for manufacturer of cellular and tissue-based products shall be required to have been obtained regarding this place.

16. Control of documents and records (related to Article 16 as applied mutatis mutandis to Article 21)

(1) This Article prescribes matters on control of documents and records.

(2) When creating and revising the procedures for quality control operations, based on the provision in Item 2, the responsible person for creating and the date of creation, and the responsible person for revision, revision date, revision items, and the reason for revision shall each be indicated in their documents.

Section 3 Qualification Criteria

1. Compliance status to the Articles prescribed in the GQP Ordinance (related to cellular and tissue-based products) shall be evaluated according to each manufacturing site and each product item based on the "Qualification Criteria for Each Article of the GQP Ordinance (related to cellular and tissue-based products)"(hereinafter referred to as the "GQP Ordinance Qualification Criteria") in the Attachment 3. In this evaluation, necessary items shall also be regarded as matters pertaining to the product item and shall be evaluated regardless of the product item.

2. GQP Ordinance Qualification Criteria shall be a criteria indicating the endpoints in the form of questions according to each Article. The final evaluation results of conformity status according to each Article shall be determined after explaining the reasons for the evaluation to the persons subject to this conformity inspection, and after thoroughly hearing opinions from the persons subject to this conformity inspection.

3. Basic principles for operating the GQP Ordinance Qualification Criteria shall be to evaluate as Rank A (conforming) if matters indicated in the question is appropriately conducted (including cases where immediate improvement is made on-site); as Rank D (serious defect) if there is apparent conflict with the criteria; and as Rank B and C from the following perspective.

(1) Rank B (mild defect) shall be for cases where although there is not much problem regarding influence on cellular and tissue-based product quality, improvement is necessary for completeness in terms of operation regarding the criteria.

(2) Rank C (moderate defect) shall be for cases where influence on cellular and tissue-based product quality cannot be denied and improvement is necessary in terms of operation regarding the criteria.

4. Conformity status shall be evaluated via the following criteria using the evaluation results for each Article obtained according to the procedure indicated in the above section "3."

(1) Conforming : Only As.

(2) Generally conforming : As and Bs, or only Bs.

(3) Require improvement : The number of Cs is half of all items or less, and there are no Ds.

(4) Not conforming : Does not fall under any of the above.

5. Evaluation on relevance to Article 23-21, Item 1 of the Act:

(1) Manufacturing sites corresponding to "conforming": Quality control methods do not correspond to Article 23-21, Item 1 of the Act.

(2) Manufacturing sites corresponding to "generally conforming": Items in which the evaluation results of conformity status for each Article were categorized as B shall require improvements to be instructed via document to those subject to conformity inspection and shall require reports of those improvement results or improvement plan. In this case, conformity status can be re-evaluated as "conforming" by having those subject to conformity inspection submit a detailed report on improvement results or a specific improvement plan during the period until the next renewal of licensing, and may be handled according to the above section "(1)". However, if there is no submission of a detailed report on improvement results or a specific improvement plan within the period until the next renewal of licensing (in case of new license application, before disposition upon such application), a detailed report on improvement results shall be submitted within 30 days from the day of completing the improvement. Furthermore, conformity inspection shall be conducted as necessary if the confirmation of improvement status is required on-site.

(3) Manufacturing sites corresponding to "improvement required": The provision of (a) shall be applied mutatis mutandis to items in which the evaluation results of

conformity status for each Article were categorized as B. Items in which the evaluation results of conformity status for each Article were categorized as C can be re-evaluated as "conforming" by having those subject to conformity inspection submit a detailed report on improvement results or a specific improvement plan and if the improvement is completed during the period until the next renewal of licensing (in case of new license application, before disposition upon such application), and may be handled according to the above section "(1)". However, if the improvement is not completed, the conformity status shall, in principle, be re-evaluated as "not conforming" and shall be handled according to the below section "(4)".

(4) Manufacturing site corresponding to "not conforming": Quality control method shall correspond to Article 23-21, Item 1 of the Act. However, items whose evaluation results of conformity status for each Article were categorized as D can be handled according to the matters categorized as C of the above section "(3)", only if improvement is expected to be completed promptly.

[Attachment 1]

Qualification Criteria for Each Article of the Regulations for Buildings and Facilities
(Related to Cellular and Tissue-based Products)

1. Buildings and facilities at manufacturing sites of manufacturers of cellular and tissue-based products in the general category (related to Article 14)

No	Article of the Ministerial Ordinance	Question
1	Article 14, Item 1	Is the manufacturing site equipped with facilities and equipment necessary for manufacturing the product?

No	Article of the Ministerial Ordinance	Question
2	Article 14, Item 2	Are products, etc., and packaging and labeling materials positioned so as to prevent confusion and contamination and to enable smooth and appropriate operation without any impediment, and are they easy to be cleaned and maintenanced?

No	Article of the Ministerial Ordinance	Question
3	Article 14, Item 3	Is there a facility for hand washing, a dressing room, and other necessary sanitation facilities?

No	Article of the Ministerial Ordinance	Question
4	Article 14, Item 4	Are such areas for receiving raw materials and storing products separated from other areas where products are manufactured?

No	Article of the Ministerial Ordinance	Question
5	Article 14, Item 5	Do such areas for receiving raw materials and storing products have their necessary buildings and facilities?

No	Article of the Ministerial Ordinance	Question
6	Article 14, Item 6	Do work areas meet the following requirements? (a) Lighting and ventilation are appropriate and clean. (b) Are clearly separated from places of regular residence and unclean places. (c) Have sufficient amount of area that allows operations to be carried out without any impediment. (d) Have buildings or facilities to protect against dust, insects, and mice. (e) Have facilities or equipment necessary for disposing waste water and waste. (f) Have facilities for disposing poisonous gases if handled depending on the products, etc.

No	Article of the Ministerial Ordinance	Question
7	Article 14, Item 7	Do the work rooms at the work area meet the following requirements? (a) There shall be no entrances or exits opening directly to outdoors, provided, however, that this shall not apply to the cases where there are necessary buildings and facilities for preventing contamination from outdoors. (b) Entrances, exits, and windows shall be those that can be closed. (c) Indoor drainage facility shall be of a structure that prevents contamination of the work room. (d) The ceiling of the work room shall be of a structure with no risk of waste falling off. (e) Such indoor facilities as pipes and ducts shall be of a structure in which waste will not accumulate on their surfaces, provided, however, that this shall not apply if they can be easily cleaned.

No	Article of the Ministerial Ordinance	Question
8	Article 14, Item 8	Do work rooms or working control areas at the work area have buildings and facilities that allow maintenance and control of temperature and humidity (humidity shall be limited to cases where its maintenance and control are necessary)?

No	Article of the Ministerial Ordinance	Question
9	Article 14, Item 9	Do controlled clean areas, aseptic areas, etc., at the work area meet the following requirements? (a) The surfaces of ceilings, walls, and floors shall be smooth with no cracks, and shall be those that do not generate dust. They shall also be easy to be cleaned and shall be those that withstand spray cleaning, such as with antiseptic solutions. (b) Facilities and equipment shall be those that can be sterilized or disinfected. (c) Drainage facilities shall be of a structure that prevents contamination due to toxic waste water. (d) Clean areas shall have no drainage outlets. If there is any inevitable reason, however, drainage outlets shall be of a structure that prevents contamination of the work room. (e) Aseptic areas shall meet the following requirements: (1) There shall be no drainage outlets. (2) There shall be no sinks.

No	Article of the Ministerial Ordinance	Question
10	Article 14, Item 10	Are the areas at the work area where inspections and testings using animals or microorganisms and where animal tissues or microorganisms that are not necessary for product manufacturing are handled clearly separated from other areas for manufacturing the product and have a separate air-handling system?

No	Article of the Ministerial Ordinance	Question
11	Article 14, Item 11	Do aseptic areas at the work area use clean filtered air and have buildings and facilities necessary for appropriately controlling differential pressure?

No	Article of the Ministerial Ordinance	Question
12	Article 14, Item 12	Do areas at the work area where pathogenic microorganisms, etc., are handled have buildings and facilities necessary for appropriately controlling differential pressure?

No	Article of the Ministerial Ordinance	Question
13	Article 14, Item 13	Is there a facility for cleaning, disinfecting, and sterilizing equipment that were used in aseptic areas, and is there a facility for disposing waste fluid, etc.?

No	Article of the Ministerial Ordinance	Question
14	Article 14, Item 14	Is the air-handling system of an appropriate structure that prevents contamination of products, etc., due to microorganisms, etc.?

No	Article of the Ministerial Ordinance	Question
15	Article 14, Item 15	Are piping, valves, and vent filters of a structure that can be easily cleaned or sterilized depending on their intended use?

No	Article of the Ministerial Ordinance	Question
16	Article 14, Item 16	Does the facility for controlling animals meet the following requirements? (a) The area for inspecting and testing animals is isolated from other areas. (b) Has a facility for storing food where there is no risk of pest invasion. (c) Has a breeding room for animals for manufacturing and a breeding room for animals for inspecting and testing. (d) The air-handling system at the breeding room for animals is separated from other areas, provided, however, that this shall not apply for animals that are considered appropriate for outdoor breeding. (e) Has an inoculation room if animals are to have antigen, etc., inoculated? In this case, the inoculation room shall be separated from the necropsy room.

No	Article of the Ministerial Ordinance	Question
17	Article 14, Item 17	Are there necessary facilities for sanitary and safe storage of products, etc., and packaging and labeling materials where they can be stored separately?

No	Article of the Ministerial Ordinance	Question
18	Article 14, Item 18	Is the storage facility furnished with thermostat, thermometer, and other necessary meter?

No	Article of the Ministerial Ordinance	Question
19	Article 14, Item 19	Are the following testing facilities and equipment furnished? Provided, however, this shall not apply in cases where testing will be conducted without any impediment under the responsibility of the manufacturers of cellular and tissue-based products using other testing facilities of these manufacturers, or other testing institutions. (a) Facilities and instrument for sealed testing in cases where sealed testing is necessary (b) Facilities and equipment for testing for any foreign matters (c) Facilities and equipment for physical and chemical testing of products, etc., and packaging and labeling materials (d) Facilities and equipment for sterility test (e) Facilities and equipment for pyrogenicity testing in cases where pyrogenicity testing is necessary (f) Facilities and equipment for biological testing in cases where biological testing is necessary

2. Buildings and facilities at the manufacturing site of manufacturers for cellular and tissue-based products in the category of packaging, etc. (related to Article 15)

No	Article of the Ministerial Ordinance	Question
20	Article 15, Item 1	Are there necessary buildings and facilities for sanitary and safe storage of products, etc., and packaging and labeling materials?

No	Article of the Ministerial Ordinance	Question
21	Article 15, Item 2	Is there a sufficient amount of area that allows appropriate operation without any impediment?

No	Article of the Ministerial Ordinance	Question
22	Article 15, Item 3	Are necessary facilities and equipment furnished for testing products, etc., and packaging and labeling materials? Provided, however, this shall not apply in cases where testing will be conducted without any impediment under the responsibility of the manufacturers of cellular and tissue-based products using other testing facilities of these manufacturers or other testing institutions.

[Attachment 2]

Qualification Criteria for Each Article of the GCTP Ordinance

1. Quality risk management (related to Article 4)

No	Article of the Ministerial Ordinance	Question
1	Article 4	When implementing manufacturing control and quality control at the manufacturing site, are manufacturers, etc. considering use of quality risk management?

2. Manufacturing Department and Quality Department (related to Article 5)

No	Article of the Ministerial Ordinance	Question
2	Article 5, Paragraph 1	Have manufacturers, etc. established a Manufacturing Department and Quality Department for each manufacturing site under the supervision of a Manufacturing Manager?

No	Article of the Ministerial Ordinance	Question
3	Article 5, Paragraph 2	Is the Quality Department independent from the Manufacturing Department?

3. Manufacturing Manager (related to Article 6)

No	Article of the Ministerial Ordinance	Question
4	Article 6, Paragraph 1	Is the Manufacturing Manager carrying out the following duties? (1) To supervise activities for manufacturing and quality control, and to manage/direct so that they can be properly and smoothly implemented. (2) When there are quality defects or in other cases where there is risk of significant effect on product quality, to confirm required measures are being promptly taken and the status of their progress, and as necessary to instruct to implement necessary measures such as of improvement.

No	Article of the Ministerial Ordinance	Question
5	Article 6, Paragraph 2	Are the manufacturers, etc. making an effort for the effective performance of the duties of the Manufacturing Manager?

4. Personnel (related to Article 7)

No	Article of the Ministerial Ordinance	Question
6	Article 7, Paragraph 1	Have the manufacturers, etc. appropriately appointed Managers according to the organization and scale of the manufacturing site as well as types of duties?

No	Article of the Ministerial Ordinance	Question
7	Article 7, Paragraph 2	Have the manufacturers, etc. appointed an appropriate number of Managers according to the organization and scale of the manufacturing site as well as types of duties?

No	Article of the Ministerial Ordinance	Question
8	Article 7, Paragraph 3	Have the manufacturers, etc. secured an adequate number of personnel who are capable of properly implementing the manufacturing and quality control duties?

No	Article of the Ministerial Ordinance	Question
9	Article 7, Paragraph 4	Have the manufacturers, etc. properly documented responsibilities and a management system of personnel (including Manufacturing Manager and Managers) engaged in the manufacturing and quality control duties?

5. Product master formula (related to Article 8)

No	Article of the Ministerial Ordinance	Question
10	Article 8	Have the manufacturers, etc. prepared and retained a product master formula for each product (excluding intermediate products; the same applies hereinafter in this article) describing the below-mentioned matters at each manufacturing site involved in the manufacture of the product, and received approval of the Quality Department? (1) Approved product information (2) Standards prescribed in the provision of Article 42, Paragraph 1 of the Act, and matters regarding quality prescribed in laws on pharmaceutical affairs or in orders or dispositions based on these law (3) Manufacturing procedures (excluding matters set forth in Item (1)) (4) The name, nature, description, active ingredients and their contents, and other specifications of a material obtained from humans, animals, plants or microorganisms provided as the source material (5) Specification of animals used for manufacturing or inspection and testing (including donor animals; hereinafter referred to as "utilized animals") (6) Other necessary matters

6. Procedures (related to Article 9)

No	Article of the Ministerial Ordinance	Question
11	Article 9, Paragraph 1	Have the manufacturers, etc. at each manufacturing site prepared and retained sanitation control standard code presenting sanitary control of buildings and facilities as well as of personnel and other necessary matters?

No	Article of the Ministerial Ordinance	Question
12	Article 9, Paragraph 2	Have manufacturers, etc. at each manufacturing site prepared and retained manufacturing control standard code, describing the storage of products, etc., the control of manufacturing processes, and other necessary matters?

No	Article of the Ministerial Ordinance	Question
13	Article 9, Paragraph 3	Have manufacturers, etc. at each manufacturing site prepared and retained a quality control standard code, mentioning a method for sample collection, a method for assessing inspection and testing results, and other necessary matters?

No	Article of the Ministerial Ordinance	Question
14	Article 9, Paragraph 4	Have manufacturers, etc. at each manufacturing site prepared and retained the following documents concerning procedures for properly and smoothly implementing manufacturing control and quality control in addition to those set forth in the preceding three paragraphs? (1) Procedures for control of release from a manufacturing site (2) Procedures for validation or verification (3) Procedures for review of product quality (4) Procedures for change control in matters set forth in Article 16 (5) Procedures for deviation control set forth in Article 17 (6) Procedures for handling quality information and quality defects (7) Procedures for recall action (8) Procedures for self-inspections (9) Procedures for training (10) Procedures for document and record control (11) Other procedures necessary for properly and smoothly implementing manufacturing control and quality control

No	Article of the Ministerial Ordinance	Question
15	Article 9, Paragraph 5	Have the manufacturers, etc. retained operation procedures at their manufacturing sites?

7. Buildings and facilities (related to Article 10)

No	Article of the Ministerial Ordinance	Question
16	Article 10	Do buildings and facilities at manufacturing sites of products meet the following requirements? (1) That cleaning and maintenance are properly carried out according to their usage, and as necessary, sterilization is implemented in accordance with the operating procedures, and their records are prepared and retained. (2) That facilities for disposal of poisonous gases, if handled depending on products, etc., are equipped. (3) That among the work areas, a work room or working control area shall be provided with adequate buildings and facilities for maintaining and controlling cleanliness according to the types,

No	Article of the Ministerial Ordinance	Question
		structures, characteristics and manufacturing processes of products. (4) That the work room shall meet the following requirements: (a) The work room shall be provided with buildings and facilities for preventing contamination by dust or microorganisms according to the types, structures and manufacturing processes of products, provided, however, that this provision shall not apply to the case where the same effects are obtained from the functions of the manufacturing facilities; (b) The work room shall have facilities necessary for properly drying and storing containers after washing; (c) The work room shall have sterilization equipment necessary for manufacturing according to the types of products; (d) An area for performing aseptic operations shall be provided with clean air processed through a filter and have buildings and facilities necessary for properly controlling differential pressure; and (e) When manufacturing products related to injections, the liquid-contacting piping of pipes and other relevant materials affecting sterility assurance shall be of a structure to facilitate cleaning and enable sterilization. (5) That the work room for the drying and sterilization operations of containers after washing shall be used exclusively for that purpose, provided, however, that this provision shall not apply to the case where there is no risk of contamination of containers after washing. (6) That work rooms for the weighing operations of raw materials, the formulating operations of products, and the filling operations of products or sealing operations of containers shall be constructed so as not to allow passage for personnel other than those working in the room, provided, however, that this provision shall not apply to the case where there is no risk of contamination to products by personnel other than those working in the room. (7) That work rooms for the formulating operations or the filling operations of products or sealing operations of containers shall be separated from work rooms other than these or the working control area but used exclusively for those purposes. Also, the working rooms shall have dressing rooms for exclusive use by personnel engaged in these operations. (8) That when products, etc. which are suspected to have serious effects on other products by cross-contamination are manufactured, work rooms related to the products, etc. shall be exclusively for them, and the air-treatment system shall be separated, provided, however, that this provision shall not apply to the case where validated inactivation processes and cleaning procedures or either one of them is established or maintained. (9) That facilities for supply of water of the quality and quantity needed for the manufacturing of products (including cleaning water for facilities, apparatuses and containers) shall be equipped. (10) That facilities to supply distilled water, etc. for the manufacturing of products shall be of a structure to prevent contamination of distilled water, etc. by foreign matters or microorganisms.

No	Article of the Ministerial Ordinance	Question
		(11) That the work area shall be provided with the following facilities in rooms clearly separated from other rooms, provided, however that the facilities found to be unnecessary for the manufacturing of the product according to the types, manufacturing methods, etc. of products are excluded: (a) Storage facility for cells, microorganisms, etc.; (b) Facilities for keeping animals for use in manufacturing or inspection and testing after inoculation of microorganisms, etc.; (c) Facilities for treating animals for use in manufacturing or inspection and testing; (d) Facilities for transferring cells or microorganisms, etc. into culture media, etc.; (e) Facility for culturing cells, microorganisms, etc.; (f) Facilities for collecting, inactivating, sterilizing, etc. cultured cells or microorganisms, etc.; and (g) Facilities for disinfecting apparatus and appliances that have been used in manufacturing or inspection and testing. (12) That the room provided with the facilities mentioned in Items (d) and (f) of the preceding item and the room provided with the facilities for sterility tests among the facilities necessary for inspecting and testing products, etc. and packaging and labeling materials shall meet the following requirements: (a) Work rooms shall be aseptic, provided, however, that this provision shall not apply to the case where the work room is provided with facilities having function enabling to perform aseptic operations without problem according to the types, manufacturing methods, etc. of products; and (b) The aseptic room set forth in Item A shall have an adjacent anteroom which usually allows exclusive passage of personnel to and from the work room and whose entrances and exits are not opening directly to the exterior. (13) That the work area shall be provided with the following facilities in addition to those specified in Item (11): (a) Facilities necessary for breeding and managing animals for use in manufacturing or inspection and testing; (b) Facilities for preparing culture media and diluents for the media; (c) Facilities for washing and sterilizing in advance apparatus and appliances, containers, etc. which are used in manufacturing or inspection and testing; and (d) Facilities for properly treating animal carcasses and other wastes as well as for purifying sewage.

8. Manufacturing control (related to Article 11)

No	Article of the Ministerial Ordinance	Question
17	Article 11, Paragraph 1	Are the manufacturers, etc. having the Manufacturing Department properly carry out the following duties related to manufacturing control in accordance with the operating procedures? (1) That the manufacturing order describing instructions, precautions and other necessary matters during manufacturing processes shall

No	Article of the Ministerial Ordinance	Question
		be prepared and retained. (2) That products shall be manufactured in accordance with the manufacturing order. (3) That records on the manufacturing of products shall be prepared and retained by lot (by manufacturing number for products not constituting a lot; the same applies hereinafter). (4) That whether or not the packaging and labeling materials of products are appropriate shall be checked by lot, and the records of its results shall be prepared and retained. (5) The products, etc. by lot, and packaging and labeling materials by control unit shall be appropriately stored and released, and the records thereof shall be prepared and retained. (6) That the cleanliness of the buildings and facilities shall be checked, and the records of its results shall be prepared and retained. (7) That periodic inspection and maintenance of the buildings and facilities shall be performed, and the records thereof shall be prepared and retained. Also, meters shall be properly calibrated, and the records thereof shall be prepared and retained. (8) That it shall be checked through records of manufacturing, storage, release and sanitary control that manufacturing control is properly implemented, and its results shall be reported in writing to the Quality Department. (9) That for work rooms or working control areas, according to the types, structures, characteristics and manufacturing processes of products to be manufactured, as well as the contents of operations to be carried out in the work rooms or working control areas, the control level of work environment such as cleanliness shall be appropriately set and managed. (10) That for the products, etc., and packaging and labeling materials, according to the types, structures, characteristics, manufacturing processes, etc. of products to be manufactured, necessary control items such as the counts of microorganisms, etc. shall be appropriately set and managed. (11) That necessary measures for preventing contamination of the products, etc. and packaging and labeling materials by microorganisms, etc. during manufacturing processes shall be taken. (12) That for critical processes for ensuring the sterility of products, according to the types, structures, characteristics, manufacturing processes, etc. of products to be manufactured, control values necessary for process control shall be appropriately set and managed. (13) That for manufacturing water, according to its usage, control values related to necessary microbial and physicochemical items shall be appropriately set and managed. (14) That when microorganisms, etc. contained in the products, etc. are inactivated or eliminated during the manufacturing processes, measures necessary for preventing contamination by the products, etc. that have not gone through the process of inactivation or elimination shall be taken. (15) That when biochemical technology is applied during the manufacturing processes, continuous measurements of

No	Article of the Ministerial Ordinance	Question
		temperature, a hydrogen ion index, etc. necessary for the control of the manufacturing processes shall be performed. (16) That when equipment for column chromatography is used during the manufacturing processes, measures necessary for preventing contamination of the equipment by microorganisms, etc. shall be taken, and measurements of endotoxins, if needed, shall be carried out. (17) That in employing the culture method to provide a continuous supply of culture media to an incubation tank and to perform continuous discharge of liquid media during the manufacturing processes, measures necessary for maintaining incubation conditions in the incubation tank during the incubation period shall be taken. (18) That any article that has been contaminated by microorganisms, etc. (limited to those contaminated during the manufacturing processes), shall be disposed of so as not to cause hazards to the public health and hygiene. (19) That records on the handling of cell strains to be used for manufacturing shall be prepared for the following matters, and the records shall be retained: (a) Name of cell strain and number given to each container; (b) Date of being transferred, and the name and address of a person who has transferred (in case of a corporation, name and address); (c) Biological properties and date of testing; and (d) Status of subculture. (20) That for raw materials derived from organisms (excluding plants) (hereinafter referred to as "biological-origin raw materials for regenerative medicine products") to be used for manufacturing, it shall be confirmed that the biological-origin raw materials for regenerative medicine products are appropriate by reference to the product master formula of the product, and records of the confirmation shall be prepared and retained. (21) That the manufacturers, etc. shall retain by themselves the records of biological-origin raw materials for regenerative medicine products to be used for manufacturing of the product with respect to matters as specified by the Minister of Health, Labour and Welfare for a period set forth in Article 22, Item 3, (a) or (b), or close a contract with a firm collecting raw materials of the biological-origin raw materials for regenerative medicine products, and the records shall be properly retained by the raw materials collecting firms, etc. based on the contract. (22) That records set forth in Item (8) and the preceding two items shall be prepared for each lot of products to be manufactured, and the records thereof shall be retained. (23) That in handling of the cells or tissues collected from different donors or donor animals, measures necessary for preventing confusion and cross-contamination of the cells or tissues shall be taken. (24) That it shall be confirmed based on records on the following matters that cells or tissues as raw materials are appropriate, when received, by reference to the product master formula of the product, and the records of the confirmation results shall be

No	Article of the Ministerial Ordinance	Question
		prepared and retained: (a) Facilities where the cells or tissues have been collected; (b) Date on which the cells or tissues have been collected; (c) When the cells or tissues are derived from humans, the status of diagnosing donors based on their interview and tests for the donor screening (referring to performing a diagnosis based on interview and tests of donors to decide whether or not they are fully eligible to provide their cells or tissues as the raw materials of products); (d) When the cells or tissues are derived from animals, the status of receiving donor animals as well as conditions of the inspection and testing, and breeding and keeping of such animals for the donor screening (referring to performing inspection/ testing and breeding/ keeping of donor animals to decide whether or not they are fully eligible to provide their cells or tissues as the raw materials of products); (e) Course of operations to collect the cells or tissues; (f) Course of transporting the cells or tissues; and (g) Requirements for ensuring the quality of the products in addition to those mentioned in Items (a) to (f). (25) That when collecting cells or tissues as raw materials from donor animals, measures necessary for preventing contamination by microorganisms, etc. during the collection shall be taken, and records of such measures shall be prepared and retained. (26) That for products, the names of the destination facilities, date of distribution and lot shall be understood for each product, and the records thereof shall be prepared and retained. (27) That for distribution, measures necessary for ensuring the quality of products shall be taken, and records of such measures shall be prepared and retained. (28) That records set forth from Item (24) to the preceding item shall be prepared by lot (product for the records in Item (26)) and retained. (29) That the sanitary control of personnel shall be implemented in accordance with the following requirements: (a) To restrict as much as possible for persons other than personnel engaged in manufacturing operations to go in or out of the work area; (b) To restrict as much as possible for personnel to go in or out of the controlled clean area or aseptic operation area where actual operations are carried out; (c) To specify strict procedures for preventing contamination by personnel engaged in duties related to culture of human or animal cells or microorganisms, etc. and other processing (excluding those actually used as raw materials in the manufacturing), and not to allow the personnel to go in or out of the work room or working control area for products except for the case where such procedures are compiled; and (d) To have personnel engaged in manufacturing operations not assign to activities related to controlling utilized animals (excluding those actually used for the manufacturing process).

No	Article of the Ministerial Ordinance	Question
		(30) That the sanitary control of personnel working in the controlled clean area or aseptic operation area shall be implemented in accordance with the following requirements: (a) To have personnel engaged in manufacturing operations wear work clothes, shoes, caps, masks and gloves that have been disinfected; (b) To have personnel engaged in manufacturing operations properly change clothing according to the level of control of the concerned area when entering in the controlled clean area or aseptic operation area; (c) To have personnel undergo medical checkups at intervals not exceeding 6 months in order to confirm that they do not have diseases that are suspected to contaminate the products, etc. by microorganisms, etc.; (d) When personnel having their health conditions that are suspected to contaminate the products, etc. with microorganisms, etc. (including skin or hair infections, cold, wound, or symptoms such as diarrhea or fevers of unknown cause), to have the personnel not engage in operations in the controlled clean area or aseptic operation area; (e) When personnel handle microorganisms, etc. that may contaminate cells or tissues immediately before collecting or treating the cells or tissues, to have the personnel not engage in operations in the controlled clean area or aseptic operation area; and (f) To prepare and retain records on the preceding Item and Items A to E. (31) Other duties necessary for manufacturing control.

No	Article of the Ministerial Ordinance	Question
18	Article 11, Paragraph 2	Are records on products specified in the preceding paragraph retained so as to appropriately confirm a series of records from biological-origin raw materials for regenerative medicine products provided in manufacturing to a product manufactured with the biological-origin raw materials for regenerative medicine products?

9. Quality control (related to Article 12)

No	Article of the Ministerial Ordinance	Question
19	Article 12, Paragraph 1	Are manufacturers, etc. storing reserve samples of the products at an amount twice or more than the necessary amount (however, an appropriate quantity if the quantity cannot be secured) for all the required inspections and testings, for each lot (in the case of specified regenerative medicine products not constituting a lot, for biological-origin raw materials for regenerative medicine products used in the manufacturing, for each manufacturing number of the product or from each lot of the biological-origin raw materials for regenerative medicine products) and under proper conditions of storage for periods set forth in each of the following items from the date of manufacturing? Provided, however, this provision shall not apply to specified regenerative medicine products not constituting a lot

No	Article of the Ministerial Ordinance	Question
		under a contract, already closed between the manufacturers, etc. and raw materials collecting firms, etc. specifying that the raw materials collecting firms, etc. shall store a reserve sample for periods set forth in each of the following items. For products constituting a lot, after a period of the expiry date plus one year, the storage of the biological-origin raw materials for regenerative medicine products, which have been provided in manufacturing the product, may be substituted for storage of the product: (1) A period of the expiry date plus 10 years for specified regenerative medicine products; and (2) Appropriate duration for regenerative medicine products (excluding products set forth in the preceding item).

No	Article of the Ministerial Ordinance	Question
20	Article 12, Paragraph 2	Are manufacturers, etc. having the Quality Department systematically and appropriately perform the following duties related to the quality control of products in accordance with the operating procedures? (1) That samples necessary for carrying out inspection and testing shall be collected by lot for products, etc. and by control unit for packaging and labeling materials as well as the records thereof shall be prepared and retained. (2) That the inspection and testing (including inspection and testing implemented under the responsibilities of the manufacturers, etc. using other inspection and testing facilities of the manufacturers, etc. or other inspection and testing institutions, and such use is found to be acceptable; the same applies hereinafter) of the collected samples shall be conducted by lot or control unit as well as the records thereof shall be prepared and retained. (3) That the periodic inspection and maintenance of the facilities and apparatuses for inspection and testing shall be carried out as well as the records thereof shall be prepared and retained. Also, meters for inspection and testing shall be properly calibrated as well as the records thereof shall be prepared and retained. (4) That the results of the inspection and testing set forth in Item (2) shall be assessed, and the results shall be reported in writing to the Manufacturing Department. (5) That samples shall be separated by the proper labeling of identification in order to prevent confusion and cross-contamination of the samples. (6) That at the proper stage of manufacturing processes, the inspection and testing important for the quality control and impracticable in the product shall be performed. (7) That any article that has been contaminated by microorganisms, etc. (limited to those contaminated during the inspection and testing), shall be disposed of so as not to cause hazards to the public health and hygiene. (8) That records on the use of cell strains for inspection and testing shall be prepared for the following matters, and the records shall be retained: (a) Name of cell strain and number given to each container; (b) Date of being transferred, and the name and address of a

No	Article of the Ministerial Ordinance	Question
		person who has transferred (in case of a corporation, name and address); (c) Biological properties and date of testing; and (d) Status of subculture. (9) That records on the results of inspection and testing shall be prepared for each lot of products to be manufactured, and the records thereof shall be retained. (10) That inspection and testing of donor animals at the time of or after their receipt and other necessary duties shall be performed by the manufacturers, etc. themselves or by a person designated beforehand according to the contents of the duties. (11) That records on the duties specified in the preceding item shall be prepared and retained. (12) Other duties necessary for quality control.

No	Article of the Ministerial Ordinance	Question
21	Article 12, Paragraph 3	When the procedures to evaluate conformity with the standards for manufacturing control and quality control in an exporting country are found to be equivalent to those in Japan, inspection and testing (excluding visual inspection) specified in Item (2) of the preceding paragraph may be substituted for confirmation of records of the inspection and testing conducted by the foreign manufacturers of regenerative medicine products in an exporting country. In such a case, are the manufacturers having the Quality Department properly implement the following duties? (1) To periodically check that the products, etc. have been manufactured in accordance with the appropriate manufacturing procedures, etc. (2) To periodically verify that the manufacturing sites of the foreign manufacturers of regenerative medicine products meet the standards for manufacturing control and quality control in that country. (3) To prepare and retain records of confirmation in the preceding two items. (4) To check the records of inspection and testing on the concerned product carried out by the foreign manufacturers of regenerative medicine products, and to prepare and retain the records of the confirmation.

No	Article of the Ministerial Ordinance	Question
22	Article 12, Paragraph 4	Are records on products specified in the preceding three paragraphs retained so as to appropriately confirm a series of records from biological-origin raw materials for regenerative medicine products provided in manufacturing to a product manufactured with the biological-origin raw materials for regenerative medicine products?

No	Article of the Ministerial Ordinance	Question
23	Article 12, Paragraph 5	Are manufacturers, etc. having the Quality Department verify by lot

No	Article of the Ministerial Ordinance	Question
		the results of confirmation on manufacturing control reported by the Manufacturing Department pursuant to the provision of Paragraph 1, Item 8 of the preceding article in accordance with the operating procedures?

10. Control of release from the manufacturing site (related to Article 13)

No	Article of the Ministerial Ordinance	Question
24	Article 13, Paragraph 1	Are manufacturers, etc. having the Quality Department implement duties to properly evaluate the results of manufacturing control and quality control, and determine whether or not the product can be released from the manufacturing site in accordance with the operating procedures?

No	Article of the Ministerial Ordinance	Question
25	Article 13, Paragraph 2	Do persons who carry out the duties set forth in the preceding paragraph have an ability to properly and smoothly perform the said duties?

No	Article of the Ministerial Ordinance	Question
26	Article 13, Paragraph 3	Are manufacturers, etc. making an effort for the effective performance of the duties assigned to the persons who implement the duties set forth in Paragraph 1?

No	Article of the Ministerial Ordinance	Question
27	Article 13, Paragraph 4	Are manufacturers, etc. not releasing the product from the manufacturing site until the decision set forth in Paragraph 1 is properly made?

11. Validation or verification (related to Article 14)

No	Article of the Ministerial Ordinance	Question
28	Article 14, Paragraph 1	Are manufacturers, etc. having a person, designated beforehand, perform the following duties in accordance with the operating procedures? (1) Validation shall be implemented in the following cases, provided, however, that if validation cannot be carried out due to compelling reasons, verification shall be conducted: (a) When the manufacturing of a new product is started at the manufacturing site; (b) When there are changes in the manufacturing procedures, etc. that may significantly affect the quality of the product; and (c) Other cases where it is found to be necessary for properly implementing the manufacturing control and quality control of the product. (2) To report in writing to the Quality Department plan and results of

No	Article of the Ministerial Ordinance	Question
		validation or verification.

No	Article of the Ministerial Ordinance	Question
29	Article 14, Paragraph 2	Are manufacturers, etc. taking required measures when it is found necessary to improve manufacturing control or quality control based on the results of the validation or verification set forth in Item 1 of the preceding paragraph, as well as prepare and retain the records of the said measures?

12. Review of product quality (related to Article 15)

No	Article of the Ministerial Ordinance	Question
30	Article 15, Paragraph 1	Are manufacturers, etc. having a person, designated beforehand, perform the following duties in accordance with the operating procedures? (1) That a review on the quality of products shall be implemented periodically or as necessary for the purpose of validating the consistency of manufacturing processes and the validity of the specifications of the products, etc. (2) That the results of the review set forth in the preceding item shall be reported in writing to the Quality Department. (3) That the report set forth in the preceding item shall be confirmed by the Quality Department.

No	Article of the Ministerial Ordinance	Question
31	Article 15, Paragraph 2	Are manufacturers, etc. having the Quality Department prepare and retain the records of the confirmation set forth in Item 3 of the preceding paragraph in accordance with the operating procedures and properly report them in writing to the Manufacturing Manager?

No	Article of the Ministerial Ordinance	Question
32	Article 15, Paragraph 3	Are manufacturers, etc. taking required measures when it is found necessary to improve manufacturing control or quality control, or to implement validation or verification based on the results of the review set forth in Paragraph 1, Item 1, as well as prepare and retain the records of the said measures?

13. Change control (related to Article 16)

No	Article of the Ministerial Ordinance	Question
33	Article 16	When changes in the manufacturing procedures, etc. which may affect the quality of the product, are to be made, are manufacturers, etc. having a person, designated beforehand, implement the following duties in accordance with the operating procedures? (1) To evaluate the effect of the said changes on the quality of products, obtain approval of the Quality Department for the changes based on the results of the evaluation, and prepare and