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Proposed regulatory scheme for personalized medical devices, including 3D-printed devices

Views expressed by Materialise NV, represented by Materialise Australia Pty Ltd

March 29, 2019

Materialise NV
Technologielaan 15
3001 Leuven, Belgium

Introduction

Materialise incorporates 29 years of 3D printing experience into a range of software solutions and 3D printing services, which together form the backbone of the 3D printing industry. Materialise's open and flexible solutions enable players in a wide variety of industries, including healthcare, automotive, aerospace, art and design, and consumer goods, to build innovative 3D printing applications that aim to make the world a better and healthier place. Headquartered in Belgium, with branches worldwide, Materialise combines the largest group of software developers in the industry with one of the largest 3D printing facilities in the world.

Specifically in the field of medical devices, Materialise offers a wide range of products and services. A first group of products includes medical device software mainly intended for 3D visualization of medical imaging data, and subsequent analysis, simulation, treatment planning and/or case handling. Output files of our medical device software can also be used for the fabrication of physical replicas of the output file using (traditional) additive manufacturing methods. Many of these products are CE-marked and have received US FDA 510(k) clearance. They are all developed within a management system that has received ISO 13485:2016 certification.

Secondly, and in part using the aforementioned software, Materialise develops personalised surgical guides for osteotomy and joint replacement surgery, which are often marketed in collaboration with third-party implant manufacturers. Health Practitioners can rely on Materialise's state-of-the-art Engineering on Anatomy expertise, upon which Materialise will design the unique surgical device that exclusively meet the needs and indications of the instructing health practitioner and the patient. These surgical guides are medical devices which, in Europe and in Australia, currently have the status of custom-made devices. A significant market for these products is the USA, where the products are regular class II devices. For certain pathologies, in the USA, Materialise offers solutions by making use of the custom-made device exemption as described on page 26 of the consultation paper.

Thirdly, Materialise offers patient-specific 3D printed titanium implants. The main applications include craniomaxillofacial plates and implants, and implants for shoulder and hip arthroplasty. Making optimal use of its technological capabilities, Materialise targets and/or is approached by surgeons for applications that are not served with conventionally manufactured mass produced implants. For example, Materialise's aMace acetabular implant system targets hip revision cases where patients suffer from severe bone loss or bone defects, and where they have typically not benefitted from conventional solutions.

Fourthly, Materialise's product offering includes instrumentation and screws as accessories to implant solutions mentioned above.

Finally, Materialise offers various types of 3D printed anatomical models, ranging from generic models for training purposes, to patient-specific models intended to assist clinicians in evaluating and planning medical interventions.

This overview serves to demonstrate that Materialise is a full medical device company, having built management systems that have been audited and certified by regulatory agencies and notified bodies to comply with regulations and legislation. Evidence of compliance with Essential Principles of safety and performance, through adherence to international standards and norms, is an integral part of these systems – as is also currently required by various regulations. Materialise strongly supports the need for regulation of medical devices, and is committed to compliance.

From our experience, we also know, however, that certain rare conditions are underserved by the medical device industry, simply because the fixed costs, of which regulatory and quality costs are a considerable part, prohibit offering a product in an economically justified way. It is crucial to the advancement of medicine and effective, personalized patient treatment, that

flexible regulatory regimes continue to exist, in which a balance is found between minimizing patient risk, and a sustainable product offering.

Materialise is pleased to be allowed to offer its opinion to the TGA consultation paper. In the following chapters, we follow the structure of the consultation paper and will respond to the different proposals.

1. Introduction of new definitions

- *Medical devices that fit the harmonized definition of custom-made, which is more detailed than the current Australian definition, will still be eligible for the exempt status, with limited regulatory oversight.*
- *The patient-matched category of devices, which currently falls under the custom-made definition in Australia, will no longer be eligible for this exemption, and instead will require third party regulatory oversight according to the device risk classification.*

We are supportive of the introduction of regulatory oversight for personalized devices. We are not fully supportive of the current definitions and distinctions made in the definitions between custom-made and patient-matched, because of the following reasons:

Established products such as high-volume 3D printed surgical guides matched to the patient anatomy, are recognized for their specificity as patient-matched, but can fit within a general regime from a regulatory point of view, in line with how such devices have been reviewed by the US FDA for example.

However, when looking at the definition of custom-made devices, we would like to argue that 'Specific Design Characteristics' ordered by a healthcare professional are typical to custom-made, and that this automatically excludes the potential characterization of a medical device as patient-matched based on a specified design envelope. In fact, we make use of single and validated processes for different jurisdictions, regardless of the categorization as custom-made, patient-matched or generic in these different jurisdictions. One could argue that there is no such thing as 'Specific Design Characteristics' that cannot be validated within a design envelope, which would *de facto* mean that the categorization of custom-made is non-existent.

At the same time, Materialise offers a truly custom-made acetabular implant to orthopedic surgeons who wish to restore mobility in patients suffering from pelvic bone defects categorized as Paprosky type 3B. These patients, who have often gone through repeated hip implant surgeries, have needs that cannot be appropriately met by alternatives on the market. The design characteristics are given by the healthcare professional through a series of interactive planning sessions in collaboration with skilled biomedical engineers. Building upon the current approach of the US FDA, the processes behind the design and production of these devices are validated just like any other device. **Therefore, these devices have attributes of both custom-made and patient-matched devices. The proposed definitions framework fails to adequately and unambiguously decide on the correct classification.**

In addition to the above, the context of the medical device development is rapidly evolving – making this determination of custom-made a continuous dynamic process.

To ensure compliance with the new definition of patient-matched, resources will have to be invested in the compilation of a technical file meeting the MDR requirements, incl. the obtaining of sufficient clinical data. The cost for the review of these files by a NB alone is roughly estimated at 10k EUR. Current labels and labeling will have to be updated according to the MDR requirements. Depending on the prioritization of internal resources, availability of third parties such as a notified body, implementation of new labeling and documentation, we anticipate that a CE-marking of the current custom-made devices might easily take 1 year. This does not yet include the ARTG listings with the Australian Therapeutic Good

Administration, after sponsor agreements are established. We strongly believe that these additional measures will significantly increase the business risks for SME, whereby the increased costs only impose higher business risks. The devices are currently classified as custom-made and function well, additional controls and business costs will not necessarily increase the safety and effectiveness of the devices, but increase the costs in a possibly uncontrolled way, leading to the possibility that certain devices will no longer be offered in certain jurisdictions despite the lack of safety/effectiveness concerns, which is a less favorable outcome than before this regulatory change.

1.b. Change in the requirements for supplying custom-made medical devices

*It is **proposed to change the regulatory requirements for custom-made devices** to require:*

- *that the manufacturer's statement about a custom-made device is provided to the patient receiving the device*
- *that the TGA be allowed to enter and inspect custom-made device manufacturing sites, in accordance with the authority it has to inspect all other medical device manufacturers*
- *that a manufacturer in Australia, or a sponsor of an overseas-manufactured custom-made device, provides an annual report to the TGA of the custom-made devices it has supplied, and*
- *that documentation about an implantable custom-made device is retained for a minimum period of fifteen (15) years; as the current specification of a five (5)-year retention period is considered inadequate.*

Materialise does not have any significant concerns with the changed requirements, imposed on the new class of patient-matched medical devices. We believe the cost and effort of implementation of these additional requirements for custom-made devices are minimal: our Process Engineering System is set-up to have documents shipped with the devices; a small procedure change is needed for government inspections for custom-made devices, we already provide the TGA with annual reports for our procedure packs, and we are compliant with the documentation retention requirements of 15 years for other jurisdictions.

1.c MDPS requirements for lower risk without need to have a manufacturing certification

MDPSs, like other systems, would be considered to be medical devices and would be included in the ARTG. They would be classified and assessed according to the device they are intended to produce. The production equipment and consumable raw materials used in a MDPS would not be considered to be medical devices on their own, unless they fit the definition of medical device in their own right.

Healthcare providers or healthcare facilities that use MDPSs to produce medical devices for treating their patients would not be considered as manufacturers under the regulatory framework in relation to those systems. This means healthcare providers would not need conformity assessment certification for manufacturing with a MDPS.

Materialise is supportive of the introduction of a concept of a medical device production system, and the inclusion of these systems in the ARTG. We are, however, not supportive of the lack of regulatory oversight for healthcare providers or healthcare facilities that use MDPS.

We are missing a rationale on why the MDPS in health institutions would be exempted from any manufacturer assessment certification. Most hospitals are not equipped with the necessary skills, machines, processes or quality systems to safely and effectively design, develop, produce, post-process and inspect medical devices.

In reality, we believe there will not be an increased clinical expertise in Point of Care hospital labs – but these labs will rather operate with technical operators relying on engineering expertise. This will make them no different from medical device companies, making it hard to understand a difference in treatment by the regulator. In addition, due to this competitive advantage, it is likely that these 3D Printing labs will start operating in a more entrepreneurial manner, increasing the unfair competition with the industry. We suggest that the use of MDPS by health institutions should be limited to non-industrial scales to avoid this.

The actual production of a medical device only represent a small fraction of the total work required in the whole cycle (for example, but not limited hereto: personnel training, imaging protocols, software selection, printing selection, material selection, quality controls, etc.). Contrary to a medical device company, these institutions will have no oversight from any third party. Who will ensure the safety and effectiveness of these devices the moment they come out of the MDPS? The consultation paper refers to the objectives and benefits of the proposed regulatory changes. We believe that the current set-up for the MDPS is not in line with the objective of minimizing public health and safety risks, nor is it maintaining any level of consumer confidence in the regulation of medical devices. The aim to minimize 'unnecessary' regulatory burden is wrongly applied here, as the need to have regulatory oversight is very much needed.

As will be outlined in the next section 1.d, as a manufacturer, Materialise would certainly reconsider whether it wishes to offer anatomical models. Nevertheless, such models have become a requirement to many practitioners. This will have as a consequence that health practitioners may start printing themselves in a hospital setting. As mentioned in the paper, such practitioners would not be held to conformity assessments if they used a medical device production system and this system was included in the ARTG.

1.d. update the classification rule for MD that record diagnostic images so that it includes any device for this purpose and not just X-Rays, for example 3D Printed anatomical models.

> *A medical device that is intended by the manufacturer to be used to record diagnostic images is classified as Class IIa. This includes software and anatomical models intended for diagnosis or investigation of the anatomy.*

Materialise would like to seek additional input on this proposed change. On the one hand, the text is referring to medical device that are recording patient images for diagnosis, whereas it also talks about imaging records for investigation of the anatomy.

Our software does not record any images, but rather processes images by allowing segmentation and transferring existing DICOM images to a 3D model. Our software will never diagnose nor is it intended to diagnose. Output files can be used for diagnostic purposes, but this would fall outside of the scope of the software as other factors such as the materials and choice of printers are impacting factors.

In our experience, anatomical models are not used for diagnosis (diagnosis is usually already made), but are used to evaluate treatment options or to evaluate decisions related to treatments. Next to that, they are used in a non-therapeutic setting, e.g. as a communication tool to patients to inform them about planned interventions, or among clinical team members.

We offer anatomical models specifically intended to provide supplementary information to cardiologic interventionists in selection the stent size for trans-catheter cardiac valve

replacements, i.e. not as a decision tool but as an additional pointer. While, evidently, the risk related to such a model is higher, it is burdensome to apply *all* requirements applicable to any other mass-produced class IIa device to this line of products. Specifically, as the volume of this type of models is very low, costs related to full documentation, clinical evaluation and post-market surveillance, are not commensurate with the risk represented by the device. In addition, these kind of devices could be printed by hospitals as part of their Medical Device Production System, without the necessary conformity assessments, which results in unfair competition.

It is unclear to us what the basis is for the up-classification of medical devices that record diagnostic images. We could anticipate on reasons why software intended to process images to allow diagnostic use or therapeutic use, can be seen as a class IIa device. With the current proposal, it appears that the underlying media, imaging information in itself (including all derived forms such as onscreen models, printed models, etc.) are also considered a class IIa, whereas we don't believe that these represent any patient risk in itself.