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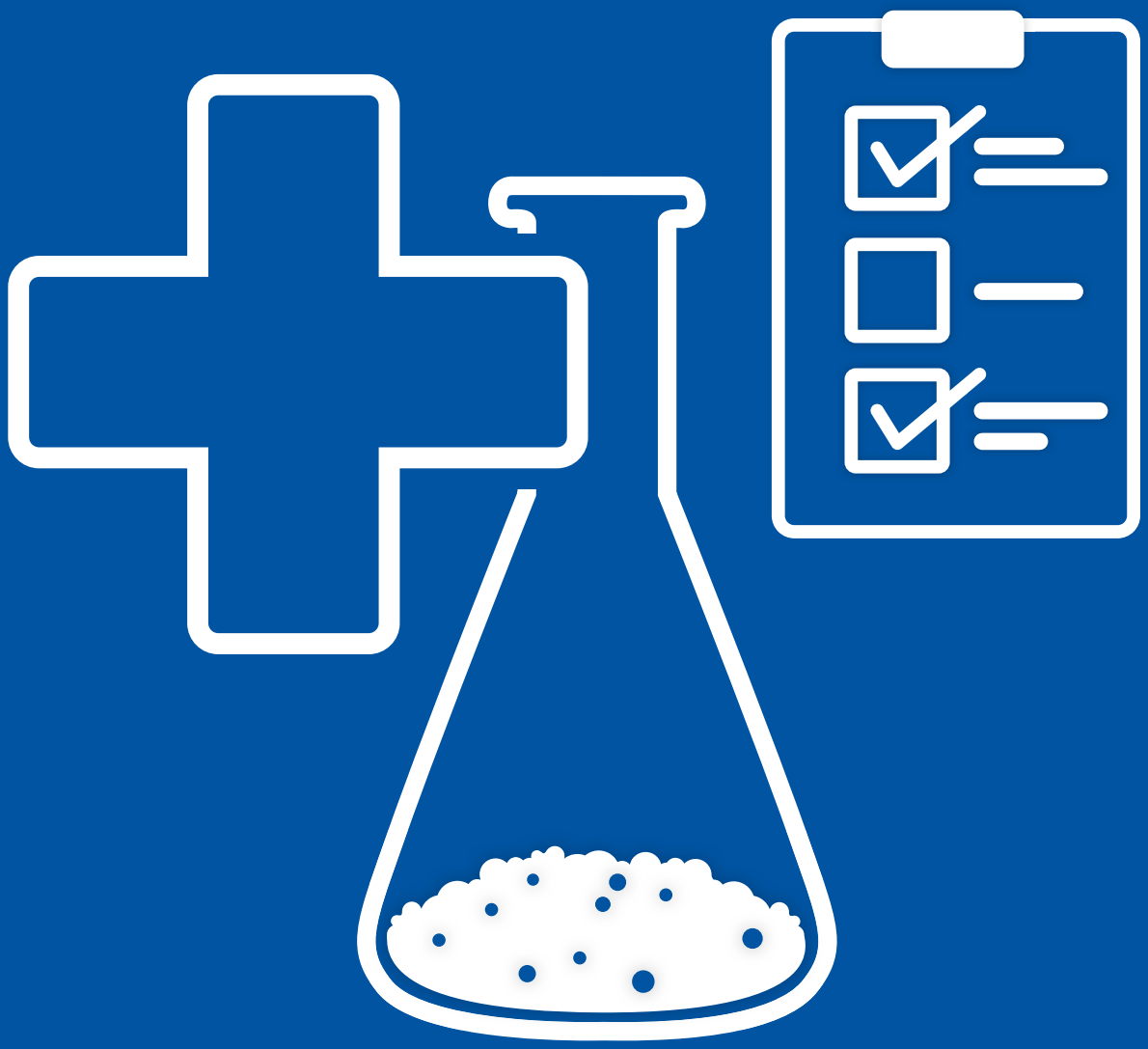
WHITEPAPER

Medical Grade Plastics –

Requirements for plastics in medical technology and the pharmaceutical



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Abstract

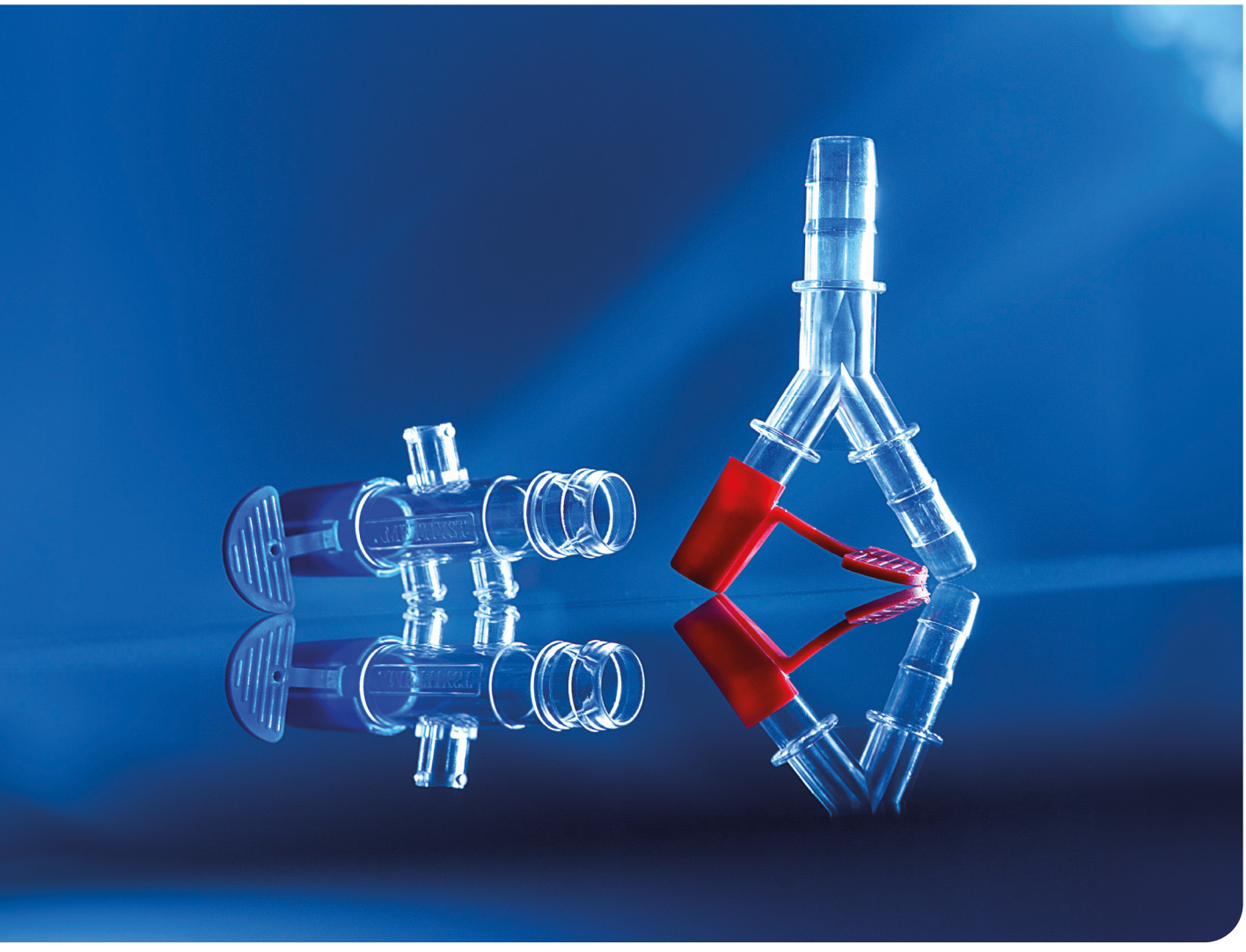
If you search for ‘plastics for medical products’ online, you’ll find plenty of hits for medical plastics, medical grade plastics or medical grade qualities from different manufacturers.

Many labels and associated data sheets indicate a specific procedure or guideline that makes these plastics inherently suitable for any type of medical device.

Yet there’s still no clear definition of ‘medical grade’.

The term really is a black box whose definition needs to be clarified. It also needs to be clarified whether the end product really needs to be medical grade.

This White Paper deals with the different definitions of medical grade—from a technical perspective (USP VI, ISO 10993, VDI) and considering regulatory aspects (MDR). The authors also provide practical instructions for choosing the right plastic to safely bring products to market. The White Paper is primarily aimed at SME manufacturers of plastic components for medical devices as well as at plastic medical device distributors without specialist material expertise.



Introduction

Plastics have long since superseded materials in medical technology such as metal or glass. Whether cannula, prosthesis or blood glucose meter: more than half of all medical products manufactured worldwide are now made of plastics. In many areas and applications, they can't be replaced by any other materials.

It's no wonder, because plastics combine many special properties: They're easy to process, virtually unbreakable, lightweight – and can be precisely adapted to a wide range of requirements profiles.

When selecting the right plastic for a medical device, developers are often guided by the 'medical grade qualities' promoted by raw material manufacturers and distributors. In other words, medical plastics with the relevant evidence of biocompatibility in accordance with US or European standards and regulations. This evidence implies that the material is adequately specified for use in medical devices.

The materials then come with a certificate confirming that the products contain no toxic substances or they comply with the MDR requirements, for example. Or biological safety tests have already been carried out on the starting material in accordance with ISO 10993 and/or the US Pharmacopoeia (USP) and confirmed by the relevant certificates (e.g., USP Class VI).

However, to the very day, no guidelines or standards exist in the USA or Europe that provide a clear definition of medical grade plastics.

In addition, merely considering the material used says nothing about the biological assessment of the end product. This is because the manufacturing process can also have a considerable influence on this assessment.

Her the ball is in the medical device manufacturer's court in every case. As the 'distributor', they are legally responsible for the safety of their product.

Patient safety comes first

Medical technology is a heavily regulated industry: The development of products, as well as the selection of suppliers or quality requirements, are more or less prescribed. The overarching regulation in Europe is the **Medical Device Regulation (MDR)**. The MDR came into force in 2017 and placed the focus even more squarely on the safety of medical devices for patients, users and third parties.

The amended MDR from 2017 was partly prompted by one of the biggest scandals in the industry: the PIP scandal. For over ten years, the manufacturer Poly Implant Prothèse (PIP) marketed breast implants made of inferior industrial silicone, which led to significantly elevated rupture rates (frequency of tearing). The manufacturer had used a silicone material not specifically declared for medical use. All approval and quality controls failed because of PIP's willful deception. The scandal reignited a major debate on medical device safety. This provided the impetus for the European Union to introduce a new law for medical devices in Europe focusing more on the safety of these products for users, patients and third parties than had previously been the case.

All legal requirements can be broken down to the basic principle:
The medical device must be safe and effective throughout its life.

This fundamental legal demand results in requirements for the product, which are often described in 'product standards' (e.g., the connection forces of medical tubes to connectors - ISO 8536), but ultimately many properties of a product can also be traced back directly to its material properties. Material selection for medical devices therefore plays a crucial role.

Material is becoming a success factor

Owing to the heightened requirements, all suppliers along the value chain (including material and raw material suppliers) are made even more accountable.

For example, the following is required:

- **Knowledge of what influence processes have on materials - DIN EN ISO 13485**
- **Knowledge about the use of CMR (Carcinogenic, Mutagenic, or Reprotoxic) substances and phthalates**
- **Knowledge on the compatibility of materials with other substances that are relevant when using the product—including drugs used**
- **Knowledge of how to mitigate the risk of materials, particles or substances released by the product**

The right material can determine whether a product is successful or not.

Irrespective of who makes the material selection decision—it should generally be critically questioned.

If the material is not prescribed, various decision-making factors should be considered and addressed to the relevant specialist departments:

Material price and availability (Purchasing)

Regulations → Purchasing / regulatory expert / material expert

Design and machining processes → Design and manufacturing

Design / haptics / optics → Users

Technical material properties → Material experts

Creating a requirements profile

In practice, the decision on the materials used can start with a requirements profile. This profile is compared with the data sheets of specific materials and/or information from potential suppliers. In-house material tests and benchmarking are also common for special or industry-specific requirements.

Example of a requirements profile

Requirement	Condition	Material A	Material B	Material C
Tensile strength	> 100 MPa according to ISO 527	Yes	No	Yes
Price	< 3 €/kg	Yes	Yes	No
Processing	MFR > 20 g / 10 min	No	Yes	Yes
Package	Bagged products 20 kg	No	No	No
Others				

Source: Polyneers

IIn this tabular form, various criteria are defined, which can then be compared with different material options. In this simplified and exemplary comparison, all materials have the same number of conditions fulfilled, which complicates selection. To facilitate selection in practice, the criteria should therefore be made stricter. For example, MUST and SHOULD criteria can be distinguished. It may also be helpful to assign quantitative weightings to the conditions.

Special requirement: Criticality

In medical technology, the law requires that patient safety comes first. The criticality factor should therefore be adopted in the material decision. Criticality refers to the risk-based assessment of what influence the property under consideration has on the safety of the end product.

Wherever possible, product requirements should be linked to measurable material requirements. Besides the classic technical and commercial requirements, the matrix is supplemented with product and industry-specific requirements such as biocompatibility, sterilizability or aging stability.

Example of a requirements profile – supplemented with the criticality factor

Requirement	Condition	Criticality	Proof
GENERAL			TECHNICAL DOCUMENTATION
Tensile strength	> 100 MPa according to ISO 527		
Price	<3€/kg		
Processing	MFR >20g/10 min		
Package	Bagged products 20 kg		
Others			
SPECIFIC			
Biological safety	ISO 10993-xx		
Sterilizability	Radiation up to 45 kGy		
Aging stability	ASTM F1980		
Supply chain reliability	2nd source		
	Security stock		
	Change Management		
Stable properties	Consistency of formulation		
	Change Management		
Others			

Source: Polyneers

Material selection in medical technology

In medical technology, materials and suppliers are selected on a risk basis. Product requirements are translated into material requirements, and the importance of each requirement is evaluated based on criticality for patient safety. Evidence such as test reports, raw data and other records are part of the technical documentation of a medical device.

On the term ‘medical grade plastics’

If one follows the previously prepared risk analysis, good pre-evaluated supplier and material criteria should ideally emerge. Nevertheless, there is still a large number of diverse suppliers and material options with different quality standards. This is because every material manufacturer or supplier defines its portfolio based on different quality characteristics and properties.

In addition, there is currently no protected term ‘medical grade’ to which direct and unified quality standards are linked. No material certification exists for use in medical technology either. USP Classes I to VI or biocompatibility testing according to ISO 10993, which are often used in this context, on their own, are by no means sufficient for product approval by the authorities.

For approval, in order to take process influences or material interactions into account, for example, the entire product must also always be tested as well. Because ultimately, the

application defines all requirements. So generally, any type of plastic can be used for any application, as long as the requirements of the application are met.

An example: Biological safety (in particular biocompatibility according to ISO 10993) applies to infusion tubing, but is not required for the housing part of an infusion pump.

Unified definition from the VDI Guideline

So why do we need a definition at all for medical grade plastics?

The greatest benefit for all participants along the value chain—from raw material manufacturers to processors and distributors—arises when the term 'medical grade' universally covers a defined range of aspects. A VDI expert committee proposed this standardization of definition in the VDI Guideline 2017.

The 'VDI Guideline 2017 on Medical Grade Plastics' is the first practical guideline for clarifying certain requirements between manufacturers and material suppliers in medical technology. In the Guideline, the safety concept for medical devices is systematically traced back to material properties.

A medical device is considered safe if it fulfills all its testable requirements during its life cycle. A medical device is therefore safe if its properties don't change. As materials and processes in the manufacture of the product have a significant influence on the properties, there is a need for systematic feedback—from stable product properties, to stable processes, and stable material properties.

Ensuring stable product properties

Three essential attributes describe this requirement:

- **Consistency in formulation**
- **Functioning change management**
- **Guaranteed supply chain reliability**

Consistency in formulation serves to ensure stable material properties and hence also product properties. A formulation is therefore considered to be consistent if the components (plastics and additives) and the production processes remain as unchanged as far as possible over the life cycle.

Changes in the raw material (components or process) during the life cycle of a medical device are unavoidable, however. To mitigate the risk, all changes to be made as part of a change management process are therefore evaluated in terms of their impact on patient safety.

In this context, an agreement prescribing timely notification of changes by the supplier is also mandatory. It serves to ensure supply chain reliability and ultimately also to safeguard patient care. Specifically, suppliers are required to provide a concept that includes, for example, alternative sources of supply (2nd source), alternative grades, alternative production lines, etc.

In practice, the above characteristics are negotiated and defined in quality assurance agreements (QAAs) between suppliers and customers (processors or distributors).

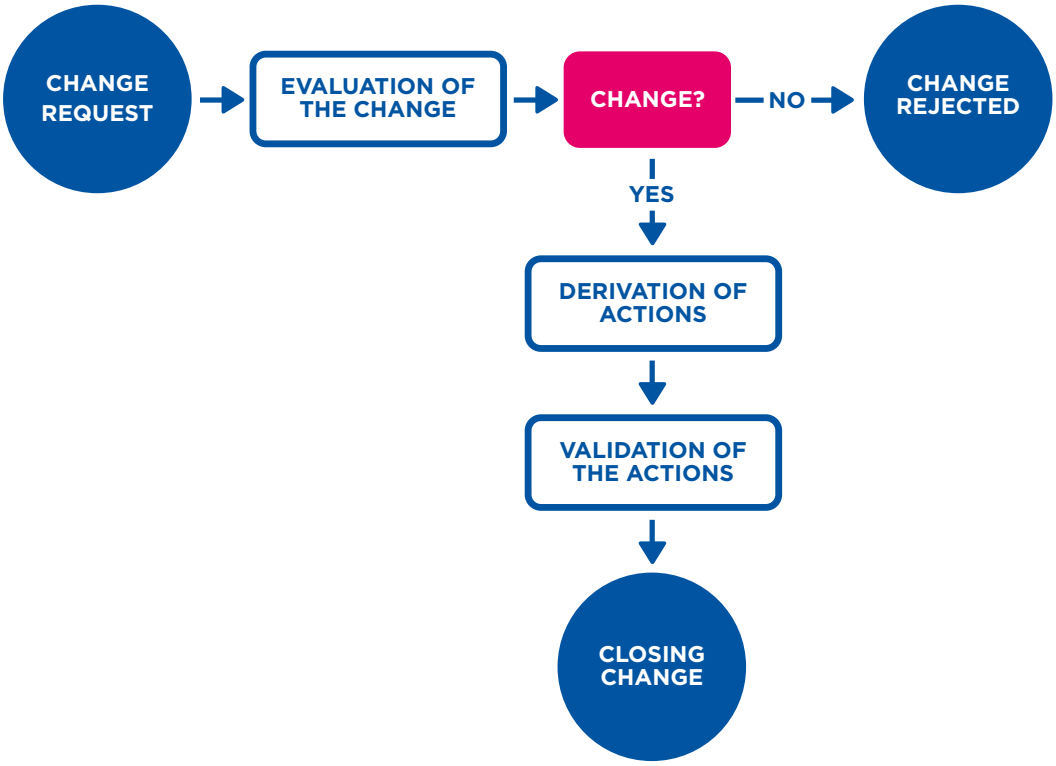
One scenario shows the importance of the customer-supplier relationship

You're a project manager at a distributor of medical devices whose product portfolio also includes medical tubing.

The European Chemicals Agency (ECHA) has included an additive in the candidate list of REACH Annex XIV which is a stabilizer in the tubing material you use. This means that from a certain date (sunset date), the distribution and use of this substance will be generally prohibited. Your material supplier decides to replace the stabilizer with an (unclassified) alternative. The changeover in production is to take effect in six months. Until then, the formulation with the current stabilizer can still be sourced (last order call). Your material supplier will notify you of the upcoming changes with an official letter.

This letter then triggers a 'chain reaction' in your company in terms of change management ('change request'). You'll be tasked with coordinating the change project.

The schematic approach could be as follows:



Explanations for the individual sections in relation to the scenario:

1. Evaluation of the change

The specialist departments (e.g., R&D, Production, Logistics or Regulatory Affairs) and the material supplier provide an assessment ('Expert Statement') of the change and evaluate the potential influence on the final medical device, in this case a catheter set for urological use.

2. Acceptance or rejection of the change request

Accepting the change request is purely a formality in the scenario described, because the upcoming change obviously has a far-reaching impact—there is the threat of inability to deliver. You form a project team.

3. Derivation of actions

Your material supplier has already proposed a possible action with the alternative stabilizer. However, there are other options:

- Use of another (unlisted) stabilizer
- Application for approval of the stabilizer already in use
- Change the tubing material with harmless additives
- Discontinuation or decommissioning of the medical device due to lack of alternatives

Together with Management, the project team now decides on the material supplier option. It is also decided to search for a second supplier (2nd source).

4. Implementation and validation of the actions

Even before validating the 'new' tubing material, take a look at the associated risk analyses for the product and check which attributes need to be revalidated. As a rule, the influence on biocompatibility and aging behavior must be retested and re-evaluated.

5. Closing change

Once all actions have been completed and the documentation for the new tubing formulation has been updated, the change process can be completed.

Depending on the "degree of innovation" of the actions, the entire change process can take between a few months to years. For this reason, it is essential to conclude a Quality Assurance Agreement (QAA). In the example shown, the QAA attributes of consistency of formulation, prenotification period in case of changes, and last order call, support this change process and future ones. To further mitigate risk, your company should still consider developing an alternative tubing material with a less harmful stabilizer class.

Conclusion

Materials selection in medical technology does not differ significantly from other sectors of industry in purely technical terms, because here too the properties and requirements of the product determine the requirements for the materials used.
In medical technology, however, additional application-specific requirements such as sterilizability or biocompatibility arise as well as the general requirements (like rigidity or transparency).

A requirement matrix can help in the selection of the right plastic. In this way, the prospective materials and suppliers are successively narrowed down based on data

sheet or database values. In case of special requirements, open exchange with material suppliers is also advisable.

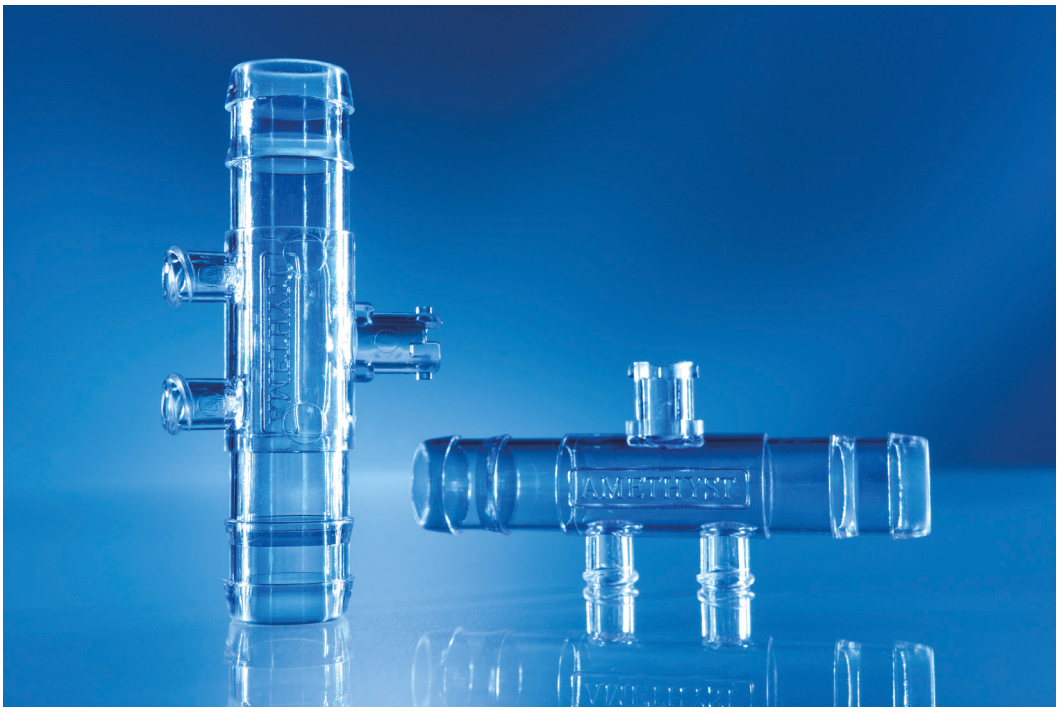
Legally, the distributor of medical devices must prove the safety and performance of its products. In particular, Article 10 in Annex I, Chapter II of the EU Medical Devices Regulation sets out some basic requirements for the use of materials, which can be summarized as follows:

The distributor must know exactly which materials are used in their product, why they use them, what influence processes have on the materials used, and they must prove that the materials used are safe.

There is no unified definition of a medical grade plastic to which requirements are directly linked or secured. So there can be no guidelines as to when a medical grade plastic should be used. As long as the material used guarantees the safety and performance of the medical device, a technical grade plastic can also be used.

But it is advisable for the distributor—as the legally responsible party—to apply certain quality standards to the materials used.

The VDI Guideline 'Medical Grade Plastics' provides useful orientation for the key aspects of consistency in formulation, change management and supply chain reliability. These and other quality attributes are typically safeguarded in the supplier relationship with a quality assurance agreement (QAA).



We're there to advise you!

Not all polymers are the same. And not every plastic is suitable for every medical application. What's more, certain requirements must be met before a product receives approval as a medical device. The VDI Guideline 2017 defines what requirements these are and thus creates the corresponding standards.
We are there to advise you on these guidelines and support you in consistently ensuring the formulation, quality and supply chain reliability of your products.

Abbreviations / terms	Explanations
ASTM	The American Society for Testing and Materials is an international standardization organization based in West Conshohocken, Pennsylvania, USA. It publishes technical standards for goods and services.
Biocompatibility (according to ISO 10993)	ISO 10993 - in contrast to USP Class VI - is a standard for assessing the biological safety of medical devices. The assessment and selection of test methods and parameters is carried out as part of a risk management process. Preliminary investigation of materials is usually performed using toxicological evaluation of extracts. The extraction study is carried out along the lines of Part 18 of the standard.
CMR substances	CMR substances are substances that are classified as carcinogenic, mutagenic or reprotoxic.
ISO 8536	DIN ISO 8536 is a standard that covers intravenous infusions and transfusions in medical practice. It specifies requirements and test procedures for infusion and transfusion devices to ensure their safe and effective use.

Abbreviations / terms	Explanations
ISO 527	ISO 527 is a standard that covers the testing of plastics and other polymeric materials. It defines standardized methods for determining the mechanical properties of plastics, such as tensile strength, strain, elongation at break, and modulus of elasticity.
ISO 10993	ISO 10993 is a standard that covers the evaluation of medical devices made of biological material. It defines standardized procedures for assessing the biological risk of medical devices, implants and other materials that come into contact with the human body.
kGy	kGy stands for kilogray and is a unit for the absorption of ionizing radiation by a material or substance. One gray (Gy) corresponds to the energy absorption of one Joule per kilogram of matter.
MDR	The European Medical Device Regulation (EU) 2017/745 (MDR) supersedes the Directives on medical devices (93/42/EEC, MDD) and active implantable medical devices (90/385/EEC, AIMDD). The MDR came into force in 2017. The effective date of the MDR was May 26, 2021. The MDR transitional provisions will continue until December 31, 2028.
MFR	MFR stands for Melt Flow Rate and is a unit for the flowability of plastics. It indicates how much plastic can flow through a standardized cylinder under a defined load and temperature within a certain time.

Abbreviations / terms	Explanations
MPa	MPa stands for Megapascal and is a unit for pressure or stress.
Phtalates	Phthalates are compounds of phthalic acid (1,2-benzenedicarboxylic acid) with different alcohols (phthalic acid esters). Phthalates are mainly used as plasticizers for plastics
QAA	The Quality Assurance Agreement (QAA) contractually regulates between the customer and the supplier which quality assurance measures the supplier must carry out in detail.
REACH Regulation	The REACH Regulation is a European Union regulation enacted to improve the protection of human health and the environment from the risks that can arise from chemicals. REACH stands for 'Registration, Evaluation, Authorization and Restriction of Chemicals'. The REACH Regulation came into force on June 1, 2007.
USP	USP stands for United States Pharmacopeia, a private (non-governmental) organization responsible for the quality and safety of medical devices and food in the USA.

Abbreviations / terms	Explanations
USP Class VI	In the USP, plastics are divided into six biocompatibility classes. USP Class VI is the strictest. It represents a series of in-vivo tests described in Chapter 88 of the US Pharmacopoeia. Biological reactivity is determined in an animal experiment using an extract (extraction agents are described in the chapter). The extract is injected into the animal.
VDI Guideline	A VDI Guideline is a technical regulation drawn up by the Association of German Engineers (VDI) in a specialist committee of experts from science and industry on certain topics within different specialist disciplines and is intended to reflect the current state of the art. These are often topics for which insufficient international regulations or standards exist or none at all.
VDI Guideline 2017 Medical Grade Plastics	This VDI Guideline focuses on patient safety, which must be legally safeguarded by the manufacturer of a medical device. This patient safety is linked to unchanging product properties and therefore also directly to unchanging material properties. The main aspects derived are: Consistency of formulation, supply chain reliability and change management

Masterflex Group Medical

Novoplast Schlauchtechnik GmbH & Fleima-Plastic GmbH

Plastics have always played a pivotal role in medical technology. As versatile as plastic is itself, products made from it can be just as varied and individual.
We develop and manufacture high-quality tubing, connectors and applications as well as customized assemblies for sophisticated applications in medical technology.

Our components are used in the areas of infusion, dialysis, endoscopy, enteral nutrition, but also in hearing aids, as examples.
We've successfully combined the two manufacturing techniques of extrusion and injection molding in sophisticated medical technology projects for many years now, offering creative solutions from a single source.

Evermore frequently, we also act as development partners and accompany medical products from the idea to the finished product.

In Halberstadt in Saxony-Anhalt, polymer materials are processed into medical tubing by extrusion in ISO Class 6 to 8 cleanrooms, while in Wald-Michelbach (Hesse), the relevant connecting parts such as clamps, adapters, connectors and protective caps are manufactured by injection molding.

On request, we assemble the individual components into customized and precisely fitting assemblies—for example by bonding (with solvent-based or UV adhesives) or ultrasonic welding.
We offer all assembly steps in the cleanroom in accordance with ISO 14644-1 ISO Class 7, depending on the cleanliness and quality requirements of the particular product.
When it comes to materials, production techniques and industry requirements, we are in a position to draw on broad and in-depth know-how.

Our products are "made in Germany".

We meet the requirements of the EU Medical Device Regulation (MDR), as well as the legal framework conditions in accordance with DIN EN ISO 13485:2016.

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Polyneers GmbH

We are a young company headquartered in Stein near Nuremberg (Bavaria).

Our core competence lies in consulting on all aspects of plastics in medical technology and their application. Our expertise is founded on 14 years of experience in the industry, specifically in the field of materials science at B. Braun Melsungen AG, among others.

We have expertise in the chemistry and physics of plastics development and testing.

We support material manufacturers in understanding applications, processes and trends in the medical technology environment. With the aim of manufacturing safe and compliant medical devices, we advise distributors and processors on the selection of suitable materials and testing strategies and support them with failure analyses.

Our services encompass:

→ Advice on the selection and optimization of plastics

→ Implementation of a medical strategy workshops and training courses on special medical technology topics (e.g., biocompatibility, medical grade plastics)

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