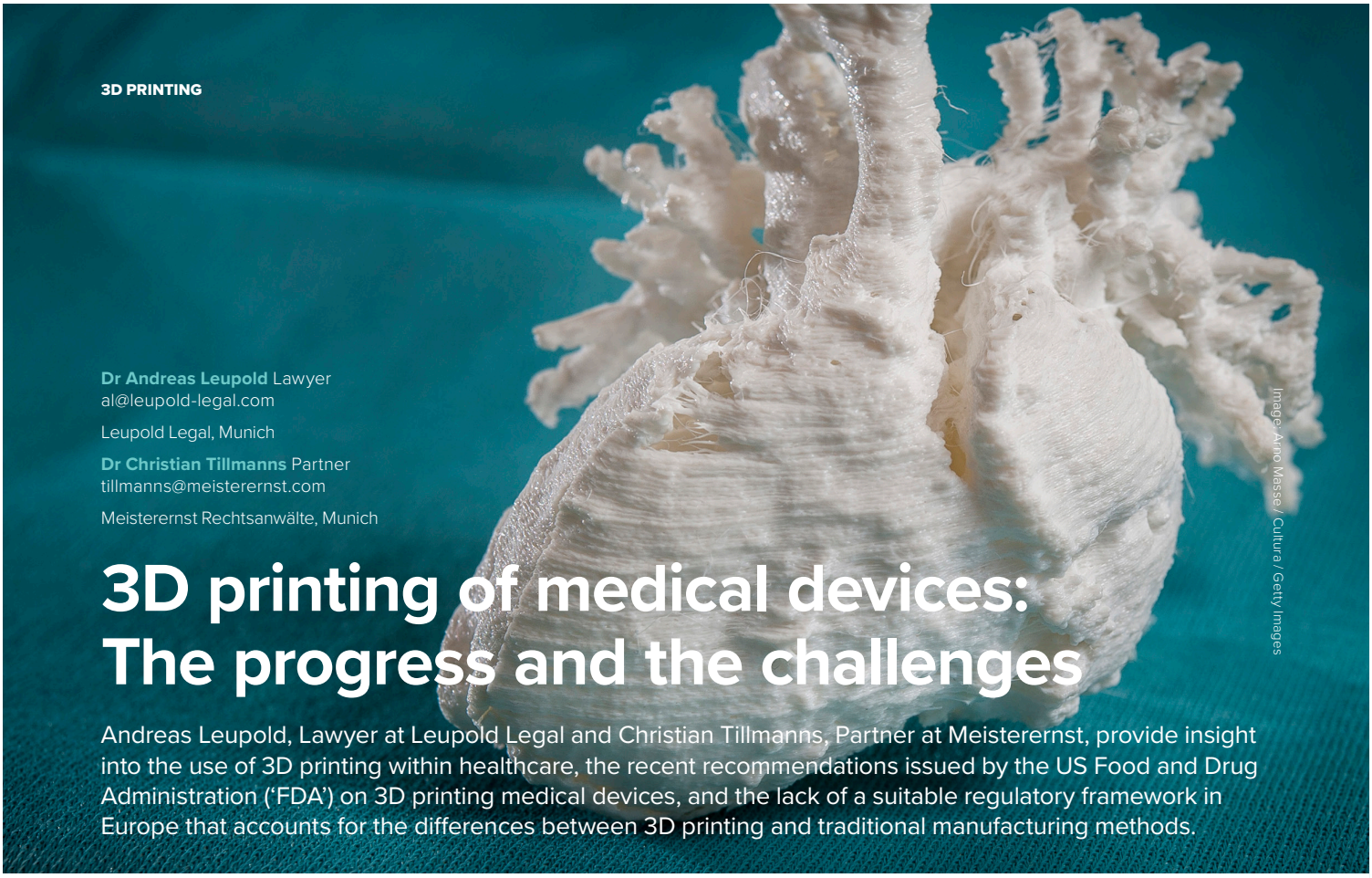

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# 3D printing of medical devices: The progress and the challenges

Andreas Leupold, Lawyer at Leupold Legal and Christian Tillmanns, Partner at Meisterernst, provide insight into the use of 3D printing within healthcare, the recent recommendations issued by the US Food and Drug Administration ('FDA') on 3D printing medical devices, and the lack of a suitable regulatory framework in Europe that accounts for the differences between 3D printing and traditional manufacturing methods.

3D printing service providers have seen it coming: The market for 3D printed prostheses and anatomic models is growing exponentially, and the healthcare sector is becoming one of the core drivers of 3D printing. Materialise, one of the largest suppliers of 3D printing software and 3D printing service providers, already supports the treatment of over 50,000 patients with 50,000 individual solutions every year. Manufacturers of industrial 3D printers such as eos[1] and 3D Systems[2] are stressing the many advantages of implants that were made with their next generation machines for patients, surgeons and hospitals. Stratasys[3] is offering multi-material 3D printing systems for manufacturing lifelike 3D models of human organs that can be used for training surgeons and which enable better preparation for operations than conventional clinical training. It is of no surprise to insiders, but the sheer speed of innovations in this field is sometimes staggering and medical applications that seemed impossible a few years ago may now become a reality in the near future.

## Medical devices: The rise of 3D printing

3D printing is different from any other manufacturing process as it relies on building the desired product layer by layer with a 3D printer without the need for conventional tools, which is why it is also referred to as 'additive manufacturing[4].' According to the latest research[5], 3D printing has not only revolutionised dentistry, craniomaxillofacial surgery[6], hearing aids and orthopedics, but has contributed significantly to the overall growth of the market for 3D printing applications and will reach $6 billion by 2027. While most hearing aids are already manufactured with 3D printers, there are plenty of other innovations that exceed even the most optimistic expectations of industry experts. If you think that 3D printing inside your body may be the stuff of your favourite science fiction TV show only, well think again. Researchers at the École Polytechnique Fédérale of Lausanne, Switzerland have just presented a new technique that will allow endoscopic in-body microprinting by means of ultra-thin fibers[7]. No less impressive is the progress in bioprinting functional human tissue: Scientists at Imperial College London have created a new process for 3D printing soft tissues that may eventually be used for printing organs from patient's own cells without the usual rejection of organs from donors[8].

These and other innovations may offer new treatment options and some of them may save lives some day, but they also raise specific issues that need to be addressed in future legislation that cannot be accommodated under the current regulatory framework. In the US, the FDA has just begun to address some of the unique characteristics of additive manufacturing processes that need to be mastered before one can apply them in practice.

## Technical guidance for 3D printing medical devices in the United States

In December 2017, the FDA published its 'Technical Considerations for Additive Manufactured Medical Devices[9].' As the FDA stresses in the introduction, this paper does not contain any binding rules and leaves room for managing 3D printing processes with alternative approaches, as long as they meet the requirements of the applicable statutes and regulations. This limitation, however, does not diminish the usefulness of the technical considerations as a practical guide that provides sound advice on how to tackle quality control for 3D printed medical devices. In a first step, the FDA discusses the differences of 3D printing versus traditional manufacturing methods and addresses the need to consider a variety of build parameters and document the manufacturing tolerances of 3D printers.

## 3D printing in the operating theatre: Exposure to product liability

The FDA then correctly points out that 3D printing is uniquely suited for patient matched designs ('PMD'). Such PMDs pose particular medical and legal challenges as they can be

modified by the device manufacturer or clinical staff to account for clinical findings. While the FDA does not address the legal issues arising from such modifications, hospitals and attending physicians will need to become aware of the fact that this may expose them to additional significant liability towards their patients that must be addressed to avoid grave consequences. This is especially true for point-of-care device manufacturing in operating theatres, orthopedic and dental practices, where doctors can become manufacturers by using 3D printers to build or modify medical devices.

### 3D printing of medical devices: Privacy pitfalls

The FDA also acknowledges the fact that many additive manufactured ('AM') devices incorporate medical imaging data that contain personally identifiable information ('PII') and protected health information ('PHI') that must be managed properly, and the segregation of personal patient data from other patients' data must be ensured at all times. The questions arising from using PII in 3D printing medical devices not only requires close scrutiny under the HIPAA privacy rules[10] in the US, but also under the forthcoming EU General Data Protection Regulation ('GDPR'). The GDPR will become especially important as significant fines for failure to handle data protection correctly will then be part of the law all over Europe.

### Failure to consider 3D printing parameters can result in liability for defective medical devices

Another potential pitfall arises from the need to convert the original 3D model created with computer aided design (CAD) software to different file formats during the printing process as any such conversion can affect the final device and component properties because of changes to product dimensions and/or geometry[11]. Unlike other manufacturing methods, 3D printing also requires the devicemaker to think about the proper placement, orientation and maximum number of devices that are printed simultaneously in the same 3D printer, as these factors impact the quality of the final product[12]. Failure to control these parameters that can vary between machines from the same manufacturer under seemingly identical environmental conditions[13], and the lack of proper process validation may result in contractual liability for defects in the final product as well as tort liability for damages such defects cause to a patient's body. The same holds true for the proper removal of support material, selection of the proper layer thickness, build paths and proper calibration of all machine parameters. These factors are interdependent and must therefore be viewed in an integrated way.

### Predictive maintenance: The need for new agreements

Predictive maintenance that enables device manufacturers to foresee and prevent product defects that are caused by the wear and tear of certain parts of the 3D printer can significantly reduce the risk of defective medical products. Hospitals and medical device manufacturers must be aware of the fact that replacing machine parts before they become prone to affecting the quality of a medical device requires a new type of contractual agreement that grants the providers of maintenance services access to the 3D printers used by their customers, as well as the right to collect and analyse the manufacturing data from such devices. Data access and data ownership are becoming essential requirements for 3D printing medical devices but are still largely neglected in agreements between manufacturers/distributors of 3D printers for medical applications and their customers. This means that existing contracts must be examined to ensure that they validly allow for predictive maintenance and access to the machine data that is therefore needed.

### Exoneration from product liability starts here: Inspection and documentation of materials and 3D printing processes

As in traditional manufacturing processes, suppliers of medical devices that avail themselves of 3D printing techniques must pay attention to the raw materials they are using and ensure that the quality is consistent[14]. To avoid undesirable difficulties of proving the true cause of a material defect in a medical device that has been manufactured additively, the FDA recommends thorough inspection and documentation of the specifications of all incoming materials, their provenance and purity[15]. The reason why this is so important lies in the fact that the material properties are shaped by the 3D printing technique chosen and can hence differ significantly from the original specifications. Consequently, it can be very difficult to establish cause and effect and the liability for defects in the final medical device if the properties of the starting materials have not been recorded. If remains of the printing material are reused, the manufacturer should in their own best interest be able to prove or, as the FDA puts it, at least 'provide a rationale' that this does not affect the quality of the final device. The documentation should also comprise a description of the post-processing techniques used, as well as possible detrimental effects they may have on the final product and a description of the measures taken to mitigate them[16]. Since 3D printing processes often require the use of support structures to prevent the medical device from becoming unstable during the manufacturing process, it must also be ensured that any residue of support material is removed during post-processing to a degree that it does not adversely affect the quality and safety of the final device[17].

Finally, the FDA points out that medical devices that have been manufactured additively can be checked for pre-market submission by means of destructive testing ('DT') or non-destructive testing ('NDT') e.g. by computer tomography or hyperspectral imaging[18]. In either case, the test and acceptance criteria must be established, and the testing process as well as all manufacturing process parameters must be thoroughly documented.

### The current situation in Europe

There is currently no official guidance on 3D printing medical devices in Europe that can be compared to the that published by the FDA in the US. This may be because medical devices are not subject to any formal approval procedures in the EU. Although manufacturers of medical devices must pass a conformity assessment procedure they are ultimately responsible for ensuring the compliance of their products according to regulatory requirements. Against this background, it is unfortunate that 3D printing is neither specifically addressed in the current Medical Devices regulatory framework ('MDD[19],' 'IVDD[20]' and 'AIMDD[21]') nor in the upcoming Medical Device Regulation ('MDR'). This leads to questions of interpretation of the new provisions that have a significant impact on the regulatory requirements with regard to 3D printing of medical devices as part of patient care[22].

### Pre- and post-marketing requirements: Status of the products, standard medical devices vs. 'custom-made devices' and/or 'hospital produced devices'

Relating safety aspects of using 3D printing technology, one of the key questions is whether 3D printed medical devices for the individual patient need to be qualified

continued

as 'custom-made' medical devices or not. If they can be qualified as 'custom-made' or 'hospital produced devices' 3D printing enjoys regulatory benefits in comparison to standard medical devices.

## The European legal regime for medical devices

The 3D printer, solely as a production tool[23], and the design software (if it is not intended to be used e.g. for preoperative or surgical planning) cannot be qualified as medical devices[24] under the current MDD[25], and unique patient-specific 3D printed devices are not qualified as mass produced but as custom-made devices in the sense of Art. 1 2. (d) MDD[26]. Having in mind 'traditional' custom-made devices such as orthopaedic shoes, the European legislator decided that custom-made devices do not have to fulfill the normal quality system requirements, they do not require the involvement of a notified body in the conformity assessment procedure, and no specific quality management system requirements apply to them. The only requirements are the manufacturer's diligence and declaration of conformity, the prescription by a qualified person and the *ex post* controls performed by competent authorities. With regard to the repeatability and standardisation of 3D printing devices and in the light of the protection purpose of the MDD, the question is raised as to whether these circumstances may eventually merit 3D printing of medical devices as the 'normal' production of devices with a high degree of customisation included in the production process, rather than the production of custom-made devices[27]. In the latter case the same regulatory burden would apply to 3D printed devices as for 'normal' devices.

## New definition of 'custom-made' devices in the Medical Device Regulation

From May 2020 the new EU Medical Device Regulation[28] will be applicable. Due to Art. 2 (3) MDR, a custom-made device is: 'any device specifically made in accordance with a written prescription of any person authorised by national law by virtue of that person's professional qualifications which gives, under that person's responsibility, specific design characteristics, and is intended for the sole use of a particular patient exclusively to meet their individual conditions and needs.' But there is one important exclusion criteria: 'However, mass produced devices which need to be adapted to meet the specific requirements of any professional user and devices which are mass produced by means of industrial manufacturing processes in accordance with the written prescriptions of any authorised person shall not be considered to be custom-made devices.'

As a consequence, the 'industrial' mass production of 3D printed devices will not be qualified as 'custom-made,' even if the devices are prescribed for specific patients. The manufacturer of such products - like manufacturers of 'normal' devices - will need to prepare full technical documentation and establish a quality management system that is appropriate with regard to the risk class of the 3D printed device. The key question in future will be, under which conditions a prescribed device with patient-specific parametrisation is mass produced by means of an 'industrial manufacturing process.'

## Exemption of 'in house'/ hospital produced devices

According to Art. 5, Sec. 5 MDR under certain conditions the (regulatory) requirements of MDR shall also not apply to devices manufactured and used

Andreas Leupold is co-author of a book on 3D printing: Leupold/Glossner, 3D Printing: Recht, Wirtschaft & Technik des industriellen 3D-Drucks: C.H.Beck Publishing House.

1. https://cdn0.scrvt.com/eos/public/66918c41e39c1b11/d05335391d6a4957d64dc29be4905963/medizinbroschuere.pdf (in German).
2. https://www.3dsystems.com/sites/default/files/2017-06/MM-504%20Rev%20A_Medical%20Device%20Design%20%26%20Manufacturing%20Brochure_WEB.pdf
3. http://www.stratasys.com/de/industrien/medical/clinical-training-models
4. While 3D printing is just one form of additive manufacturing, both terms are used interchangeably. See 3D Printing, Leupold/Glossner.
5. See 'The Future of 3D Printing for Medical & Pharmaceuticals to 2027' at https://www.smithersrapra.com/market-reports/medical-industry-market-reports/the-future-of-3d-printing-for-medical-pharmaceutic
6. The same holds true for craniomaxillofacial surgery, see http://www.materialise.com/en/resources/webinar-recording/revolutionizing-CMF-surgery-3D-printingand https://www.concept-laser.de/contact_usa/3d-metal-printing-improves-craniomaxillofacial-surgery/
7. https://www.osapublishing.org/DirectPDFAccess/03DACDBF-B872-4A40-8CC4EF75EC5273B8_380852/oe-26-2-1766.pdf?da=1&id=380852&seq=0&mobile=no
8. https://www.nature.com/articles/s41598-017-16668-9. For a non-exhaustive list of what can be 3D printed in medicine and healthcare today, see http://medicalfuturist.com/3d-printing-in-medicine-and-healthcare/
9. Technical Considerations for Additive Manufactured Medical Devices - Guidance for Industry and Food and Drug Administration Staff, Document issued on 5 December 2017, https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM499809.pdf. In 2015, the FDA approved Spritam, the first 3D printed drug for oral use as a prescription adjunctive therapy in the treatment of partial onset seizures, myoclonic seizures and primary generalised tonic-clonic seizures in adults and children with epilepsy, see https://www.aprecia.com/pdf/2015_08_03_Spritam_FDA_Approval_Press_Release.pdf
10. For a simplified collection of all HIPAA rules edited by the U.S. Department of Health and Human Services Office for Civil Rights see https://www.hhs.gov/sites/default/files/ocr/privacy/hipaa/administrative/combined/hipaa-simplification-201303.pdf
11. FDA Technical Considerations (footnote 4), p.11.
12. Ibid.
13. FDA Technical Considerations (footnote 4), p.18.
14. FDA Technical Considerations (footnote 4), p.15.
15. FDA Technical Considerations (footnote 4), p.16, 24.
16. FDA Technical Considerations (footnote 4), p.17.
17. FDA Technical Considerations (footnote 4), p.26.
18. Hyperspectral imaging uses a much broader spectrum of light than is visible and detects 'fingerprints' in the electromagnetic spectrum that are unique to the material used. For an informative introduction to hyperspectral imaging and its advantages and disadvantages, see http://www.microimages.com/documentation/Tutorials/hyprspec.pdf
19. Council Directive 93/42/EEC of 14 June 1993 concerning medical devices (OJ L 169, 12.7.1993, p. 1).
20. Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on in vitro diagnostic medical devices OJ L 331 of 7 December 1998.
21. Council Directive of 20 June 1990 on the approximation of the laws of the Member States relating to active implantable medical devices (90/385/EEC), (OJ L 189, 20.7.1990, p. 17).
22. Liability, data protection and traceability issues will not be discussed in this article.
23. The relevant quality and safety requirements regarding the 3D printer are set out in Directive 2006/42/EC of the European Parliament and of the Council of 17 May 2006 on Machinery and amending Directive 95/16 EC.
24. See also: Vinck Imgard, Vijverman An, Vollebregt Erik, Broeckx Nils, Wouters Karlien, Piët Mariel, Bacic Natalija, Vlayen Joan, Thiry Nancy, Neyt Mattias, KCE Reports 297: 'Responsible use of high-risk medical devices: the example of 3D printed medical devices,' https://kce.fgov.be/en/responsible-use-of-high-risk-medical-devices-the-example-of-3d-printed-medical-devices, p. 45 -52.
25. Regarding 3D printed medical devices that are identical to conventionally produced devices the same CE marking and conformity assessment requirements related to the risk class of the traditionally produced device are applicable.
26. See also KCE Reports 297, footnote 6, p. 51 ff.
27. See also KCE Reports 297, footnote 6, p. 55.
28. Regulation (EU) 2017/745 of the Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC.

only within health institutions (such as hospitals). Again such a qualification would enable health institutions to access a less constricting regulatory framework with regard to manufacturing and using 3D printed devices. But to enjoy these regulatory privileges there are valid restrictions that have to been fulfilled: among other things, the device cannot be transferred to another legal entity, an appropriate quality management system must be established and the health institution must justify in its documentation that the targeted patient group's specific needs cannot be met or be met at the appropriate level of performance by an equivalent device available on the market (supply gap). Again there are reasonable doubts as to whether this regulatory path will be the ideal solution for establishing 3D printed device treatment in health institutions, because according to Art. 5 Sec. 5 MDR, 'this paragraph shall not apply to devices that are manufactured on an industrial scale.'

### Summary and outlook

Due to Recital 1 of the new MDR, this new Regulation aims among other things at establishing a robust, transparent, predictable and sustainable regulatory framework for medical devices which ensures a high level of safety and health 'whilst supporting innovation.' Therefore, it would have been helpful if the EU legislator had provided specific provisions on the legal qualification of 3D printed devices and on the responsibility of individual and/or legal persons involved in producing and using these devices in the treatment of the patient.

As outlined above, there are still significant uncertainties regarding important regulatory questions that could hinder the future development and application of innovative and helpful 3D printing technologies in patient treatment. It now remains to be seen at a national level how the responsible authorities will interpret the relevant provisions (manufacturing 'at an industrial scale,' 'mass produced by means of industrial manufacturing processes') and if health institutions are willing and able to establish the necessary regulatory setup to offer patients these new and innovative treatment options. The first signs that the latter is the case can be seen in developments in Germany where a number of hospitals are offering 3D printed knee joints and are becoming increasingly interested in this promising technology for other applications.





## Cyber attack hits Norwegian health services

Sykehuspartner, the parent company of Health South East RHF, a healthcare organisation that manages hospitals in the South-East region of Norway, announced on the 15 January 2018 that it had been subject to a cyber attack on 8 January 2018. At the time of publication, the Police Security Service ('PST'), who are investigating the attack, have not determined the extent of the attack or the damage caused with any certainty. Sykehuspartner has stated that "it is a very serious situation," but so far there is no evidence to suggest that the cyber attack has had direct consequences for patient treatment, patient safety or patient data, but such outcomes cannot be excluded.

"Not many details are clear at this point other than that the PST started their investigation on 14 January," said Arve Føyen, Partner at Advokatfirmaet Føyen Torkildsen AS. "They suspect that the attack was orchestrated by a foreign state and it is being regarded as a potential violation of Section 121 of the Penal Code as espionage directed at state secrets. So far, the response of the affected healthcare services seems to be adequate, since they immediately seem to have involved the police and taken precautions. At this stage the incident does not seem likely to damage public trust, but much will depend on the further development of the case."

Due to the impending implementation of the General Data Protection Regulation ('GDPR'), which requires notification to the affected individuals of a breach of their personal data within 72 hours, some commentators have scrutinised the period of time taken before the cyber attack was announced to the public. "Data security is considered a priority in Norwegian healthcare services, and there are already extensive regulations in place," comments Føyen. "Following a heated discussion in the summer of 2017 regarding the outsourcing of IT services by Health South East RHF and Sykehuspartner, there has been an increased focus on compliance with data protection legislation. This will of course be strengthened with the incoming implementation of the GDPR on 25 May this year."

Sykehuspartner stated in its press release that the response to the attack had been in accordance with established emergency preparedness routines, that a number of measures have been implemented to remove the threat, and further measures will be implemented in the future. The Norwegian National Security Authority ('NSM') in its statement on the matter published on 15 January 2018, sought to assure the Norwegian public that the cyber attack is being taken seriously. "We have invested considerable resources to assist the health authorities and handle the situation," stated Kjetil Nilsen, Director of the NSM, in the press release. Nilsen also stressed that for the sake of incident management, further details on the attack could not be discussed at that time.

"Cyber attacks in general are increasing in number and severity in Norway, in line with what is happening in the rest of Western Europe," concludes Føyen. "Last year the number of attacks increased by about 10%. The ongoing investigations into this particular cyber attack will give us the answer as to whether the health services are adequately prepared. I do not think this will impact the digitisation of healthcare services in Norway, apart from putting an even greater focus on security and the protection of information systems."