Regarding the Consultation document:
Commission Delegated Act on Principles and guidelines on good manufacturing practice for investigational medicinal products for human use and inspection procedures, pursuant to the first subparagraph of Article 63(1) of Regulation (EU) No 536/2014

Comments from the **ADKA (German Association of Hospital Pharmacists)** regarding:

Question 2:

We prefer Option a) for the batch documentation, from our point of view the retention period as currently required is a sufficient period of time for the batch documentation.

Section 2.13. Advanced therapy investigational medicinal products

Reconstitution of an investigational medicinal product (IMP) is not considered manufacturing and therefore may be carried out in hospitals, health centers or clinics, by pharmacists or other persons legally authorized in the Member States to carry out such processes and if the investigational medicinal products are intended to be used exclusively in those institutions (Commission Directive 2005/28/EC, Art. 9 (2)). This will obviously remain unchanged by the Commission Guidelines pursuant to the CT Regulation No. 536/2014, as will the definition of the term "reconstitution" which remains the same as in Eudralex Vol. 4, Annex 13.

By German law, Advanced Therapy Medicinal Products (ATMPs) are exempt from this, a manufacturing authorization is therefore per se required for any activity concerning ATMPs (§ 13 (2b) AMG). It is not clearly defined whether the reconstitution of an ATMP may be carried out in hospitals without manufacturing authorization and the decision on that matter is currently made by the German regional commissions, not by the national competent authorities.

This jeopardizes the feasibility of clinical trials with ATMPs in Germany, and possibly Europe, since only very few hospitals and clinical trial centers in Germany have an appropriate manufacturing authorization and the diversity of ATMP products renders a general authorization for these products quite impossible.

The general requirement for a manufacturing authorization regarding any activity concerning ATMPs should be subject to discussion. As pointed out in the Consultation document, section 2.13., a risk-based approach adapted to the specific characteristics of an ATMP should not only be applicable regarding the GMP requirements, but also regarding the permission to reconstitute ATMPs at hospital pharmacies, especially for clinical trials, without manufacturing authorization.

For instance, a genetically modified organism (GMO) falls under the definition of an ATMP, but not the categorization as ATMP alone should be the decisive factor whether the reconstitution is subject to an manufacturing authorization or not. But rather the respective ATMP-specific process of reconstitution, the single steps involved and possible risks arising during that process and whether these can be appropriately handled should be the determining factors.

The environment, training and expertise found in a hospital pharmacy offers the ideal setting for patient individual reconstitution of IMPs, including ATMPs used in clinical trials. A high standard of security is implemented for the handling and preparations of CMR substances, which provides a solid basis for handling of biological hazard materials like GMOs. Aseptic preparation processes are clearly defined and regularly validated, the specialist staff carrying out the

preparation is well trained and highly experienced. Equipment and environmental conditions are kept to the appropriate technical standard.

In order to keep the performance of clinical trials with new and innovative ATMPs feasible in Europe, the handling of ATMPs and their preparation for administration should be allowed in hospital pharmacies without authorization, if a favorable product-specific risk-assessment is provided by the Sponsor and/or Hospital Pharmacy.

Authors:

Dr. Tilman Schöning, representing the ADKA committee Oncology

Dr. Lenka Taylor, representing the ADKA committee Clinical Trials

Hospital Pharmacy, University Hospital Heidelberg, Germany