Cleanliness of Orthopaedic Implants According to ISO 19227: Differences and Gaps Compared to ISO 10993-18

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INTRODUCTION: The evaluation of the cleanliness and biological safety of an orthopaedic implant is a central part of the conformity assessment procedure for market approval. There are two documents describing the cleanliness: ISO 19227 coming from the cleaning processes development and validation and ISO 10993-18 describing the chemical characterisation of medical device materials for the biological evaluation.
In this work, we have taken a closer look at the differences and gaps with regard to the evaluation of the cleanliness of implants.

METHODS: The two standards were compared in terms of their recommendations to test implant cleanliness. Differences and gaps were reported.

RESULTS & DISCUSSION: An important difference is that ISO 19227 focusses on extractable contaminants, while in ISO 10993-18 the investigations can start with the characterization of bulk and surface properties, including leachable and extractable contaminants.
Both standards mention the importance of a risk assessment based on the analysis of the contaminants. However, a limit value of 0.5 mg/implant of total hydrocarbon and organic carbon (THC & TOC) is mentioned in ISO 19227. Although it is mentioned, that this value "can serve as a starting point for acceptance levels", this does not make sense from a toxicological evaluation point of view and could give manufacturers a false sense of security if they follow this example. For example, the threshold of toxicological concern (TTC) for carcinogenic substances, which could be released from a long-term contacting medical device (> 10 years), is 1.5 µg/day (according to ISO/TS 21726). Therefore, limit values have to be determined in a case by case risk assessment, depending on the implant type, site of implantation and exposure or based on the historical clinical performance of the device.

This brings us to the next topic that is missing in ISO 19227, the analytical evaluation threshold (AET) concept. The AET is the concentration threshold below which extractables or leachables identification is not required. Thus, the chosen analytical method requires a quantification limit that is lower than the AET. This is often not the case with THC and TOC, if used as stand-alone methods.

CONCLUSIONS: ISO 19227 is very helpful in the development and validation of a cleaning process. The proposed analytical methods TOC and THC can be potentially useful for process control of an established cleaning process. However, the list of possible test methods is not sufficiently comprehensive. Focusing on specific examples of test methods and giving suggestions on how to derive an acceptance criterion could give a false sense of security.
A general acceptance limit of 0.5 mg/implant is not appropriate, as the size, complexity, manufacturing and cleaning process of implants are diverse. Thus, limit values have to be determined in a toxicological risk assessment and are usually supplemented by the requirement that the device is visually clean.
Therefore, we suggest that the chemical characterisation of orthopaedic implants should be performed according to ISO 10993-18. Surface contamination is then considered and evaluated as part of the chemical characterisation. If necessary according to the risk mitigation plan, even small amounts of contamination should be identified and quantified. If the toxicological assessment shows that the surface contamination is problematic, the cleaning process must be improved in accordance to ISO 19227.

REFERENCES: ISO 19227:2018-03*: Implants for surgery - Cleanliness of orthopedic implants – General Requirements*. ISO 10993-18:2020-01: *Biological evaluation of medical devices – Part 18: Chemical characterization of medical device materials within a risk management process.* ISO/TS 21726:2019-02: *Biological evaluation of medical devices - Application of the threshold of toxicological concern (TTC) for assessing biocompatibility of medical device constituents.*