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Proposed regulatory changes related to personalised and 3D printed medical devices

Views expressed by Materialise

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1 Introduction

Materialise incorporates 27 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 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 hip implant system targets hip implant 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.

2 Proposal 1: New definitions for personalised devices

As explained in the introduction, Materialise welcomes that considerations are made for devices intended to treat rare patient conditions or anatomy where there is no commercially available alternative.

However, we are concerned about the correct selection of the elements to distinguish custom-made from other types of medical devices.

Specifically, we believe that the following elements may not be always capable of fully distinguishing:

- "specific design characteristics", a criterion for custom-made devices, is not further defined. It seems to be positioned opposite the concept of "a medical based on a standard device template model that is matched to a patient's anatomy". In our experience, however, we believe that both types start from a common concept and design in which at least maximum and minimum dimensions, as well as key characteristics (e.g., flanges on an acetabular cup implant) are defined as a design envelope on which worst-case validation can take place.
- "A production process that is capable of being validated" is in our opinion not a criterion that exclusively fits "patient-specific medical devices"; in our experience,
  Processes and systems have been established and validated to realize unique and case-specific design and production. The complementary interaction between the clinical practitioner and the Materialise clinical engineer is of utmost importance to come to a tailored solution/approach for that individual patient. By defining the extremes, a continuum within which Clinical Engineers, doctors, technicians interact to come to a solution within validated specifications.
- It is also possible to have custom-made on prescription of a health care professional while still working a routine, commercial scale. In fact, in line with the above, a routine, validated process approach offers better guarantees towards the safety and effectiveness of custom-made devices.
- The use of the criteria: 'availability of a viable commercial alternative' without any further explanation of the limitations in assessing this allows every unique or maybe irrelevant feature to the patient to be used as a reason for differentiation.

In short, these elements create, in our opinion, an artificial distinction between custom-made and patient-specific.

Consideration should be given to medical devices from foreign manufacturers that are considered custom made in European regulations and thus are not included in the CE certification scope, and that now will have to follow a risk-based regulatory framework with third party oversight. Under the MDD 93/42, custom-made devices are excluded from CE marking.

As mentioned in the introduction, we believe that also in the market of joint-replacing implants, several conditions are not served by commercially viable (standard) product lines. Excluding these groups of conditions ex ante seems to make it prohibitively difficult to offer good solutions. This is in contrast to our experience in Europe, where Materialise has, over the course of several years, been able to change the lives of more than 500 patients and their relatives with a unique and truly custom acetabular hip cup implant solution. This has been

possible thanks to the MDD framework of custom-made devices, which we apply in an open communication with the competent authority and with a voluntarily ISO 13485 certified quality management system. With a system in place to monitor post-market experience and thorough documentation of all aspects of the lifecycle of these devices, we believe the risks and benefits of this solution are in balance.

This brings us then to the question whether the number of devices per manufacture per year should be limited. We believe that any specified number would be a rather arbitrary limit, as is also indeed the case in the USA. For some conditions, it may indeed be the case that there are 5 or less devices per year that a/any manufacturer would ever supply. For others, the demand not served sufficiently by commercially available alternatives may be a multiple of 5. We believe that there would be more value in a qualitative distinction and decision, whether a device would be considered a custom-made or a patient-specific device.

Finally, we would like to note that in the proposed definition of *medical device production system*, reference is made to products including raw materials that are intended to be used by a health care practitioner to produce a finished medical device. While the consultation paper elaborates on this in Proposal 3, we submit that, while health care practitioners are included in the design and customization process, production mostly takes place at a medical device manufacturer rather than a health care practitioner.

In conclusion, Materialise fully recognizes that regulatory regimes should not be used to engineer artificial escape routes to avoid regulatory oversight, and acknowledges that the current lack of effective oversight for high-risk devices is to be tackled. However, we don't believe that the proposed definitions create an adequate differentiation between devices which are not mass produced medical devices. A distinction that is more based on qualitative aspects (such as the Quality System Certifications of the medical device company involved) as well as considerations of market access to underserved conditions, would seem more appropriate.

3 Proposal 2: Changes to the custom made conformity assessment procedure

Materialise believes that the proposal as described will add meaningful tools for regulatory oversight on custom made devices. We do not believe the proposed changes would create unnecessary burdens.

The questions that currently seems unanswered, are

- to what standard the TGA would inspect custom made device manufacturing sites (if different from ISO 13485), and would the inspection by QMS-focused or also reviewing compliance with essential principles; and
- to what extent the TGA would control devices manufactured overseas.

4 Proposal 3: Changes to the definition of manufacturer

As Materialise is a medical devices manufacturer, the ideas expressed in proposal 3 don't significantly affect our position.

Generally speaking, Materialise endorses and supports hospitals that take action to advance medical science by making devices more patient-specific, from a general point of view. Materialise counts numerous academic and general hospitals as its customers and offers a broad range of software and consultancy services to hospitals. As an example that has been

internationally published, Materialise cooperated with the University of Michigan in the planning of the treatment of tracheobronchomalacia in an infant, where the patient received a life-saving bioresorbable custom-made tracheal splint. That being said, most hospitals are not equipped with the necessary skills, machines, processes or quality systems to safely and effectively design, develop and produce implants. If hospitals would wish to produce high-risk devices such as non-mass produced joint-replacing implants, we believe the same standards should apply to the hospital as to any other manufacturer of such devices. This is also the line followed in the new European MDR, which provides an exemption regime to health care institutions, but imposes very strict conditions for applying this exemption regime.Proposal 4: New classification for anatomical models and digital 3D print files

Materialise offers both the software needed to create virtual and printed anatomical models, as well as printed models at the request of medical practitioners.

While we believe the classification rule should indeed be updated, we are unsure about the practical consequences. For example, as a part of surgical guide product, an anatomical bone model representing the anatomy of the patient for which the patient-specific guides are produced, may be added, with the sole purpose of checking the fit of the guide. While this is, strictly speaking, part of the surgical planning, the risk related to that model at that stage is negligible from the point of view of the manufacturer. In fact, the biggest issue would likely be that the model is brought into the surgery room without proper sterilization, which is something beyond control of the model manufacturer.

At the other side of the spectrum, 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.

As a manufacturer, Materialise would certainly reconsider whether it wishes to offer such models. 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.

We believe this will be very hard to enforce and hospitals will continue to print models themselves, leading to suboptimal results. Also, considering the definition of a medical device production system, the proposal would effectively require that such systems, in which software, printer and raw materials typically originate from different parties, would be offered as one product and included in the ARTG, which, as far as we know, is not currently available as such.

This area is one where the proper use of the “custom-made” concept would be more helpful in our opinion. The provision of custom-made models for therapeutic or planning purposes is not a large business and doesn’t generate the type of revenues that allows manufacturers to bear the regulatory burden as proposed in the paper.

5 Proposal 5

No comments

6 General comments

Generalization of additive manufactured custom-made medical device classification for an international perspective should also consider the intended use, risk, and classification of the medical device. While the intended use of a device may be consistent anywhere it is used, the classification and the regulatory requirements vary to place a product on the market. As such, products may be placed on the market in some countries and not placed on the market in other countries due to local regulatory restrictions. In these cases, custom-made classification may be the best option to bring the product to these burdensome markets to be able to treat rare and unique cases while the long process of regulatory approvals are obtained but these devices are considered safe, effective, and mass produced for other markets.

It is also noted that Appendix 3, the international perspective information is incorrect for Japan. For many years, PMDA has approved 3D printed patient specific medical devices for Materialise products.

7 Conclusions

Generalization of handling additive manufactured custom made medical devices is not appropriate if it drives manufacturers to stop placing devices on the market and instead drive the manufacture of these devices by hospitals, which would be expected for the printing of anatomical models. Placing undue burden on manufacturers (driving up costs of manufacturing these devices) while hospitals can make them cheaper due to the lack of regulatory costs when additive manufacturing printers are becoming less expensive and easier to obtain by individual medical professionals.

Careful consideration should be made to the components of additive manufacture of medical devices in hospitals, in such a way that printers and resins become medical devices.