Finnish Red Cross
Blood Service

SANTE-D5-ADVANCED-THERAPIES
European Commission
DM24 02/133
B-1049 Brussels (Belgium)

Dear Sir/Madam

Submission of Comments on Public Consultation Paper on Good Manufacturing Practice for Advanced Therapy Medicinal Products

Comments from:

Name of organization: Finnish Red Cross Blood Service

The Finnish Red Cross Blood Service is a financially and operationally independent, non-profit unit within the Finnish Red Cross. It is a centralized organization with about 500 employees providing nationwide blood services in Finland.

The Finnish Red Cross is a public-law association recognized by the State of Finland. The Finnish Red Cross is the only national association in Finland that belongs to the International Red Cross and Red Crescent Movement. In its operations, it complies with the basic principles adopted at the International Conferences of Red Cross.

1. General Comments

A specific GMP guideline for ATMPs is a very welcome addition and is truly needed, since the manufacturing of ATMPs and the needed expertise is significantly different from the traditional pharmaceutical sector. The consultation document reflects well how every product is unique and needs case-by-case and risk-based evaluations and solutions. Therefore, flexible procedures and deep scientific understanding relevant to the products are required in the ATMP field.

2. Specific Comments

1. Introduction

In general, a more clear explanation of the status of this document under consultation in relation to EU GMP (ref. 3) is needed. For example, in cases of discrepancies which document is to be followed? Moreover, do general principles laid down in e.g. EU GMP Annex 1 still apply?

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Line 64: Academic institutes should be added as possible sites for early phases of research of ATMPs.

2. GMPs for ATMPs: general principles

Q1: The principles are relatively well-adapted to the specific characteristics of ATMPs.

The sentence on line 110 strengthens this by highlighting that some flexibility in the application of GMP requirements should be applied.

3. Personnel

Q4: The principles are relatively well-adapted to the specific characteristics of ATMPs.

Definition of adequate practical experience of the personnel is appreciated as it strengthens the specific requirements needed for the intended operations and responsibilities in manufacturing of ATMPs.

4. Premises

Q5: The principles are relatively well-adapted to the specific characteristics of ATMPs.

5. Equipment

Q9: The principles are relatively well-adapted to the specific characteristics of ATMPs.

6. Documentation

Q10: The principles are relatively well-adapted to the specific characteristics of ATMPs.

7. Starting and raw materials

Q13: The principles are relatively well-adapted to the specific characteristics of ATMPs.

8. Seed lot and cell bank system

Q14: The principles are relatively well-adapted to the specific characteristics of ATMPs.

The specification on lines 554-558 is appreciated and reflects a pragmatic approach.

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9. Production

9.2. Handling of incoming materials and products

Q15: The principles are relatively well-adapted to the specific characteristics of ATMPs.

Lines 606-609: this paragraph in its current form is somewhat confusing and unclear. Although identification tags /labels are always needed throughout the manufacturing steps the listed actions seem too detailed and heavy to add any value. Especially, if the production facility only manufactures one product per time and according to a clear batch record.

10. Qualification and validation

Q16: The principles are relatively well-adapted to the specific characteristics of ATMPs.

Especially the following is appreciated: the definition of validation versus qualification, validation of manufacturing process for ATIMP production on lines 711-716 and continual improvement during the development phase and early phases of clinical trials on lines 717-721.

11. Qualified person and batch release

Q18: The principles are relatively well-adapted to the specific characteristics of ATMPs.

Lines 768-769: It is appreciated that a detailed knowledge of the product type and manufacturing steps for which the QP is taking responsibility is needed. Therefore, in-depth qualification and experience in biological sciences should be emphasized.

12. Quality Control

Q19: The principles are relatively well-adapted to the specific characteristics of ATMPs with the exemption of chapter 12.2. sampling.

12.2. Sampling

The text on lines 930-932 is highly appreciated and demonstrates a pragmatic approach and understanding about the realities of the field. Nevertheless, this chapter in its current form is too extensive and unrealistic for ATMPs and needs revision. The biological nature of starting materials, raw materials and finished products should be taken into account. Especially the limited availability of material and the stability of samples should be considered.

12.3. Testing

In general a good chapter specifically adapted to the testing of ATMPs, especially the paragraph on lines 976-978.

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12.4. Stability monitoring system

It is appreciated that stability monitoring programs are expected only after marketing authorization.

13. Outsourced activities

Q20: The principles are relatively well-adapted to the specific characteristics of ATMPs.

14. Quality defects and product recalls

Q21: The principles are relatively well-adapted to the specific characteristics of ATMPs.

16. Reconstitution of product after batch release

Q22: Yes, it is agreed that where reconstitution of the finished ATMP is required, the manufacturer's responsibility is limited to the validation of the process of reconstitution and the transmission of detailed information about the process of reconstitution to the end users.

Q23: Yes, it is agreed that that reconstitution is not manufacturing and therefore is outside GMP.

Q24: Assembly of transport vessel, identification of product, preformulation before administration, infusion devices and protocols bedside are considered as reconstitution.

17. Automated production of ATMPs

Q25: If the automated device produces an end product, which with current EU regulation is classified as an ATMP, the GMP requirements for processing/manufacturing should apply for the user no matter location. Therefore, the end user in the hospital should also ultimately be responsible for the quality of the ATMPs. A quality system which fulfils ATMP GMP requirements should be in place. Process validation and aseptic validation for ATMP production by automated devices/systems should be performed according to ATMP GMP principles in order to ensure the quality of ATMPs. Furthermore, ATMP GMP compliant batch records allowing full traceability should be in use. The end user could also outsource the process validation and other quality system work required for the use of automated devices/systems if the organization lacks the needed knowledge.

It should, however, also be in the interest of the manufacturer of the automatic processing device to produce enough evidence of safety and efficacy (both nonclinical and clinical) of the ATMP produced by the automatic device and respective processing protocol.

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November 10th 2015, Helsinki

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