KCE REPORT 297Cs

Federaal Kenniscentrum voor de Gezondheidszorg
Centre Fédéral d'Expertise des Soins de Santé
Belgian Health Care Knowledge Centre

SUMMARY

RESPONSIBLE USE OF HIGH-RISK MEDICAL DEVICES: THE EXAMPLE OF 3D PRINTED MEDICAL DEVICES





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HEALTH TECHNOLOGY ASSESSMENT

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RESPONSIBLE USE OF HIGH-RISK MEDICAL DEVICES: THE EXAMPLE OF 3D-PRINTED MEDICAL DEVICES

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FOREWORD

New technologies are often very appealing to those who live at the same speed as that with which such technologies are developed today. Yet we must ask ourselves whether they always result in real progress. Everyone who is involved in healthcare must therefore be very exacting, and put quality, safety and efficacy first. The belief that the welfare of the patient must always take priority can however be undermined by the fear of missing the train of innovation. Caregivers must always therefore proceed very cautiously.

The policymakers of the care system share this concern, but frame it in a budgetary context. Thus they are also concerned about the relationship between cost price and efficacy, and the accessibility of care. And the latter in particular matters to the patient. Because what sense is there in inventing new techniques from which not everyone can benefit if they offer advantages?

The stencil era saved students many hours of copy work, and then turned seamlessly into the period of the photocopy. Today the creations of the mind and human intelligence are three-dimensionally printed, and that can be considered great progress. But although we hope that ‘new’ in healthcare is equivalent to ‘better’, the proof of that has not yet been convincingly provided at present.

On the other hand, we also do not want to obstruct technological progress. Therefore we are open to the (conditional or limited) reimbursement of safe 3D-printed medical devices. But not under any condition whatsoever, or at any price whatsoever. In addition, we urge caution with 3D-printed products that still await validation with regard to safety, quality and efficacy. This must come after limited use, in order to be able to examine the various effects. In this way we must arrive at not only the belief, but also the proof that they offer added value to patient and caregiver, and so to the entire care system.

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Christian LÉONARD
Interim General Manager

CORE MESSAGES

- 3D printing makes it possible to make a fully custom-made medical device for an individual patient. In addition it is also possible to produce medical devices that are adapted to the patient via a standardised production process in large quantities.
- At present there are few scientifically demonstrated advantages of 3D printing applications for the patient (risk of complications, quality of surgery, etc.). Proponents also claim an advantage in the form of time gain in the operation itself. However, this too is not uniformly supported by the scientific literature.
- At present the cost price of 3D-printed medical devices for which the added value compared to an existing alternative has not (yet) been demonstrated can however be charged to the patient or the hospital. It is not certain whether patients are aware in this connection of the scientific uncertainty on 3D-printed applications or the existence of alternatives.
- As long as there are adequate guarantees of safety, 3D-printed medical devices for which the added value has not (yet) been demonstrated could be reimbursed at the level of the alternative. In this way innovation is not blocked, the patient gets a safe medical device, and he/she decides him/herself to accept the risk of a (possibly) innovative technique. For the RIZIV/INAMI [*National Institute for Health and Disability Insurance*] this is a budget-neutral action, because reimbursement is at the level of the alternative.
- If no alternative exists (e.g. for a custom-made 3D-printed facial prosthesis), an evaluation per individual case is indicated.
- Companies can be supported by the government in collecting scientific evidence to guarantee safe use in patients and to support reimbursement decisions. The existing administrative databanks already contain data (e.g. on mortality, readmissions, etc.) that can be very useful. The traceability data can be used to link these data to the medical device of the patient. The existing traceability systems would have to be modified for this.
- The data on patient and procedural outcomes in the existing administrative databanks often do not suffice to demonstrate the added value of a 3D-printed medical device. It is then up to the company to set up a study and collect these data.

SUMMARY

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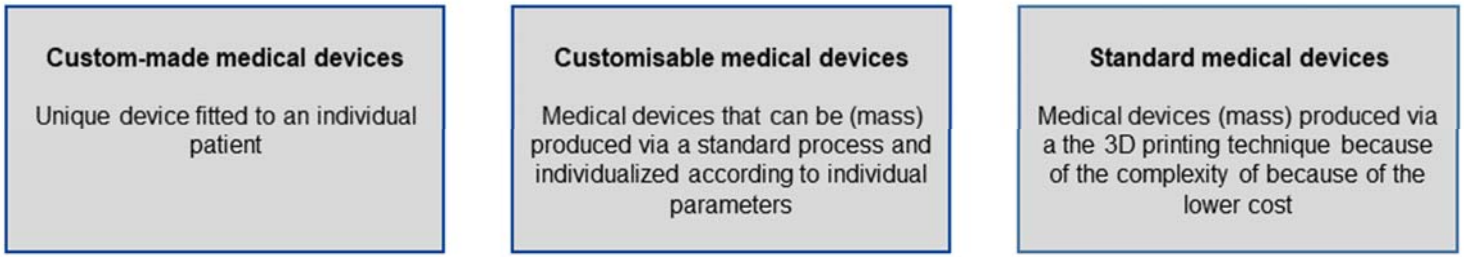
1. THE MEDICAL SECTOR AND 3D PRINTING

1.1. Various medical applications of 3D printing

3D printing is a production technique in which a digital file is converted into a tangible object. This object is built up layer by layer by the 3D printer. In the medical and especially in the orthopaedic and dental sector, 3D printing has experienced increasing growth and interest in recent years. Today this sector has become the greatest user of this technique after industry and aerospace.[a]

Unlike 'standard' medical devices, which are made in large numbers but in a more limited number of shapes, 3D printing offers the possibility of making for example a **"custom-made" prosthesis or implant for each individual patient**. With the 3D printing technique, several variants of a design for a medical device can also be made and **customised ("tailored")**, by adjusting certain parameters. Finally, it is also possible to produce **large quantities of standard products or components**, in which 3D printing can offer added value due to the complexity or the lower production price.

Figure 1 – Typology of 3D-printed medical devices

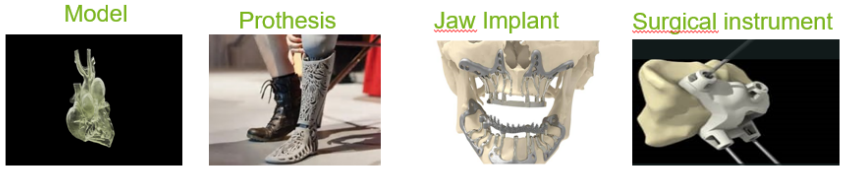


[a] Wohlers Report 2015: 3D Printing and Additive Manufacturing State of the Industry Annual Worldwide Progress Report, Wohlers Associates, 2015.

In addition to **prostheses** and **implants** (see Figure 2), 3D printing is also often used in the medical field to make a **model (**see Figure 2) of e.g. a joint or organ of a specific patient. The 3D images, taken with Magnetic Resonance Imaging (MRI) or a Computer Tomography (CT) scanner, still had to be viewed in two-dimensional slices until recently, but the arrival of 3D printing changed all that. On the basis of the scans a 3D model can now be made of, for example, a complex fracture. The surgeon can then view this model from all sides before the procedure and try out various options in advance, so that he no longer has to make important decisions in the operating theatre itself. In addition, the model is also useful for surgeons in choosing the appropriate instruments, deciding where and in how many places they will attach an implant and in practicing this in advance. During an operation surgeons can also make use of 3D-printed **patient-specific surgical instruments** (see figure 2).

Belgium is one of the prominent players in the field of 3D printing in the medical sector. In 2011 surgeons at Ghent University Hospital conducted one of the most complex face transplants to date, in which they made 3D printouts of the skull of the patient in advance to prepare for the procedure and to use as a surgical guide. In February 2012 the first jaw transplant with a custom-made 3D-printed prosthesis was successfully conducted in an 83-year-old woman with chronic bone disease in the East Limburg Hospital (ZOL).[b] Today at Leuven University Hospital, 3D prints are already routinely made of the jaw joint of patients to prepare for a jaw correction.

Figure 2 – Types of 3D-printed medical applications



Sources: www.materialise.com en https://www.forbes.com/sites/tjmccue/2014/08/31/3d-printed-prosthetics/#3ebb1f9b33b4).

Text Box 1 – How is 3D printing of a medical device done?

In an initial (preoperative) phase the device must be designed. For this the physician must provide patient data and other relevant medical information, by among other things making the necessary scans of the body part where the device will be implanted or of which a model will be made. The 2D images from the scan are converted into 3D images and are then processed by an engineer with the aid of special software (computer aided design - CAD) according to the instructions of the physician. The CAD file is finally uploaded to the 3D printer, which builds up the medical device or model three-dimensionally. The material of which the object is made usually consists of plastic, ceramic or metal in powder form and is introduced into the machine as in an inkjet printer. The printer starts to print the lower part of the object and keeps accumulating a new layer on top of it that adheres to the previous one. So the medical device is gradually formed.

[b] http://www.zol.be/sites/default/files/publicaties/zolarium/pdf/zolarium-2015-55.pdf

The following components are needed for 3D printing a medical device:

- a printer
- the material (plastic, ceramic, metal, etc.)
- software to operate the printer
- Computer Aided Design (CAD) software to design the device
- data that are used by the software to print out the specific device (product specifications).

There are also a number of production steps after printing, e.g. polishing, disinfection and sterilisation.

3D printing can be done in the hospital itself or subcontracted to an external supplier.

1.2. Topic of the study

An innovative technique such as 3D printing in the medical sector presents the various participants with a number of new challenges. For the surgeon and especially for the patient there is the aspect of safety and efficacy. For health insurance there is the question of whether and how certain 3D-printed applications should be reimbursed. Producers, distributors and other parties in the production and distribution chain have important questions on the legal conditions with which the various products and their components must comply. Finally, in the interest of public health the government should provide a framework that allows safe and responsible use of 3D-printed medical applications. In the current report, the KCE aims to offer a guideline for all these various parties. In this, the focus will first of all be on high-risk medical devices in particular (see Text Box 2), since they involve the most risk for the patient and are often also the most expensive for health insurance. The intention is not to examine whether a certain 3D application should or should not be reimbursed.

The following research questions are examined further:

- Are 3D-printed medical devices safer and/or more effective than standard devices?
- Is the use of 3D-printed medical devices cost-effective?
- What is the legal and policy framework of 3D printing with regard to among other things market access, liability, personal data protection, patient rights, traceability, reimbursement and intellectual property rights in the EU in general and specifically in Belgium and in four other countries (the Netherlands, the UK, France and the US)?

This report does not consider 3D printing of medications and bioprinting (printing of organs, tissues and the like). In addition we limit ourselves to the 3D printing process. Virtual 3D preoperative planning that does not lead to a printed product does not belong to the scope of this study. Moreover, the production steps after the printing process, such as polishing and sterilisation, are not addressed, since in an evaluation of the medical literature the general safety and efficacy of a procedure is first of all examined. If there are e.g. problems with safety, it can often not be directly deduced what the underlying cause is, and it requires further investigation. The safety of the raw materials used also falls outside the scope. These aspects fall under the authority of the FAMHP.

Text Box 2 – What are high-risk medical devices?

High-risk medical devices include among other things implants that are often permanently implanted into the body, or devices that come into contact with the heart or brain. Examples are hip prostheses, pacemakers, stents, and heart valves.

2. IS THE USE OF 3D-PRINTED MEDICAL DEVICES SAFE AND EFFECTIVE?

2.1. How did we proceed?

We studied the international medical literature on (custom-made) 3D-printed medical devices, more specifically implants, preoperative models (of joints and bones, among other things) and surgical instruments.

We conducted a systematic literature review in the database of the Cochrane Library, Medline and Embase. We also searched for systematic reviews and meta-analyses of randomised controlled studies (RCTs) and additional individual RCTs in which a group of patients in whom 3D-printed applications had been used was compared with a control group that had been treated in the standard way. We identified 35 relevant RCTs. You can find more details on the methodology used in section 3.2 of the scientific report.

2.2. Few demonstrated advantages for the patient and conflicting results with regard to reduction in operating time

Most of the RCTs concerned the use of a 3D surgical instrument during orthopaedic surgery, particularly during total knee arthroplasty (total replacement of the knee joint). From these studies it appears that the advantages for the patient (risk of complications, quality of surgery, etc.) are very limited. According to proponents of 3D printing this technology would reduce the duration of an operation, which would ensure a less fatigued surgical team that makes fewer mistakes. In addition costs would be saved, because the operating rooms are occupied for a shorter time. From the literature however we cannot convincingly deduce that operating time is significantly reduced by the use of 3D-printed medical devices (see also Chapter 3 of the scientific report).

For most other indications (custom-made implants, models for operating plans, surgical instruments for other orthopaedic procedures and for maxillofacial surgery) the RCTs were too small and/or they established no significant effects. In general there are presently no convincing data that demonstrate that a procedure with 3D-printed medical devices is more effective or safer than a ‘standard’ procedure. Moreover, in the studies concerned few relevant endpoints were measured (e.g. replacement of the implant).

3. IS THE USE OF 3D-PRINTED MEDICAL DEVICES COST-EFFECTIVE?

3.1. How did we proceed?

We searched the databases of Medline, Embase, EconLit (Ovid), CRD (Centre for Reviews and Dissemination), HTA and the National Health Service Economic Evaluation Database. In addition we consulted the websites of members of INAHTA (International Network of Agencies for Health Technology Assessment) and several other websites, such as that of the British NICE (National Institute for Health and Care Excellence). We also examined the reference lists of relevant review papers and economic evaluations.

After selection this ultimately yielded eight (partial) economic evaluations of 3D printing, one of them Belgian.[1] Four studies concerned maxillofacial surgery; the other four cardiovascular, cranial and back surgery and dentistry. Most of the studies used 3D printing for multiple purposes, but in the majority the technique was in any event used to make preoperative models. In addition, in a number of studies 3D-printed custom-made implants were compared with standard implants. You can find more details on the search strategy and the evaluations considered in section 4.1 of the scientific report.

3.2. Varying quality of the studies

The quality of the studies was very diverse; some studies include only a summary description of the methods used, sources and input. The number of patients was also limited (usually fewer than 20 per group), and the time horizon was often very short (usually only the (pre)operative phase or the hospitalisation time), so that the clinical and economic effects in the long term were not included.

3.3. Results

The studies give varying results.

Three studies on maxillofacial and dental surgery indicate on the basis of prospective and retrospective study that 3D models for operation planning and 3D implants shorten the (pre)operative time (and length of stay in Baj et al.[2]) and consequently are less expensive than the standard techniques. However, two other studies, also on maxillofacial surgery, report no significant reduction in the operating time, and also no difference on costs, with sometimes even an increase.[3 74, 4 76]

In two studies on back and cranial surgery the costs also increased, without a significant difference in (pre)operation time[5 73] or length of hospital stay, or even a significant drop in operating time or length of hospital stay.[5 73, 6 80]

In general there are presently no convincing data demonstrating that the use of 3D printing is more cost-effective or even cost-saving than the current treatment. This is, given the observations in the medical section, not surprising.

Some assert that 3D printing is especially time-saving in highly labour-intensive, specialised surgery.[7 72] Yet the results from four studies of highly labour-intensive maxillofacial surgery are also not convincing.

In no study are the results expressed in QALY (see Text Box 2), which hinders assessment of the cost-effectiveness of 3D printing.

Text Box 3 – How is cost-effectiveness calculated?

A cost-effectiveness analysis expresses the advantages of a procedure in 'life years gained' or in 'life years gained corrected for quality of life' (QALY – Quality-Adjusted Life Years) for the patient. When a procedure costs less and has more advantages for the patient than the current standard practice, the decision is obvious. But often a procedure does improve health, but also costs more than the standard treatment. In that case the ratio between the additional cost of the procedure and the lifespan gained (adjusted or not for the quality of life) is calculated. This is the so-called ICER (Incremental Cost-Effectiveness Ratio).

The assertion that 3D printing reduces operating time and costs is still not scientifically proven, especially not if the investment cost of the equipment and the time that surgeons devote to making scans and designing and producing the print are also taken into account. In the future the purchase price of the equipment may fall and the technology will undoubtedly still improve. Whether this will also ensure a cost reduction will have to be re-examined in quantitative, prospective studies with larger sample sizes and longer follow-up times. In addition a full economic analysis should be conducted.

4. LEGAL ASPECTS OF 3D PRINTING OF MEDICAL DEVICES

We also investigated the following legal aspects at the EU level, at the Belgian level and in four other countries (the Netherlands, the United Kingdom, France and the US):

- requirements for market access (see section 5.4. and 5.5. of the scientific report)
- liability (see section 5.6 of the scientific report)
- protection of patient data (see section 5.7 of the scientific report)
- patient rights (see section 5.8 of the scientific report)
- intellectual property rights (see section 5.11 of the scientific report)

4.1. How did we proceed?

For the portion on the legal aspects we analysed the legislation, case law and legal doctrine of the EU, Belgium and the aforementioned four countries. You can find the sources we consulted in section 5.3 of the scientific report.

4.2. Requirements for market access

4.2.1. *Current regulations: no CE label for custom-made and customised 3D-printed medical devices*

At present (autumn of 2017) the legal framework for 3D-printed medical devices consists of the European Medical Devices Directive (MDD)[c], the In-vitro Diagnostic Medical Devices Directive (IVDD)[d] and the Active Implantable Medical Devices Directive (AIMDD),[e] which have been integrated into Belgian legislation.[f] At present there is no consensus at the European level on whether 3D-printed models should be classified as medical devices, and thus fall under the European legislation on medical devices. Models seldom have a purely diagnostic or therapeutic purpose; they are used particularly in the preparatory phase of an operation. However, if a producer *itself* indicates that a medical device should be used with a model so that it can be employed optimally, the model can be regarded as an accessory to the medical device.

Which rules are applicable to putting 3D-printed medical devices on the market depends on their classification as a standard, customisable or "custom-made" device (see **Error! Reference source not found.**).[g]

In contrast to **'standard'** medical devices, manufacturers of **custom-made** medical devices, regardless of the risk profile, do not need to apply any CE marking to their product, there are no specific quality system requirements[h], and for the higher risk classes there is no prior external evaluation of the device by a notified body[i]. Manufacturers do have to[j] draw up a statement (Annex VIII MDD) with identification data and characteristics of the device, the identity of the patient (coded or not), the prescribing physician, and as applicable the hospital concerned. They must in addition declare that the essential requirements of Annex I MDD (among others, justification of material choice, biocompatibility requirements, and sterility requirements[k]) are fulfilled. However, they need not demonstrate that the 3D-printed device is safer or more effective than (possibly) existing alternatives (this is by the way also not a requirement for CE marking).

According to law, every Belgian manufacturer must also register *every* custom-made device that it puts on the Belgian market individually with the Federal Agency for Medicines and Health Products (FAMHP). In practice it generally suffices for the manufacturer to give a general description of the *category* of devices that it is putting on the market (e.g. orthopaedic devices).[l] The FAMHP can conduct checks in retrospect with regard to the design, manufacture and performance of the device. Finally, custom-made

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c Council Directive 93/42/EEC of 14 June 1993 concerning medical devices, OJ L 169, 12/7/1993, pp. 1-43.

d 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, 7/12/1998, pp. 1-37.

e Council Directive 90/385/EEC of 20 June 1990 on the approximation of the laws of the Member States relating to active implantable medical devices, PB L 189 of 20/7/1990, pp. 17-36.

f RD of 18 March 1999 on medical devices, *Belgian Official Gazette,* 14 April 1999 and RD of 14 November 2001 on in-vitro diagnostic medical devices, *Belgian Official Gazette,* 12 December 2001.

g It should be remarked that in the IVD sector there are no personalised medical devices, so that the relevant rules are not applicable.

h There are general requirements such as reporting of incidents and post-marketing surveillance.

i A notified body is an inspection or test institute designated by a government that must test whether products comply with the applicable valid (European) directives.

j Only for class IIa, IIb and class III devices

k http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CONSLEG:1993L0042:20071011:en:PDF

l Personal communication by the FAMHP

medical devices can only be obtained via a prescription by a qualified person.

3D printing of medical devices now also makes it possible to (in addition to custom-made production of a unique product and production of a standard product (see **Error! Reference source not found.**)) produce **individually adapted medical devices ("customisable")** on a larger scale via a controlled production process ("mass customisation"). With the software models used, by adjusting certain parameters the production process can be largely repeated. That reproducibility and standardisation make the process comparable to that for a standard production process.

Yet these 3D-printed medical devices are regarded as prescription devices that are made once for a certain patient. The consequence is that they are usually classified with the custom-made devices. The question therefore arises whether such medical devices should not be considered 'standard' medical devices to the individual.

Along the same lines, it can also be asked whether it is justifiable to allow medical devices in higher risk classes (e.g. orthopaedic implants) that are produced on a large scale without any prior assessment and without having an overview before large-scale dissemination on the market. Future regulations try to address this (see 4.2.2).

In addition to the 3D-printed medical devices, the printer, the software and the material used must also comply with certain quality and safety conditions.

- The **3D printer** does not fall under the regulations with regard to medical devices but must comply with certain quality and safety requirements in the European Directive concerning machinery.[m]
- **Software** used for 3D printing can in certain cases be classified as a medical device. This is the case for software that is used in itself as a therapeutic or diagnostic tool, such as software for preoperative or surgical preparation and/or simulation. The consequence of this is that it must be CE marked and must comply with the other requirements for medical devices. The design and production software for making a 3D printed medical device is however not used in itself as a therapeutic or diagnostic tool. It is therefore not regarded as a medical device. For this software, standards for good software development and safety are applicable (e.g. EN IEC 62304 for software for clinical purposes and possibly IEC 82304 for software in healthcare).

  Sometimes however software is supplied in a total package, so that it is no longer clear to which portion the stricter requirements are applicable. Here, the FAMHP can participate in recasting the existing guidelines on classification of software used in healthcare within the legislative framework of medical devices[n] and clarify the specific requirements with which the various types of software must comply.
- The **material** for printing the 3D medical device is not classified as a medical device in itself, but it is checked in the assessment whether a medical device complies with the essential requirements of Annex I of the MDD. For certain materials specific legislation is applicable (see 5.4.1.1 of scientific report).

Belgian legislation has added additional restrictions on distribution, advertising and offering of premiums or benefits to caregivers to promote 3D medical devices to the conditions for market access (see 5.5.2.1 of scientific report). This has no more impact on 3D-printed devices than on standard devices.

[m] Directive 2006/42/EC of the European Parliament and of the Council of 17 May 2006 on machinery, amending Directive 95/16/EC, PB L 157 of 9/6/2006, pp. 24–86.

[n] Meddev. 2.1/6 Guidelines on the qualification and classification of stand-alone software used in healthcare within the regulatory framework of medical devices.

4.2.2. New regulations: stricter requirements for customisable 3D medical devices made in larger quantities

The new regulations, namely the Medical Devices Regulation (MDR) and the In Vitro Diagnostics Regulation (IVDR) were published on 5 May 2017 and took effect on 25 May 2017.[o] The new regulations will be directly applicable in the member states after a transition period of 3 years for the MDR (spring of 2020) and 5 years for the IVDR (spring of 2022). Under the new legislation much stricter requirements are imposed on clinical data, more and more specific essential requirements are imposed, the role of the European databank for medical devices will become much greater, market surveillance is more harmonised between the member states, etc.

The big difference in the new regulations for this specific topic is however that not every customisable 3D-printed medical device can still be considered a custom-made device. According to the MDR a device is especially custom-made on the basis of a medical prescription with specifications, and it is intended exclusively for a certain patient. Medical devices that are made in larger quantity and that must be adapted to the specific requirements of each professional user, and devices that are made in *industrial manufacturing processes* on the basis of a medical prescription are not considered custom-made devices. This means that customisable medical devices will have to comply with the same conditions as standard medical devices for market access.

Customisable 3D-printed devices will probably fall under the definition above. It could be argued that an industrial manufacturing process is characterised by a standard production method. In this, every device is produced in exactly the same way, but adaptations are possible by changing a number of parameters. Thus customisable mass-produced 3D-printed medical devices would fall under this.

In related areas too, such as medications for advanced therapy (ATMPs, advanced therapy medicinal products), the authorities have been quick to confirmed in the past that the production of cells or tissues of ATMPs, even in the smallest batches, is classified as production via an industrial manufacturing process. In this way, by the application of the strictest regulations, safety and quality are best guaranteed.

An exception to the stricter legislation for standard medical devices was made for medical **devices that are made in hospitals** (5 (5) MDR). Aside from the essential requirements of Annex I, the requirements of the MDR (among others, CE marking, assessment by a notified body for certain risk classes) are not applicable under a number of conditions.

To benefit from this exception, no equivalent device may be available on the market, a hospital may not carry out mass production on an industrial scale (which should still be better defined by legislation), and appropriate quality management systems (this too should be further defined) are to be present. The devices may not be moved to another legal entity (e.g. another hospital), and the volume and production process may not take place routinely or in a standardised way. Moreover the member states can also exercise control over the quality of these (3D-printed) medical devices by requesting information and conducting inspections in the hospitals. In addition they can limit the use and production of certain devices in hospitals or forbid outsourcing of certain 3D printing activities for reasons of public health. Finally, the European Commission can set stricter requirements in Annex I of the MDR on the technical documentation for these devices via legislation. If hospitals do not fulfil the conditions for exemption, the general rules with regard to standard medical devices are simply applicable.

The new regulations also stipulate that manufacturers of **class III custom-made implantable devices** must have a compliance assessment of their quality management system conducted by a notified body.

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[o] Regulation (EU) 2017/745 of the European 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 (hereinafter referred to as Medical Devices Regulation (MDR)) and Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on in-vitro diagnostic medical devices and repealing Directive 98/79/EC and Commission Decision 2010/227/EU (hereinafter referred to as In-Vitro Diagnostics Regulation (IVDR)).

4.3. Liability

A jawbone that must be implanted is produced in 3D on the basis of a surgeon's design. A year later the jawbone breaks due to a defect in the medical device, with all sorts of complications for the patient as a consequence.

Who is liable for this? According to the principles of product liability the producer is liable for any defect in its product. In 3D printing, however, there is a deviation from the traditional chain of production, distribution and use. Who is the producer here? Many parties are involved in the production of 3D devices: the surgeon who makes the initial design, the software engineer who develops the 3D design, the producer of the 3D printer, of the material, of the software and of the implant, the implanting surgeon, the hospital, etc.

4.3.1. The European directive with regard to product liability

The Product Liability Directive (PLD)[p] states that member states 'must impose strict liability on' producers when their products are defective and cause bodily injury, without the need for the victim to demonstrate that the producer has committed an error. The PLD also encompasses all medical devices that are made in the EU or imported. This strict liability is however only applicable to 'industrially made products'. It has not yet been determined by the EU whether 3D-printed medical devices fall under this PLD, and no EU case law yet exists on the concept 'industrially produced'. The MDR does however explicitly refer to the PLD (Art. 10, 16°) so that it can be assumed that 3D-printed medical devices fall under the scope of the PLD. In further analysis we therefore assume that the PLD is applicable to 3D-printed medical devices.

4.3.2. Belgian legislation

The European product liability directive was transposed into Belgian legislation by the Product Liability Law of 25 February 1991.[q]

According to this law the producer is liable for damage caused by a defect in its product, also without the need for the victim to demonstrate the fault of the producer. The burden of proof is thus reversed; it is the producer that must prove that it has made no error in making the device. We examine whether and how these general principles can be applied to 3D-printed medical devices.

According to the Product Liability Law every tangible movable item is considered to be a "**product**". All the components of 3D printing (see Text Box 1) therefore fall under the law, with the exception of the design and CAD files and the software.

The law considers a product to be **defective** when it does not offer the safety that can be expected, taking account of all the circumstances. A 3D medical device is for example considered defective if it is made of faulty material.

As stated previously, a large number of participants are involved in the development of 3D devices. In the sense of this law, "producer" is understood to be the manufacturer of an end product, a part of an end product, or a raw material, and everyone who presents himself as a manufacturer or producer by applying his name, brand or other identifying mark to the product. Importers of products into the EU are also considered producers. If no producer or importer can be identified, the supplier of the product can be considered the producer.

[p] Council Directive 85/374/EEC of 25 July 1985 on the approximation of the laws, regulations and administrative provisions of the Member States concerning liability for defective products, PB L 210 of 7/8/1985, pp. 29–33.

[q] Law of 25 February 1991 concerning liability for defective products, *Belgian Official Gazette*. 22 March 1991.

The following participants can for example be regarded as producers in the sense of the Product Liability Law:

- the developer of the website from which the software was downloaded
- the producer of the material and the 3D printer
- anyone who prints the product: a traditional producer or a physician, pharmacist, hospital employee, etc.
- a hospital that prints 3D devices itself in the hospital.

If multiple persons appear to be liable, they are jointly and severally liable for payment of the full damages.

Invocation of the Product Liability Law does not prevent the victim from also calling on the rules of contractual or non-contractual liability, e.g. to involve parties that do not fall under the Product Liability Law, such as the developer of the CAD files. The victim will therefore have to prove the error, damage and causal relation, which is less favourable for him than in product liability. Damages for defective software or CAD files could also be claimed in certain cases via the Medical Accidents Law of 31 March 2010. In practice the defect in the software will also express itself in a defect in the end product, so that the patient, even if the producer of the software does not fall under the Product Liability Law, can still address the producer of the end product on the basis of this law.

In reality however an agreement is often concluded **between the producer of 3D devices and the hospital or physician.** In addition agreements are made on the liability (and insurance obligation) of each party. In principle the parties are free in this, and they can even specify that the product liability legislation is also applicable to the software developer. This is a more favourable arrangement for the patient, because he then does not bear the burden of proof of the error. Despite this contractual freedom a producer can however never limit or preclude its liability toward patients in the agreement with the hospital or the physician.

For more details on contractual and non-contractual liability, criminal liability, liability with regard to the guarantee obligation (Art 1641 Civil Code) and medical experiments, the medical accidents law, liability of the government and the insurance obligation, see section 5.6.2 of the scientific report. For liability in foreign examples, see sections 6.1.4 through 6.1.7 of Appendix 3.

4.4. Protection of personal data

The 3D printing process unavoidably also involves the processing of health data of the individual patient. In addition these data can be used for other than therapeutic purposes, e.g. for scientific research or reimbursement purposes (see below). The Privacy Legislation protects the processing of personal data and has developed rules for this.[r] It is very important to know who is regarded as "responsible for processing" by the law. This person is in fact charged with almost all the legal obligations to guarantee protection of the processed data.

[r] EU: Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data, PB L 281 of 23/11/1995 pp. 0031 - 0050 and Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC, PB L 119 of 4/5/2016, pp. 1–88; Belgium: Law of 8 December 1992 on the protection of privacy in relation to the processing of personal data, *Belgian Official Gazette*, 18 March 1992 and its implementation decrees.

Hospitals will generally be regarded as responsible for processing the personal data of the patient that are required for the 3D printing process. If hospitals outsource 3D printing to an external producer, they will have to conclude a processing agreement with it.

If the conditions of the privacy legislation are met, no specific problems arise in 3D printing. For more details see Chapter 5.7 of the scientific report.

4.5. Right of patient to information

Today there is still insufficient reliable scientific evidence on the effectiveness and safety of 3D-printed devices. This means that the patient must be sufficiently informed on this to be able to give valid informed consent. The caregiver must be truthful in this on the scientific uncertainty. The greater the uncertainty, the more comprehensively the patient must be made aware of the relevant risks and of the more standard alternatives.

If the patient revokes his consent in the course of the printing process, it is legally possible to request that he pay the already incurred costs of a custom-made medical device, unless he has been insufficiently informed in advance by the caregivers (see 5.8 scientific report).

4.6. Intellectual property rights

For details on intellectual property rights, see section 5.11 of the scientific report.

5. TRACEABILITY OF (3D) MEDICAL DEVICES

Medical devices are fully traceable if all the stages of the production chain (from design to use in the patient) are known. Labelling, registers and coding systems, among other things, can be used for this.

As was made clear in the scandal of the leaking PIP breast implants in 2012, this traceability is crucial for patient safety. Because the PIP implants were not traceable, identification of possible victims and recall of the products not yet used was hindered.

We examined the current and future EU and national traceability requirements for 3D-printed medical devices, especially for the higher-risk invasive devices and implants. Subsequently we investigated what measures have been taken in several other countries (the Netherlands, the United Kingdom, France and the US).

5.1. Current EU requirements

At present there are no measures specifically applicable to 3D-printed devices, and the general measures with regard to traceability of medical devices are applicable. Current EU regulations[s] require that **all medical devices** be accompanied by a **label** with among other things the name of the manufacturer and a serial code or number, so that the manufacturer and the product can be identified.

The PIP scandal has demonstrated however that this does not suffice, because if the label is applied to the device itself (which is not required), it is often no longer visible once it is in the body of a patient. Therefore in 2013 the European Commission called for a 'unique identification system' (UDI) that will be provided in future legislation (see below).

European regulations provide specific rules for **custom-made (3D) devices,** and the current legislation regards customisable 3D-printed medical devices as custom-made devices (see 4.2.1); in addition to the

[s] Annex I, 13.3 MDD

aforementioned **label** they must be made on the basis of a **medical prescription with the specific characteristics of the patient concerned**. Moreover the maker must include with every device a **statement** (the so-called 'Annex VIII statement') with among other things its name, data that make identification of the device and the patient possible, the name of the caregiver and as necessary the hospital, and the characteristics of the product. The maker must save these data and make them available to the patient.

For low-risk devices (class I) this statement must also be drawn up, but it need not be supplied. The prescription of the caregiver can suffice for tracing.

In addition to the traceability of the product itself it must also be possible to identify the market participants (among others manufacturers, importers, distributors, but not the patient) in the distribution chain. Thus market participants must keep a record of market participants to whom they have provided their product and/or from whom they have bought products.[t]

5.2. Future additional EU regulations: more collaboration, unique code and implant card

5.2.1. General requirement: collaboration among those involved

As a reaction to the PIP scandal, the new European regulations[u] provide measures to improve the traceability of medical devices. First and foremost there is the general requirement that distributors and importers must collaborate with manufacturers, so that every participant can identify the previous and next participant in the supply chain.

5.2.2. Specific additional measures: unique code and implant card

Furthermore, in addition to the already planned label, the following specific measures are provided:

- a unique identification code (Unique Device Identification - UDI) for every (3D-printed) medical device, consisting of a code specific to the manufacturer and model of the device (Device Identifier – UDI-DI) and a number that can trace the production (Product Identifier – UDI-PI) (e.g. serial number, batch number, expiry date, software identification, etc.). Only the manufacturer will have available the data behind the UDI-PI. It is up to the manufacturer to keep track of the traceability of the product components on the basis of the production file (batch record).
- registration of the (3D) medical device in the UDI databank by the manufacturer;
- registration of the manufacturers, representatives and importers of (3D) medical devices in a databank of the European Commission;
- an overview of the safety data and clinical performance of the device, which must be publically available;
- inclusion of all the aforementioned items in the EUDAMED database; the UDI-PI will however not be included in the EUDAMED database.

[t] The 'Blue Guide' on the implementation of EU product rules 2016; http://ec.europa.eu/DocsRoom/documents/18027

[u] Medical Devices Regulation (MDR) and the In Vitro Diagnostics Regulation (IVDR)

- an implant card for each patient, with which the implanted device and its manufacturer can be identified.

These measures are **not applicable to 3D-printed medical devices made in a hospital**. The hospital will only have to register its name and address and the data needed to identify the device.

The aforementioned measures, with the exception of the UDI, are applicable to **custom-made 3D-printed medical devices**.

In contrast to the current legislation, **customisable 3D-printed devices** are no longer regarded by the new European legislation as custom-made devices, but as standard medical devices (see 4.2.2). Therefore they will have to fulfil all the stricter traceability requirements cited above.

For **class III implantable devices** the **market participants** ensure that the UDIs of the devices that they have supplied or received are (preferably electronically) stored and retained.

Care institutions also ensure that the UDIs of the **class III implantable devices** they have supplied or received are (preferably electronically) stored and retained. However, this does not mean that they also know in which patients these medical devices are used. The member states can require that this too be done for other devices.

In addition member states can require that **caregivers** store and retain (preferably electronically) the UDIs of the **devices** supplied to them.

In the future the new European regulations will be directly applicable in Belgium. As previously stated, the EU will probably then no longer regard customisable 3D-printed devices as custom-made medical devices, but as standard devices.

5.3. Current Belgian legislation: registration with the FAMHP

Belgium has already included traceability requirements in its legislation.[v]

Before they can put their device on the Belgian market, **manufacturers** of (3D) class 1 or custom-made medical devices, systems and procedure packs established in Belgium must **register themselves and the description of their product with the FAMHP** (Federal Agency for Medicines and Health Products).

In addition **distributors** that provide devices in Belgium must register themselves and the risk classes of the devices they distribute in Belgium with the FAMHP. In this way the FAMHP can conduct a risk analysis, and possibly conduct inspections on the basis of this.

Distributors and exporters of medical devices with a CE label must also keep a register ensuring the traceability of the medical devices.[w]

However, these measures do not optimally guarantee the traceability of each individual medical device. Supplementary measures are therefore necessary:

- For **custom-made medical devices (which includes most 3D-printed devices under the current system**) the European label and the Annex VIII statement act as a tracing tool. Moreover every Belgian manufacturer must **report**, in addition to itself, a description of the product it puts on the Belgian market to the FAMHP. This requirement is however insufficient for full traceability, because the manufacturer is not required to notify the FAMHP of the distribution and use of that device. The Annex VIII statement of the manufacturer can be used to trace the device to a physician, hospital or patient. However, there is no

[v] RD of 18 March 1999, RD of 14 November 2001 and law of 15 December 2013

[w] It is advisable to do this on the basis of batch numbers/serial numbers, but this is not a legal requirement except when sold in the framework of the ministerial decree of 18 May 2005; see FAMHP guidelines on good distribution practices for distributors of medical devices with a CE marking.

central registration of these statements, so that the FAMHP must request statements from every manufacturer separately.

- As a reaction to the PIP scandal, Belgian legislation specifies an additional, specific regulation for **(3D) implants,** but this regulation is not yet in effect. A **caregiver** who implants, removes or replaces such a device must:
  - enter the information needed to identify the patient and the implant in the **Central Implant Tracing Register of the FAMHP**. This register should not be confused with the already existing registers (QERMID) for reimbursement of certain types of implants (e.g. coronary stents, hip and knee prostheses).
  - give the patient an **implant card** with information on the implant.

This registration will take place using the RIZIV/INAMI notification number (see 6.2.1.1). In the future the current RIZIV/INAMI notification will take place with the FAMHP. Custom-made (3D) implants do not have such a number, and therefore they cannot be registered, and the patient cannot receive an implant card. Nevertheless they are (at the time the report was written) not legally exempt from these obligations. As of 2021 registration in the tracing register will however take place on the basis of the UDI. As the UDI is not applicable to custom-made medical devices, these too will not be included in the tracing register in the future.

Despite the legal basis for the central traceability register, its use is not yet required because an implementation decree that governs the modalities for notification in the register is still needed. Such a traceability system is also a necessary condition for the use of patient and process outcomes for scientific and reimbursement purposes (see 6.5.3).

Table 1 – Traceability requirements under the current and future system by type of medical device

	Current situation		Future situation	
	EU	**Belgium**	**EU**	**Belgium**
All Medical Devices (MDs)	• Label • Identification of market participants in distribution chain	• Label • Registration of **distributors** that supply MDs in Belgium + product characteristics with FAMHP • FAMHP guidelines: distributors must keep register that guarantees traceability	• Label • **Distributors and importers** must collaborate with manufacturers to achieve an adequate level of traceability.	• Label • Registration of **distributor** + product characteristics with FAMHP
Standard MD	• See all MDs	• See all MDs	• UDI • registration in the UDI databank by the manufacturer; • registration of **manufacturers**, representatives and **importers** in a European Commission databank; • overview of the data on safety and clinical performance of the device that is publically available; • inclusion of all the aforementioned instruments in the EUDAMED database; • For class III implantable devices, market participants and care institutions ensure that the UDI of the devices they have supplied or that have been supplied to them are stored and kept.	• See EU • FAMHP guidelines: **distributors** must keep register that guarantees traceability
Custom-made medical devices	• Prescription • Label • Annex VIII MDD statement by manufacturer	• Prescription • Label • Annex VIII MDD statement by manufacturer • Registration of manufacturer + product with FAMHP	• Same as current situation	• Same as current situation
Implants	• See all or custom-made MDs	• See all or custom-made MDs	• See standard MDs+ • Implant card • For class III implantable devices, market participants and care institutions ensure that the UDI of the devices they have supplied or that have been supplied to them are stored and kept.	• See all MDs + • Implant register • Implant card
Medical devices produced in the hospital	• Not regulated	• Not regulated	• Hospital must make public details of MD, name and address of manufacturer-hospital, etc.	• Hospital must make public details of MD, name and address of manufacturer-hospital, etc. The Belgian government can require that additional info be sent to the FAMHP.

Comment: 'customised' medical devices are considered 'custom-made' medical devices in the current regulations. In future regulations they will fall under 'standard' medical devices.

6. REIMBURSEMENT OF 3D-PRINTED DEVICES

6.1. Member states of the EU decide on reimbursement themselves

Reimbursement for medical devices is not governed at the European level. The member states can thus decide autonomously which medical devices are reimbursed by their health insurance, and under what conditions.

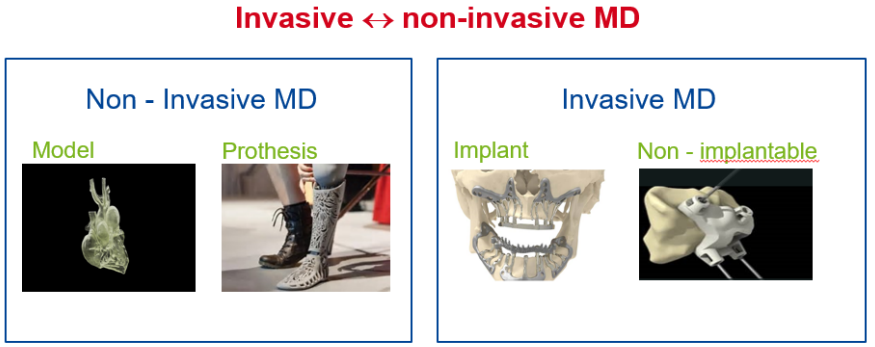
An exception to this is cross-border healthcare, in which an EU citizen has himself treated in another member state. For this a specific reimbursement system exists within the EU (see section 6.5.2 of the scientific report).

6.2. General legislation applicable to medical devices

There are at present no specific Belgian regulations for reimbursement of 3D-printed devices and the associated services (e.g. the design of the 3D device). Thus we must take as a basis the legislation applicable to the reimbursement of "standard" medical devices.

In reimbursement of medical devices a distinction is made between invasive[x] and non-invasive devices (see **Error! Reference source not found.**).

Figure 3 – Invasive versus non-invasive medical devices



**There is no consensus at the EU level at the moment as to whether models should be regarded as medical devices.*

In our country 3D printing occurs primarily for custom-made[y] and invasive medical devices. Therefore a producer of 3D devices primarily follows the procedure below.

6.2.1. Reimbursement for invasive medical (3D) devices and implants

Custom-made (3D-printed) medical devices do not need to bear a CE label and need not be reported to the RIZIV/INAMI. Yet they can, just like their standard counterparts, be reimbursed by Belgian health insurance on condition that the procedures are followed and that they fulfil certain conditions.

[x] Device that partially or wholly enters the body, either through an orifice or through the body surface.

[y] Implants are by definition also invasive medical devices.

6.2.1.1. Reimbursement by the RIZIV/INAMI

The procedure for obtaining, modifying or revoking reimbursement for a (3D) implant or an invasive medical device for long-term use[z] is governed by the Royal Decree (RD) of 25 June 2014, which amended the Belgian reimbursement system for implants and invasive devices as of 1 July 2014 (see Chapter 5.10.2.1 of the scientific report). The reimbursement of certain dental implants does not fall under this (see 5.10.2.1. of the scientific report).

After a CE label has been received and the RIZIV/INAMI has been notified (not needed for (3D) custom-made devices), the manufacturer or the Minister of Social Affairs and Public Health can request reimbursement from the RIZIV/INAMI, and more specifically from the Commission for the Reimbursement of Invasive Medical Devices and Implants (*CRIMDI*). The CRIMDI itself can also take initiatives in that direction, e.g. if the producer makes no request and the CRIMDI considers that there is sufficient scientific evidence.

If a decision is made to reimburse a (3D) medical device, this is added to (one of the) two annexes of the RD[aa]:

- Annex I contains a list of provisions within a number of medical specialities (e.g. neurosurgery, ophthalmology, etc.), and the reimbursement conditions.
- Annex II contains the nominative list of implants and invasive medical devices that are reimbursed, with their detailed data (e.g. name of device, name of producer, price, etc.). Each individual device on this list has an identification code and is linked to a provision from the list of Annex I.

The RIZIV/INAMI pays a fixed amount (lump sum) or reimbursement on the basis of their individual (maximum) price for the devices on these lists, depending on their category (A, B, C, D, E, F).

Innovative medical devices for which uncertainty still exists on the added value in comparison with existing alternatives can be reimbursed within the following two categories:

- In the framework of a 'limited clinical application'[bb] (Cat G): the CRIMDI can propose temporary reimbursement on condition that additional research is still done.
- In the framework of a contract concluded with the RIZIV/INAMI[cc] (Cat H): if no reimbursement is proposed in the framework of a limited clinical application, the applicant can ask the Minister of Public Health to negotiate a contract between the applicant and the RIZIV/INAMI.[dd]

Table 9 of the scientific report contains an overview of all the custom-made 3D devices that are now (2017) reimbursed

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z Generally, intended to be used uninterruptedly for more than 30 days.

aa http://www.riziv.fgov.be/nl/professionals/individuelezorgverleners/verstrekkers-van-implantaten/Paginas/terugbetaling-implantaten.aspx#.WYRFk4R97IV

bb Art. 57 to 65 RD of 25 June 2014 establishing the procedures, terms and conditions with regard to reimbursement of the required insurance for medical care and benefits in the costs of implants and invasive medical devices, *Belgian Official Gazette*. 1 July 2014

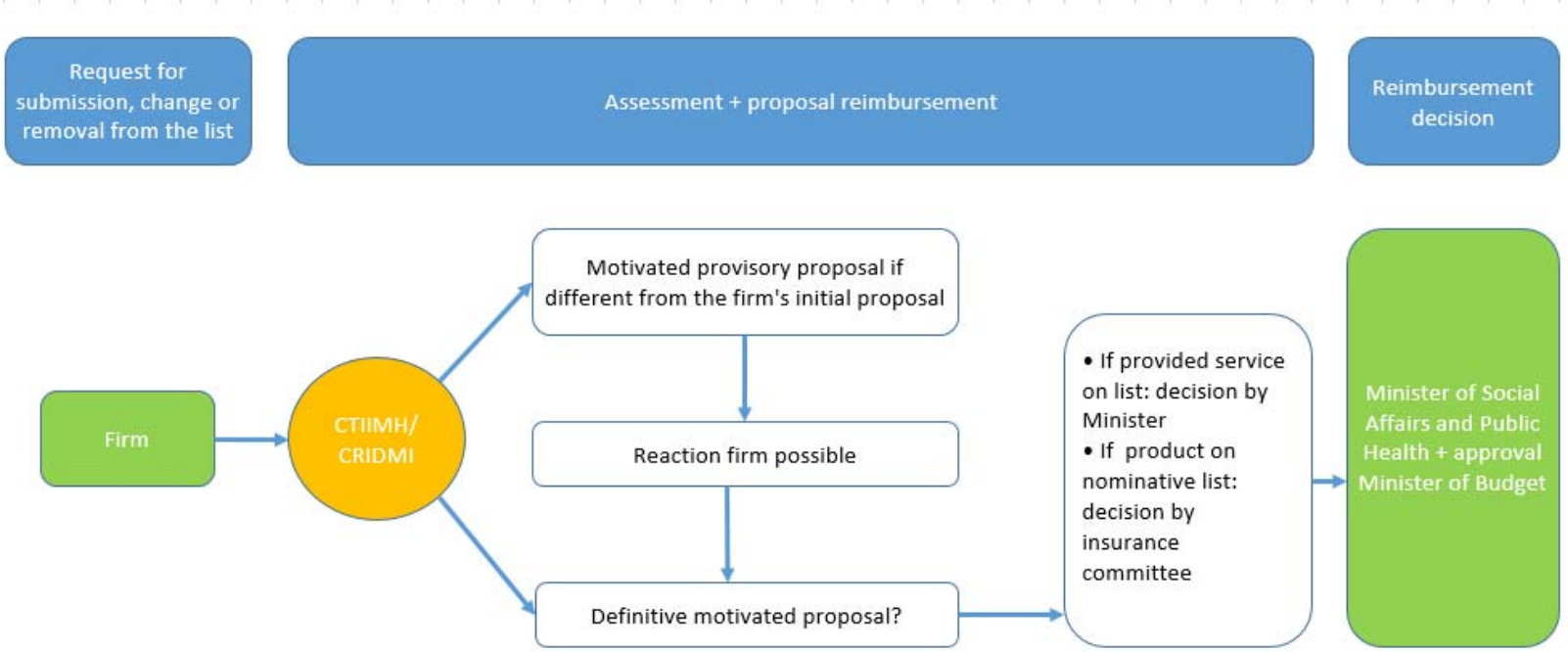
cc Art. 66-71 RD of 25 June 2014

dd Art. 66 to 71 RD of 25 June 2014

For some custom-made **(3D) devices** the CRIMDI can decide that reimbursement is only possible **after an assessment by individual case** by the College of Physicians-Directors (*College van Artsen-Directeurs*, CAD) of the RIZIV/INAMI, composed of physicians from the health insurance funds and the RIZIV/INAMI. One of the conditions for reimbursement that often arises is that use of a standard, non-custom-made implant was not possible.

When all the possible means for reimbursement have been exhausted, **custom-made** (**3D) devices** can also be eligible for reimbursement under very strict conditions by the **Special Solidarity Fund (*Bijzonder Solidariteitsfonds*)**. This fund constitutes a supplement to the required health insurance and serves to intervene financially in (expensive) procedures for, among other things, treatment of rare illnesses and innovative techniques and medical devices that are not (yet) reimbursed by the RIZIV/INAMI (see section 5.10.2.2 of the scientific report).

Figure 1 – Procedure for inclusion in, modification of or removal from the list – request by the company (*)



** The Minister of Social Affairs and Public Health and the CRIMDI can also make a request for inclusion in, modification of or removal from the list on their own initiative.*

6.2.1.2. (Partial) reimbursement from the hospital budget

The Hospital Act (*Ziekenhuiswet*) (Art 102.4) specifies that the costs of **implants** must be borne by the hospital budget (Budget of Financial Means - BFM) in certain cases. This is the case for:

- implants that have not been reported, while they are subject to the notification requirement;
- implants that are not reimbursed after evaluation by the CRIMDI because their quality has been found to be inferior or because they have harmful side effects.

In the following cases the hospital bears (part of) the costs of **implants and invasive medical devices**:

- implants and invasive medical devices for which the producer charges a price that is higher than the lump-sum amount that the RIZIV/INAMI reimburses; the hospital must pay the surplus for this.
- Implants and invasive medical devices for which the price lies above the maximum price established by the RIZIV/INAMI; here the hospital must bear the total cost of the device.

Non-reimbursed invasive medical devices are chargeable to the hospital.

6.2.1.3. Sometimes the patient must assume the costs

Sometimes the costs for an **implant** are chargeable to the patient. That is the case for implants that are not on the reimbursement lists of the RD of 25 June 2014, for the following reasons:

- no request for reimbursement was submitted;
- a request for reimbursement was submitted and the result was positive, but the decision for reimbursement is not yet in effect.
- a request for reimbursement was submitted, but a negative reimbursement decision was made for one of the following reasons:
  - there is insufficient scientific evidence OR
  - there is an insufficient budget OR
  - the price of the device is too high in relation to the added value of the product versus the already existing alternatives.

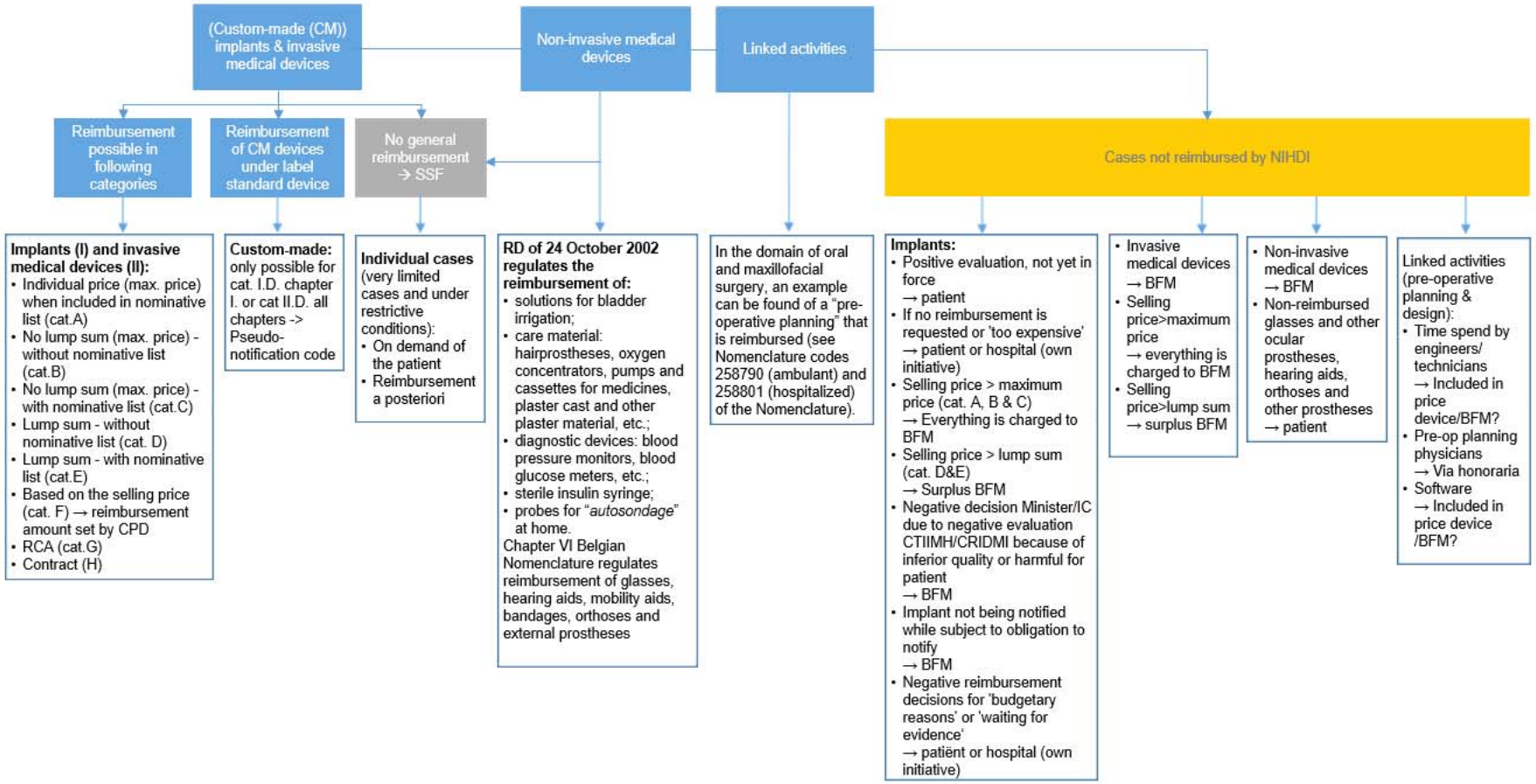
According to the law on patient rights, the patient must be made aware in advance of these costs and of the existence of equivalent (reimbursed) alternatives, so that he/she can make an informed decision. In some cases the hospital can decide to take on the costs itself.

6.2.2. Reimbursement of non-invasive medical (3D-printed) devices

The Technical Council for Diagnostic Devices and Care Material is authorised to make the decision to reimburse certain categories of non-invasive medical devices (see 5.10.2.1 scientific report).

Chapter IV of the Nomenclature governs the reimbursement of eyeglasses and other eye prostheses (Art. 30 list), hearing aids (Art. 31 list), bandages (Art. 27 list), mobility equipment (Art. 28 §8 list), orthopaedic devices and other prostheses (Art. 29 list). Reimbursement conditions differ according to the category of device and are specified in the Convention Committees of the respective sectors (see section 5.10.2.1. of the scientific report).

Figure 2 – Reimbursement options for 3D medical devices in Belgium



**Abbreviations in the diagram: MDs = medical devices; BFM= Budget of financial means; IC= insurance commission; CRIMDI = Commissie Tegemoetkoming Implantaten en Invasieve Medische Hulpmiddelen [Committee for the Reimbursement of Invasive Medical Devices and Implants], CAD= College van Artsen-Directeurs [College of Physicians-Directors], LCA = limited clinical application.*

6.3. Possible problems and solutions in reimbursement of (3D-printed) medical devices and related services

As noted above, a medical device – whether or not 3D-printed - can be used without being reimbursed, and without its medical efficacy being demonstrated. Often in this case the patient must bear the costs. Moreover this can lead to large-scale dissemination of high-risk devices on the market and this can lead to an indirect pressure to reimburse them.

In the cases where no reimbursement request has been submitted or where it has been declined, the producers themselves can determine the price and can charge it (at least partially) to the patient. Some hospitals therefore have 'innovation funds' for this to contribute to the costs, but it must be asked whether patients or hospitals should assume the risk and costs for (possibly) innovative devices.

Moreover it is not certain whether patients are always aware that they are being treated with a medical device for which the added value has not (yet) been demonstrated. Surgeons do have the duty to inform their patient of existing alternatives, but the legislation does not explicitly require that a surgeon also justify why he chooses a certain product over the alternative.

The following options should offer a solution for these possible problems. They hold not only for custom-made 3D-printed medical devices, but also more generically for non-3D-printed (standard or custom-made) medical devices.

6.3.1. A reimbursement request is submitted for a safe (custom-made) 3D-printed device for which the added value has not been demonstrated. A (custom-made) alternative is available.

We propose that, if there are adequate guaranties for the safety of the patient, a 3D-printed device for which the added value has not been demonstrated should receive the same reimbursement as an already existing alternative.

This is a beneficial arrangement for all the parties concerned. Because the 3D-printed device is safe, there is no risk to the patient's health, and he/she does not bear the costs of a medical device for which the added value in comparison to the existing alternative has not yet been demonstrated. For the RIZIV/INAMI the budgetary risk is as high as for the alternative. The innovative activities of the producers are not impeded because their product is reimbursed like the alternative until its added value can be demonstrated and a higher price may be justified.

Moreover the government can support companies by collecting data on the results in the existing databanks (e.g. number of deaths, readmissions, etc.) (see 6.5.3). In all of this the patient must be made aware that he is being treated with a device for which a suitable reimbursed alternative exists, and for which the added value has not yet been demonstrated.

In practice the challenge will primarily consist of determining in a transparent way what a "suitable" alternative is. Sometimes there are various (custom-made) highly comparable medical devices for the same indication. Given that highly specialised cases in small patient populations that require specific expertise are often involved, clinical (possibly foreign) experts should be involved in assessment of the existing alternatives.

6.3.2. A reimbursement request is submitted for a 3D device for which no suitable (custom-made) alternative is available.

When no suitable alternative is available, it is difficult to determine a price and the level of scientific evidence. If there is no (custom-made) alternative, comparison can be made with “wait and see”. In this case the aforementioned reimbursement at the level of the alternative cannot be applied and an assessment by individual case is needed.

6.3.3. No reimbursement request has been submitted, the decision is negative due to too high a price, or the producer requests that reimbursement be revoked

Sometimes producers submit no request for reimbursement, e.g. if the evidence is too weak. In theory they can even ask to have their product removed from the list, e.g. because they find the reimbursement too low. In these cases, just as when reimbursement has been declined due to too high a price, the device can still be used without limitations by surgeons. The patient and/or the hospital then (partially) assume the costs.

To optimally protect patients, the care provider should explicitly inform the patient that he/she will pay the cost for a non-reimbursed (3D-printed) product for which no sufficient added value has yet been demonstrated, while a reimbursed alternative (possibly) exists.

6.3.4. Separate reimbursement for preoperative planning?

It is typical of 3D-printed medical devices that their development during the preoperative phase demands a great deal of time and effort, which is often much less the case for standard devices. Because now in theory only the 3D-printed device is reimbursed, some argue that health insurance should also have to reimburse the costs of preoperative planning. Now the time that the surgeon devotes to design and development of a 3D-printed device is usually included in his fee, just as for a standard device. An exception to this exists in the field of oral and maxillofacial surgery. There the RIZIV/INAMI has in fact been prepared to separately reimburse the 3D analysis that takes place before the actual 3D printing of the surgical instrument.

The time that engineers devote to developing the medical device together with the surgeon in the preoperative phase is also not separately reimbursed by the RIZIV/INAMI[ee].

The costs for the preoperative phase may possibly be charged by companies at present in the price of the 3D-printed medical device. As the cost structure is not transparent at present, it cannot be ascertained how much is charged for which items.

The only argument for an extra reimbursement could be that the services in the preoperative phase offer demonstrable added value compared to the alternative approach. As previously stated in Chapter 2, this has however not (yet) been convincingly demonstrated.

The claim that 3D technology significantly reduces operating time is also not always supported by the literature. Even if this were the case, this yields an added value for the hospital (which can save on the costs for operating time) and for the surgeon (who can carry out more procedures) first of all. From the point of view of the patient or the RIZIV/INAMI there is no demonstrated added value and consequently there are no good reasons to allocate this additional reimbursement.

[ee] In radiotherapy the financing for the reimbursement of the physicists (or engineer, as the case may be) takes place via B3. A part of the remittance that radiotherapists make to the hospital may also be used for this.

6.4. The IDEAL model for safe use of innovative high-risk devices and data collection

Today we see that producers of custom-made (3D-printed) devices regularly cite added costs compared to the non-custom-made alternative in the reimbursement request. In addition the amounts for highly comparable custom-made (3D) devices sometimes differ significantly (e.g. surgical guides for osteotomy). Nevertheless a higher price can only be granted if an added value can be demonstrated.

As appears from Chapter 2, at this time there is however little evidence that invasive 3D medical devices offer added value.

Often the objection to this is that it is not easy to provide this scientific evidence; the patient groups are often small and it is ethically problematic to compare procedures with high-risk medical devices with the traditional methods. But these arguments can be countered with e.g. transcatheter aortic valve implantations (TAVIs). This procedure has already been performed for years in the EU and the data from thousands of patients have already been registered. In the absence of a control group, the possible added value of the procedure cannot however be reliably demonstrated. However, in the US relevant randomised clinical studies were in fact successfully conducted.[ff]

Before a new procedure is introduced on a large scale, a formal scientific evaluation of this procedure in which it is compared with existing alternatives is strongly recommended. A suitable study design must be used for this. The IDEAL model can be used to introduce and use innovative (3D) medical devices safely. It was designed by a group of, among others, surgeons and experts for the introduction of innovative surgical procedures. IDEAL stands for 'Idea, Development, Exploration, Assessment and Long-term study'. This describes the steps to be followed in developing and assessing new invasive techniques and procedures[8].

Idea/proof of concept: when a surgeon tries out a procedure for the first time.

All new procedures must automatically be reported to the hospital and kept in an online register accessible to all surgeons. In particular, adverse effects and failures must be published to prevent repetitions in the future.

Development: if the initial reports give the impression that the procedure provides benefits, others can also try out this procedure.

The procedure is applied in a limited group of patients. In this phase experience is gained and the technique is refined or modified. Precautionary measures are taken to prevent negative consequences for patients by e.g. working with mentoring during the learning curve. All procedures must be collected in a register with clear reporting of ALL outcomes.

Exploration/learning: understanding the potential advantages and drawbacks.

As soon as the procedure has been described and the most important technical aspects have been developed, exploratory prospective clinical studies without a control group can be set up. This can take place in parallel with the launch of a RCT.

Assessment: Is this technique more clinically effective and cost-effective than the existing alternatives?

This phase is intended to assess the efficacy/effectiveness versus the current alternatives. RCTs are the most suitable for this, and the choice of the comparator is very important.

Long-term study: In this stage established procedures are assessed for rare and long-term outcomes, making use of a register.

There is no exact point in time that indicates when an "innovation" evolves from one phase to the next phase. Transparent reporting of study protocols and results is necessary in every phase.

[ff] https://kce.fgov.be/nl/publication/report/transcatheter-aortakunstklep-implantatie-tavi-een-health-technology-assessment-ac

The incorporation of IDEAL seems to us to be a responsible choice that offers various advantages:

- It requires the care provider to consider the responsible use of high-risk medical (3D) devices. It can lead to use of such devices without reliable evidence on the added value for the patient being limited and/or their being used in a responsible setting.
- A specialist can only make a decision on use of a high-risk medical (3D) device and justify this if he himself has the relevant data. This can indirectly ensure that the producers (must) make the results of clinical studies available transparently.
- Due to such assessment from the field, new high-risk procedures can quickly be identified and assessed for their suitability for research or routine use.
- The liability risk for the caregiver is limited if he has followed the step-by-step plan properly.

6.5. How can the IDEAL model be launched in Belgium?

6.5.1. Basic principle: demonstrate safety and added value compared to existing alternatives

An efficient system should not only allow the safety of (3D-printed) high-risk medical devices (retrospective, e.g. reaction only if multiple cases of damage occur) to be demonstrated but also the safety (e.g. adverse events in the patient) and added value compared to existing alternatives. At present the demonstration of safety and added value for the patient is not required by European legislation. It is thus up to the national governments to develop such a system.

Below we go over a number of exploratory avenues for safe introduction of (3D-printed) high-risk medical devices and joint establishment and development of a system that can systematically assess the safety and added value of (3D-printed) high-risk medical devices by the FAMHP, RIZIV/INAMI and Healthdata.be.

However, a number of practical and legal uncertainties and obstacles exist in this. Further reflection and close collaboration by the parties concerned is therefore necessary.

6.5.2. Action 1: limit the use of 3D-printed devices in the developmental phase to certain reference centres

Working with a limited number of hospitals that act as reference centres offers a number of advantages; it can lead to better results for the patient because expertise is concentrated. In addition, for devices without evidence of efficacy, the number of procedures within those centres can also be limited and the data needed can be collected.

Possible criteria for such centres can be the experience of the physicians and medical teams, the research expertise of the team, the requirement to train other specialists, etc.

6.5.3. *Action 2: improvement in the use of the existing registers by linking patient and procedure outcomes to a unique identifier of a device*

As stated previously, data on patient and procedure outcomes are often lacking for 3D printing. In the initial phase and long-term follow-up, registers can be useful (see 6.4).

The existing administrative databanks can be used as scientific tools with which knowledge can be developed (among other things, data on 30-day mortality[gg], readmission[hh], etc.). Collection of these data can provide important observational data for devices not yet reimbursed and can also be imposed as a condition for reimbursement (up to the level of the alternative – see above).

In this way knowledge of a specific device or a certain category of devices can be improved and problems can be identified more quickly. This information can thus be useful both for the physician who uses the devices in the initial phase and for the reimbursing government that, for example, wants to know whether e.g. more complications occur than with 'standard' medical devices before reimbursing 3D-printed medical devices. Patient data can be used by health insurance without the need for patient consent (Art. 7 §2c of Law of 8 December 1992 on the protection of privacy in relation to the processing of personal data).

In addition this system offers an advantage for the company, which can use these data without having to make an investment itself for this. The data in the existing administrative databanks have their limitations too, however. If a company wants to demonstrate that its 3D-printed product is better than the alternative and also wants to receive a surcharge for it, it will usually have to set up a study itself (with e.g. a comparative arm and end points other than those in the administrative databanks).

Moreover, better use of the existing registers is useful not only for 3D-printed medical devices, but also for other (high-risk) medical devices (see Text Box 4).

Text Box 4 – Example: metal-on-metal hip prosthesis

"In mid-2010 British orthopaedists reported that some patients with a so-called metal-on-metal hip prosthesis, consisting of a large metal head and a metal socket, had complaints. These complaints were caused when very small metal particles were released during normal physical activity. In some patients they caused a local inflammatory reaction of the tissues around the hip. Increased concentrations of metal in the blood could also occur. Although initially only metal-on-metal hip prostheses of a certain brand seemed to be involved, it has since become clear that these problems could also occur with equivalent hip prostheses of other brands."[ii]

The use of registers has an advantage over post-marketing surveillance in cases where complications often lead to readmissions (with a repeat procedure or replacement as with the hip prosthesis) in that problems can be traced faster and there is no dependence on reporting by third parties. Currently manufacturers, persons who sell medical devices, notified bodies, physicians, and persons responsible for reception and/or delivery of the devices are to report incidents with medical devices. The patient should also be able to report incidents via a standardised form.

The data registered can only be useful if they can be linked to a unique (patient-specific) identifier of a device. At present the data collected in

gg These data can be found in the National Register

hh These data can be found in the Minimum Hospital Data (*Minimale ziekenhuisgegevens*, MZG) linked to the Anonymous Hospital Stays - Day Hospitalisation (*Anonieme Ziekenhuisverblijven-Daghospitalisatie*, AZV-ADH)

ii https://www.tjongerschans.nl/pati%C3%ABnten/specialismen/orthopedie/metaal-op-metaal-(m-o-m)-heupprothesen

hospitals on patient and procedure outcomes could be linked to the medical device used in the patient via the nomenclature code. This would however only be possible for reimbursed medical devices. Moreover the nomenclature code does not always indicate what e.g. the manufacturing method was (3D versus other technique).

6.5.4. Possibilities for using traceability data linked to (existing) patient and procedure outcomes

In the future, most 3D-printed medical devices will have a UDI (see 4.2.2). It will be possible to ascertain which implants (UDI- DI) have been used in which patient on the basis of the Central Tracing Implant Register. A link of the data from the Central Tracing Register to the data from the administrative databanks (on the basis of the INSZ [*social security identification*] number) would thus be an ideal solution for being able to use existing patient and procedure outcomes. For this it would be necessary to be able to distinguish 3D-printed medical devices from non-3D-printed on the basis of the UDI-DI and to recognise use of various materials.

We go over three possible options below:

6.5.4.1. Explicit inclusion of material specifications and manufacturing methods in the UDI-DI

The UDI consists of a code specific to the manufacturer and model of the device (Device Identifier – UDI-DI) and a number that can trace the production (Product Identifier – UDI-PI) (e.g. serial number, batch number, expiry date, software identification, etc.). Only the UDI-DI will be included in a central database. The UDI-PI, which contains more detailed product information, will only be available from the manufacturer. The type of manufacture (e.g. 3D-printed versus other method) or the type of material (e.g. metal-on-metal hip prostheses versus ceramic) is information that will not be contained in the UDI-DI. This information may possibly be in the UDI database if the manufacturer itself chooses this (see Annex VI Part B, 13° in the MDR). For high-risk medical devices the explicit inclusion of material specifications and manufacturing methods - which are necessary for proper identification - in the UDI-DI would be an optimal solution for setting up the proposed system. In this case the explicit addition of these extra fields would make it possible to directly check the type of device involved (e.g. 3D-printed versus other manufacturing method or metal versus ceramic), without the intervention of the manufacturer or the user.

The feasibility of and need for extra fields in the UDI-DI should however be investigated further.

6.5.4.2. Medical devices with a different manufacturing process or manufactured from a different material get a different UDI-DI

Another possibility for making the distinction between medical devices with a different manufacturing process or made of a different material possible is allocation of a different UDI-DI.

- For medical devices from a ***different manufacturer*** this is already the case (e.g. a 3D-printed surgical instrument from company X will have a different UDI than an equivalent instrument from company Y). Even with different UDI-DI codes it will still be necessary to count on the cooperation of the implanting physicians or the manufacturer to know the devices behind the UDI code precisely. The MDR specifies that member states can require that physicians keep the UDI codes of the medical devices supplied to them (Art. 27.9 MDR).
- If medical devices with a different manufacturing process (e.g. 3D-printed versus alternative manufacturing method) or made of a different material (e.g. metal versus ceramic) come *from* ***the same manufacturer***, it is in principle possible that they have the same UDI-DI, if they are considered to be of the same 'model'. An ideal solution would be for the notified bodies to allocate a different UDI-DI code for every essential difference in manufacturing method or material. Manufacturers can however submit one technical file for a group of medical devices with equivalent properties. It is highly probable that notified bodies cannot require a different technical file (and so no different UDI-DI) for products that are made of the same material but that came about via another manufacturing process (3D versus other manufacturing method).

6.5.4.3. *Essential changes in the manufacturing process or the use of different essential components lead to a new UDI-DI*

The MDR already requires a new UDI-DI if a change in the medical device can lead to misidentification or more difficult traceability (3.9 Annex VI). It also gives a non-exhaustive summary of situations in which a new UDI-DI is required, e.g. a new version or model of a medical device. Here too it is unlikely that a change in the manufacturing process (e.g. 3D-printed version of a medical device that was initially manufactured in another way) or a replacement of an essential component (e.g. a different battery with an altered operating life) would be regarded as a new version and so would require a new UDI-DI.

6.5.4.4. *Additional limitations*

Although use of the UDI code offers quite a few possibilities in principle, there are a number of additional limitations. Thus, the UDI code is not applicable to medical devices produced in the hospital (these fall under Art. 5 (5) MDR – see 4.2.2) and custom-made medical devices.

As previously stated, the bulk of 3D-printed medical devices will be regarded as standard medical devices in the future, and the UDI will also be applicable. Unique custom-made 3D-printed medical devices will thus be rather limited in number. Moreover it will be difficult to collect data on a wide range, since unique items are involved.

The number of medical devices produced in the hospital (which fall under the special system of Art. 5 (5) MDR) will probably also be very small. One of the conditions is after all that mass production on an industrial scale may not be involved.

Finally, only the implants from the Central Tracing Register could initially be linked to the data from the administrative databanks. In an initial phase this will primarily involve high-risk implants. This means that invasive non-implantable medical devices and implants with a lower risk are not initially included. A step-by-step approach with priority given to high-risk implants seems the most feasible choice, however. Collaboration between FAMHP, RIZIV/INAMI and Healthdata.be in developing this system is essential.

7. JUSTIFICATION FOR RECOMMENDATIONS

At present, 3D-printed customisable medical devices are generally regarded as custom-made medical devices.

The traceability requirements for standard medical devices, to which 3D customisable medical devices will also belong in the future, will be made more stringent. Thus among other things a unique product identifier will be allocated (UDI). This UDI will not be applicable to custom-made medical devices and medical devices produced in the hospital.

The current traceability data are difficult to use or even unusable for research purposes. At present the Belgian central tracing register for implants and the European UDI system are not yet operational. The format of the databanks concerned does not include all medical devices and is only intended for traceability, and not the demonstration of added value and safety in comparison to existing alternatives. To optimise the potential of such databanks and make them useful for research and reimbursement purposes, we are formulating recommendations on supplementation of the registration and use of the existing traceability data. This can be done by linking them to the patient and procedure outcomes from the existing administrative databanks.

Close collaboration among the parties concerned (RIZIV/INAMI, FAMHP, Healthdata.be, etc.) is necessary for development of such a system. It must also be ensured that the investments of the parties concerned are not disproportional. For this reason we recommend that the government take charge of the linkage, e.g. via Healthdata.

The existing data in the administrative databanks will however often not suffice for a comparative analysis in support of a reimbursement file (the A phase of IDEAL). A link with the existing administrative databanks can however be useful in the first phases of the IDEAL concept. Thus data can be automatically collected prospectively and continuously without extra burden on the specialist physicians, which can offer guarantees for safe introduction of high-risk medical devices. Currently useful data are in fact already automatically collected on e.g. mortality (National Register) or (re-) hospitalisations (data of the Technical Unit for management of hospital data) (see recommendation on traceability and research).

Currently it is possible that the patient or the hospital must cover the cost price of a medical device for which the added value has not (yet) been demonstrated. If a reimbursed alternative exists, this seems irresponsible to us. Therefore we formulate recommendations on informing the patient of the existence of alternatives, the scientific uncertainty and the financial implications.

From a social perspective too, a higher reimbursement in comparison to existing alternatives is only warranted if (insofar as possible) an added value can be demonstrated (see recommendations on reimbursement and informing the patient).

RECOMMENDATIONS

To the Minister of Public Health, the RIZIV/INAMI, FAMHP, Healthdata.be, care providers/scientific associations and institutions: Traceability and research

- **We recommend that care providers apply the IDEAL model (see 6.4) in development/introduction of new technologies:**
  - **All new procedures would automatically have to be registered, regardless of whether or not they have been conducted successfully;**
  - **In the developmental phase the use of high-risk (3D-printed) medical devices would only be allowed in a selection of expertise centres (phase I and D). This is to avoid having high-risk medical devices already used in many hospitals without a thorough evaluation of safety and added value having been conducted;**
  - **Before an innovation becomes widespread, a formal scientific evaluation would have to take place within an appropriate study design in which a comparison is made with existing alternatives (phase A);**
  - **The government can (co-)finance a system to use the existing administrative databanks (see following recommendation). The producer should first finance a study to evaluate outcomes that are not present in the administrative databanks (such as comparative effectiveness in quality of life).**
- **In addition to the possibilities for use of data that exist in the framework of reimbursement, we recommend that the government set up a system with the parties concerned (among others, Healthdata.be, RIZIV/INAMI and FAMHP) that allows linkage between the traceability data and other relevant (existing) data (among other things, 30-day mortality, rehospitalisation, etc.) to support the collection of scientific information, even before there is an issue of any reimbursement. These data can then be used for both research purposes and reimbursement purposes by e.g. the producer and/or the RIZIV/INAMI.**
  - **To this end, we recommend that a working group be set up with the parties concerned (FAMHP, RIZIV/INAMI and Healthdata.be) in which the intended objectives and the type of data that will be collected are specified with a view to a long-term strategic vision.**
  - **In the practical development, the options with regard to use of the UDI-DI in linking the traceability data to (existing) patient and procedure outcomes will have to be studied further.**

- **A step-by-step approach with priority given to high-risk 'standard' implants seems to be the most feasible choice. In the long term it can be examined whether this system can also be extended to all high-risk medical devices, thus also to custom-made 3D implants and invasive medical devices.**
- **To be able to study relevant data on patient safety on a larger scale, it is appropriate to also be able to use data originating from other countries. The advantage of use of the UDI is that it will be used at the European level, which facilitates this international use.**

To the FAMHP:

- **We recommend that input be given on the interpretation and further development of the concepts in the European Medical Devices Regulation, such as industrial production processes, mass production, UDI, etc., from the FAMHP.**
- **Complementary to setting up the system for the use of existing administrative data (e.g. rehospitalisations), we recommend making it possible for the patient to also report adverse reactions, adverse events and/or incidents to the FAMHP online/via a standardised form.**

To the RIZIV/INAMI: Reimbursement

- **If an alternative exists, this should be used to establish the price and as a comparator for demonstrating the added value. If the patient's safety is adequately guaranteed, we recommend reimbursing the (3D-printed) medical device at the level of the alternative. In this way the producer is given an incentive to submit a reimbursement file and make evaluation possible if it wishes to receive a surcharge.**
- **We recommend reimbursing a higher price for a (3D-printed) medical device only if the added value with regard to existing alternatives has, insofar as possible, been demonstrated.**
- **If no (suitable) alternative exists, a unique solution for the patient is involved and reimbursement should be assessed case by case (individually or by indication).**
- **For the preoperative phase too we recommend that reimbursement only be considered if sufficient added value can be demonstrated.**

To care providers: Information and responsible introduction of new high-risk medical devices

- **We recommend giving the patient complete information on the existing alternatives and as necessary on the scientific uncertainty that the 3D-printed medical device concerned would be safer or more effective than the existing alternative.**
- **We recommend that the financial implications for the patient related to use of the various alternatives be clearly communicated. Thus the caregiver must inform the patient explicitly that he/she will pay the cost of a non-reimbursed (3D-printed) implant for which adequate added value has not yet been demonstrated, while a reimbursed alternative exists.**
- **We recommend properly informing the patient that the cost price of a custom-made 3D-printed medical device can be charged if he/she should decide not to want to use the custom-made device once it is printed without valid reasons.**

REFERENCES

1. Tack P, Annemans L. Preliminary cost-effectiveness assessment of 3D printed anatomic models for congenital heart diseases. Value in Health. 2016;19(7):A692.
2. Baj A, Bolzoni AR, Giannì AB. Virtual planning and patient-specific implants in mandibular reconstruction surgery: A micro-costing analysiss. Value in Health. 2016;19(7):A723.
3. Prisman E, Haerle SK, Irish JC, Daly M, Miles B, Chan H. Value of preoperative mandibular plating in reconstruction of the mandible.[Erratum appears in Head Neck. 2016 Jun;38(6):939; PMID: 27166754]. Head Neck. 2014;36(6):828-33.
4. Rogers-Vizena CR, Sporn SF, Daniels KM, Padwa BL, Weinstock P. Cost-Benefit Analysis of Three-Dimensional Craniofacial Models for Midfacial Distraction: A Pilot Study. Cleft Palate Craniofacial Journal. 2016;3:3.
5. Lethaus B, Bloebaum M, Koper D, Poort-Ter Laak M, Kessler P. Interval cranioplasty with patient-specific implants and autogenous bone grafts--success and cost analysis. J Craniomaxillofac Surg. 2014;42(8):1948-51.
6. Chen H, Wu D, Yang H, Guo K. Clinical Use of 3D Printing Guide Plate in Posterior Lumbar Pedicle Screw Fixation. Medical Science Monitor. 2015;21:3948-54.
7. Choonara YE, du Toit LC, Kumar P, Kondiah PP, Pillay V. 3D-printing and the effect on medical costs: a new era? Expert Rev Pharmacoecon Outcomes Res. 2016;16(1):23-32.
8. McCulloch P, Altman DG, Campbell WB, Flum DR, Glasziou P, Marshall JC, et al. No surgical innovation without evaluation: the IDEAL recommendations. Lancet. 2009;374(9695):1105-12.

COLOPHON

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