GMP Annex 1 Revision 2022 - Impacts on the patient-specific preparation of parenterals in pharmacies

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The final revision of Annex 1 of the EU GMP Guideline was published on August 25, 2022. As in the previous version, it describes requirements for the sterile manufacture of medicinal products in the European Union, but in a much more detailed and precise manner than before. The requirements relate to all aspects of the manufacturing process, namely suitable premises, equipment, utilities, personnel, specific production and packaging technologies as well as monitoring and control measures. The revision was carried out as a collaboration between the European Medicines Agency (EMA), the World Health Organization (WHO) and the Pharmaceutical Inspection Co-operation Scheme (PIC/S). In this way, a comprehensive standardization of all requirements could be achieved. The new Annex 1 therefore also forms an important basis for the preparation of ready-to-administer parenteral medicinal products in pharmacies. However, whether the preferred barrier technologies – RABS and isolators – meet the needs of patient-specific preparation of (toxic) drugs has been the subject of controversial discussions since publication two and a half years ago.

In order to gain more clarity on this issue, it is first worth looking at the manufacturing conditions for which the new Annex 1 is intended. The focus here is primarily on industrial production, i.e. the manufacture of uniform products in large quantities through repetitive processes. Under these conditions, RABS and isolators enable the desired separation of product, environment and personnel, so that product safety can be increased. But are these devices also the best solution for the sterile preparation of individual medications as part of local care? Our answer is: Rather not, as under these conditions it is essential to be able to work safely, flexibly and without ergonomic restrictions. In addition, RABS usually offer insufficient protection against exposure to toxic substances.

The new Annex 1 allows alternative approaches to the use of RABS and isolators. In fact, as long as direct human interventions are an essential part of the preparation process, proven technologies in the form of suitable safety cabinets are not just tolerated niche products, but continue to represent the best solution with regard to product and occupational safety for the preparation of patient-specific parenterals. Together with other implications from the new Annex 1, these technical requirements are presented and discussed in the context of implementation in pharmacies.