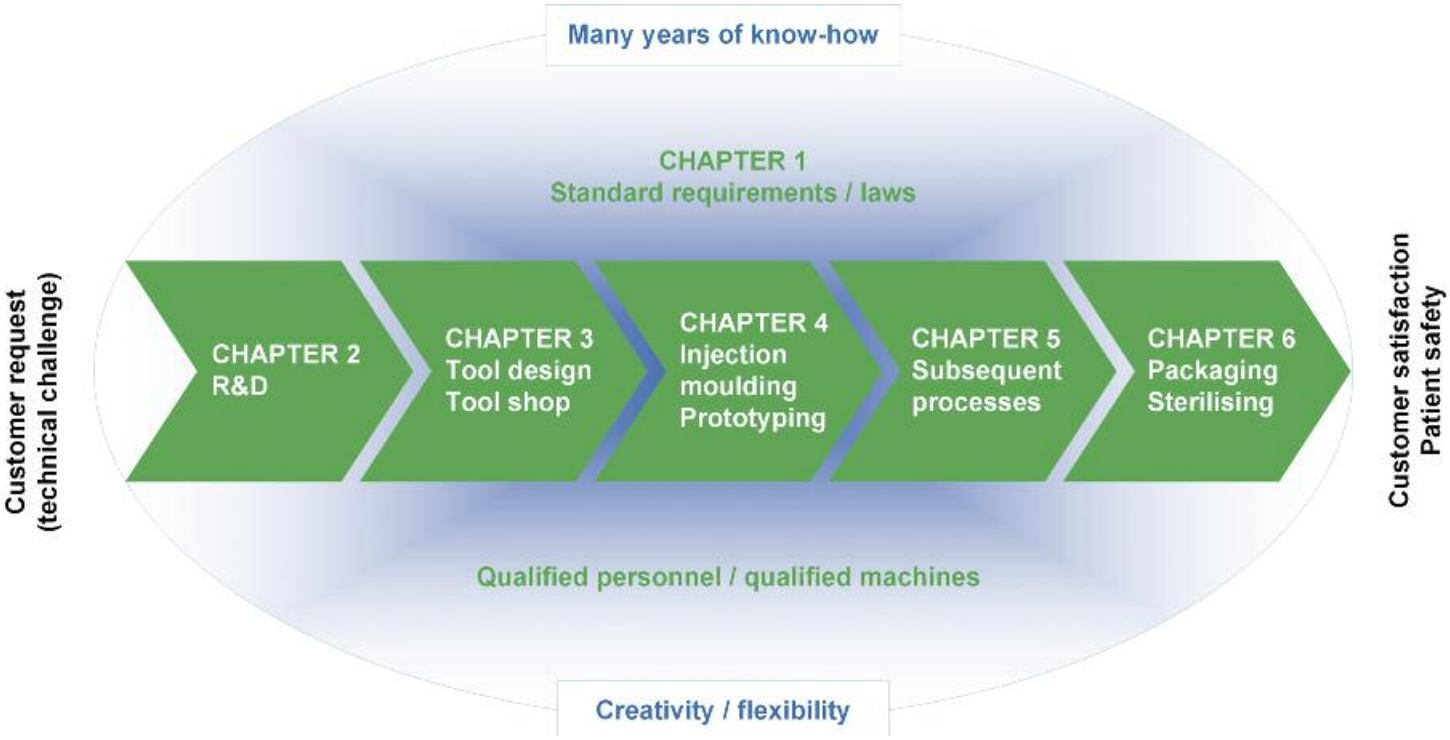
Plastic is the future
... is flexible

SAMAPLAST AG
PLASTICS TECHNOLOGY

The way from product idea to customer/patient



... test our know-how, creativity and flexibility.

SWISS MADE BY SAMAPLAST AG

www.samaplast.ch

The quality fundament

The basis for achieving the high quality requirements from the first product idea to the customer or patient? In addition to a modern company and high-tech machinery, it takes qualified and motivated employees with many years of know-how.

With a well-maintained company culture, continuous training and further education and constant improvement, we create an attractive workplace that guarantees low fluctuation and retains long-term know-how carriers. This is how we achieve customer satisfaction and business excellence.

Basic requirements (standards and laws)

How we at SAMAPLAST implement our customers' product ideas is determined by the end product and the applicable standards and laws.

As a subcontractor, we develop thermoplastic injection moulded parts, finished and tested assemblies up to sterile end-packed medical products and implants according to your ideas.

We take responsibility for product development in the form of sample or prototype production, as well as article and tool design for these products.

In addition, we manufacture the necessary injection moulding tools and produce the plastic parts with a unit weight of 0.01 to 1000g on the most modern injection moulding machines and carry out subsequent processes, e.g. printing, embossing, bonding, soldering, laser marking, etc.

Figure 1: Technical part

SAMAPLAST AG has introduced and implemented a quality management system in accordance with EN ISO 9001, DIN SPEC 17071 and EN ISO 13485 to ensure compliance with and optimisation of your quality requirements, efficient structures and perfect company organisation. In addition, the following legal requirements must be met for the manufacture of medical devices:

- MDD 93/42 EEC: European Medical Device Directive
- MDR 2017/745: European Medical Device Regulation (replaces progressively MDD 93/42 EEC)
- 21 CFR Part 820: Quality Systems Regulations der U.S. Food and Drug Administration (FDA)
- RDC-16/2013: Brazilian Good Manufacturing Practice Guide of ANVISA
- MHLW MO 169: Ministerial Ordinance on Standards for Manufacturing Control and Quality Control for Medical Devices and In-Vitro Diagnostics of the Japanese Authorities (JPAL)

A key point of the various normative and legal requirements, especially in the manufacture of medical devices, is the validation of processes if they cannot be 100% verified, e.g. injection moulding, cleaning, packaging and sterilisation processes, bonding, welding, laser marking.

Figure 2: PEEK cages

Integrated CAQ system

For support and efficient QM process design, SAMAPLAST relies on a fully integrated CAQ system linked to the ERP system. This software is used, among other things, to implement the central QM processes such as: document, training, complaints and risk management. But also in the area of quality assurance, test planning and test data acquisition as well as test equipment management and maintenance/servicing are implemented digitally.

Basic information on process validation

The validation of a process is intended to prove that the application of a method under given circumstances consistently results in products that meet the predetermined requirements.

Process validation at SAMAPLAST AG is implemented in accordance with the following standards and guidelines:

- GHTF document: "Quality Management Systems - Process Validation Guidance"
- FDA guideline: "Process Validation: General Principles and Practices"
- PICs/GMP Guide: "Guide to Good Manufacturing Practice for Medical Products"

In the offer phase, SAMAPLAST AG uses the "Classification and Responsibility Matrix" to pre-define the processes to be validated for the manufacture of the medical device. In the course of the project phase, these are then determined together with the customer using the decision matrix.

Basic requirements (framework conditions) for carrying out the validation:

- Defined GxP environment
- Qualified main and ancillary facilities
- Qualified equipment (e.g. injection moulds and devices)
- Validated process software
- Calibrated instruments or test/measuring equipment
- Capable test/measurement systems (proof of capability by means of MSA)
- Specified and approved materials
- Trained and qualified personnel

These requirements result in the following process structure with corresponding basic requirements:

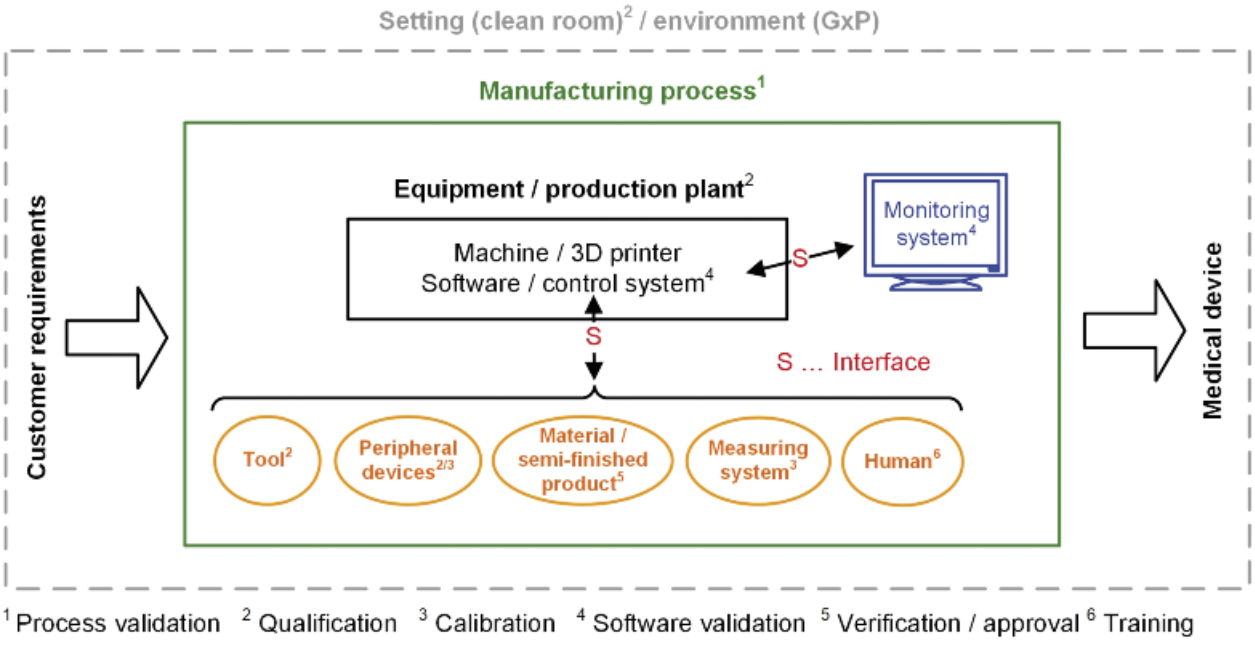


Figure A: Process structure and basic requirements (framework conditions)

Qualification of plants, machinery and equipment

The qualification serves as documented proof that the systems/machines have been designed, installed and tested in accordance with GMP and specifications and that they function in accordance with the specifications.

The qualification is implemented by means of the following qualification model (Fig. B).

The basis for this is the performance of a risk analysis to identify the critical functions (GxP relevance), definition of the requirements (URS) and the scope of qualification (qualification plan).

The focus is on the risk-based impact of the investment with reference to the product. This means that the GEP tests are referenced, "only" GMP-relevant tests are planned and carried out on a risk basis.

In the course of the design qualification (DQ), the requirements of the user requirement specification (URS = requirement of the user) are checked against those of the functional specification.

After construction of the plant/machine, acceptance takes place at the supplier's premises in the course of the factory acceptance test (FAT) and, if necessary, acceptance at SAMAPLAST AG by means of the site acceptance test (SAT) after the installation qualification (IQ).

Figure 3: Clean room 1 SAMAPLAST AG

The operational qualification (OQ) is the final check to determine whether the plant is operating as planned and whether proper functioning is guaranteed over the entire range of process-critical parameters determined in the course of a risk analysis.

With the qualification report (QR), the plant/machine is formally commissioned and integrated into the maintenance and requalification program. It is subject to change management until it is decommissioned.

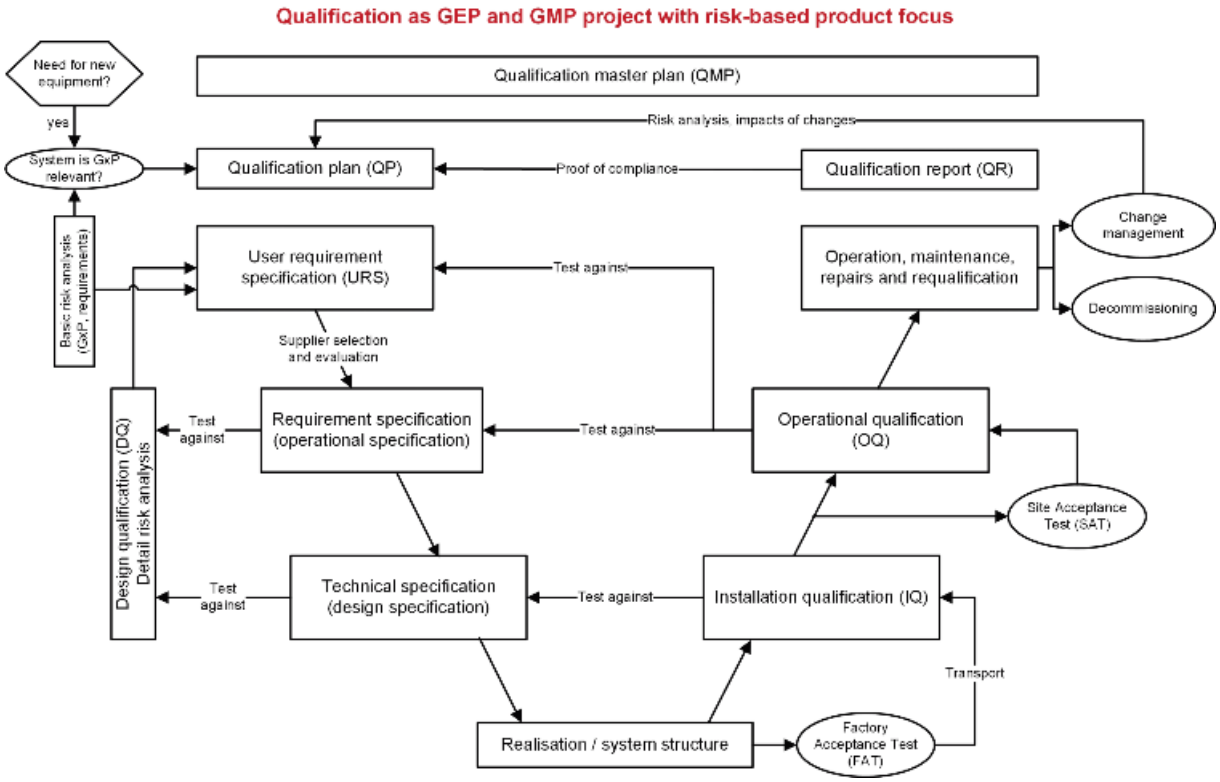


Figure B: Qualification model (V model)

Process validation - general implementation

Process validation serves as documented proof that the manufacturing process continuously produces a product that meets the specified requirements.

Validation at SAMAPLAST AG is implemented using the following validation model (Fig. C).

The basis for this is the execution of a process risk analysis to determine the scope of validation (validation plan), which is carried out together with the customer based on the customer's design FMEA.

In the course of the installation qualification (IQ), the framework conditions are defined. In addition, the qualification and calibration status of the main and auxiliary equipment, measurement methods (MSA), the implementation of software validations and the release of raw materials are checked.

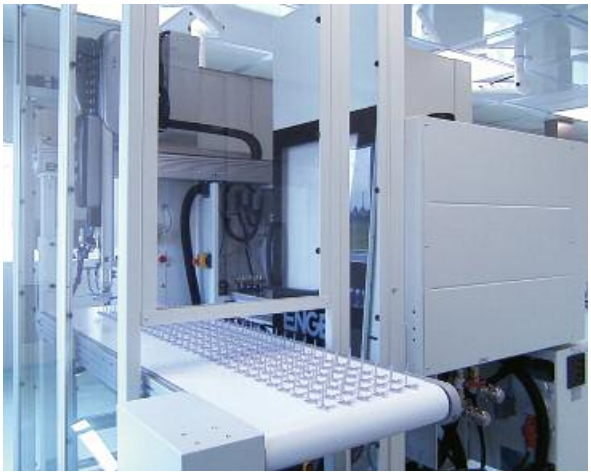


Figure 4: Clean room production SAMAPLAST AG

During operational qualification (OQ), the process parameters are examined under worst-case conditions with the main focus on the capability test of the machine in order to determine machine-related influences on the manufacturing process. Subsequently, during the performance qualification (PQ), proof of long-term process stability with consideration of process fluctuations is usually provided by at least three routine production batches.

With the validation report (VR), the manufacturing process (including training of personnel) is formally introduced and is subject to change management until the product phase-out.

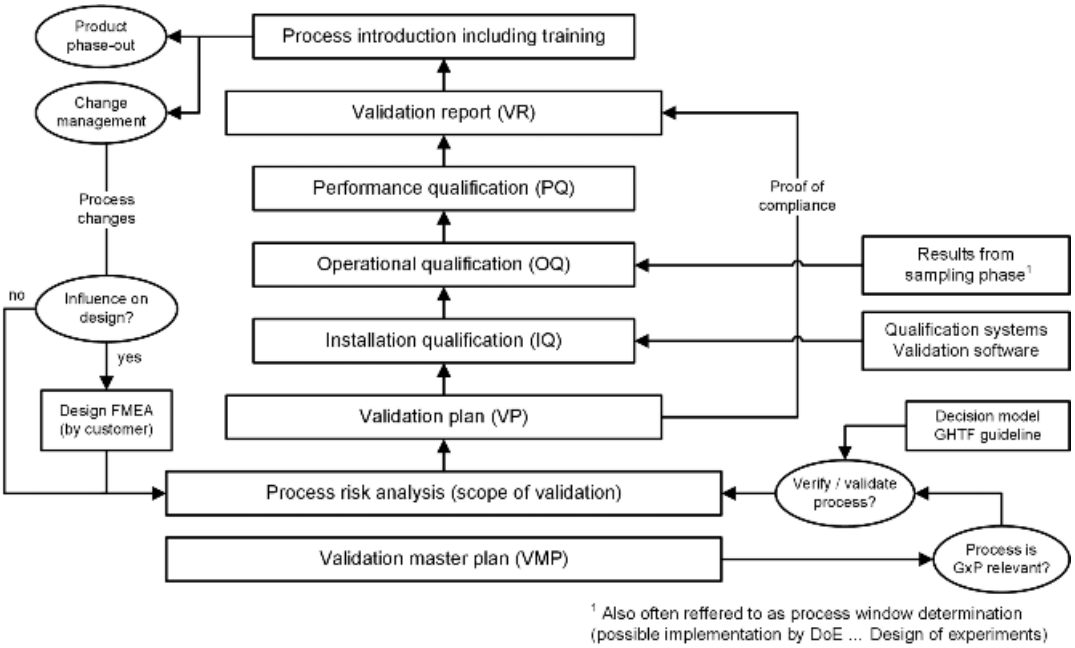


Figure C: Validation model

Computer-supported system (CSV)/software validation of the process software

For documented proof that the software used, including interfaces, works according to the specification, it is validated according to the GAMP 5 guidelines before the process validation is carried out.

The validation effort for the software validation is determined with the classification of the software and hardware into the GAMP categories and subsequent risk analysis and is specified in the validation plan (VP).

After implementation and release of the individual validation phases, installation qualification (IQ), operational qualification (OQ) and performance qualification (PQ), the software is released for operation by means of a validation report (VR) and included in the change management.

Development - this is where your component is created

We leave nothing to chance and develop a tailor-made and market-driven product from your ideas and wishes.

Our systematically structured development process enables us to support our customers in every phase of product development. On request, we can take care of everything from design to prototype production and carrying out the necessary measurements and tests.

In order to maintain a close dialogue with our customers, we consistently use modern development tools such as CAD, injection moulding simulation and specific calculation programmes. Our processes are trimmed to short lead times and direct communication both internally and with the customer.
In the end, you receive the optimised product data as a 3D CAD file as well as a component drawing, which was created by combining your and our know-how.

Based on the standards, internal processes and specifications of the customer (URS), the component development takes place with the following phases:

1. Design development

Based on the customer's requirements (e.g. drawing) and the many years of experience of our engineers, the specifications are developed and made available to the customer.

2. Design review/evaluation

With the standard use of development tools such as injection moulding simulation (MOLDFLOW), the design is analysed and checked for optimisation possibilities of component and process.

In order to consolidate the design and ensure the function, additional calculations and simulations (FEM, simulation...) are carried out according to need and risk.

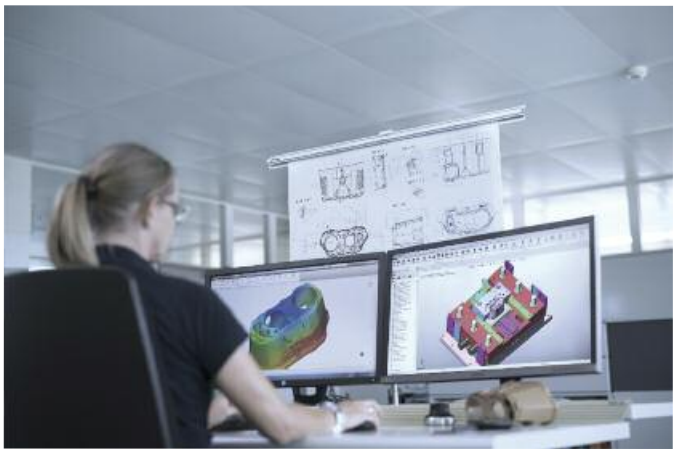


Figure 5: Design development/evaluation

3. Prototypes and small series

For initial functional tests, e.g. surgery handling, for marketing purposes, but also for biocomp tests or initial clinical studies, additive manufacturing (AM) or rapid tooling can be used to produce prototypes and very small series.

- Rapid prototyping master models (SLA, SLS, FDM, 3D printing, freeforming)
- Mechanical manufacturing processes
- Vacuum casting
- Rapid tooling

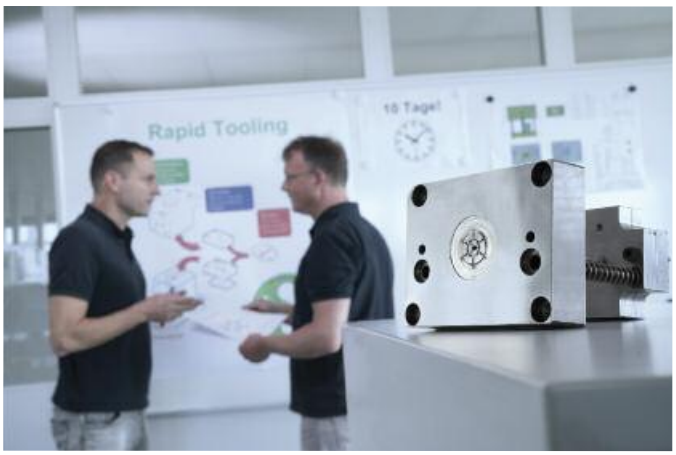


Figure 6: Discussion of tool concept

4. Design verification

As a preliminary step to design validation and to prove that the specifications are met, SAMAPLAST supports the customer with measurements and tests (e.g. material or functional tests, tensile tests, aging, CTs).

Tool design - implementation of the development ideas

Based on the design, the engineering department creates the tool concept and thus determines the strategy for the tool manufacture and production of the plastic injection moulded part.

Wrong decisions can drive up the tool costs and make the product unmouldable. At SAMAPLAST AG, the first milestone in project implementation is therefore a risk assessment based on the initial design idea with all key functions. In this way, we avoid errors and accelerate throughput times.

From idea to product

Based on the approved product design, the customer's specifications (URS) and the findings from the injection moulding simulation (MODLFLOW), our design department uses a 3D CAD system (NX) to design an injection mould that meets the product requirements. It also allows us to produce high precision and temperature resistant injection moulds for the technical or medical device industry and implantalogy.

Necessary workpiece mounts, assembly fixtures or test fixtures/gauges are designed project-specifically in the sense of POKA YOKE and LEAN as required.

They are produced in additive manufacturing (AM) from the original material of the product, if reasonable and in order to avoid cross-contamination of medical devices.

Continuity - a decisive factor

In order to reduce the interface risk, all cross-divisional production steps and quality-relevant processes are carefully planned, checked and introduced in the course of the design work for each new project.

In addition, we use a consistent data model from design to construction to the creation of the milling programmes (CAM).

The focus and goal of mould design is to create injection moulds that fully meet our customers' demanding accuracy, quality, delivery and cost requirements right from the start.

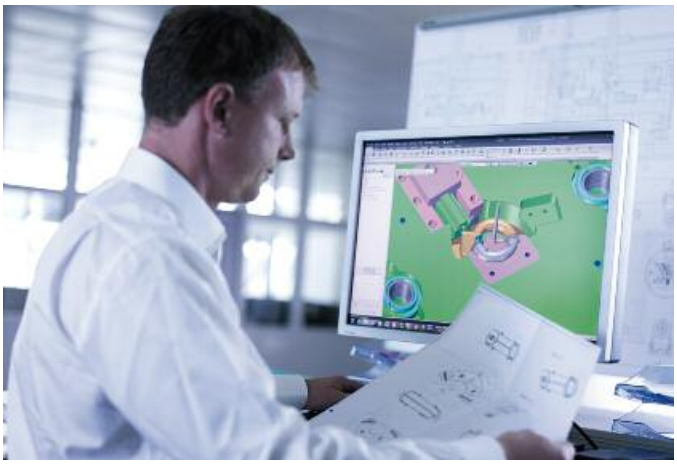


Figure 7: CAD - tool design

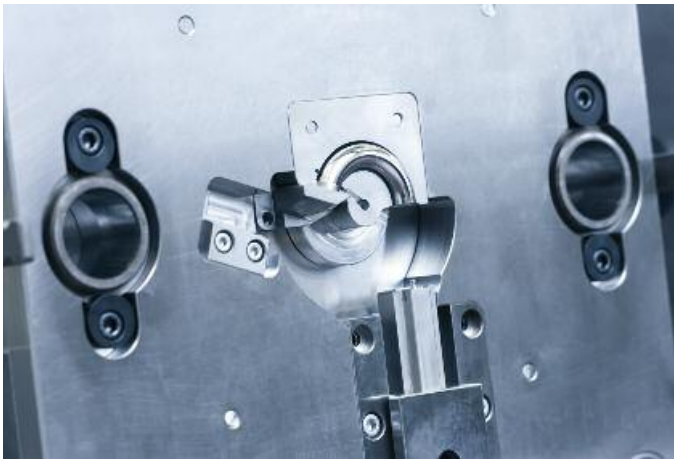


Figure 8: Injection mould

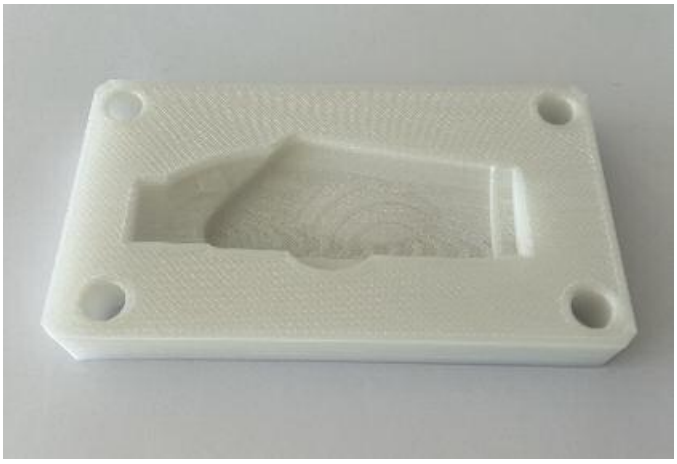


Figure 9: POKA-YOKE fixture made with AM

Toolmaking - guarantor for excellent quality

The precision and perfection of the injection moulds ultimately determine the quality and reproducibility of the injection moulded parts. In addition, these are the prerequisites for low wear and a long service life of the tools.

The decisive factor here is the optimal implementation of the designers' ideas during tool manufacture and stable process maturation in production (initial sampling and design of experiment).

The solution: consistent modern infrastructure paired with qualified employees with many years of know-how and cross-departmental project communication to minimise the interface risk.

Consistency in tool production

After the tool design, the data for the tool production is transferred to the tool shop. The toolmaking department has a direct interface with the development/ design department.

It enables the creation of CNC programmes for mechanical processing directly from the 3D data model with the help of the integrated CAM module (e.g. electrode production or hard milling).

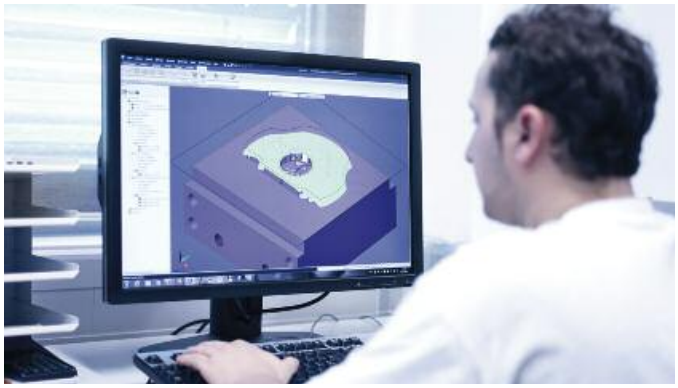


Figure 10: CAM processing

Modern infrastructure and qualified, long-term employees

Our qualified, long-term employees manufacture the tool components with high precision on a high-tech machine park.

Modern sink erosion and wire erosion machines support us to produce the most complex shapes and contours.

Figure 11: Mechanical processing

Nothing is impossible

In technology, everything should become smaller and more accurate. This trend is also noticeable in the injection moulding process.

To ensure that even the smallest moulded parts can be produced with the highest precision, the manufacturing process must already be carried out with the utmost precision during the tool production.

Figure 12: Micro insert - for resorbable screws M1.5

One system for many applications

In order to achieve the high quality requirements at competitive prices, SAMAPLAST AG has developed a modular mould system which reduces the manufacturing costs for an injection mould and guarantees the highest precision.

The perfect tool in less time

To reduce tool adaptation and sampling loops, SAMAPLAST AG relies on state-of-the-art measurement and calculation technologies. Compensation in 3-dimensional space is carried out via the reverse engineering and the target CAD data, and from this the CAM data for the tool machining machines.

Highly precise complex shapes and contours

With modern sink erosion and wire erosion equipment, the most complex shapes and contours can be produced with the highest precision and accuracy.

Wire cutting:

- Wire thicknesses up to 0.05mm
- Corner radii of 0.04mm
- Height from 10mm
- Accuracy of ± 0.001mm

SAMAPLAST is the leader in Switzerland in defined rotary cutting:

- Indexing with simultaneous B-axis in 0.001mm range
- Diameter 0,50mm with surfaces and contours
- Corner radii 0.06mm (see Figure 16)

With sink erosion, we achieve an accuracy of ± 0.005mm with the graphite electrodes produced in-house, depending on the surface condition.

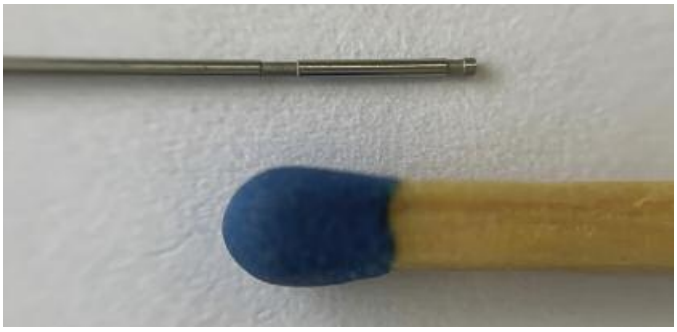


Figure 16: Rotating cutting with indexing at
⌀ 0.4mm with accuracy of 0.002mm

Figure 13: Interchangeable inserts/modular form (master form)

Figure 14: Wire erosion

Figure 15: Sink erosion

Free of machining residues due to ultrasonic cleaning

The production of injection moulds requires machining processes, e.g. milling, turning, drilling, grinding, but also the use of technologies such as spark and wire erosion.

Lubricants, coolants and various substances such as dielectric fluid are required for erosion.

These media, as well as oils for the preservation of injection moulds and the cleaning agents used for the cleaning process, must be removed without residue before the injection mould is used, so that they do not impair the quality of the medical devices and thus do not endanger patient safety.

Figure 17: US purifying plant

The residue-free (= free of machining residues) removal of chemical impurities from the production, storage or preservation and cleaning of injection moulds is achieved at SAMAPLAST AG by means of the validated ultrasonic cleaning process.

Subsequent phases were implemented in the course of validation:

- Definition of worst-case contaminants, parameters and products
- Determination of analytical procedures/testing methods (including validation)
- Determination of the permissible limit and alarm values
- Provision of the medical certificate (OQ and PQ)
- Monitoring

Our ultrasonic cleaning process:

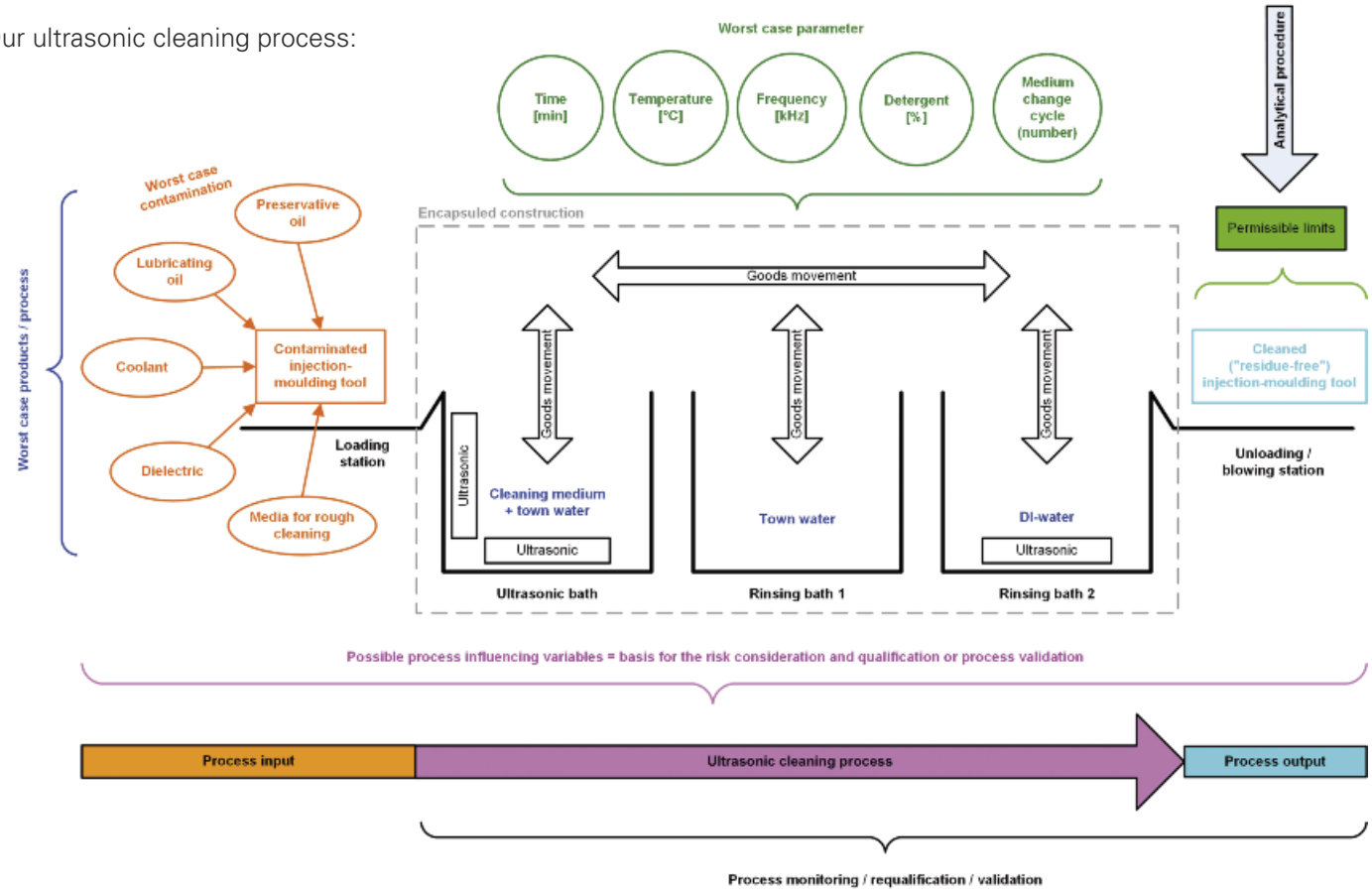


Figure D: Principle of the ultrasonic cleaning process

Injection moulding, our core competence

Innovative, precise, flexible - these attributes describe our view of production and customer service.

Paired with the experience of many decades, our know-how in the processing of high-tech plastics and absorbable materials is at the highest level. With the most modern injection moulding machines we process all thermoplastics and produce highly precise plastic parts with different weights.

Injection moulding machines:

- Microprocessor controlled
- 150 - 4000 kN clamping force
- Products weighing from 0.01 to 1000 grams

Processing of:

- Bulk plastics (PP, PE, POM, PA, PC etc.)
- High temperature plastics (PEEK, PEKK, PSU etc.)
- Resorbable plastics

Fillers:

- Dyes
- Radiopaque fillers
- Carbon or glass fibres etc.

Figure 18: Fabrication

Automation

For larger series, we have automated our injection moulding machines to such an extent that the parts are automatically removed from the injection mould using a freely programmable handling device.

In the automation cell shown here, the use of further peripheral devices has enabled automatic cutting of the gate, milling of the gate and stacked depositing in the transport box, including insertion of the intermediate inserts.

This enables autonomous production over a longer period of time.

Figure 19: Automation (spraying, milling and stacking)

Insert technology

Over the years we have perfected our insert technology. In addition to simple inserts, we now also use multifunctional combinations of inserts in the injection moulds.

Figure 20: Combination of a special threaded bushing connected to a functional antenna and another threaded bushing inserted in a second injection moulding process.

The result is a multifunctional product made of different materials such as plastic, steel and brass, which are ideally matched to each other and can therefore optimally fulfil their functional task.

Advantages of the insert technique:

- increased punctual mechanical strength
- firm connection due to optimum demoulding
- direct connection of functionally relevant components (e.g. plastic parts, sheet metal, bushings, etc.)

Figure 20: Insert technology

We get to the bottom of it

With us, man and machine form a unit that gets to the bottom of specific tasks.

In our technical laboratory we have modern analysis tools for the characterisation of the flow behaviour (moulding mass test) and for the proof of the residual moisture.

In addition, our specialists have a DSC analysis device at their disposal for the quality control of the raw materials and the manufactured components. Furthermore, the device can be used for damage analysis.

Assistance and safety in production

We can prove the effectiveness of the drying of the raw material by means of residual moisture testing.

Also in the event of production problems (e.g. surface defects - moisture streaks), the cause can be analysed or confirmed.

The MVR (melt volume rate) tester can be used to characterise the flow behaviour on the one hand, and on the other hand to check compliance with the material properties in the course of an incoming goods inspection or to analyse or confirm the cause of production problems (fillability).

Figure 21: Technical laboratory (MVR and residual moisture)

Root cause analysis to generate solutions

With the help of our DSC analyser (differential scanning calorimetry) we have the possibility to get to the bottom of things and to carry out cause research in the following areas:

- Identification of raw materials (granules)
- Quality control (correct processability of materials)
- Damage analysis (correct workability, raw material or mixture)

The Mettler Toledo DSC 1 system allows us to perform automated analyses on 34 samples in a temperature range of -35 to 700°C (± 0.2 °K) and, if necessary, in a nitrogen atmosphere.

Figure 22: Technical Laboratory (DSC)

Risk-based approach to process validation of the injection moulding process

Due to the variety of products available to customers in the injection moulding process, SAMAPLAST AG has developed a riskbased approach to implementing process validation of the injection moulding process. This was developed, among other things, under economic aspects and under consideration of the scope and type of project.

In the course of a customer-neutral basic validation, SAMAPLAST has provided evidence that the injection moulding process can be considered fundamentally valid, provided that the necessary framework conditions for process validation are met.

With this knowledge, the customer can carry out an economic project-related process validation (without PQ) with referencing to the basic validation on the basis of

- the customer's design FMEA,
- the process FMEA from the basic validation and
- the potential impact on patient safety and product quality.

If this is not possible, a validation of a specific customer project according to the state of the art must be carried out in full.

Figure 23: Dental parts

Basic validation of the injection moulding process and possibilities for the implementation of customer projects:

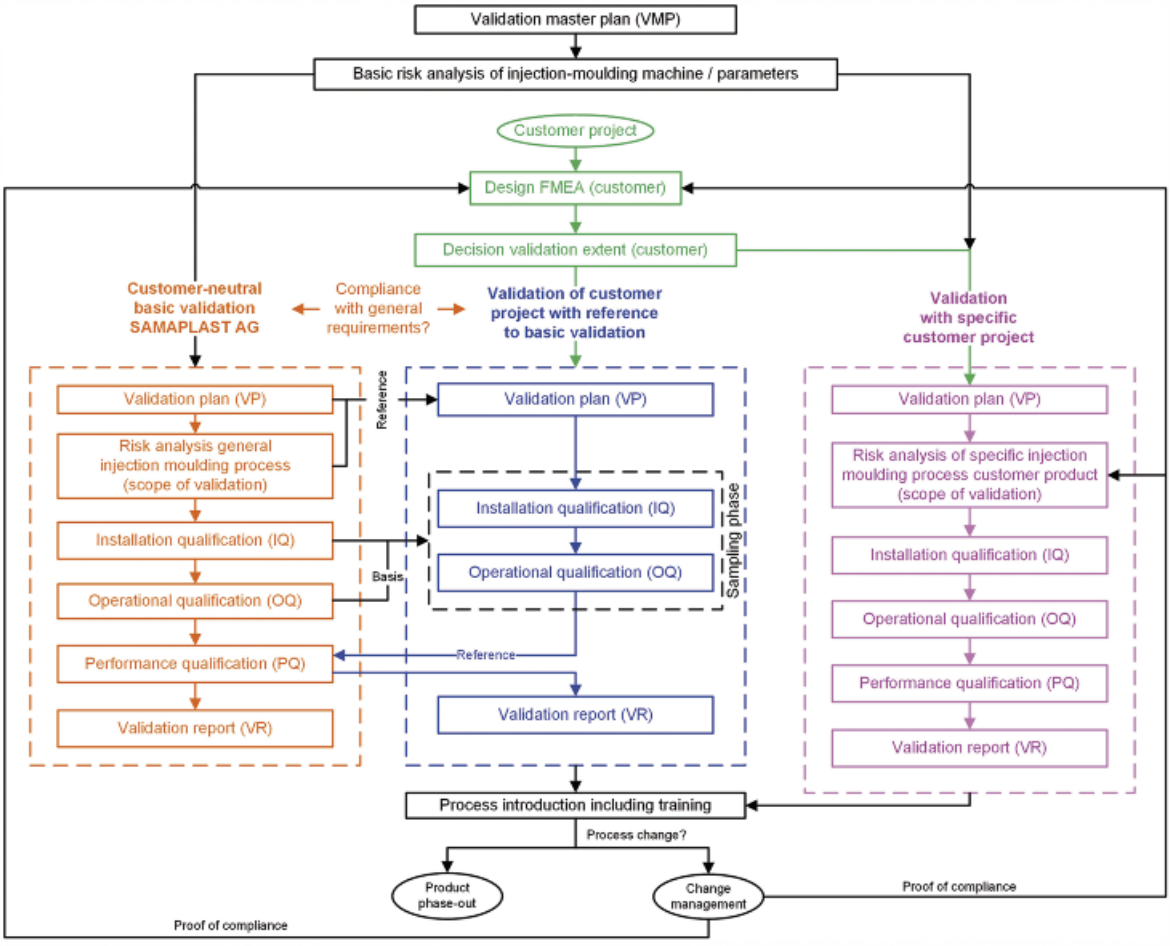


Figure E: Model for the risk-based approach to process validation of the injection moulding process

Prototypes from hardened steel tools in 10 days

Already since 2016, prototypes made of hardened steel are produced in 10 days with the Rapid Tooling concept and that also for the medical world. How is that possible?

- Prefabricated, hardened inserts made of approved materials are always in stock.
- In suitable master forms, sampling can be carried out without delay.
- Clamping devices and tools are standardised.
- All operational processes have been optimised.
  - Quotation preparation within one working day
  - Data creation in 3D-CAD with CAM coupling
  - Milling of the mould sections overnight
  - Injection moulding process on series machines in the selected environment (normal conditions, clean room ISO 7 or ISO 8 in operation)

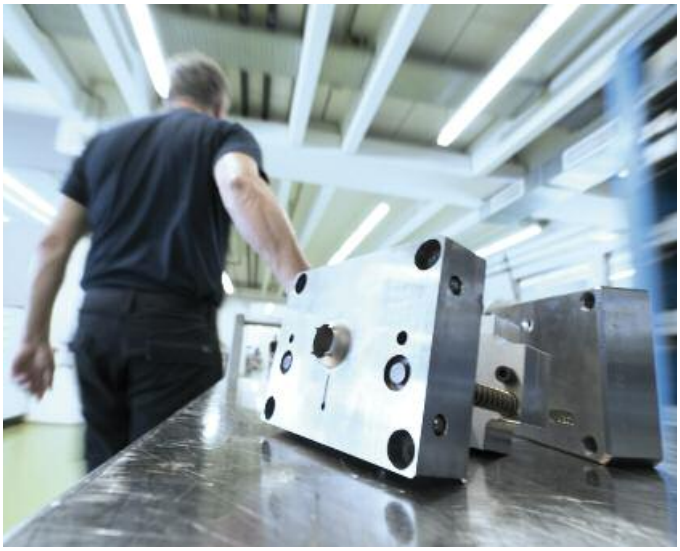


Figure 24: Rapid Tooling concept

The concept closes the gap between generatively or conventionally manufactured prototypes from the series tool. Testing on the "serial product" is now possible without high costs and long delivery times.

In most cases, the project lead time will be reduced. The risk can be significantly reduced at a very early stage. Particularly in the medical device sector, this opens up new possibilities, as the necessary evidence and tests can be started at an early stage.

Advantages for the customer:

- Delivery time for first samples: 10 working days
- Practically all plastics can be processed, including high-performance materials such as PEEK, PSU and highly reinforced plastics.
- Part size: up to 70x70x30mm; inserts are possible.
- Process control as in series production; production in a clean room is possible.

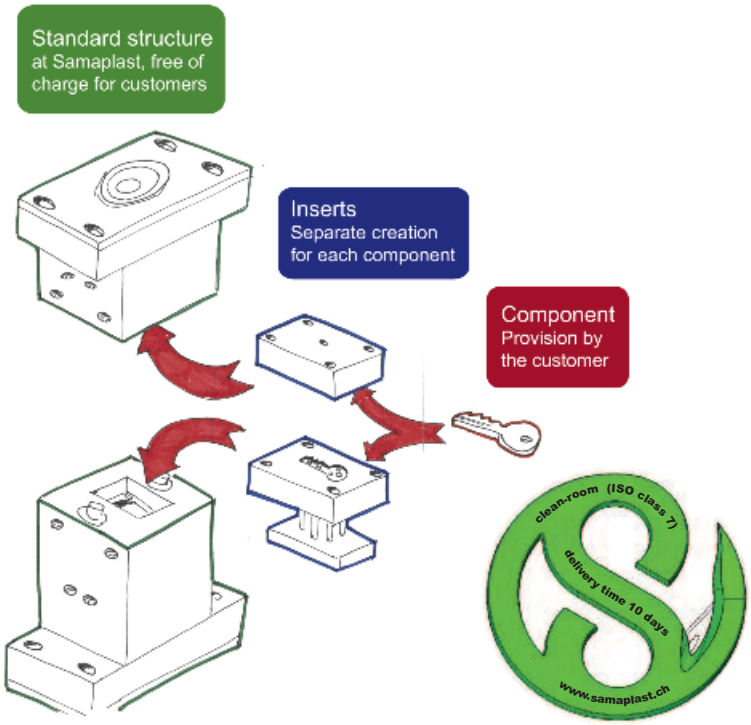


Figure 25: Rapid Tooling concept

The "time-to-market", a decisive competitive factor, can be significantly reduced.

Additive manufacturing (AM) - implants for humans and animals

Implant technology has come a long way in the meantime. Whereas in the past spare parts were produced in standard sizes, additive manufacturing is being used to produce more and more individual parts.

With the aim of implementing the production of medical devices using the validated additive manufacturing (AM) process for very small series up to batch size 1, SAMAPLAST AG has been using additive manufacturing with freeforming and FDM printing since 2018.

Today it is impossible to imagine life without this technology, because we use it to implement solutions that would not be possible with the classic injection moulding process.

One advantage of the prototyping process is that it reduces the risk of project failure. Why? Because critical function, handling and also biocompatibility tests, e.g. on cytotoxicity, can be carried out on near-series parts at an early stage.

Figure 26: Peek cages produced with AM

Key points in prototyping or AM

So what are the requirements for using products manufactured using additive manufacturing for medical devices or even as implants?

The first step is the procurement of equipment, the necessary process know-how and efficient project planning. Subsequently, the critical influencing variables and their effects must be developed in the course of a risk analysis and processed step by step:

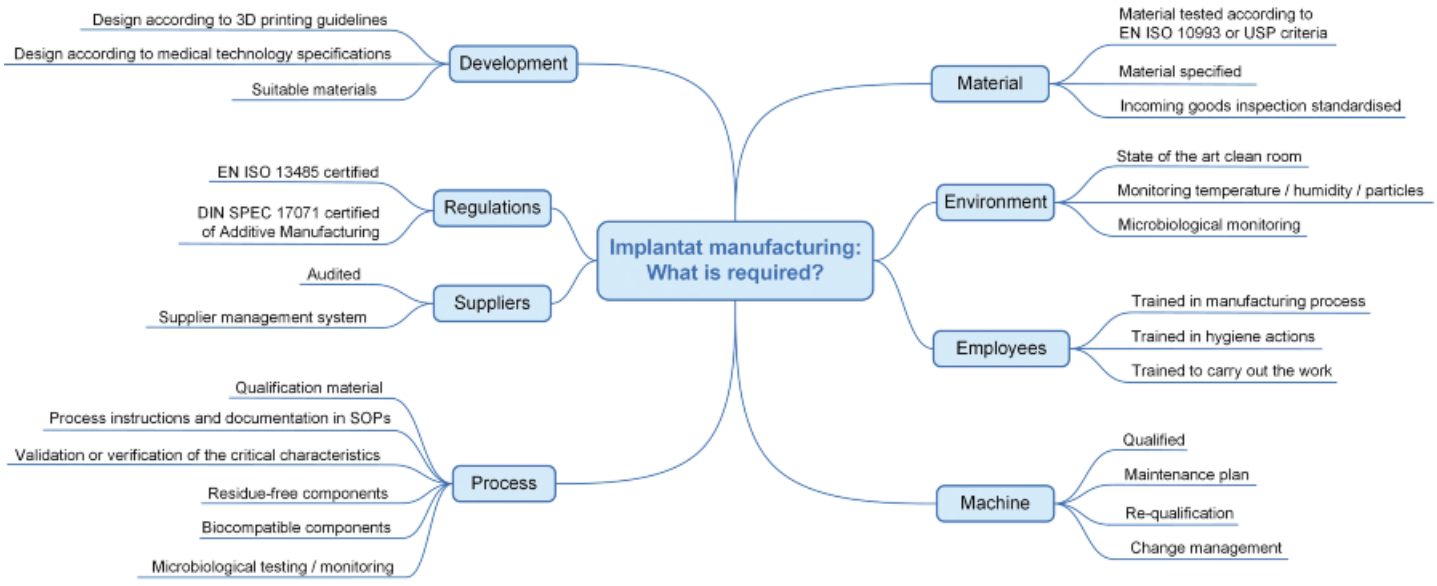


Figure F: Critical influencing variables and actions in AM production

Other key sticking points in additive manufacturing (AM) that need to be examined and resolved, especially in the manufacture of medical devices or implants:

- AM production within the defined framework of a management system
- Certification according to DIN SPEC 17071 (later ISO ASTM 52920)
- Interfaces to medical production according to EN ISO 13485 considered and transferred into a holistically functioning system
- Residue-free and biocompatible components
  - Carrier plates/materials: Checking or eradication of the possible risk of error
  - Qualified machines or 3D printers
  - Controlled environment (e.g. clean room ISO 8)
- Close cooperation with the manufacturers of materials and carrier raw materials, especially in the case of highly sensitive materials (e.g. absorbable materials or implant raw materials)

Bild 27: Resorbable C and Y plates

The art of the AM process

The process is based on the two pillars 3D printer and material. It appears simple, but requires high precision.

The big difference to injection moulding, where function and precision are controlled by the injection mould: With 3D printing, this is done exclusively through the component design, the strategy of the component construction and the fine tuning of the parameters.

The precise knowledge of the process and raw material guarantees printed components with the required reproducible quality over a long period of time and over several productions, comparable with a process validation in the classical sense.

Figure 28: Clean room (ISO 8) for prototyping

Material qualification as a guarantee for success

In order for a customer-specific process validation in additive manufacturing to function at all, a material qualification is necessary, based on a DoE (Design of Experiment).

The basis for this is at SAMAPLAST a large number of basic qualifications ("treasure chest") with minimum requirements (CTQ), which have been carried out on a wide variety of material types. In the case of customer projects, a series of tests is carried out on the basis of the "treasure chest" and the feasibility is thus fundamentally confirmed.

If possible and useful for the project, an in-depth DOE, worst case perspectives (WCP) and process validation (IQ, OQ, PQ) or verification are carried out for further data acquisition or to achieve optimal process consistency and as a basis for CE certification using specific customer data (D-FMEA, CTQ/function and design).

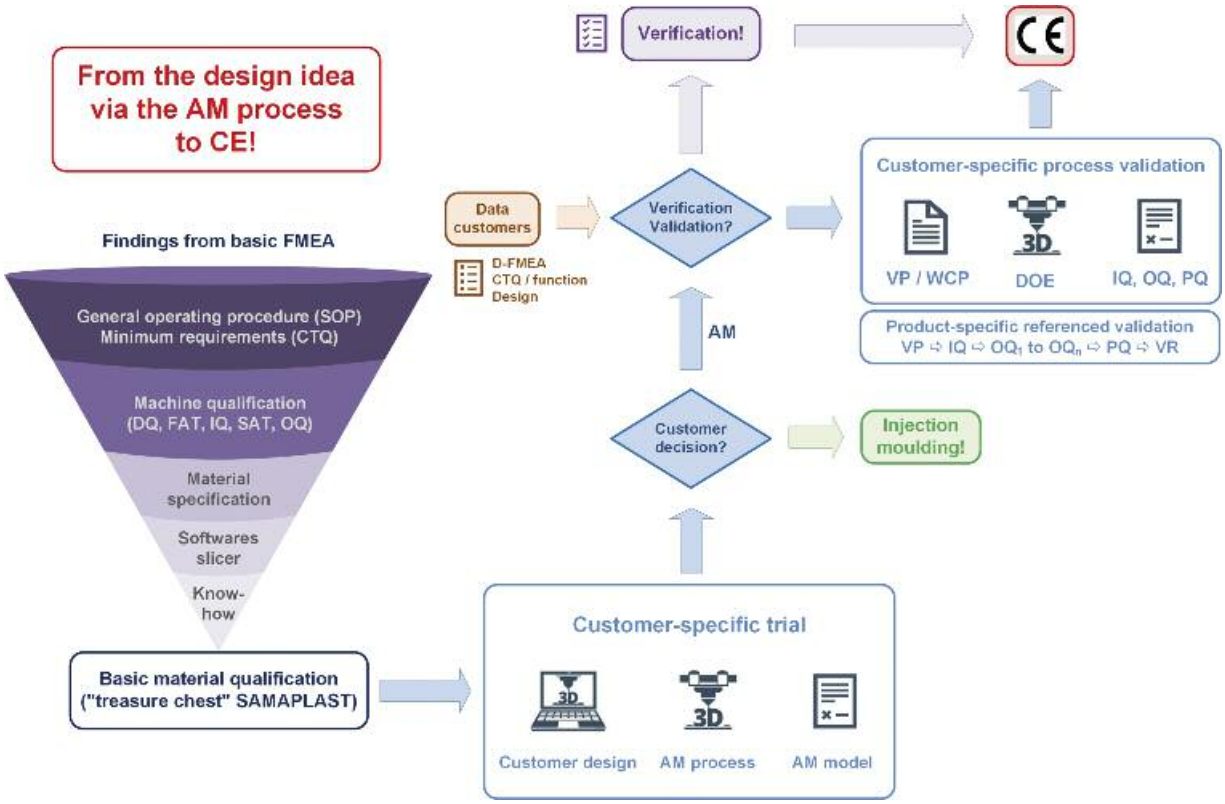


Figure G: Material qualification concept

Meaningful use for AM

However, 3D printing is not always able to deliver the solution or the success of a project/product idea right away. As with other technologies, those responsible must first ask themselves the question of feasibility and meaningfulness. The company currently uses 3D printing for the following tasks:

- Design finding: development of product ideas
- Design optimisation: risk minimisation
- Material specification/testing: quality
- Product support: biocompatible handling systems and devices in lightweight design
- Production of the tools: printed tool inserts for injection moulds
- Process optimisation: DoE as a basis for process validation and process freeze
- Series production: GMP-compliant manufacture of medical devices

Downstream processes - further processing

We make everything out of plastic, but there is no doing things by halves

We produce plastic injection moulded parts of the highest quality and precision. That's one thing. But we are also specialists in further processing and fully automatic production. Everything from a single source.

Mechanical processing as a supplement to injection moulding

Our programmable 3-axis CNC milling centres enable us to carry out the subsequent mechanical processing (e.g. gate milling, contour milling, engraing) in-house.

With the milling equipment and fixtures produced in-house by the tool shop, the optimised milling programmes and the project-specific working environment, mechanical machining can be implemented effectively and economically in the sense of lean management.

Figure 29: Milling

Flexible marking and labelling

With our pad printing systems we can print up to three different colours in one operation. In addition, the ink application and discharge on the X/Y positions and the print sequences/positions are easily programmable.

The possibility of programme/parameter storage, fully automatic pad cleaning and the specially developed clamping system based on the POKA YOKE principle support us in the flexibility and automation of the process.

Figure 30: Pad printing

Figure 31: Pad printing robot (automation)

Bonding as an alternative to US welding

Adhesive bonding can be a useful joining technique depending on the situation. We have many years of know-how in bonding technology with two-component or UV adhesives.

Additional equipment such as UV curing units or semi-automatic machines enable fast, accurate bonding and ensure controlled curing of the adhesive.

To ensure the tightness of the bonded joints, we have e.g. leak testers at our disposal.

Figure 32: Bonding

Joining components by soldering

With our top trained personnel in the fusion soldering process, we guarantee homogeneous connections (i.e.: no cold soldering, no cavities, no interrupted connections) of two electronic components (e.g. cable to antenna plate) and thus achieve the required electrical conductivity.

Proof of a perfect solder connection is provided by testing the electrical conductivity (e.g. testing the antenna signal) on a project-specific basis.

Figure 33: Soldering

From the idea to the fully assembled module

We assemble individual plastic and bar turning parts project-specifically in small batches, but also for semi- or fully-automatic assembly with high-tech assembly systems in large batches up to the fully assembled module.

If necessary, we integrate automatic testing, inspection and removal into the assembly.

In all processes, but especially in assembly, we try to optimise the processes through sustainable lean management in such a way that the process and product quality is improved.

To achieve this, we consistently use a wide range of LEAN tools such as set-up time optimisation, value stream analyses, shop floor management.

This enables us to implement all customer requirements flexibly, efficiently and cost-effectively.

Figure 34: Assembly in One-Piece Flow (LEAN)

Cleaning (washing or rinsing) of components or medical devices

For washing and rinsing with our HAMO T-21 cleaning system, only HPW water in accordance with the valid Ph. Eur. is used, which is produced with our qualified BWT ultrapure water system.

For the treatment of drinking water in highly purified water (HPW) the following phases are passed:

- Complete softening
- Reverse osmosis in downstream electrical mixing bed and ultrafiltration using sterile filter
- Storage in ultrapure water tank and sterilisation with ozone
- Prior to removal, ozone is degraded by means of a UV system

In addition to the qualification (DQ/FAT/IQ/SAT/OQ), the water treatment process was validated according to the state of the art with consideration of the worst-case parameters listed below, which are also checked in the course of regular monitoring.

- Conductance at 20°C ≤1.1 or at 25°C ≤1,3 µS/cm
- TOC <500 ppb (0,5 mg/l)
- Aerobic mesophilic germs <10 CFU/100ml
- Nitrate ≤0,2 ppb
- Bacterial endotoxins <0.25 EU/ml

Figure 35: HPW water treatment plant

Figure 36: HPW water treatment plant

Figure 37: Ultrapure water purification system

Medical devices or parts for clean room production made of titanium, POM, PEEK, PPSU etc. are cleaned with the qualified HAMO T-21 clean water washing machine with sluice function. For the defined standard cleaning processes (rinsing and washing) for metal or plastic parts, a cleaning validation was carried out according to GMP requirements.
In the course of this validation, the following influencing variables were considered, for which worst-case scenarios (WCS) were run:

- Degree of purity of the products before cleaning
- Worst case products and position (on product)
- Worst case inoculation position
- Cleaning equipment
- Filling level of the cleaning system

The process suitability in the course of the process validation of the individual WCSs was confirmed using the following analysis methods and parameters:

- Visual check for dryness
- Conductance
- Chemical residues on product
- Microbiological status (bioburden)
- Detection of bacterial endotoxins using the LAL test
- Cytotoxicity test according to EN ISO 10993-5

Marking and labelling with laser

With our qualified equipment, which operate using vector technology, we are not only able to mark products (e.g. CE mark, material) but also to apply lettering (e.g. UDI-compliant direct marking or logos for marketing purposes) to a wide variety of materials (e.g. plastics, metals).

For medical devices, this is also possible under controlled conditions in an ISO-7 clean room (in operation).

Compliance with the quality criteria (e.g. readability) is checked in the course of monitoring (IPC).

Furthermore, the maintenance of biocompatibility (abrasion problems) for medical devices after laser marking has been proven in the course of process validations on various materials (e.g. PEEK, PPSU).

In the course of the validation, the following influencing variables were considered, for which worst-case scenarios (WCS) were run:

- Worst case products (e.g. materials)
- Worst case laser parameters (intensity)
- Worst-case laser treatment (area)

The process suitability of the individual WCSs was confirmed using a wide range of tests from EN ISO 10993.

Figure 38: Laser marking systems

Figure 39: Laser treatment of a test head

US welding method for joining various components

With the help of the ultrasonic welding process, various materials with different properties can be joined together to form a product up to a sonotrode size of 100mm x 140mm.

For US welding of medical devices, qualified ultrasonic welding equipment with integrated control is used, which complies with the requirements of 21 CFR Part 11. Thus, the basic prerequisite for precise, versatile and economical US welding according to defined conditions was created at SAMAPLAST AG.

In addition, on the basis of a risk analysis in the course of process validation, documented proof of suitability was provided that the ultrasonic welding process welds plastic parts together reproducibly over a longer period of time, taking process fluctuations into account.

In the course of the validation, the following influencing variables were considered, for which worst-case scenarios (WCS) were run:

- Amplitude (amplitude of oscillation)
- Welding and trigger force
- Welding path
- Welding and holding time

The process suitability of the individual worst-case scenarios was confirmed by means of a wide range of test procedures/testing relating to the critical characteristics of the product or product group.

Figure 40: Ultrasonic welding system

Figure 41: C-Port^{CT} catheter system

Final packaging of sterilisable medical devices

According to MDD RL 93/42 EEC Annex I or MDR 2017/745, medical devices must be designed, manufactured and packaged in such a way that their operational characteristics and performance do not change during storage and transport, taking into account the information provided by the manufacturer.

To meet these requirements, the packaging equipment has been qualified (DQ/FAT/IQ/SAT/OQ) and the packaging process has been validated (IQ/OQ/PQ) by our packaging specialists with regard to the sealing parameters in accordance with EN ISO 11607-2.

In order to minimise the time and costs involved in the development process and project management, SAMAPLAST AG has determined standard medical device packaging for pouches and blisters of various sizes and materials and validated the sealing parameters for these.

In order to reduce the risk when carrying out the packaging validation of the final packaging, the effectiveness and reproducibility of the heat-sealing process was additionally demonstrated taking into account the influence of sterilisation and real-time ageing for the individual packages.

Figure 42: Qualified packaging machine

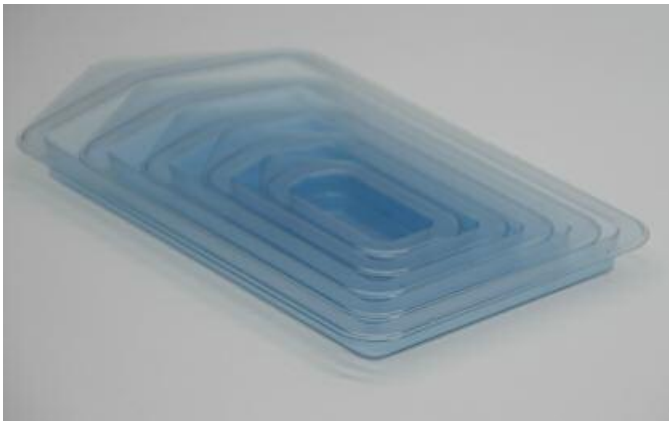


Figure 43: Validated standard packaging blister

Figure 44: Packaging examples

Validated standard packaging

When defining the standard packaging, care was taken to select packaging sizes and types that cover a broad portfolio of articles and corresponding sterilisation types.

Standard medical device packaging POUCHES

Material	Sizes
OPA-PE-Peel	45 x 95 mm to 250 x 500 mm
OPA-SiOx-PE-Peel	85 x 150 mm to 200 x 380 mm
OPA Aluminium PE-Peel	45 x 110 mm to 250 x 500 mm
Tyvek Peel tubular pouches	width 70 mm to 400 mm

Figure H: Standard medical device packaging POUCHES

Standard medical device packaging BLISTER

Material	Sizes
Blister material PETG Sealing film medical Tyvek	L=67.5 bis 179.5 mm B=35 bis 103 mm H=max. 85 mm

Figure I: Standard medical device packaging BLISTER

The implementation of phase 1 "Validation sealing process" from the packaging validation final packaging can be omitted if a validated standard packaging can be used. This significantly reduces the time and financial effort required.

Packaging validation final packaging

The aim of packaging validation is to provide documented proof that the specific requirements (sterility and function) of the final packaged medical device are met throughout the entire life cycle, i.e. up to the time of use.

To implement the requirements for packaging validation, SAMAPLAST AG has developed a validation concept in four phases based on EN ISO 11607:

- Phase 1: Validation of the sealing process
- Phase 2: Stability validation
- Phase 3: Durability validation 1
- Phase 4: Durability validation 2

This standard concept serves as a guideline for determining the project/product-specific validation procedure and should be planned together with the customer already in the development phase in order to reduce risk and save time.

Phase 1 "Validation of the sealing process" can be omitted if validated standard packaging is used, as the sealing parameters for this packaging have been validated in accordance with EN ISO 11607-2, taking into account the influence of sterilisation and ageing (5 years).

Phases 2 to 4 should take place in the course of a combined stability and packaging validation according to EN ISO 11607-1. In this validation, subsequent tests or parts thereof are carried out in the individual test phases with reference to the defined final packaging.

These tests are carried out partly in-house or by our accredited partners.

Test systems/test methods	Standard
Environmental simulation/ performance test	ISTA 1A, 2A, 3A
Pressure simulation test	ASTM D 6653
Accelerated ageing	ASTM F 1980
Visual inspection	ASTM F 1886
Peel test	ASTM F 88
Dye penetration test	ASTM F 1929
Burst and creep test	ASTM F 1140
Bubble emission test	ASTM F 2096
Testing the germination tightness	DIN 58953 Part 6

Figure J: Test systems/test methods

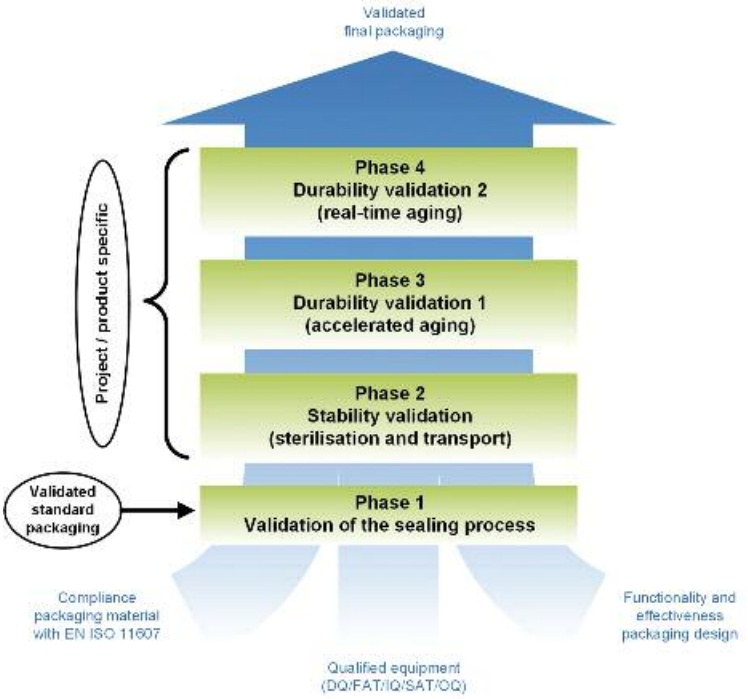


Figure K: Validation concept final packaging

Figure 45: Validated final packaging (bag)

Figure 46: Sealed seam inspection

Sterilisation of medical devices

Various methods can be used to achieve sterility of end-packaged medical devices. Two established methods are sterilisation by irradiation (gamma or X-Ray) or ethylene oxide (ETO).

Since adequate assurance of sterility of devices cannot be achieved by random testing, MDD 93/42 EEC or MDR 2017/745 requires validation of sterilisation processes according to harmonised standards that provide evidence of a Sterility Assurance Level ≥ 10^{-6} (SAL ≥ 10^{-6} means that there is a maximum of one living germ per 1,000,000 sterile medical devices)

Sterilisation by irradiations according to VD_{max}^{25}

The EN ISO 11137-1 to 3 series of standards proposes several procedures for sterilisation using irradiations. The most widely used method is the VD_{max}^{25} method, which uses a selected sterilisation dose of at least 25kGy and is applicable to products with a microbial load of ≤ 1000. It is divided into three phases:

- Microbiological validation (dose determination)
- Dosimetric validation (dose mapping)
- Auditing (dose monitoring)

In the course of the dose determination, a trial is conducted to confirm that sterility can be achieved for a non-sterile product with a verification dose determined on the basis of the hygiene status (bioburden) from three batches.

In auditing, this result is confirmed every three months, provided that production takes place during this period.

Dose mapping is used to confirm compliance with the defined irradiation dose for the specified packaging in all areas of the specified MIN and MAX loading on three independent runs.

Figure 47: Validated final packaging

Ethylene oxide sterilisation (ETO) - half cycle method (overkill)

In most cases, the half-cycle procedure according to EN ISO 11135-1 is used for sterilisation by means of ETO, which is divided into three phases:

- Half cycle ⇨ 3 runs
- Full cycle ⇨ 2 runs
- Short cycle ⇨ 1 run

In the half-cycle phase, three sterilisations provide microbiological evidence that a SAL of 10^{-6} is achieved with half the gas exposure time when loading MIN and MAX at the worst-case point of the product unit.

Figure 48: Validated final packaging (Tyvek pouches)

Subsequently it is confirmed that after two sterilisations with full gas exposure time with loading MIN a SAL of 10^{-6} is achieved, the residues of ETO (ethylene oxide) and ECH (ethylene chlorohydrins) show an acceptable level according to EN ISO 10993-7 and the function of the medical device or stability of the packaging is guaranteed.

In addition, the suitability of the test method and the proof of sterility are demonstrated on the "real product" in the course of a short cycle with low gas exposure time (= 1/6 of the full cycle) at maximum loading. It is also evident that the biological indicators (BI) are more difficult to sterilise routinely than the germs on the product, as well as their worst-case positions.

In addition, it is proven over all three phases that with loading MIN and MAX the physical parameters are maintained over the sterilisation cycle according to the specification.

Biocompatibility of medical devices

According to MDD 93/42 EEC Annex I or MDR 2017/745 humans must be protected from possible biological risks arising from the use of medical devices.

The extent for the implementation of this requirement and the procedure is regulated in the EN ISO 10993-1 to 20 series of standards. The basis of EN ISO 10993 is the decision model from EN ISO 10993-1 (Figure 1), which is shown schematically below:

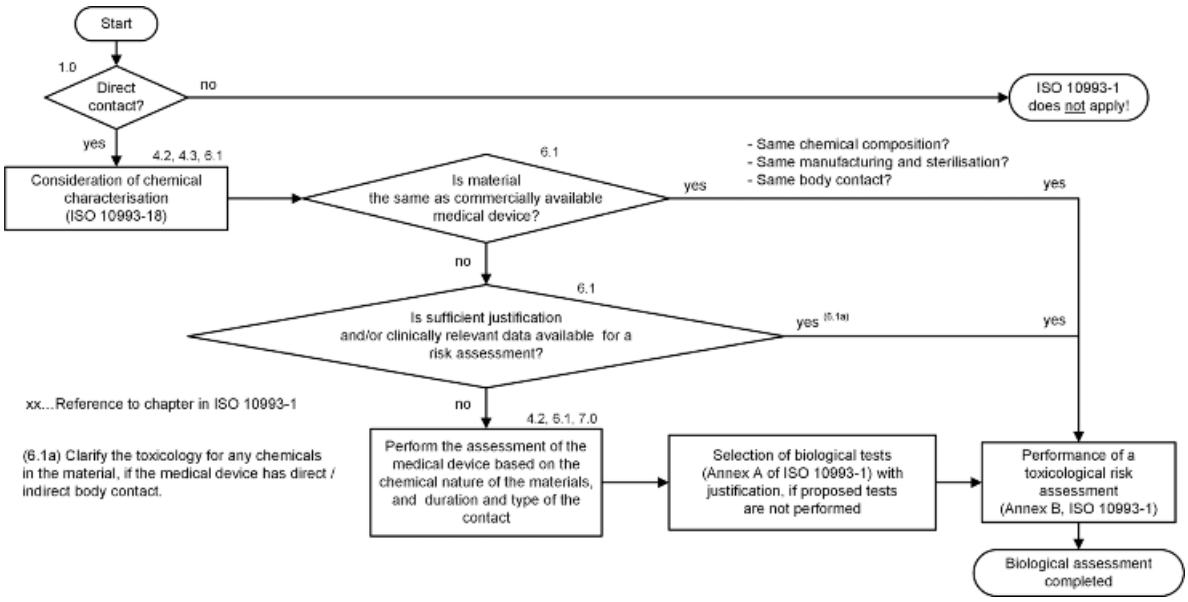


Figure L: Schematic representation of the decision model (Figure 1) from EN ISO 10993-1

From the consideration of EN ISO 10993-1 and the decision model, the following points emerge, which have to be considered or checked:

1. A biological assessment is necessary when there is direct physical contact.
2. The final product should be considered in the ready-to-use state, including the sterilised product where appropriate. EN ISO 10993 is basically not intended for the assessment of raw materials. There are regulations for these, such as USP Class VI (United States Pharmacopeia).
3. Provided that sufficient information is available regarding the chemical characterisation of the material (EN ISO 10993-18), that the material corresponds to that of a commercially available medical device, that it has the same chemical composition and that the manufacturing and sterilisation and body contact are the same, the biological evaluation can be completed after a toxicological risk assessment has been carried out.
4. Where there is sufficient justification and/or clinically relevant data (chemical or biological) for a risk assessment, the biological assessment may be completed after a toxicological risk assessment has been carried out.
5. Where points 3 or 4 do not apply, biological tests (see EN ISO 10993-1 Annex I) must be carried out on the basis of the chemical nature of the materials (EN ISO 10993-18) and the nature and duration of the contact. Once these tests and a toxicological risk assessment have been carried out, the biological evaluation can be completed.

Figure 49: Supporting medical product for bio-cages

Quality assurance with measurement competence

Quality is our job

Developing products and bringing them to market is one thing. Optimal quality you can rely on, the other. That is why quality assurance has top priority at SAMAPLAST AG.

We take a close look at the quality of our products

For the most accurate optical assessment of our micro injection moulded parts or surface conditions of the products or injection mould components, we have a digital 3D microscope with an infinitely variable wide-range zoom lens with a magnification of 20 to 1,000 times.

This is also equipped with a multifunctional vision system and a controller, scanner and surface measurement module, supported with optimising and vibration function. This allows us to create a depth of field composition in real time and 3D image creation.

Thus, even the smallest detail does not remain hidden from us.

Figure 50: Keyence 1000 times optic

Precision is measurable

For the automated measurement of our plastic parts we use a tactile 3D coordinate measuring system with a maximum measuring range of X=650, Y=1000, Z=500mm and an active damping device.

With the interface module, 3D data in a wide variety of formats can be read in, on which the measuring programmes are based. The coordinate measuring machine, the workpiece and the measurement results can be displayed in the 3D graphic.

Figure 51: Tactile 3D coordinate measuring machine

Optical measurement as an alternative

As an alternative to tactile 3D coordinate measurement, SAMAPLAST AG has an optical, programmable 3D coordinate measuring machine with video system available with a maximum measuring range of X=220, Y=150, Z=100mm and a magnification of 40 up to 120 times.

With these non-contact measuring systems, smallest parts or plastic parts with moving areas or components can be measured with very high measuring accuracy and speed without deforming or damaging the products.

Figure 52: DeMeed optical 3D coordinate measuring machine

The right strength for every product

To measure the tensile and compressive strength and determine the modulus of elasticity, we use the Zwick & Roell Z010 tensile/ compressive testing machine for a force of 100N to a maximum of 10KN.

The qualified testing machine is equipped with a macro extensometer which allows to perform a tensile test according to DIN EN ISO 527-1.

The determined data and curves are managed in the TestXpert software and can be edited or evaluated in any user-defined way.

In addition to the tensile tests, project-specific tensile and compression tests are carried out.

Figure 53: Tensile and pressure test

Too soft or too hard?

In a wide variety of cases, the hardness of the plastic injection moulding can play a decisive role.

To prove the correct hardness we use a digital hardness tester according to Shore, which allows us to carry out a hardness test Shore A or D according to DIN 53505 or ASTM D 2240.

The determined data are evaluated and managed by means of user software.

Figure 54: Shore hardness tester

Green is not always green

In most cases, an assembly consists of different components of different materials with the same colour. Depending on the type of component (painted aluminium housing or plastic injection moulding), there are differences in colour.

To ensure that colour differences remain within acceptable limits, SAMAPLAST AG determines the colour characteristics of the plastic parts with the aid of a Konica Minolta colour measuring device (spectrophotometer) or compares them with a standard (e.g. reference part) or another component.

The evaluation of the measurement is done with a special software based on the L*a*b color system (brightness L* and the color coordinates a* and b*).

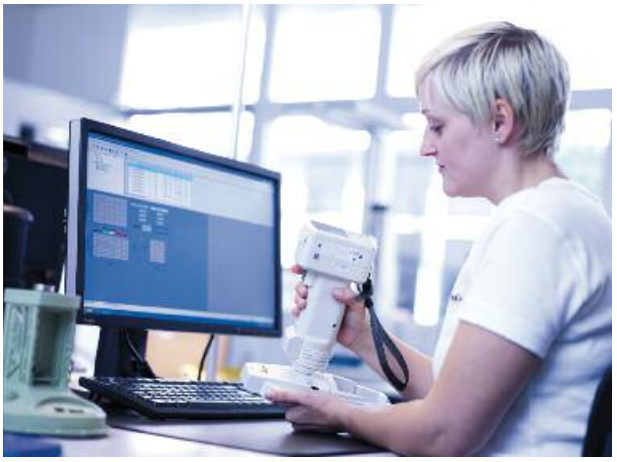


Figure 55: Colour measurement

Risk-based approach for measurement system analysis (MSA)

Measurement system analyses for the manufacture or testing of medical devices are increasingly required as a prerequisite. Due to the variety of products for its customers, SAMAPLAST developed such a risk-based approach for the measurement system analysis including economic aspects.
Basic MSAs were performed on the most common test equipment/test methods with a focus on worst-case conditions to fundamentally demonstrate capability within defined criteria.

In order to apply referenced MSAs in project implementation, the following worst-case criteria must match the customer-specific characteristics and be confirmed using a statement/rational.

- Measuring type of the measuring equipment/measuring system.
- Geometry of the features.
- The dimension of the characteristics should be within the minimum/maximum dimension of the worst case parts from the basic MSA (deviation max. 30% from the minimum/maximum dimension).
- Material characteristics (for contact measurement methods).
- The surface/measuring area must meet the criteria.
- The measuring position on the measuring equipment must match (e.g. caliper leg front/centre/rear).
- The tolerance/range must be comparable and meet criteria.

If a referenced MSA is not possible, a specific MSA according to the state of the art must be carried out in full.

Figure 56: Gear made of PEEK

The following diagram shows on the one hand the procedure of the basic MSA in general, and on the other hand possibilities for the implementation of customer- or project-specific MSA:

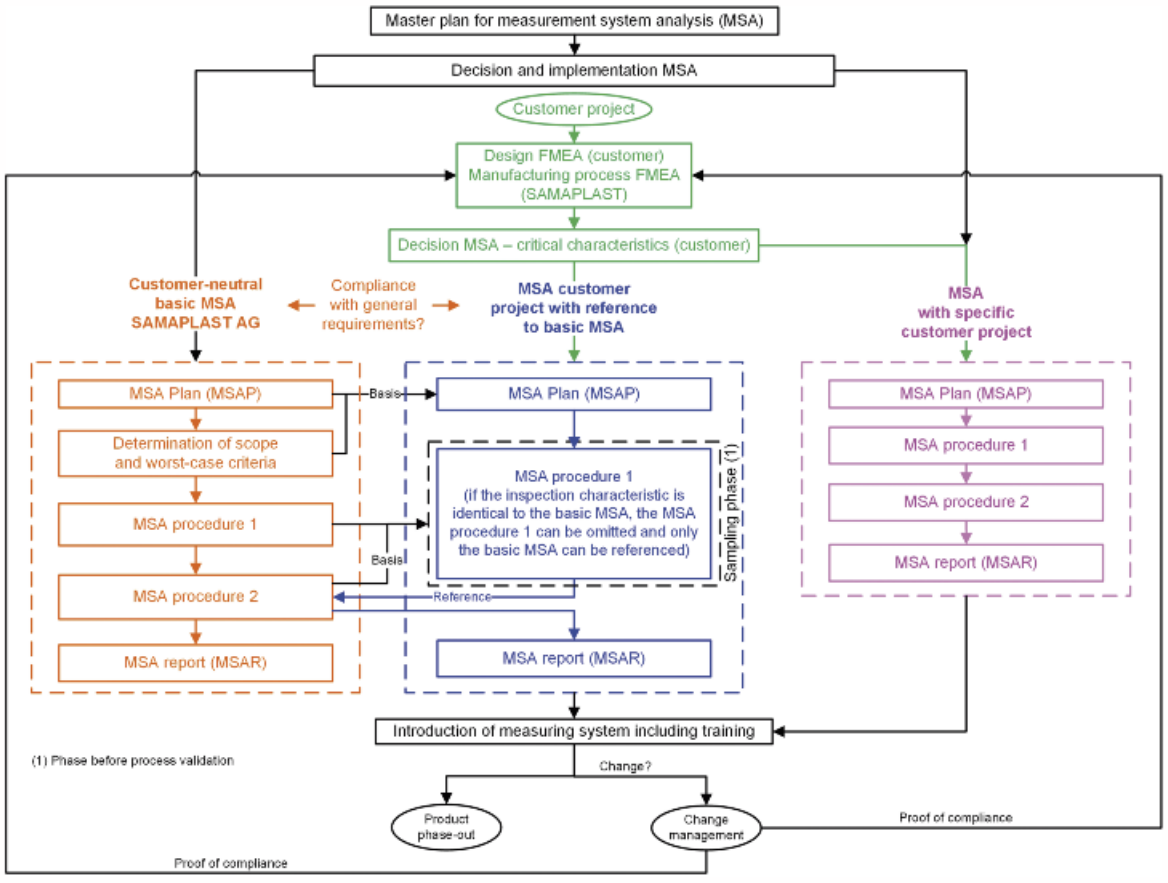


Figure M: Model for the risk-based approach to measurement system analysis (MSA)