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HIGH-PERFORMANCE CERAMICS

# BUILDING THE SAFE ROUTE TO 3D-PRINTED MEDICAL DEVICES

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# 1. INTRODUCTION

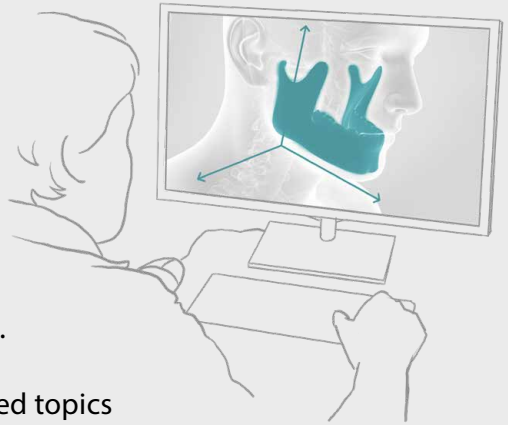
Recent developments in **additive manufacturing** (i.e. 3D printing), especially when considering high-performance **ceramics** and bioresorbable ceramics, enable a whole **new spectrum of applications** in the field of **medical devices.**

In contrast to the growing technological possibilities in development and manufacturing, the **regulatory frameworks** for medical devices tend to **become stricter**. New technologies such as additive manufacturing are very often not yet considered by those regulations and the authorities responsible.

This may discourage many potential developers and manufacturers of medical devices to implement such methods and materials.

In this article it will be discussed which **cornerstones** have to be set for the **safe** and **reliable design** and **manufacturing** of **medical devices** via **additive manufacturing**.

## 2. DEVICE DESIGN



The **safety** of the device itself **starts** with the **device design**. In this specific context, design does not refer to the geometry or look alone but to the complete specification of the medical device.

Some of the most important related topics shall be discussed in the next chapters.

### 2.1 RISK MANAGEMENT

Before even starting with the design of the actual device, an **appropriate risk management system** has to be established. The standard ISO 14971 describes the requirements for a systematic risk management system and is the backbone for successful implementation.

Risk management is not only related to the device design in terms of **materials or functionalities**, but shall also accompany the device during its **whole lifecycle**. This will therefore involve the later **manufacturing process** and **quality control measures**.

**Decisions** taken during the device's lifecycle shall be **risk based**. This also gives manufacturers the opportunity to optimize their efforts e.g. by reducing them for tasks that have been identified as low or negligible risk.

### 2.2 INTENDED USE

The **first step** in the development of the medical device is the definition of the **intended use**. All other requirements, especially requirements regarding safety, are derived from this starting step.

Taking into account the possibilities of additive manufacturing, one major scenario includes **patient-specific medical devices**. Such devices are specifically made in accordance with a written prescription and is intended for the sole use of a particular patient exclusively to meet their individual conditions and needs.

Of course, **mass-produced medical devices** are another possibility of additive manufacturing that make sense in certain cases.

### 2.3 SELECTION OF MATERIALS

The **device material** must be **carefully selected** by considering the desired **properties** and functional **safety** of the final part. **Biocompatibilty** is extremely important in medical applications.

For example, calcium phosphate-based **ceramics** such as β-tri calcium phosphate or hydroxyapatite can be used for applications where **biodegradation, bioactivity, osteoinduction** etc. are required. In such cases, the **highest level** of **biocompatibility is mandatory**.

The **device manufacturer** must deliver **proof** that it is **biocompatible** and pass the tests for the relevant standards e.g. ISO 10993.

By selecting materials **previously tested** by the manufacturer, unexpected results during the final testing can be **avoided**.

Such information and test results for biocompatibility from the material manufacturer are also **substantial input for the risk management** and the device design history file.

The device manufacturer should involve the material manufacturer **as early as possible** in the process.

This is not only related to data regarding biocompatibility or the suitability for use in medical devices per se, but also to the **material**

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**manufacturers design guidelines** for manufacturing components. These guidelines are also **essential** for all later process steps in the future manufacturing process.

## 2.4 DOCUMENTATION

According to applicable regulations, the whole **device design** and **process** has to be **properly documented**.

A proper quality management system according to e.g. ISO 13485 or FDA 21 CFR Part 820 shall be installed.

It is necessary to include **third party documentation** to the design file, including from the **raw material manufacturer** and information about the **equipment** being used.


# 3. MANUFACTURING PROCESS

## 3.1 RAW MATERIALS

The **raw material** used during manufacturing can majorly influence the **reliability** of the process. The manufacturer of the device should communicate any previously defined specific requirements, such as **special purity grades** or conformity to certain standards, to the material supplier. In such cases it is advisable to ask for a **certificate of conformity** from the material manufacturer to declare that the material has been manufactured according to **appropriate procedures** and offer data including chemical analysis, viscosity, refractive index etc.

To ensure **traceability**, this information shall be provided on the material batch base by the manufacturer.

If it is part of the **device manufacturer's** quality management system, it may also be required that the manufacturer of the material **holds a valid ISO 13485 certification**. The device manufacturer may also negotiate the right to audit the material manufacturer.

## 3.2 ENVIRONMENT

A **well-controlled production environment** avoids any problems caused by the surrounding conditons (e.g. humidity, temperature). Recommendations given by the material manufacturer should be followed, with environmental conditions being **documented**.

## 3.3 EQUIPMENT QUALIFICATION

All **equipment** used during the process shall be **qualified** – in particular, the **3D printer** and **post-processing** tools used (e.g. debinding and sintering ovens). The medical device manufacturer must ensure that the

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equipment configuration and process parameters are **not altered** without notice by implementing **proper access levels** and **documentation** and by reaching out to the equipment manufacturer for **IQ** (installation qualification) and **OQ** (operational qualification) plans if needed.

Once completed, IQ and OQ changes to the equipment may only be performed under **change control regimes**. The device manufacturer must also be aware that the CAD software being used to design the device may be subject to **software validation** – especially when deriving patient-specific geometries from CT scans.

### 3.4 PROCESS VALIDATION

Once the equipment has been qualified, the manufacturing process must be **validated** to ensure the delivery of parts with **consistent specifications**. Specification limits for the devices must be defined during the design phase, with limits possibly including geometrical dimension, strength or surface characteristics. Limits must be validated on the intended equipment with the necessary process parameters.

When manufacturing high-performance ceramics, the process ranges from data preparation to 3D printing and cleaning, and finally to debinding and sintering.

Periodical **control runs** should be carried out using, for example, test tokens with well-defined and quantifiable geometries. Data from test runs are subject to **statistical process control**, as discussed later in this white paper.

With there being a large number of **variables** throughout the process that can impact upon the final part, as many as possible should be kept **constant**. Any use of **inappropriate consumables** can heavily **impact** upon the final part, e.g. using unspecified cleaning fluid to remove excess material after printing may introduce unwanted elements and **directly affect mechanical properties**.

As such, the device manufacturer should only use aids recommended by the material/equipment manufacturer – where not possible, the material manufacturer should be **consulted** regarding compatibility.

Consequently, **change management** applies not only to process parameters and equipment but also **consumables** and other materials.

### 3.5 MANUFACTURING RECORDS

The **materials** and **equipment** used, process **parameters** and critical **consumables** shall all be **recorded**.

Ideally, the manufacturing equipment supports this process by generating **electronic records** of the process parameters and materials used. If regulations require it, **data integrity** rules have to be observed in this context.

It is advisable to consult the equipment manufacturer for system features or available options for **electronic record generation** (e.g. with 21 CFR part 11 compliance).


# 4. QUALITY CONTROL

## 4.1 PRODUCT RELEASE TESTING

One advantage of additive manufacturing is the possibility to generate **very complex geometries**, including intricate internal features.

Complex geometries and internal features may require more advanced quality control and measuring methods. Due to this, a **decision** based on risk management (see beginning of this article) has to be made to determine **which release criteria** is going to be used.

In some cases, **adequate process validation** may reduce complex release methods; in other very demanding applications, it may be necessary e.g. to have a **100% inspection by means of micro-CT**.

## 4.2 STATISTICAL PROCESS CONTROL

As mentioned during the discussion of process validation, **data gained** during the manufacturing process **shall be statistically evaluated**. This data may, for example, be part-to-part dimensional accuracy either in green/white bodies or sintered condition or the density of the sintered parts.

This allows for an early detection of trends towards process limits and helps parties to **better understand** the manufacturing process.

Trends may be related to equipment and materials, therefore it is recommended to consult the supplier in such cases.

## 5. CONCLUSION

**Additive manufacturing** gives new **opportunities** for medical device manufacturing and offers a **safe and reliable** process output if the guidance given in this document is followed.

**Lithoz** offers the **expertise** of their in-house experts to support their customers throughout the whole production development chain, from material and application **development** through to the selection of adequate equipment and regulatory questions. Alongside the broad variety of solutions to further simplify the production of your medical device, Lithoz also offers **highly customized consultations** to best support you in your developments.

In any case, having **all parties** – such as material and equipment manufacturers, regulating agencies and notified bodies – **involved and consulted** at an early stage will shorten the path from inital design to final component.

# Contact

*"KLS Martin has been working with Lithoz for 5 years. Since 2015, we have had a CeraFab 7500 3D printer and have used it to produce jaw implants (CMF implants) for human use. These have been met with great success in numerous patients and we have had optimal results in terms of the accuracy of fit, tolerance and healing success. Lithoz supports us with our certification of the products and we look forward to further cooperation with Lithoz in the future."*

**Frank Reinauer | Head of Innovation at KLS Martin**


**Dr. Daniel Bomze**
Email: sales@lithoz.com
Phone: + 43 1 9346612 – 200

**Sandra Balnik**
Email: sbalnik@lithoz.com
Phone: + 43 1 9346612 – 230





**Lithoz GmbH**
Mollardgasse 85a / 2 / 64 – 69 | 1060 Vienna • Austria
Tel: + 43 1 9346612 – 200 | Email: office@lithoz.com