

Introduction:

GMP checklist for ATMP manufactures is based on Part IV- GMP Requirements for Advanced Therapy Medicinal Products of the EudraLex - Volume 4 - Good Manufacturing Practice (GMP) guidelines and contains specific questions about quality work at the GMP facility with references to the corresponding requirements of the regulations and supporting documents. The checklist applies only to Advanced Therapy Medicinal Products (ATMP) and should be read and used as a guidance for the understanding and interpretation of the legislation applying to ATMPs.

Part IV of *EudraLex - Volume 4 - Good Manufacturing Practice (GMP) guidelines* contains guidelines on Good Manufacturing Practice specific to Advanced Therapy Medicinal products. These guidelines do not apply to medicinal products other than ATMPs. The part IV states that:

“Compliance with good manufacturing practice (GMP) is mandatory for all medicinal products that have been granted a marketing authorization. Likewise, the manufacture of investigational medicinal products must be in accordance with GMP. Advanced therapy medicinal products that are administered to patients under Article 3(7) of Directive 2001/83/EC1 (so called “hospital exemption”) must be manufactured under equivalent quality standards to the manufacturing of advanced therapy medicinal products with a marketing authorization.”

How to use this guide:

This checklist should be used as a guidance for the understanding and interpretation of the legislation and annexes applying to GMP for ATMP, not as a replacement. It should be considered as a help to check compliance with the rules. Careful reading of the original guidelines and relevant legal framework is recommended before commencing using this checklist.

The checklist is divided into 17 chapters, reflecting the 17 chapters of the EudraLex GMP Part IV. Each chapter contains a number of questions with tick-boxes, defined as below:

- Fulfilled: completed, documents/checklists in place
- Control needed: uncertain status, need verifying
- Action needed: not in place, actions to be taken
- Not applicable: not applicable for the user of the checklist

This way, the checklist identifies non-compliance and actions needed in order to comply with the EudraLex GMP Part IV. The checklist may be used in the onset of ATMP production, or as an ongoing tool for self-inspections.

Each chapter begins with a quote from EudraLex GMP Part IV. For each question there is a reference to the specific paragraph in EU-GMP part IV “Guidelines on Good Manufacturing Practice specific to Advanced Therapy Medicinal Products” where more information can be found. There is also a column containing more information, suggested documents or guidance documents.

‘Guidance documents’ are references to other guidelines, directives and/or regulations. These references contain important information and/or helpful instructions for GMP-compliance.

‘Suggested documents’ are examples of instructions, policies, checklists needed in the pharmaceutical quality system (PQS) to ensure GMP-compliance. The list is non-exhaustive and suggestions only. Different approaches might give the same result.

‘Notes’ are the authors comments on cross-references to other part of the legislation.

This guide was created by:

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Disclaimer:

The following guide are produced and designed as a support for users within the ATMP-field. The project group aims to ensure that the guide available on the website are up to date but cannot provide any guarantees. Users themselves are therefore responsible for checking that the content is correct and current with applicable regulations.

Document History:

Version number	Date	Revision description
1.0	2019-05-09	First version
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TABLE OF CONTENTS

1. Introduction – scope, general principles	2
2. Risk-based approach	5
3. Personnel	7
4. Premises	10
5. Equipment	14
6. Documentation	16
7. Starting and raw material	24
8. Seed lot and cell bank system	29
9. Production	31
10. Qualification and validation	37
11. Qualified person and batch release	41
12. Quality control	43
13. Outsourced activity	46
14. Quality defects and product recalls	48
15. Environmental control measures for ATMPs containing or consisting of GMOs	50
16. Reconstitution of product after batch release	51
17. Automated production of ATMPs	52

1. Introduction – scope, general principles

“Compliance with good manufacturing practice is mandatory for all medicinal products that have been granted a marketing authorization. Likewise, the manufacture of investigational medicinal products must be in accordance with GMP. Advanced therapy medicinal products that are administered to the patient under Article 3(7) of Directive 2001/83/EC so called hospital exemption must be manufactured under equivalent quality standards to the manufacturing of advanced therapy medicinal products with a marketing authorization”.

	Question	Comments	Notes
1.21	Do you have a pharmaceutical quality system (PQS) as defined in 1.22?	<p><i>Guidance documents:</i></p> <ul style="list-style-type: none"> • ICH Q10 Pharmaceutical quality system. • EMA/CHMP/ICH/214732/2007 • PIC/S GUIDE TO GOOD PRACTICES FOR THE PREPARATION OF MEDICINAL PRODUCTS IN HEALTHCARE ESTABLISHMENTS PE 010-4 <p>Note; it is the manufacturer that needs to have a PQS, however, the sponsor is responsible for ensuring the existence thereof.</p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
1.23	Do you demonstrate effectiveness of the PQS at site level?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> • <i>Management review</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
1.24	Does the PQS include and ensure training of personnel?	<p><i>Note: see chapter 3 for detailed GMP-requirements.</i></p> <p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> • <i>Instructions for training.</i> • <i>Validation of training</i> • <i>Re-training policies</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
	Does the PQS include allocation of responsibilities?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> • <i>Organizational charts</i> • <i>Job descriptions</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
	Does the PQS ensure suitable premises and equipment, and maintenance thereof?	<p><i>Note: see chapter 4, 5 for detailed GMP-requirements.</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]

	Question	Comments	Notes
1.24	Does the PQS include a documentation system for specifications, production instructions and record keeping?	<i>Note: see chapter 6 for detailed GMP-requirements.</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed Not applicable <i>[room for notes]</i>
	Does the PQS ensure an adequate manufacturing process that ensures a consistent production and a product compliant with specifications?	<i>Note: see chapter 9 for detailed GMP-requirements.</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
	Does the PQS contain a quality control system independent from the production?	<i>Note: see chapter 12 for detailed GMP-requirements.</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
	Do you have system for Change Control?	<i>Suggested documents:</i> <ul style="list-style-type: none"> • <i>Change Control SOP</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed Not applicable <i>[room for notes]</i>
	Does the PQS include a system for identification of quality defects including CAPA?	<i>Note: see chapter 14 for detailed GMP-requirements.</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed Not applicable <i>[room for notes]</i>
	Does the PQS include a system for traceability of ATMPs and starting and critical raw material?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
1.25	Does the PQS ensure that all quality attributes or critical parameter processes are trended and checked?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
	Does the PQS include self-inspections, and ensure that the records and corrective actions are kept?	<i>Suggested documents:</i> <ul style="list-style-type: none"> • <i>Self-inspection scheme</i> • <i>Self-inspection checklist</i> <i>Note; this checklist may be used as a checklist for self-inspection.</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
1.26	For authorized ATMPs; Does the PQS include a program for annual quality reviews?	<i>Suggested documents:</i> <ul style="list-style-type: none"> • <i>Product quality review (PQR)</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>

	Question	Comments	Notes
1.27	Is the result of the quality review evaluated by the manufacturer?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>
1.27	If the market authorization holder is a different legal entity; Is the result of the quality review evaluated by the market authorization holder as well as the manufacturer?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>

2. Risk-based approach

“The risk-based approach (RBA) is applicable to all types of ATMP. It applies in an equal fashion to all types of settings. The quality, safety and efficacy attributes of the ATMPs and compliance with GMP should be ensured for all ATMPs, regardless of whether they are developed in a hospital, academic or industrial setting”.

	Question	Comments	Notes
N/A	Do you have a quality risk management system (QRM) in place?	<p><i>Guidance documents:</i></p> <ul style="list-style-type: none"> ICH guideline Q9 on quality risk management CHMP/ICH/24235/2006 <p><i>Note: The Level of effort and documentation depends on level of risk. The use of informal risk management processes may be acceptable, see section 2.18. 2.20-2.24</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>
	For each manufactured ATMP; have you done a risk assessment, identifying all risks and risk factors for patients, environment and/or human health?	<p><i>Guidance documents:</i></p> <ul style="list-style-type: none"> Guidelines relevant for advanced therapy medicinal products Guideline on human cell-based medicinal products (EMA/CHMP/410869/2006) Guideline on the risk-based approach according to annex I, part IV of Directive 2001/83/EC applied to Advanced therapy medicinal products EMA/CAT/CPWP/686637/2011 Guideline on quality, non-clinical and clinical aspects of medicinal products containing genetically modified cells EMA/CAT/GTWP/671639/2008 ICH guideline Q8 (R2) on Pharmaceutical Development <p><i>Note: For content of the risk assessment, see also section 2.10, 2.12, 2.15, 2.16.</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
	Did you identify and implement control/mitigation measures based on the risk assessment?	<p><i>Note: Identify control and mitigation measures that are most appropriate in each case.</i></p> <p><i>The manufacturer is responsible to put in place the necessary measures to address the risk of the product, see section 2.14</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>
2.17 - 2.22	For investigational ATMPs: Do you have a system to ensure that risk assessments are based on current scientific knowledge and accumulated experience, and the strategy to ensure quality is updated as knowledge and experience increase?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>

	Question	Comments	Notes
2.25	For authorised ATMPs; Is the application of the described risk-based approach executed in accordance with the marketing authorization?	<i>Note: A risk-based approach and identification of mitigating strategies can be used to justify deviations from standard expectations in the marketing authorization application.</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>

Note: chapter 2 of GMP-ATMP contains non-exhaustive list of examples to illustrate risk-based approach. In this checklist, risk-based strategies and needs thereof has been incorporated into respective chapter.

3. Personnel

“The ATMP-manufacturer should have an adequate number of personnel with appropriate qualifications and adequate experience relating to the intended operations”.

“All personnel should receive training on the principle of GMP that affect them and receive initial and periodic training relevant to their tasks.”

	Question	Comments	Notes
3.10 to 3.11	Do you have an adequate number of personnel with appropriate training and adequate practical experience relevant to the intended operation?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> • <i>Policy Staff Education & Training</i> • <i>Checklist Staff Education & Training</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
3.11	Do you have job descriptions for all staff, indicating the staff's duties and responsibilities?	<ul style="list-style-type: none"> • <i>Job Descriptions for key personnel: for example Qualified Person, Quality Assurance, Quality Controller, Head of Production, production personnel, cleaning staff</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
3.12 to 3.13	Does personnel receive initial and periodic training relevant to their tasks, and initial and periodic training in GMP?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
3.14	Do you train your personnel specifically in aseptic manufacturing, and is this documented?	<p><i>Guidance documents:</i></p> <ul style="list-style-type: none"> • PIC/S recommendation on the validation of aseptic processes 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
3.15	Have all personnel involved in routine aseptic manufacturing participated in process simulation tests?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
	Do you document training and compliance of gowning requirements?	<i>Note: see 3.25-3.28 for gowning requirements.</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
	Do you re-assess gowning compliance annually?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
3.16	Do you monitor all personnel working in A/B for microbial contamination after critical operations and when leaving the A/B area?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> • <i>Environmental monitoring program</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>

	Question	Comments	Notes
3.16	Do you have a program for disqualifying personnel based on results, with retraining and requalification?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
3.17	Do you train personnel in preventing communicable diseases from raw and starting materials to operators and vice versa?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
	Have personnel handling GMO's received training to prevent cross-contamination and potential environmental impacts?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>
3.18	Have cleaning and maintenance personnel received training?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
3.19	Do you have records of all training of personnel?	<i>Suggested documents:</i> <ul style="list-style-type: none"> • <i>Checklist Staff Education and Training</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
	Do you assess all training for effectiveness?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
3.20 to 3.33	Do you have a hygiene program?	<i>Suggested documents:</i> <ul style="list-style-type: none"> • <i>Hygiene program to cover aspects of 3.20 – 3.33</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
3.25 to 3.28	Do you have an instruction that describes the clothing required for the clean areas?	<i>Suggested documents:</i> <ul style="list-style-type: none"> • <i>Instruction for gowning</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
3.32	Do you ensure that personnel with infectious diseases or open lesions do not participate in production?	<i>Suggested documents:</i> <ul style="list-style-type: none"> • <i>Hygiene regulation or policy</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
3.33	Do you vaccinate personnel involved in production, maintenance, testing and internal control if considered necessary?	<i>Suggested documents:</i> <ul style="list-style-type: none"> • <i>Hygiene regulation or policy</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>

	Question	Comments	Notes
3.34	Are key personnel appointed by senior management?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
3.35	Do you have clear, defined and communicated roles and responsibilities for key personnel?	<i>Suggested documents::</i> <ul style="list-style-type: none"> • <i>Job Descriptions</i> • <i>Organization charts</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
3.37	Is there a unit responsible for quality assurance? If yes, are the responsibilities shared with the person responsible for production and the person responsible for quality control?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>
3.40	Is the person responsible for production separated from the person responsible for quality control in every single batch? is this documented?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>

4. Premises

“Premises must be suitable for the operations to be carried out. In particular, they should be designed to minimize the opportunity for extraneous contamination, cross-contamination, the risk of errors and in general, any adverse effect on the quality of products.”

	Question	Comments	Notes
4.11 4.64 to 4.66 4.71 to 4.74	Are your premises for production, quality control, storage and ancillary areas suitable (clean, maintained, with good lightning and ventilation etc.)?	<p><i>Guidance documents:</i></p> <ul style="list-style-type: none"> • PIC/S Guide to good manufacturing practice for medicinal products part I • Guide to good manufacturing practice for medicinal products annexes • EudraLex EU Guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use, Volume 4, Part 1 Chapter 3: Premises and Equipment 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
4.12	Are your premises qualified?	<p><i>Guidance documents:</i></p> <ul style="list-style-type: none"> • PIC/S Validation Master Plan Installation and Operational Qualification Non-Sterile Process Validation Cleaning Validation PI 006-3 • EudraLex EU Guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use, Volume 4, Part 1, Annex 15 Qualification and validation <p><i>Note: See 10.1 Qualification of premises and equipment</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
4.13 to 4.16	For multi-product facilities; have you risk assessed concurrent manufacturing?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>
4.18 to 4.26	Do you separate different batches/products in time and or in place?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> • Policy for concurrent manufacturing of different batches/products 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>

	Question	Comments	Notes
4.27 to 4.36	Does the production area comply with the standards for design and construction to avoid contamination?	<p><i>Guidance documents:</i></p> <ul style="list-style-type: none"> • ISO 14644-1 • ISO 14698-1 • FEDERAL STANDARD 209E • cGMP Annex 1 <p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> • Site Master File. <p><i>Note: Site Master File to include logistic charts (personnel, goods, product, waste) describing the flow of materials and personnel in the premises.</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
4.37 to 4.38	Have you risk assessed the premises in regards to classification and aseptic handling for the product to be produced?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
4.39	Have you classified the clean rooms according to ISO 14644-1?	<p><i>Note: For classification, airborne particles equal to or greater than 0,5 µm should be measured.</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
4.40	Have you qualified the clean rooms based on measurement of the microbial load in operation?	<p><i>Note: Qualification of the microbial load in operation should include air sampling, settle plates and contact plates. The qualification could be included in the process validation report.</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
4.42	Have you validated cleaning of clean areas?	<p><i>Note: see 10.2 cleaning validation</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
4.42	Do you use sterile disinfectants, detergents, and cleaning materials in grade A/B?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> • Cleaning SOP • Specifications with acceptance criteria for disinfectants, detergents and cleaning materials • Cleaning validation <p><i>Note: To avoid the development of resistant strains and to achieve a broader range of bio-decontamination activity it's recommended to use more than one type of disinfectants. Also, the efficacy thereof should be checked.</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable [room for notes]

	Question	Comments	Notes
4.43	Do you have an environmental monitoring program with trended results?	<p><i>Suggested document:</i></p> <ul style="list-style-type: none"> SOP describing the environmental control program including classification, qualification and monitoring. <i>Validation Master Plan</i> <p><i>Note: The results shall be recorded, trended and the results summarized in a yearly report, along with a statement of compliance or non-compliance with the set limits depending on the class of the area.</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
4.44 to 4.47	Have the monitoring positions, the number of samples, volume, frequency of monitoring and actions limits been chosen based on locations posing the highest risk of contamination and the control strategy for the site and does it include the biosafety cabinets/isolators?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> <i>Risk analysis over the production activities to design the control strategy (aiming for “worst case” and high risk).</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
4.48 to 4.54	Do you monitor non-viable particles during critical operations and at set intervals at rest, with set alert and alarm levels, and have action plans in case of deviations covering grade A-D?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> <i>SOP describing the defined alert limits and the action limits.</i> <p><i>Note: The recommended action limits are listed in 4.50.</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
4.55	Do you monitor particles $\geq 5\mu\text{m}$ in grade A and B areas?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>
4.56 to 4.60	Do you monitor viable-particle during critical operations and at set intervals at rest, with set alert and alarm levels, and have action plans in case of deviations covering grade A-D?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> <i>SOP describing the defined alert limits and the action limits.</i> <p><i>Note: The recommended maximum limits are listed in 4.59.</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>
4.61	Do you identify microbes detected in a grade A area on species level?	<p><i>Note: All microorganisms found in a grade A area should be identified to species level and actions taken, based on the result.</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
4.61	Do you assess the impact of identified species on product quality and the suitability of the premises?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>

	Question	Comments	Notes
4.62	Do you monitor air pressure, with set alert and alarm levels, and action plans in case of deviations?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> <i>SOP describing the defined alert limits and the action limits.</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
4.62 to 4.63	Does adjacent rooms of different grades have differential pressure?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> <i>SOP describing the defined values for air pressure differential between areas of higher and lower cleanliness. The SOP should include the actions to be taken in case of pressure failure.</i> <p><i>Note: The differential pressure guidance value between rooms of different grades is 10-15 Pa. The pressure should be continuously monitored and with alarm settings.</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
4.66 to 4.69	Do you monitor storage areas?	<p><i>Note: The temperature should be monitored and the rH where relevant.</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
	<p>Do you have sufficient storage areas to store and separate various categories of material and products:</p> <ul style="list-style-type: none"> starting and raw material packaging materials intermediate, bulk and finished products products in quarantine, released, rejected, returned or recalled? 		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
4.70	Do you store highly reactive materials/products safe and secure?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>

5. Equipment

“Equipment used in production or control operations should be suitable for its intended purpose and it should not present any hazard to the product. Parts of production equipment that come into contact with the product should not have unwanted reactive, additive, adsorptive or absorptive properties that may affect the quality of the product. In addition, parts of the equipment that come into contact with cells/tissue should be sterile.

	Question	Comments	Notes
5.10	Are parts of the equipment that come into contact with the product sterile, and free from reactive, additive, adsorptive or absorptive properties?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
5.11	Have you identified all major equipment?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
5.13	Have you placed and installed equipment at suitable locations?	<i>Note: see 9.40 and 9.46 for requirements for open and closed production.</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
5.14	Are balances and measurement equipment of appropriate range and precision?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
5.16	Do you prevent use of defective equipment?	<i>Note: defective equipment should be removed from production area, or at least be clearly labelled as defective.</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
5.17	Do you have a process, and a validation scheme, for calibrating, inspecting and checking equipment at defined intervals?	<i>Suggested documents:</i> <ul style="list-style-type: none"> • <i>Validation Master Plan</i> • <i>Validation Scheme for Equipment</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
5.17	Are all ventilation filters qualified and maintained and changed at appropriate intervals?	<i>Suggested documents:</i> <ul style="list-style-type: none"> • <i>Instruction for control and maintenance of the cleanroom.</i> • <i>Room book with specification of filter type and class, location, air supply etc.</i> <p><i>Note: Filter ID and certificates of all filters should be received at installation and kept for traceability.</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>

	Question	Comments	Notes
5.17	Are all replaced filters tested for integrity after installation?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> • <i>Instruction for control and maintenance of the cleanroom</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
5.18	Do you use single-use cleaning materials whenever possible?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
5.19	Are maintenance and repair performed outside the production area?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
	If repair and maintenance cannot be performed outside the production and control area, have you verified the premises prior to restart production?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
5.20	Do you have a policy for the movement of equipment within the production areas?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>

6. Documentation

“Good documentation is an essential part of the quality system and is a key element of GMP. The main objective of the system of documentation utilized must be to establish, control, monitor and record all activities which directly or indirectly may affect the quality of the medicinal products. Records required to ensure traceability should also be kept.”

The amount of document and records/reports should be adjusted to the type of product and the stage of development. For investigational ATMPs, the level of detail of the specifications and instructions should be adapted to the type of product and to the stage of development.

	Question	Comments	Notes
6.13	Do you have measures to protect data against accidental loss or damage and from unauthorized manipulation?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> • <i>Instruction for computerized systems including backup of data</i> <p><i>Note:</i> <i>Measures should be taken to protect the data from manipulation (preventing unauthorized entry to the system (for ex. use of keys, pass cards, personal codes with passwords)).</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
	Do you have measures to ensure accuracy, completeness, availability and legibility of documents?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> • <i>Document control policy</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
6.16	Do you have clear and detailed specification and instructions to ensure compliance with the marketing authorization/clinical trial authorization and product consistency? and manufacturing ?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> • <i>Specifications for all material and finished product.</i> • <i>Manufacturing instructions/SOPs.</i> <p><i>Note: The specifications and instructions must comply with the terms of the MA/CTA, product consistency and the required quality of the product.</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
6.17	Do you have a process for revision control and implementation of new documents and routines?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> • <i>Document control policy</i> • <i>Instruction for training</i> <p><i>Note: The document control policy should describe revision and approval of documents, implementation/training of new routines and removal of old versions.</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]

	Question	Comments	Notes
6.17	Are all documents containing specifications and instructions approved, signed and dated by authorized persons and is there a date of entry into operation?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> • <i>Document control policy</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
6.18	Do you periodically re-assess and update specifications and instructions, and can the old documents be traced?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> • <i>Document control policy</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
6.19	Do you have a process for change control?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> • <i>Change control policy</i> • <i>Change control log</i> • <i>Report for change control</i> <p><i>Note: See also section 1.24</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
	Do you seek approval from the authorities if manufacturing requirements or substantial modifications in the manufacturing process are done?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
6.20	Does all raw material have specification?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> • <i>Documents for specification of the materials (raw materials, bulk, intermediates and packaging materials).</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
6.20	Does all starting material have a specification?	<ul style="list-style-type: none"> • <i>Documents for specification of Starting Material.</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
	Do all intermediate and bulk products have specifications?	<p><i>Note: The specification of raw materials should include a description of the item, the approved suppliers and, if reasonable, the original producer of the material; the quality requirements with acceptance limits, the identification of species and anatomical environment (raw materials of biological origin), instructions for sampling and storage, transport conditions and precautions.</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>
6.20	Does primary packaging materials have specifications?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>

	Question	Comments	Notes
6.20	Are there specifications for other materials used in the manufacturing process that can have a critical impact on quality (e.g. medical devices)?	<p><i>The specifications of the starting materials should include a description of the starting materials including the anatomical environment from where the materials origin (or when applicable; identification of the cell-line or master cell bank) and with instructions for sampling and storage, transport conditions and precautions.</i></p> <p>Guidance documents:</p> <ul style="list-style-type: none"> • PIC/S GMP GUIDE (PART I: BASIC REQUIREMENTS FOR MEDICINAL PRODUCTS) (4.13-4.16) • <i>The starting material should comply with 2004/23/EG</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable [room for notes]
	Have you defined the batch size for all ATMPs produced?	<p><i>Note: Products generated from different starting materials should be considered a distinct batch.</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
	Do you have manufacturing instructions?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
	Does finished products have specifications?	<p>Suggested documents:</p> <ul style="list-style-type: none"> • <i>Defined specification for the finished products.</i> <p><i>Note: The specification should cover contents of section 6.20 viii</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
	Do you have packaging instruction for each product?	<p>Guidance documents:</p> <ul style="list-style-type: none"> • <i>(EC) No 1394/2007, article 11 and 12 (labelling requirements)</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
	Do you comply with labelling requirements?	<p>Guidance documents:</p> <ul style="list-style-type: none"> • <i>For hospital exemption, the labelling should comply with LVFS/2011:3 and LVFS/2008:12, consolidated HSLF-FS 2017:32.</i> • <i>For clinical trial, the labelling should comply with LVFS/2011:19, consolidated HSLF-FS 2019:40 and LVFS/2008:12, consolidated HSLF-FS 2017:32</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]

	Question	Comments	Notes
6.22 - 6.24	For Investigational ATMPs: Do you have a Product Specification File?	<i>Suggested documents:</i> <ul style="list-style-type: none"> • <i>Product specification file (PSF)</i> <i>Guidance documents:</i> <ul style="list-style-type: none"> • Annex 13 Investigational Medicinal Products 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>
6.22	For clinical trials using blinded products; do you have an instruction of the blinding process and does it allow for identification of the product when necessary?	<i>Note: See 9.83 The blinding system should be described in the Product Specification File.</i> <i>Production of a placebo product also require a manufacturing authorization by the competent authorities (Läkemedelsverket).</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>
6.25	Do you make and complete records at the time of each action taken?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
6.26	Do you keep receipt records for each delivery of materials, starting materials, bulk, intermediate as well as primary packaging materials?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
	Do you keep batch processing records for each batch processed?	<i>Note: batch records to contain all relevant information as in 6.26</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
	Do you keep results from release tests?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
6.26	Do you keep environmental monitoring records?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
	Do you record outcome from self-inspections?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
6.27	Do you record, investigate and take appropriate corrective measures in case of deviations?	<i>Suggested documents:</i> <ul style="list-style-type: none"> • <i>Non-conformance handling</i> • <i>CAPA system</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>

	Question	Comments	Notes
6.28	Do you have a documented routine for qualification of premises and equipment?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> • <i>Validation master plan (VMP) should include the routines for qualification of equipment.</i> <p><i>Guidance documents:</i></p> <ul style="list-style-type: none"> • <u>PIC/S Validation Master Plan Installation and Operational Qualification Non-Sterile Process Validation Cleaning Validation PI 006-3</u> • <i>EudraLex EU Guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use, Volume 4, <u>Annex 15 Qualification and validation</u></i> <p><i>Note: See 10.1 Qualification of premises and equipment</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
	Do you have a documented routine for validation of manufacturing process?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> • <i>Validation master plan (VMP)</i> <p><i>Note: Processes and procedures should undergo periodic critical re-validation to ensure that they remain capable of achieving the intended results.</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
	Do you have a documented routine for validation of analytical methods?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> • <i>Validation master plan (VMP)</i> <p><i>Note: Processes and procedures should undergo periodic critical re-validation to ensure that they remain capable of achieving the intended results.</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
	Do you have a documented routine for maintenance and calibration of equipment?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> • <i>Validation master plan (VMP)</i> • <i>A maintenance schedule can be used to document maintenance of equipment.</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>

	Question	Comments	Notes
6.28	Do you have a documented routine for cleaning procedures?	<p>Suggested documents:</p> <ul style="list-style-type: none"> • SOPs describing the cleaning procedure including the detergents and disinfectants to be used • A checklist to document the cleaning process. 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
	Do you have a documented routine for environmental monitoring?	<p>Suggested documents:</p> <ul style="list-style-type: none"> • SOPs describing the environmental monitoring routine including set limits and a checklist to document the monitoring. <p>Note: The results could preferably be documented in an excel file for trend analysis purpose.</p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
	Do you have a documented routine for investigations of deviations and non-conformances?	<p>Suggested documents:</p> <ul style="list-style-type: none"> • A non-conformance report containing a description of the non-conformance, the immediate corrective actions taken, the Root Cause Analysis and further Corrective and Preventative Actions that needs to be taken. 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
	Do you have a documented routine for handling quality complaints and recall of products?	<p>Note: There should be a procedure for receiving complaints about products. The causes of quality defects should be investigated and appropriate measures taken to prevent reoccurrence.</p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
6.29	Do you have a logbook for all equipment?	<p>Suggested document:</p> <ul style="list-style-type: none"> • Logbooks for equipment <p>Note: The logbook should be used to record in chronological order, calibrations, maintenance, cleaning or repair operations, including the dates and identity of people who carried these operations out.</p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]

	Question	Comments	Notes
6.31	Do you have a Site Master File?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> • <i>Site Master File</i> <p><i>Guidance documents:</i></p> <ul style="list-style-type: none"> • Site Master File PIC/S Explanatory Notes on the preparation of a Site Master File. PE 008-4 • Volume 4, Good Manufacturing Practice Medicinal Products for Human and Veterinary Use Explanatory Notes on the preparation of a Site Master File <p><i>Note: A Site Master File (SMF) is a document describing the GMP related activities of the manufacturer.</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
6.32	For market authorized products: Do you keep batch process record for at least a year after expiry of the batch, or for 5 years after release of QP, whichever is the longest?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> • <i>Archiving policy</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable [room for notes]
	For investigational ATMP: Do you keep batch process record for 5 years after the formal discontinuation of the last clinical trial in which the batch was used?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> • <i>Archiving policy</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable [room for notes]
6.34	For market authorized products; Do you retain critical documentation, incl. raw data, whilst authorization remains in force?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> • <i>Archiving policy</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable [room for notes]
6.35	Do you have a manual or electronic system that enables the bidirectional tracking of cells/tissues contained in ATMPs from the point of donation to finished product?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> • <i>System for traceability</i> <p><i>Guidance documents:</i></p> <ul style="list-style-type: none"> • (EC) 2004/23/EG • 2006/86/EC 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
6.37	Do you retain the donor identification code, or information permitting the identification of the donor, for at least 30 years?	<p><i>Guidance documents:</i></p> <ul style="list-style-type: none"> • 2006/86/EC • (EU) 2015/565 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]

	Question	Comments	Notes
6.37	Do you retain the internal code, or other system for identifying cells/tissues used as starting material up to batch release – for at least 30 years?	<i>Suggested documents:</i> <ul style="list-style-type: none"> • <i>Archiving policy</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
	Is the link between the donor identification code (or equivalent) and the internal code (or equivalent) established and maintained for at least 30 years?	<i>Suggested documents:</i> <ul style="list-style-type: none"> • <i>Archiving policy</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
	Do you retain the identification, including batch number of critical raw material and other substances that may have an impact on the safety of the ATMP, for at least 30 years?	<i>Suggested documents:</i> <ul style="list-style-type: none"> • <i>Archiving policy</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
	Do you retain the identification of all other active substances contained in the ATMP for at least 30 years?	<i>Suggested documents:</i> <ul style="list-style-type: none"> • <i>Archiving policy</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>
6.38	Do you keep data permitting the identification of the donor animal for 30 years?	<i>Note: When using xenogeneic cell as starting material</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>
6.39	Are the traceability data auditable and can data rapidly be accessed in case of an adverse reaction?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
6.40	If the responsibility of the traceability data transferred to the marketing authorization holder/sponsor, is there a written agreement?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>

7. Starting and raw material

“The quality of starting and raw material is a key factor to consider in the production of ATMPs.”

	Question	Comments	Notes
7.11	Have you removed any antimicrobials used in the production process as soon as possible?	<i>Note: all antimicrobial should be removed to prevent them from interfering with the sterility testing and from contaminating the final product.</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable [room for notes]
7.12	Have you demonstrated that culture media is suitable for its intended purpose?	<i>Suggested documents:</i> <ul style="list-style-type: none"> <i>Instruction for control of growth promotion properties of cell culture media</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable [room for notes]
7.13	Does all raw material, where possible, comply with Ph Eur 5.2.12?	<i>Guidance documents:</i> <ul style="list-style-type: none"> <u>Ph Eur 5.2.12 general chapter on raw materials of biological origin for the production of cell based and gene therapy medicinal products.</u> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable [room for notes]
	If applicable: Have you risk assessed the use of research grade raw materials, and checked those materials suitability?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable [room for notes]
7.14	Have you documented all decisions whether a raw material is critical?	<i>Note: see section 6.2</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]

	Question	Comments	Notes
7.14	Do you have specifications for raw material covering aspects of production, testing, control, handling and distribution?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> • <i>Raw Material Specifications</i> <p><i>Notes; raw material of human or animal origin needs to comply with the following documents;</i></p> <ul style="list-style-type: none"> • <u>ICH Topic Q 5 A (R1) Quality of Biotechnological Products: Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin CPMP/ICH/295/95</u> • <u>Notes for guidance on virus validation studies CPMP/BWP/268/95</u> <p><i>Materials of biological origin must be considered for viral and microbial safety and Transmittable Spongiform Encephalopathy (“TSE”).</i></p> <p><i>Guidance documents:</i></p> <ul style="list-style-type: none"> • <u>Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents’</u> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable [room for notes]
	Do you select control strategies for raw materials based on risk assessments?	<p><i>Guidance documents:</i></p> <ul style="list-style-type: none"> • <u>PAS 157:2015 Evaluation of materials of biological origin used in the production of cell-based medicinal products.</u> <p><i>Note: control strategies may include qualification of suppliers, performance or suitable functional testing.</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
	For authorized ATMPs: are set specifications agreed by the supplier?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable [room for notes]
7.15	Do you check compliance of raw materials to set specifications?	<p><i>Note: level of supervision and testing should be based on a risk analysis. Raw material should be risk assessed on basis of their impact on product quality, patient safety, efficacy and intrinsic properties. See section 7.2, and section 2.30</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]

	Question	Comments	Notes
	Have you qualified your suppliers?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> • <i>SOP Qualification of Suppliers.</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>
7.16	Do you filter raw material not stating to be mycoplasma free?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>
7.18	Do you label stored raw materials in compliance with the legislation?	<p><i>See 7.18 (i-v)</i></p> <p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> • <i>A color-coding labelling system could be used to visualize and separate released materials from material in quarantine and rejected materials. For example, using red labels (rejected), yellow labels (quarantine), on test (blue) and green labels (released)</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
7.20	Does the person responsible for quality control release all raw materials?	<p><i>Suggested document:</i></p> <ul style="list-style-type: none"> • <i>QC Job Description</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
7.21	Can you track all critical raw materials used in case of a suppliers recall or in cases of alerts regarding quality and safety issues?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
7.22	Do you collect, procure and test starting material in compliance with Directive 2004/EC/23, or, if blood-derived products in compliance with Directive 2002/98/EC?	<p><i>Guidance documents:</i></p> <ul style="list-style-type: none"> • <i>Directive 2004/EC/23</i> • <i>Directive 2002/98/EC</i> • <i>cGMP annex 14</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
7.22	Is the supplier of starting material accredited, designated, authorized or licensed in compliance with Directive 2004/EC/23 or Directive 2002/98/EC?	<p><i>Technical directives:</i></p> <ul style="list-style-type: none"> • <i>2006/17/EC</i> • <i>2006/86/EC</i> • <i>2005/61/EC</i> • <i>2005/62/EC</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>

	Question	Comments	Notes
7.23	For starting material consisting of cells/tissues outside the scope of the Directive 2004/EC/23 or Directive 2002/98/EC: Have you taken appropriate steps to ensure quality, safety and traceability?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable [room for notes]
7.24	Are specifications for starting material agreed by the supplier?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
7.25	Do you verify compliance of starting material with the agreed specifications?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
7.26	Do you have an agreement with the Tissue establishment and/or the Blood establishment and does the agreement include the audit of the blood establishment and tissue establishment?	<i>Suggested documents:</i> <ul style="list-style-type: none"> • <i>Agreement Tissue Establishment</i> <i>The agreement should cover aspects relating to 7.27</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
7.27	Does the agreement contain provisions about the transfer of information, particular on tests results, traceability data, transmission of health donor information?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
7.28	Have you considered the risks of contaminating starting materials with particular emphasis on viral and microbial safety and Transmittable Spongiform Encephalopathy ("TSE")?	<i>Guidance documents:</i> <ul style="list-style-type: none"> • Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents' 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
7.29	Does the person responsible for quality control release starting material?	<i>Suggested document:</i> <ul style="list-style-type: none"> • <i>QC Job Description</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
7.30	Have you risk assessed the use of starting material released without results from tests?	<i>Suggested documents:</i> <ul style="list-style-type: none"> • <i>Risk Assessment Starting material</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable [room for notes]
7.31 to 7.32	Do you label stored starting material in compliance with the legislation?	<i>Note: see 7.31 (i-v). Labelling can be done either manually or in a computerized system.</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable [room for notes]

	Question	Comments	Notes
7.33 - 7.34	Do you process/manufacture from starting material in a GMP environment?	<i>Note: steps like washing or preservation can take place at the tissue establishment.</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
7.35	For the exceptional use of starting material which have been processed prior outside the GMP environment; Have you done a risk analysis to address all aspects of safety and efficacy of the product?	<i>Note: the competent authorities should agree to the control strategy.</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable [room for notes]
7.36	Have you made sure that starting material in form of plasmids or gene vectors from suppliers have been manufactured in GMP environment?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable [room for notes]
7.37	Have you addressed additional risks of using xenogeneic cells/tissues?	<i>Note: All donor animals should be bred in captivity, raised in SPF-conditions and be health monitored.</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable [room for notes]
7.38	Have you implemented measures to identify and prevent incidents that negatively affect the health of the donor animal?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable [room for notes]
7.39	Have all instances of ill-health in the herd been investigated as described in the legislation?	<i>Note: see 7.39</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable [room for notes]
7.40	Do you document withdrawal periods for therapeutic agents used to treat source/donor animals?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable [room for notes]

8. Seed lot and cell bank system

“When seed lots and cell banks, including master and working generations are used, they should be established under appropriate conditions, including compliance with GMP as provided in this guideline”.

	Question	Comments	Notes
8.11	Is all handling of cell seeds and cell banks carried out in a GMP-compliant manner?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
8.12	Has the limited number of cell doublings and passages been defined and has this been specified in the MA or clinical trial?	<i>Suggested documents:</i> <ul style="list-style-type: none"> • <i>Product specification</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
8.13	Are there documentation available from stages prior to the master seed or cell bank generation (initial sourcing and early development) that could support traceability including used components?	<i>Note: see 8.14 for exemptions.</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
8.14	If the seed lot and/or cell bank in use was established prior to Regulation 1394/2007 (meaning that all information is not available), has an extensive characterization been performed and has this strategy been approved by Läkemedelsverket?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>
8.15	Are the seed banks and cell lots stored and used under conditions that prevent mix-ups and cross-contamination?	<i>Note: for example, store in sealed containers, in the vapour phase of LN₂.</i> Guidance documents: <ul style="list-style-type: none"> • ICH guideline Q5D10. 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
8.16	Do you have a stock inventory?	<i>Note: for cell stock it is desirable to split the stock and store splits at different locations in a controlled environment.</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
	Do you monitor storage temperatures?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
8.16	Do you retain temperature records?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>

	Question	Comments	Notes
8.16	Do you record deviations from set limits?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
8.17	Do you document stability and recovery for seeds and banks in a manner to allow for trending of the results?	<i>Note: for investigational AMTPs, the requirements increases with increasing real-life data.</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
8.18	Do you have a system to ensure that containers removed from storage only are returned after documented adequate storage conditions?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
8.19	Are access limited to authorized personnel only?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
8.21	Do you split stocks and do you store the split stocks at different locations to minimize the risk of total loss?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
8.23	For cell stocks/cell banks established prior to 1394/2007: Have you done a risk analysis to identify measures needed to ensure the quality of the starting material?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
8.24	Have you sought approval from the competent authorities for such cell stock/cell bank?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>

9. Production

“Procedural operations, including filling, packaging, and –as applicable – cryopreservation should follow clearly defined procedures designed to ensure the quality of the product, consistent production (appropriate to the relevant stage of development), and to comply with the requirements set in the relevant manufacturing and marketing/clinical trial authorization”

“In cases of investigational ATMPs, the knowledge and understanding of the product may be limited... It is therefore acknowledged that the manufacturing process (including quality controls) may need to be adapted as the knowledge of the process increases” .

	Question	Comments	Notes
9.14	Are deviations from instructions/procedures approved in writing, and are deviations investigated in order to identify root cause and implement corrective and preventive measures?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
9.15	Do you handle all materials and products as described in written procedures?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
9.17	Do you quarantine incoming materials or products prior to release for use?	<i>Note: should be physically or administrate separated.</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
9.18	Does the person responsible for quality control release intermediate and bulk products prior to use?	Suggested document: <ul style="list-style-type: none"> • QC Job Description 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable [room for notes]
9.20	Do you label all materials, containers, major items of equipment and/or rooms during production?	<i>Note: see section 9.21 for notes on labeling.</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
9.21	Have you verified the labels suitability for storage or processing conditions?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
9.22	Are containers cleaned when necessary, and are damages to containers reported to QC?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
9.23	Is the water used in manufacturing ATMP of appropriate quality, and is it checked regularly to verify absence of contamination?	<i>Note; purchase of pre-packaged water excludes the need of demonstration appropriateness. See section 9.26</i> <i>Absence of contamination (chemical, biological and as appropriate endotoxins) should be checked.</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]

	Question	Comments	Notes
9.25	Do you have written instructions for sanitizing water pipes?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
	Do you have action limits for microbiological contamination of water pipes?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
9.26	Is there a procedure to ensure rinsing post-sanitizing water pipes to ensure removal of sanitizing agent, and has the procedure been validated?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
9.27 - 9.28	Are gases that come in contact with product compliant with European Pharmacopoeia? If not, are the risks of using technical grade gas assessed?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
9.29	Are gasses taken into aseptic area or coming in contact with product passed through sterilization filters, and are the critical gas filters checked regularly for integrity?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
9.30	Has the water used to generate steam been demonstrated to be of appropriate quality?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
9.31	Do you ensure that work area and equipment are clean and free of materials, residues or documents not required for the operation?	Suggested documents: <ul style="list-style-type: none"> • SOP Line Clearance • SOP Sanitization 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
9.32 - 9.33	Have you assessed the risk of cross-contaminating your product?	Suggested documents: <ul style="list-style-type: none"> • Risk assessment, per product Guidance documents: <ul style="list-style-type: none"> • Guideline on the risk-based approach according to annex I, part IV of Directive 2001/83/EC applied to Advanced therapy medicinal products EMA/CAT/CPWP/686637/2011 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]

	Question	Comments	Notes
9.34 - 9.36	Have you implemented mitigating measures?	<i>Note: for examples of risk-reducing measures, see 9.35, i-viii. The sum of the measure should assure absence of contamination.</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
9.37	Is the effectiveness of the control strategy assessed regularly?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
9.38	Are there validated decontamination procedures for accidental spillages?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
9.40	For closed system production; Is your closed system fulfill the requirements to be placed in clean area grade D?	<i>Note: production can take place in a clean area grade D, provided that the system is closed, see section 9.44, and validated, see section 9.43. and monitored, see section 9.43. If not, production cannot be seen as closed.</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable [room for notes]
9.45	For ATMPs produced in operating theater, have you demonstrated that the expected clinical benefit outweighs the risks?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable [room for notes]
9.46	For open system production; Does your production take place in a critical clean area A with a background clean area grade B for aseptic preparation and filling? Exceptions; <ul style="list-style-type: none"> - Preparation of solutions which are to be sterile filtered can be done in C. - Viral vectors; the expansion phase can be performed in A/C, the filtration and filling needs to be A/B, unless closed system. - Investigational ATMPs, please see 2.3.4 - Production inside sterile disposable kits, grade C may be acceptable. 		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable [room for notes]
9.50	Do you use double-ended sterilizers' or H ₂ O ₂ locks to prevent contamination when introducing materials, equipment into clean areas?	<i>Note: sterilization elsewhere is acceptable if using multiple wrappings, see 9.51. If materials cannot be sterilized, risk mitigation measure must be in place, see section 9.52. Use of filters should be used when possible (9.53)</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]

	Question	Comments	Notes
9.51	Have you validated your sterilization process?	<i>Note: Multiple wrappings should be used. If possible in numbers equal- or above-the number of stages of entry to the clean area.</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
9.52	If sterilization of articles, materials or equipment is not possible, have measures been implemented to minimize the risks?	<i>Note: For example treatment of biopsy with antibiotics, sterile filtration of raw materials, disinfection of materials)</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
9.55	Have you done process simulation tests for your product?	<i>Note; for guidance on process simulation tests, see section 9.55 - 9.65</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
9.60	Do you identify and investigate all contaminants if found in a process simulation test?	<i>Note: If indicative on a potential systematic failure, the impacts on batches produced since the last successful process simulation test should be assessed.</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
9.61 To 9.64	Are process simulation tests repeated as per legislation?	<i>Note: see section 9.61 to 9.64 The relevance of media fill test for the training of operators to ensure aseptic manufacturing should be considered when deciding the frequency of the simulation test.</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
9.66	Have you validated your sterilization methods for starting material, raw materials, excipients with regards to sterility and preserving the activity?	<i>Note: particular attention if the sterilization method is not in accordance with European Pharmacopeia.</i> <i>Guidance document:</i> <ul style="list-style-type: none"> • cGMP Annex 1 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
9.68	For solutions or liquids that cannot be sterilized in the final container: Do you filter through a sterile filter with 0.22 µm or less micron, into a previously sterilized container?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
9.69	Do you verify integrity of sterilizing filters before use, and/or after use?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
9.70	Do you monitor identified critical quality parameters?	<i>Note: if possible, continuous monitoring.</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>

	Question	Comments	Notes
9.74	Have you ensured the suitability of the primary packaging material used?	<i>Note: In regard to the characteristics of the product and the storage conditions. The level of documentation regarding the demonstration of suitability should be adapted to the phase of the development.</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
9.75	For authorised ATMPs: Have you documented selection, qualification approval and maintenance of supplier of primary packaging materials?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
9.76	Is the ATMP suitably packaged to maintain the quality of the product during storage, handling and shipping?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
9.76	For authorised ATMPs: Have you validated the primary packaging materials with regards to closure?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
	Do you regularly verify the effectiveness of the closure procedure?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
9.77	Do you have a system in place to ensure checks of electronic code readers, label counters or similar devices?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
9.78	Do you have written instructions to make sure working area is clean and free from any product, material or document not required?	<i>Suggested documents:</i> <ul style="list-style-type: none"> • <i>Line Clearance Product Labelling</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
9.79	For investigational ATMPs: Have you taken special precautions when packaging and labelling investigational ATMPs?	<i>See 9.80-9.83</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>
9.84	Are finished products checked, held in quarantine, released or rejected under the right conditions?	<i>See 9.84-9.87</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>

	Question	Comments	Notes
9.88	Do you handle rejected, recovered and returned materials in the right manner?	<i>See 9.88-9.91</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>

10. Qualification and validation

“Premises and equipment used in the manufacture of ATMP should be qualified. Through the qualification of premises and equipment, it is established that the premises and equipment are adequate for the intended operations.”

“Decisions on the scope and extent of the qualification should be based on a risk-assessment, which should be documented”.

Definitions:

- *Design qualification (DQ)- Demonstrates that the proposed design will satisfy all the requirements that are defined and detailed in the User Requirements Specification (URS). Satisfactory execution of the DQ is a mandatory requirement before construction (or procurement) of the new design can be authorised.*
- *Installation qualification (IQ) – Demonstrates that the process or equipment meets all specifications, is installed correctly, and all required components and documentation needed for continued operation are installed and in place.*
- *Operational qualification (OQ) – Demonstrates that all facets of the process or equipment are operating correctly.*
- *Performance qualification (PQ) – Demonstrates that the process or equipment performs as intended in a consistent manner over time*

	Question	Comments	Notes
10.12	Are all clean areas qualified in accordance with ISO 14644-1, and requalified in accordance with ISO 14644-2.	<i>Guidance documents:</i> <ul style="list-style-type: none"> • ISO 14644-1 • ISO 14644-2 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
10.13	Are the computerized systems validated in proportion to their impact on quality?	<i>Guidance documents:</i> <ul style="list-style-type: none"> • <i>Good Manufacturing Practice Volume 4, Medicinal Products for Human and Veterinary Use</i> Annex 11: Computerised Systems • PIC/S: PI 011 Good Practices for Computerised Systems in Regulated "GxP" Environments • USA: 21 CFR Part 11 Electronic Records, Electronic Signature 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable [room for notes]
10.14	If the product is an investigational ATMP, has the air quality been verified and critical aspects of the room and/or equipment qualified?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable [room for notes]
10.15	Are there documented routines for assessing the need of re-qualification of clean areas for each type of ATMP to be produced?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]

	Question	Comments	Notes
10.16	Are facilities and equipment re-evaluated at appropriate times?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> • <i>Validation Scheme</i> • <i>Validation Master Plan</i> <p><i>Guidance documents:</i></p> <ul style="list-style-type: none"> • PIC/S Validation Master Plan Installation and Operational Qualification Non-Sterile Process Validation Cleaning Validation PI 006-3 • <i>EudraLex EU Guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use, Volume 4, Annex 15 Qualification and validation</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
10.17	Has URS been set for the premises and equipment to ensure critical quality attributes?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> • <i>URS= User requirement specification</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
10.18	Is compliance of the URS with GMP demonstrated and documented? (design qualification?)	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> • <i>DQ (Design qualification)</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
10.19-10.25	Has premises and equipment been qualified?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> • <i>Qualification documents (qualification plan, -protocol and -report) to include Installation Qualification (IQ), Operational Qualification (OQ), and Performance Qualification (PQ).</i> <p><i>Note: For more details about the qualification requirements see 10.19-10.25</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
10.26	Is this documented in a qualification report?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
10.28-10.34	Has the cleaning of re-usable tools and equipment that come in contact with product been validated and documented in accordance with 10.28-10.34?	<p><i>Guidance documents:</i></p> <ul style="list-style-type: none"> • PIC/S Validation Master Plan Installation and Operational Qualification Non-Sterile Process Validation Cleaning Validation PI 006-3 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>

	Question	Comments	Notes
10.35	For investigational ATMPs, has cleaning been verified?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable [room for notes]
10.37	Is there a process validation protocol?	<p><i>Guidance documents:</i></p> <ul style="list-style-type: none"> • EMA/CHMP/BWP/187338/2014 Guideline on process validation for the manufacture of biotechnology-derived active substances and data to be provided in the regulatory submission <p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> • Process Validation Plan • Process Validation Report <p><i>Note: The process validation protocol should as a minimum define critical process parameters, critical quality attributes and acceptance criteria. A specified list of content in the process validation protocol is listed in 10.38. Generally three consecutive batches constitute a validation of the process but an alternative number could be accepted if justified, see 10.39.</i></p> <p><i>See 9.5.2 for guidance on aseptic process validation.</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
10.41	If validation occurs with surrogate materials, has the representativeness of the surrogate material been evaluated?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable [room for notes]
10.46	For investigational ATMPs, has (as a minimum) the aseptic processes and sterilizing processes been validated?	<p><i>Guidance documents:</i></p> <ul style="list-style-type: none"> • PIC/S RECOMMENDATION ON THE VALIDATION OF ASEPTIC PROCESSES PI 007-6 • FDA Sterilization Process Validation, January 1993 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable [room for notes]
10.47	Are process validation/evaluation data collected throughout the development?	<p><i>Note: To demonstrate that the manufacturing process ensures a consistent production</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable [room for notes]

	Question	Comments	Notes
10.48	Are the analytical methods validated/verified to ensure suitability to its purpose?	<p><i>Guidance documents</i></p> <ul style="list-style-type: none"> • <i>Ph.Eur. monograph on Method of analysis (2.7.23.) Numeration of CD34/CD45+ cells in haematopoietic products. Version 7.2</i> • <i>Ph.Eur. monograph on Method of analysis (2.7.28.) Colony-forming cell assay for human haematopoietic progenitor cells. Version 7.2</i> • <i>Ph.Eur. monograph on Nucleated Cell Count and Viability (2.7.29.)</i> • <i>Ph.Eur. monograph on Nucleic Acid Amplification Techniques (2.6.21.)</i> • <i>Ph.Eur. monograph on Flow Cytometry (2.7.24.)</i> • <i>Ph.Eur: (2.6.27) Microbiological control of cellular products</i> • <i>Ph.Eur: (2.6.1.) Sterility</i> • <i>Ph.Eur: (5.1.6) Alternative methods for control of microbiological quality</i> • <i>Ph.Eur. monograph Mycoplasmas (2.6.7.)</i> • <i>Ph.Eur. monograph on Bacterial endotoxins (2.6.14.)</i> • <u>ICH GUIDELINE VALIDATION OF ANALYTICAL PROCEDURES: TEXT AND METHODOLOGY Q2(R1)</u> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
10.50	For investigational ATMPs; are the analytical methods validated in accordance with the clinical development of the product?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable [room for notes]
10.51	Are transport conditions defined in writing?	<i>Note: Temperature, type of container etc.</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
10.52	Are the defined transport conditions demonstrated to be adequate?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> • <i>Transport validation report</i> <p><i>Note: Temperature, type of container etc.</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]

11. Qualified person and batch release

“Each manufacturing site of ATMPs in the EEA must have at least one Qualified Person.”

“Batches of ATMPs should only be released for sale, supply to the market or for use in clinical trials after certification of a QP. Until a batch is released, it should remain at the site of the manufacture or be shipped under quarantine to another authorized site.”

	Question	Comments	Notes
11.11	Do you have a system for ensuring that non certified batched aren't released?	<i>See 9.8 and 9.9</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
11.12	Does the QP has the right qualifications?	<i>Supporting documents:</i> <ul style="list-style-type: none"> • Article 49 of Directive 2001/83 • LVFS 2004:7, consolidated HSLF-FS 2018:61 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
11.13	Do you have a document describing the responsibilities of QP?	<i>Suggested document:</i> <ul style="list-style-type: none"> • <i>Job Description QP</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
	Does the document cover clear definition of responsibilities if more than 1 QP is involved?	<i>Note; the QP job description should cover 11.22-11.25</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>
11.15 to 11.19	For imported ATMPs: Is there a written instruction on certification of ATMPs produced and/or tested in third countries? Does this instruction cover transport and storage checks?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>
11.26-11.34	Do you have system for batch certification and release?	<i>Suggested documents:</i> <ul style="list-style-type: none"> • <i>SOP describing the Certification and Release process</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
11.37-11.42	Does your system include batch release prior to obtaining the results of quality control tests?	<i>Note: due to short shelf-life some ATMP must be released before completion of all QC tests. You must have a procedure in place for handling OoS test results after batch release, see 11.41.</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
11.43-11.51	For decentralized manufacturing: Do you have a system for batch certificate and release for decentralized manufacturing?	<i>Suggested documents:</i> <ul style="list-style-type: none"> • <i>SOP describing the Certification and Release process</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>

	Question	Comments	Notes
11.51	For decentralized manufacturing: Are all deviations investigated and approved by the central site?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>
11.52	Do you have a system in place to ensure that all deviations regarding production are handled and completed prior to certification and release?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
11.41-11.42 11.53	Do you have a procedure for handling of Out of Specification (OOS) batches?	<i>Suggested documents:</i> <ul style="list-style-type: none"> • <i>SOP for out of specification batches</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
11.54	Do you report out of specification batches to the competent authorities?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
	Do you document the acceptance of out of specification batches by the physician?	<i>Suggested documents:</i> <ul style="list-style-type: none"> • <i>Document for acceptance of out of specification batches</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
	Do you evaluated and notify the physician of the risks using ATMPs OoS?	<i>Suggested documents:</i> <ul style="list-style-type: none"> • <i>SOP for out of specification batches</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
	Do you have a system for informing the relevant competent authorities about administration of OOS batches?	<i>For investigational products: The manufacturer should immediately inform the sponsor and in turn inform the relevant authorities.</i> <i>For authorized products: The manufacturer should immediately inform the marketing authorization holder and the supervisor authority.</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>

12. Quality control

“Quality control is intended to ensure that the necessary and relevant tests are carried out, and that materials that are not released for use, nor products for sale or supply, until their quality has been judged satisfactory. Quality control is not confined to laboratory operations, but must be involved in all decisions which may affect the quality of the product”.

	Question	Comments	Notes
12.11	Do you have a designated person responsible for quality control?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
	Do you have a description of responsibilities for person responsible for QC?	Suggested documents: <ul style="list-style-type: none"> • Job description with responsibilities for QC 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
12.13	Do you keep records of the QC activities?	Suggested documents: <ul style="list-style-type: none"> • Instruction for reception and control of incoming materials incl. a system for quarantine, approval and rejection of materials. • Specifications including Acceptance Criteria • Instructions for sampling and testing • Quality Control Records • Agreements (out sourced activities) 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
	Do you have written procedures in place for the QC activities?	Note: See 12.12, iii to vii	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
12.14	Does QC have access to premises and documents needed to carry out his/her obligations?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
12.15	Are the sampled bulk containers and the samples taken during processing activities properly identified?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
12.16	Do you have written instructions for the sampling procedure including labelling of the sampled containers ?	Suggested documents: <ul style="list-style-type: none"> • Instructions for sampling 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]

	Question	Comments	Notes
12.17	Do you retain reference samples?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> • <i>Policy for reference samples</i> <p><i>Note: Samples should be retained for analytical and identification purpose (retention sample of the fully packed unit from a batch of finished product see 12.19).</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
12.18	Is the number and size of samples sufficient for two full analytical controls of the batch, if applicable?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
12.19	Are retention samples (a fully packaged unit from a batch of finished product) retained?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> • <i>Policy for retention samples</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
12.21	Do you have a documented sampling plan?	<p><i>Note: See 12.21 to 12.28</i> <i>The sampling plan should cover raw materials, starting materials, active substances and intermediate products, primary packaging material and retention samples (a fully packaged unit). However some exemption from above may apply in special cases.</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
12.29-12.30	Do you perform in process controls at appropriate stages of production?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> not applicable [room for notes]
12.31	Are your test methods validated?	<p><i>Note: see 10.4</i> <i>For investigational ATMPs, the level of validation should be commensurate with the development phase and the criticality of the test results considering the risk for the patient.</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
12.32	Do you keep records in connection with performed tests?	<p><i>Note: See 12.32 (1)-(ix) for the required documentation</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable [room for notes]
12.34	If testing methods are transferred from one laboratory to another; do you have a detailed protocol for this?	<p><i>Note: See 12.35 for the required parameters in the protocol</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable [room for notes]

	Question	Comments	Notes
12.37 to 12.39	<p><i>For ATMP with marketing authorization;</i> Do you have an ongoing stability program?</p>		<p> <input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable </p> <p><i>[room for notes]</i></p>

13. Outsourced activity

“Activities that are outsourced to a third part (including consultancy work) should be governed by a written contract that establishes the responsibilities of each party. As appropriate, the role and responsibilities in the event of detection of quality defects should be clearly established in the contract, as well as where applicable, the obligations of each party regarding traceability.”

	Question	Comments	Notes
13.10	Do you have a written contract for each outsourced activity, clearly establishing responsibilities in the event of quality defects, and traceability?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> • <i>Agreements outsourced activities</i> <p><i>Note: Should include access for audits (13.19), non-use of subcontracts to third party (13.18), assess to test records (13.14, 13.17, and supply of detailed instructions (13.13).</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
13.11	Are all contract acceptors assessed for suitability?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> • <i>Assessment of contractors</i> <p><i>Note: suitability is the ability to carry out outsourced activities in GMP compliance and accordance with the clinical trial/marketing authorization</i></p>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
13.12	Are all contract acceptors GMP-certified?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>
	If the contract acceptor is not GMP-certified do they comply with other suitable quality standards (e.g. ISO) and is this duly justified?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>
13.13	Are the contract acceptor given all necessary information about the product/manufacturing process to be able to carry out operations correctly.		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>
13.14	Do you as a contract giver review and assess the records and results related to the outsourced activities?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>
13.15	Do you as a contract acceptor take all measures to carry out the outsourced activities (e.g. adequate premises, equipment, trained personnel, etc.)?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>

	Question	Comments	Notes
13.16	Do you as a contract acceptor inform the contract giver and wait for approval before introducing any changes related to the outsourced activity?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>
13.17	Do you as a contract acceptor transfer records to the contract giver or is it possible for the contract giver to be granted access?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>
13.18	Do you as a contract taker inform the contract giver and wait for approval before subcontracting to a third party?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>
13.19	Do you as a contract acceptor accept audit/inspections by the contract giver or the competent authorities?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>

14. Quality defects and product recalls

“A system should be put in place to ensure that all quality related complaints, whether received orally or in writing, are recorded and that they are thoroughly investigated. Personnel responsible for managing complains and quality defects investigations should be independent from marketing and sales department unless otherwise justified. If the QP involved in the certification of the concerned batch(es) does not participate in the investigation, it should be informed in a timely manner.”

	Question	Comments	Notes
14.10 - 14.11	Do you have a system for managing quality complaints and defects?	<i>Suggested documents:</i> <ul style="list-style-type: none"> SOP describing the system for recording and investigation of incoming complaints and defects. 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
14.11	In case of a quality defect, are there SOPs describing actions to investigate, identify and address to root cause, and the need for corrective or protective measures, CAPA?	<i>Suggested documents:</i> <ul style="list-style-type: none"> SOP describing the action plans in case of the receipt of a complaint 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
14.15	Do you review the CAPA system for effectiveness?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
14.16	Do you retain all quality defect records and use them to evaluate recurring problems?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
	Are the competent authorities (Läkemedelsverket) informed in a timely manner of confirmed quality defects?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
14.18	For investigational AMTPS: can you rapidly unblind in case of recall?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable [room for notes]
14.20 14.23	Is there a written procedure for product recall and for informing competent authorities (Läkemedelsverket)?	<i>Suggested documents:</i> <ul style="list-style-type: none"> SOP describing the product recall procedure 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
14.21	Can the recall procedure be initiated promptly and at any time?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]

	Question	Comments	Notes
14.22	In case of authorized ATMPs: Have you performed a mock-recall?	<i>Note: May not be appropriate in certain settings for example for autologous products, donor-matched allogenic products of when the time between the manufacturing and the administration is very short.</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>
14.24	Do you have an action plan for recalled products already administrated?	<i>Suggested documents:</i> <ul style="list-style-type: none"> • <i>SOP describing the action plans in case of a recall</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed
14.26	Do you have a detailed inventory of shipments to facilitate recalls?	<i>Suggested documents:</i> <ul style="list-style-type: none"> • <i>A listing of the shipments made</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>

15. Environmental control measures for ATMPs containing or consisting of GMOs

“The handling of ATMPs containing or consisting of GMOs may pose a risk for the environment, requiring the implementation of additional control measures”.

	Question	Comments	Notes
15.10	Have you risk assessed and categorized the product as having negligible, low, moderate or high risk for the environment?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> <i>Environmental Risk assessment of GMOs</i> <i>Risk Management Plan including containment measures</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
15.11	Do you have containment measures based on the risk posed by the GMO?	<p><i>Guidance documents;</i></p> <ul style="list-style-type: none"> <i>Scientific Requirements on environmental risk assessment for gene therapy medicinal products.</i> <i>CHMP/GTWP/125491/06</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
15.12	Do you handle viral vectors in a segregated area, and in biological safety cabinet or isolator?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
15.13	Are there decontamination measures when moving from GMO-area to non-GMO-area or when moving between areas containing different GMO?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
15.14	Do you have an emergency plan for accidental releases of GMOs into the environment?	<p><i>Suggested documents:</i></p> <ul style="list-style-type: none"> <i>Emergency Plan</i> 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
15.15	For authorized ATMPs: Does the Risk Management Plan contain risk assessment as in 15.10, containment measures as in 15.11, and emergency plans as in 15.14?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>

16. Reconstitution of product after batch release

“Reconstitution activities can be performed at the administration site outside a GMP environment.”

“The term reconstitution covers activities required after batch release and prior to the administration of the ATMP to the patient, and which cannot be considered as a manufacturing step. No activity that entails substantial manipulation can, however, be considered reconstitution. Substantial manipulations should be conducted under GMP”

	Question	Comments	Notes
16.12 – 16.13	Does the activities qualify as reconstitution activities?	<i>Note: See 16.12 and 16.13</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
16.14	Do you provide instructions for reconstitution procedures to the administration site, and are those instructions detailed and clear?	<i>Suggested documents:</i> <ul style="list-style-type: none"> • <i>Information leaflet</i> <i>Note: The information leaflet should contain instructions on the reconstitution process, equipment to be used and requirements at the site of administration</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
16.15	Have you provided or specified any solvents or other material needed for reconstitution?	<i>Suggested documents:</i> <ul style="list-style-type: none"> • <i>Information leaflet</i> <i>Note: The information leaflet should include a list of required solvents or materials needed</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>
16.16	For authorized ATMP, Have you validated the reconstitution procedures?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <input type="checkbox"/> Not applicable <i>[room for notes]</i>

17. Automated production of ATMPs

“If the output of an automated production system meets the definition of ATMP, the requirements of the Regulation No 1394/2007 apply. Accordingly, in the case of authorized ATMPs or ATMPs used in clinical trial setting, GMP requirements apply”.

“The use of automated equipment may ease compliance with certain GMP requirements and may also bring certain advantages in respect to product’s quality”.

“The manufacturer is responsible for the quality of the ATMP, and therefore, has to ensure the suitability of the automated equipment for the specific intended purpose”.

	Question	Comments	Notes
17.12 17.13	Can you demonstrate the automated equipment’s suitability for its intended use?	<i>Note: If the automated equipment has a CE mark relevant for ATMP production, and the equipment used as intended the level of effort to demonstrate suitability is reduced</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
17.15	Did you qualify the equipment according to section 10.1?	<i>Suggested documents:</i> <ul style="list-style-type: none"> • URS for each equipment • Qualification Plan for Equipment 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
17.16	Has the manufacturer provided enough information for the ATMP producer to fully understand the functioning of the automated equipment?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
17.18	Do you have a SOP for each equipment?	<i>Note: see chapter 5 equipment and 6.29 for logbook requirements</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
17.19	Do you maintain the equipment as instructed to ensure function?	<i>Suggested documents</i> <ul style="list-style-type: none"> • Validation master plan • Program for services/calibration 	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
17.20	Is there a program for services/calibration of the automated equipment?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]
17.21	Have you validated the equipment for aseptic processing?	<i>Note: see 17.28 for description of media fill simulation. When a closed system is used for the manufacturing of an ATMP, the process simulation should focus on the steps related to the connections to the closed system, see 9.57.</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed [room for notes]

	Question	Comments	Notes
17.22	Do you keep batch and traceability records?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
17.23	Are all personnel trained in handling of the equipment?	<i>Note: see chapter 3 Personnel</i>	<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
17.24 17.25	Are all closed equipment placed in at least a grade D room, or, if appropriate in a controlled but non-classified environment? See 9.5.1		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
	Have you validated the transfer of material in and out of the room for risk of contamination?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
17.26	Do you define the manufacturing processes in regards to starting and finishing moments?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
17.27	Do you monitor in-process controls for the critical process parameters?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
	Are data on process parameters kept as part of batch records?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>
17.29	Are ATMPs produced under automated equipment batch certified by QP?		<input type="checkbox"/> Fulfilled <input type="checkbox"/> Control needed <input type="checkbox"/> Action needed <i>[room for notes]</i>