SUMMARY OF THE RESPONSES TO THE TARGETED STAKEHOLDER CONSULTATION ON THE DEVELOPMENT OF GOOD MANUFACTURING PRACTICE FOR ADVANCED THERAPY MEDICINAL PRODUCTS PURSUANT TO ARTICLE 5 OF REGULATION 1394/2007

1. GENERAL REMARKS

Article 5 of Regulation (EC) No 1394/2007 on advanced therapy medicinal products (hereafter "ATMP Regulation")[1] requires the European Commission to draw up Guidelines on good manufacturing practice specific for advanced therapy medicinal products (hereafter, "ATMPs").

With a view to prepare these Guidelines, the Commission services launched a targeted stakeholder consultation on 23 July 2015. On the basis of the comments received during the consultation as well as input from consultation with the European Medicines Agency and competent authorities in the Member States, the Commission services developed draft Guidelines on Good Manufacturing Practice ("GMP") specific to ATMPs.

With a view to give an additional opportunity for concerned stakeholders to express their views on the GMP requirements that should apply to ATMPs, the draft Guidelines on Good Manufacturing Practice specific to Advanced Therapy Medicinal Products was the subject of a new targeted stakeholder consultation (launched on 28 June 2016).

This document presents a summary of the responses to the consultation. It does not represent the views of the European Commission.

2. CONTRIBUTORS TO THE STAKEHOLDER CONSULTATION

The number of contributions received during the consultation period was 53. While in a few cases it is unclear whether the contributions received emanate from individuals/entities involved in the development, manufacturing or commercialisation of ATMPs, all stakeholder contributions received during the consultation period are made public for transparency reasons.

It is noted that a number of entities have submitted two or more separate contributions. In contrast, some contributions have been submitted on behalf of several entities and, in some cases, the same contribution has been submitted by more than one entity.

In order to facilitate a better analysis of the responses, contributors have been classified in the following categories:

Sector	**Contributors included**
Academia	University hospitals and individuals/entities involved in the research of ATMPs not falling under the category of Industry, SMEs or Others.
Industry	Individual companies and associations engaged in the development and/or marketing of ATMPs, other than SMEs.
SMEs	Individual companies and associations representing companies engaged in the development and/or marketing of ATMPs that meet the EU definition of SME.
Others	Service providers, equipment manufacturers, consultants, public/private

[1] *Regulation (EC) No 1394/2007 of the European Parliament and of the Council on advanced therapy medicinal products and amending Directive 2001/83/EC and Regulation (EC) No 726/2004*, OJ L 324, 10.12.2007, p. 121.

	partnerships/initiatives active in the area of ATMPs.

3. OUTCOME OF THE PUBLIC CONSULTATION

The approach described in the Consultation Document was supported by the majority of the respondents. Support was particularly strong among academia and SMEs.

The additional details provided regarding the application of the risk-based approach, the pragmatic approach towards process validation developed in Section 10, as well as the sections on reconstitution and automated production are the changes introduced in the consultation document (vis-à-vis the document that was the object of the consultation in 2015) that were more favourably perceived. Other clarifications introduced in the document were also welcomed (*e.g.* clarification that same GMP standards apply to industrial developers (large and SMEs) and academia, the flexibility introduced in Section 13 regarding the outsourcing of highly specialised tests, *etc*.)

However, a significant number of submissions considered that further adaptations to the specific characteristics of ATMPs were still required, in particular in connection with the following items:

- Premises: The principle of dedicated production areas for ATMPs was deemed too stringent. Additional guidance/clarification was requested regarding the use of closed systems and biosafety cabinets, as well as regarding the handling of infected materials. A number of stakeholders also considered that it should be possible that closed systems are used in a non-classified environment.

- Aseptic manufacturing: The requirements on aseptic process validation (so-called "media fill test") was the topic that received most comments. Demands for adaptation to the specific characteristics of ATMPs were shared by academia, SMEs and industry. It was generally perceived that the standard requirements for parenteral products are not fit for ATMPs, in particular in cases where each unit is subject to sterility testing prior to the administration to the patient. Various proposals for adaptation were made.

- Requirements of the on-going stability program in Section 12: It was considered that a pragmatic approach similar to the principles outlined for process validation should apply also to the on-going stability program.

- Certification by the Qualified Person ("QP"): considering that – for many ATMPs– each unit constitutes a separate batch and taking into account the new manufacturing models that are emerging, additional flexibilities were asked regarding the role of the QP.

Other demands for clarification/adaptation of punctual aspects of the document were made. At times, the requests made were, however, outside the scope of the document (*e.g.* request

for guidance on comparability, request for modification of the QP professional training foreseen in Directive 2001/83, request for regulation of the role and responsibility of the sponsor, *etc*.).

The format of the document (stand-alone *versus* annex) was raised in a significant number of contributions. While some requested that the consultation document should be amended to explicitly exclude the application of the detailed GMP guidelines in Volume 4, others considered it preferable to have this document as an Annex to the guidelines in Volume 4. In the majority of these submissions there is an underlying concern about possible legal uncertainty if the relation between the draft Guidelines on Good Manufacturing Practice specific to Advanced Therapy Medicinal Products and the GMP guidelines in Volume 4 is not clearly established. The necessity to keep the document updated to technical progress was also voiced in a number of contributions.

The above summary of comments is not exhaustive. The Commission services will carefully analyse all the responses submitted in consultation with experts in the European Medicines Agency and the Member States.