properties. In general, it can be applied to electronic systems. Yet, ISO standards have not been developed for plasma method.

The other option is the ethylene oxide sterilization, commonly utilized of polymers and combined materials. The method can be applied for optics and electronics. Beside temperature rise (30-65°C) and rapid pressure changes, a dissolution of the gas (highly toxic) in the polymeric biomaterial and possible chemical reactions with the polymer should be measured.

If the multicomponent implantable system cannot be sterilized by a single method due to incompatibility of various material and components, the common practice is to separately apply different sterilization processes for the individual material/part and assembly the device under aseptic environment (aseptic processing).

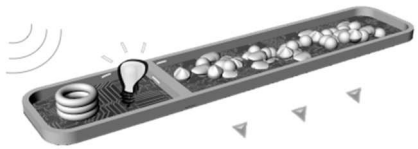

FIG. 1. Concept of wireless-powered cell-based implant for therapeutic delivery.[2]

Conclusions

The course of selection of potentially applicable sterilization methods for developed implantable bio-electronic device for therapeutics delivery was presented. Validation of these methods will be done experimentally, according to specific ISO guidance, evaluating possible alternation of physical and chemical properties of the implant, and followed by biocompatibility and functional assessment.

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References

[1] Wach R.A. et al., Wojskowa Farmacja i Medycyna, 2: 185-190, 2009.
[2] Michel F. and Folcher M., Porto Biomed. J., 2: 145-149, 2017.
[3] J. Jozwiakowska, R.A. Wach, et al., Polymer Degrad. Stab., 96, 1430-1437, 2011.