Stability and continuity

New VDI guideline 2017 Medical Grade Plastics defines requirements for plastics in medical, diagnostics and pharmaceutical packaging

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Safety for patient and user is an essential requirement for medical products, in-vitro diagnostics and pharmaceutical packaging. Subsequently, plastics grades used in medical have to fulfil particular requirements, i.e. constant properties, formulation lock or biocompatibility. Surprisingly, no standard has existed to define the requirements for medical grades so far. This gap has been filled recently by the new guideline VDI 2017 developed and launched by a work group of the German Engineer's Society (VDI). This article addresses the development of the new guideline VDI 2017 "medical grade plastics" and presents the essential requirements to be covered by medical grade plastics (MGP).

1 Introduction

Since neither user nor patient has to be subjected to any risk by a medical product, highest attention has to be paid to safe design of medical products. Therefore, legislation frameworks have been established in most countries like the recently revised medical device regulation MDR 2017/745 [1] within the European Community or by law, i.e. Code of Federal Regulation 21 CFR 820 [2] for the US market. For in-vitro diagnostics the regulation IVDR 2017/746 describes the requirements for diagnostic products [3].

All these legislative works have in its common sense to reduce the risk to patient and user to a level as low as possible. Maintaining stable and consistent product requirements over lifetime of the product are regarded as core characteristic of medical products to guarantee stability in quality of product with the purpose of products safety for patients. Consequently, stable process and hence stable material properties are essential musts for achieving stability in product properties **(fig. 1).**

Extensive efforts have to be spent during the development process on validation of product and process. For instance, for medical disposables, to ensure that product properties remain constant during lifetime it makes it necessary to verify the product properties also after physical ageing of the product. In addition, the production process has to be validated within its boundaries of the process window to be set before validation. Clinical evaluation of the product with respect to proof therapeutic use complete the validation process and hence the product development which can take four to eight years. It is followed by long-term lasting market phase of the product. Medical devices can be present and sold in the market nearly up to 20 years without hardly any change in design, process and material **(fig. 2).**

Thus, selection of appropriate material for products in medical application at the very beginning of the development process is regarded as one of the most crucial points in the development process. Therefore, materials for medical have to meet design needs such as mechanical, thermal and chemical requirements as well as special demands to biocompatibility, Furthermore, the safety of long term supply is of importance for the ladder long-term market phase.

In contrast to the high-levelled requirements of these fields of application, a com-

Fig. 1: Stable properties providing the base for safe products

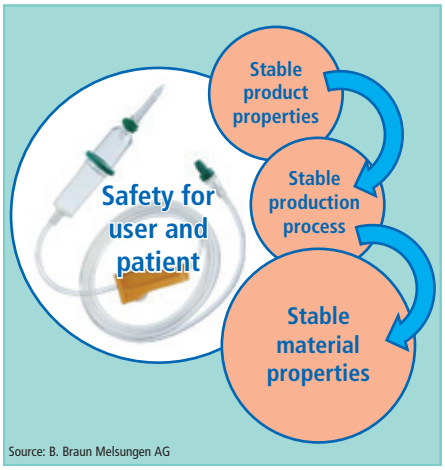
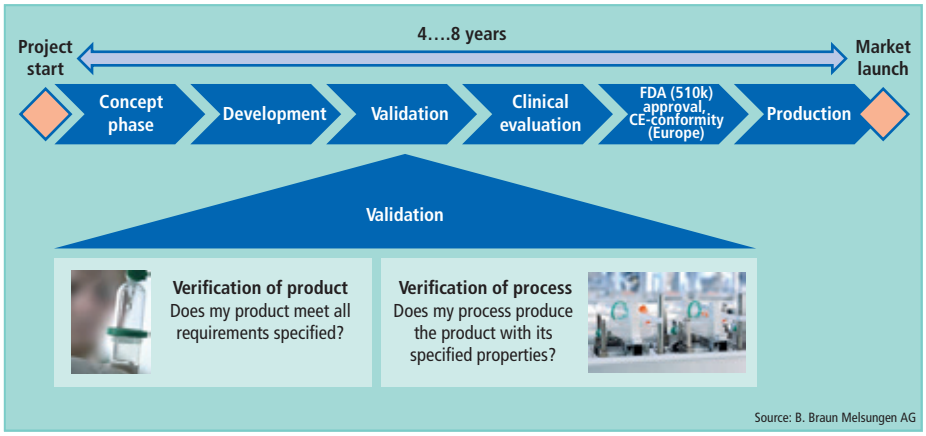


Fig. 2: Development process for medical devices



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Dedicated to Prof. Dr.-Ing. Günter Mennig on occasion of his 80th birthday

parable small volume share of plastic material is assigned to the medical field and diagnostics. Approximately 1-2 % of the annual plastic consumption goes into these fields, whereas approximately 60 % of the 500,000 t annual consumption in Europe are used for packaging, agriculture and construction [4].

For thermoplastic elastomers, an annual production of 4,5 million t is estimated for 2019, having an 8 % share going to the sector of medical and diagnostics, what equals 360,000 t of TPE dedicated to these fields [5]. TPE is widely used in the medical sector for tubing applications like catheters **(fig. 3),** infusion lines or stoppers and flexible packaging material.

Facing these enormous figures and taking the growing importance of the medical and diagnostic sector into account, surprisingly neither national nor international standard or guideline exists so far to describe the requirements to polymer or plastics grade in regard to medical application.

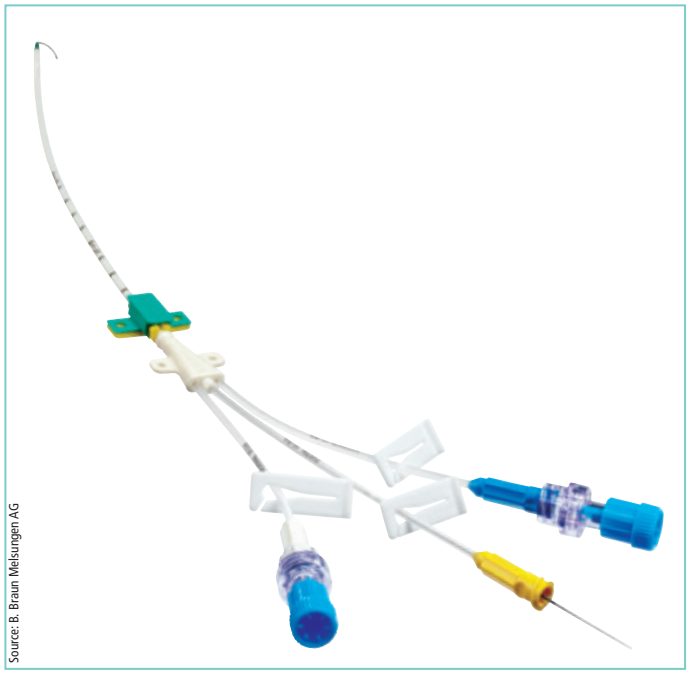
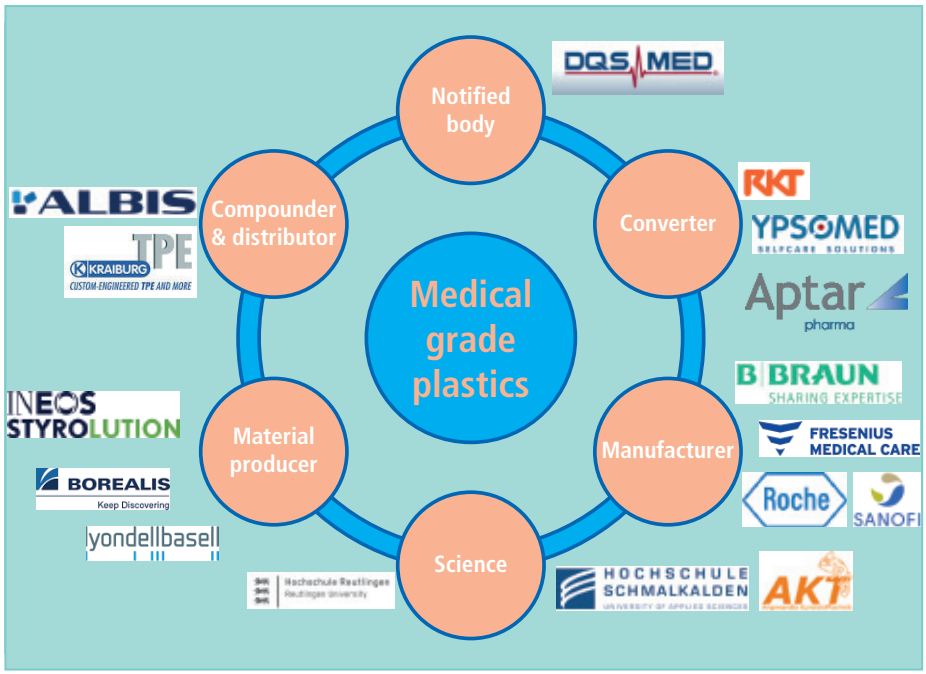

Source: B. Braun Melsungen AG

Fig. 3:
Central venous catheter made from TPU

Fig. 4: VDI expert group medical grade plastics



In practice, when it comes to material selection during the development process, the designer tends to orient to "medical grades" that are offered as such by the materials manufacturers and distributors. For these grades, proof of biocompatibility of the granule according US or European guidelines is provided by the material supplier. This indicates the medical device manufacturer that this material is expected to be suitable in general. However, it is under the obligation of the manufacturer to proof his product requirements such as biocompatibility at the final product that has been undergone all steps of processing. Up to now, no US or EU guidelines or standards exist for clearly defining the medical grade plastics.

Here, we face a gap in standardization that needs to be filled and hence this gives rise to the development of a new guideline in that field by a working committee of the German Engineer's Society. The approach to the guideline, its process of formation and the key points of this work are described in the following.

2 Starting point

The German Engineer's Society has a long lasting tradition in development of general recognized technical rules and standards for all kinds of technical areas. From its essential ideas, guidelines are developed by a technical committee of experts in a technical field where no national or international standard has been established so far. Nowadays, nearly 2,100 guidelines represent and describe state-of-the-art standards and requirements in various technical industry sectors. They act as a guideline for user and experts and setting quality standards therewith [6].

A VDI guideline does not equal formally to standards worked out by technical committees of a standard organization like ISO (International Standard Organization). It is intended by the VDI that gaps in standardization not covered by ISO, EN or DIN standards are filled by these guidelines. In order to avoid interference with "traditional" standards, VDI guidelines are rejected if a standard

is launched for the same field. The set-up and development of VDI guidelines undergoes less formal procedures, hence the time from idea to realization can be a lot shorter in comparison to the process to set in force a standard.

For the realization of a VDI guideline, technical experts come together in order to discuss and develop a guideline that is afterwards published in a first draft version as so called "green print". The green print can be regarded as a draft to be commented by public, respectively interested parties within a limited time (6 – 12 month). The expert committee deals with every comment or objection and decides finally for modification of the guideline or rejection of the comment. After this period the final version is published as "white print" and undergoes periodic review every five years. Thus, the expert group for the guideline remains active also after publication of the guideline.

The expert group for working out the VDI guideline 2017 Medical Grade Plastics was established beginning of 2017. Its founding had been triggered by various previous discussions in that field held in local networks before, i.e. network for plastics in life sciences (Partnernetzwerk für Kunststoffe in Life Sciences) AKZEPT–PP, plastic converters in medical (Interessenverbund Kunststoffverarbeiter in der Medizintechnik KiM e. V.) or VDI expert group plastics in medical (Fachgarbeitskreis Kunststoffe in der Medizintechnik des VDI). A need for clear requirements had been the essence from all these discussions and was taken up finally as a starting point for working out a guideline for it.

The expert group was constituted by representatives from material suppliers and distributors, compounders, converters, manufacturers, notified body and science in the fields of medical devices, in-vitro diagnostics and pharmaceutical packaging **(fig. 4).** Coordination of the work group was managed by Schmalkalden University of Applied Sciences, Laboratory of Applied Polymer Technology. It has been the intention to have different background and hence a heterogeneous composition of the expert group in order to win a broad base of input for the work and finally wide acceptance by all stakeholders.

Already twelve months after starting work, the green print was published in April 2018 to the public and underwent a six-month phase for commenting. More than 80 comments handed in give evidence of a strong response and interest of the industry in that topic. All these comments have been discussed by the group and helped to point out and express the content of the guideline clearer in some details. The general outline of the guideline however has not been brought into question and hence remained as provided by the draft.

Finally, in July 2019, the final version (white print) of the VDI guideline 2017 was presented at the VDI conference "Medical Grade Plastics" in Berlin to the public. It is now available at Beuth Publishing in a bilingual German-English version. Due to the valuable contribution, keen work and willingness of achieving common ground by all expert members, the guideline has been finished in an extraordinary short period.

3 Layout of the guideline

The scope of the guideline comprises the applications of medical products, pharmaceutical packaging, in vitro diagnostics and active implantable medical devices. Its basic outline and content are given by the following structure:

1. Scope of the directive
2. Terms: general, materials, parties involved
3. Abbreviations
4. Definition Medical Grade Plastics (MGP)
5. Regulatory requirements for MGPs
6. *Consistency of formulation*
   a. Scope and definition for formulation of a MGP
   b. Requirements for consistency of formulation
   c. Assessment of consistency of formulation
7. Information and documentation
8. *Security of Supply*
9. *Change Management*
10. Packaging, storage and logistics
11. Customer-Supplier relationship
12. Appendix
    a. *Example for Quality Agreement (QA)*
    b. Example for risk assessment
    c. Example for declaration of conformity for MGPs
    d. Risk factors in processing of material [6]

Some items of this guideline have to be highlighted since they represent require-

Fig. 5: Consistency of formulation

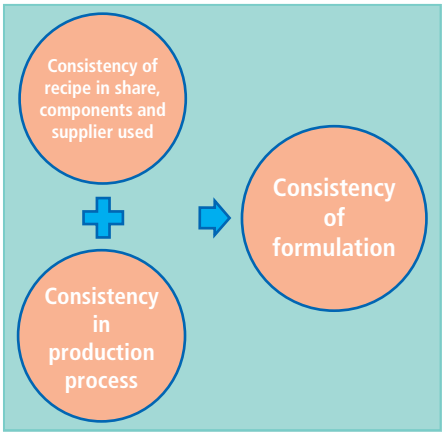


Fig. 6: Change management process

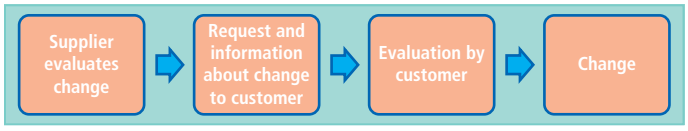
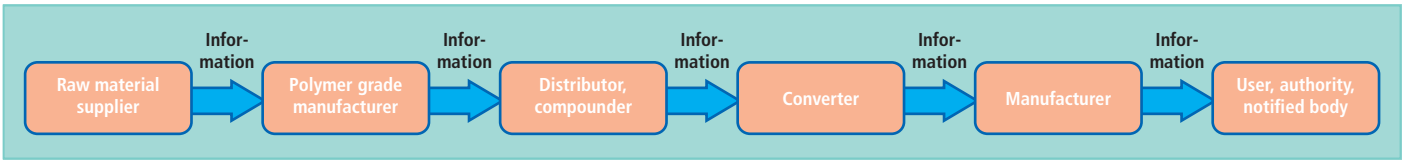


Fig. 7: Information transfer within change management process



ments and needs with highly impact on medical grades, such as *Consistency of Formulation, Security of Supply, Change Management* and *Quality Agreement* as key role document between customer and material supplier.

The consistency of a formulation is regarded as the essential requirement for constant properties. It means on one hand consistency of formulation in its content share, components and raw material suppliers used and, on the other hand, consistency in the material manufacturing process. Corresponding documentation on formulation consistency has to be presented to the customer on request. It is well noted that this information is considered as highly crucial since it represents an essential part of the intellectual property of the material supplier. However, for example, evaluation of biocompatibility by medical product manufacturer may necessitate essential information on formulation. Information transfer has to be covered by corresponding non-disclosure agreements.

It is just obvious that the already mentioned, long term running market phase of the products cannot be realized with polymer grades fixed in formulation and process for decades. From a realistic point of view, polymer grades inevitably undergo changes but they should be kept to minimum. However, this process of change has to follow a prescribed approach as displayed by **figure 6.** Changes that affect consistency have to be evaluated by the material manufacturer in a first step with respect to possible impact on product properties. If this is the case, corresponding information has to be handed over to the customer going along with a change notification. The customer has to evaluate the changes with respect to impact on his product and takes up activities necessary to implement the change for his product, i.e. verification of the product properties affected by the change. During that phase the security of supply by material that has not undergone the change yet has to be provided by the manufacturer. The installation of a change management process builds therefore another important column of requirement for medical grade plastics.

The information linked to the change has to be passed from supplier to customer starting with the raw material supplier ending up at the manufacturer respectively end use customer. It is not the sole responsibility of the material supplier to reach all possible stakeholders with the information. However, transferring the relevant information along the chain by customer-client-relationship ensures handover of information regarding the change to all parties involved **(fig. 7).**

Fig. 8: Security of supply

The aspect of maintaining the security of supply has to be kept in mind to ensure a safe and stable supply of the customer with medical products. To this end, the manufacturer respectively supplier of the medical grade plastics sets up a concept on security of supply of material to the customer. It is under the responsibility of the material supplier by what means respectively measures the supply can be guaranteed, for instance by installing a secondary production line or simply providing safety stock that can be used in case of stop of material production (force majeure). The quantity of safety stock has to be agreed upon between supplier and customer.

In addition, material suppliers have to make extraordinary precautions for ensuring safety of supply **(fig. 8).** The new guideline provides appropriate requirements for it by defining terms like:

- Notification of Change from supplier to customer in case of incident of change
- Pre-Notification Period marking the availability of current material formulation in volume previously agreed upon after announcement of change, typically 24 months) or
- Last Order Call as possibility for last ordering of stock before material change, 12-months supply recommended.

Fig. 9: Outline of quality assurance between supplier and customer

The guideline does not give explicit values and time period for these terms like last order call or pre-notification since these can differ depending on the needs of the customer and the possibilities of the supplier. It is subject to the negotiation between both parties for each case individually.

The requirements described here in detail and further ones mentioned by guideline can be agreed upon by set up of a quality agreement between material supplier and customer **(fig. 9).** It acts as a central key document, which lists the essential information and agreements upon the medical grade between both parties. A draft outline of a quality assurance is added to the guideline as appendix.

4 Discussion and outlook

All along its work, the committee has born in mind to establish a widely accepted standard that can act as a guideline as well for material suppliers as material customers. It should describe the standard and basic requirements a medical grade is expected to bring with it when declared as intended to be applied for medical application. On the one hand customers get information what to expect, on the other hand the guideline informs material suppliers about the requirements which have to be met by their materials.

Since this guideline has the intention to cover a broad range of products and applications from pharmaceutical packaging, in-vitro diagnostics up to medical devices from low to high risk classification, it follows the principle to bring all requirements for a medical grade down to the least common denominator which specifies the base in specification applied to the medical grade covering all fields described below. Additional requirements or enhanced, more tight conditions for plastics grade should be arranged between the parties involved on a bilateral base on demand, i.e. if application makes it necessary.

Started by presentation of the green print [8-11], the guideline has gained acceptance by affected parties and stakeholders already. The feedback from the industry has been positive so far. Especially the character of the guideline to define and describe the basic requirements that has to be addressed between supplier and customer for medical grade plastics has been highly appraised. This gives rise to the conclusion that the guideline is accepted and used in daily practise by all stakeholders.

For future prospect, it seems to be likely that other industries also dealing with high risk application, e.g. aeronautics or automotive, may adopt this given standard now, since they also require constant material properties for safe products providing constant and safe performance. Hence, this guideline will act as a pacemaker in regulation for plastic materials in all fields of industry that require high safety standards. The makers of the guideline are looking forward to receiving further feedback to the guideline and how its idea will prove itself. It is planned to have a first revision already after two years in order to keep the guideline up-to-date.

Finally, the new guideline VDI 2017 Medical Grade Plastics provides clarity for the description of requirements and helps to set the base for safe products from material with stable, clearly defined properties.

5 Acknowledgements

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6 Literature

[1] Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC.

[2] CFR – Code of Federal Regulation Title 21 – Food and Drugs, Subchapter H – Medical Devices, Part 820 Quality System Regulation, Food and Drug Administration (FDA), rev 1 April 2018.

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