(a) The following methods of using the electronic data processing system (electronic data processing system that connects one's electronic computer and the computer of the other party via telecommunication line).

(i) Method of sending data via telecommunication line that connects one's electronic computer and the computer of the other party and recording that data into the file provided in the computer of the other party

(ii) Method of submitting content recorded in the file of the computer of the manufacturer and recording it to the file of the computer of the other party (method of recording onto the file in the computer of the manufacturer the intent of approval or non-approval for using electromagnetic method)

(b) Method of transferring the content of the file prepared via magnetic disc, CD-ROM, or other corresponding medium that enables definite recording of certain matters

B. The above methods of using information communication technology shall be conforming to the following technical standards.

(a) The method shall enable manufacturers to create documents by outputting the content recorded in the file.

(b) Measure shall be taken to enable confirmation of whether the content recorded in the file has not been altered.

C. When concluding contracts using information communication technology, manufacturers shall indicate to the other party which method prescribed in the above section "A." will be used and method of recording in the file, and shall obtain consent via document or electromagnetic method.

D. If the manufacturers received request from the other party via document or electromagnetic method for using method other than information communication technology, the contract with this manufacturer shall not be concluded via method using information communication technology; provided, however, this shall not apply if the other party showed again consent to concluding contract using method of information communication technology.

(3) Reporting or instruction via document

When manufacturers provide reporting or instructions via document prescribed in this Article using a method of information communication technology, the above section "(2)" shall apply upon making necessary replacement in its terms.

Section 3 Validation Criteria

1. Validations prescribed in the GCTP Ordinance shall be conducted based on the below "Validation Criteria" with the consideration of the quality risk. When conducting this operation, use of quality risk management shall be put into consideration as necessary.

2. Validation Criteria

(1) Purpose of the validations

The purpose of validation and verification shall be to verify that the expected outcome of the buildings and facilities, procedures, processes, and other manufacturing control and quality control methods at the manufacturing site (; hereinafter referred to as "manufacturing processes" in this criteria) can be obtained or has been obtained, as well as to enable constant manufacturing of products conforming to the intended quality by putting this into a document. In order to achieve this target, knowledge and information accumulated via product life cycle shall be utilized, including those obtained from product development, regular confirmation of process and review of product quality. In cases where product development or establishment of technology took place in other manufacturing sites, the knowledge and information obtained there shall be enabled to be used by transferring those necessary technologies.

(2) Subject

Manufacturers shall, in principle, be required to conduct validations specified in section "(5)" on the following items.

A. Facilities (including manufacturing facility, manufacturing environment control facility), systems (including system for supporting manufacturing, such as the water supply system for manufacturing, air conditioning system) or devices (including meter)

B. Manufacturing process

C. Cleaning

(3) Procedure for validation

A. The procedure on validation prescribed in Article 9, Paragraph 4, Item 2 of the GCTP Ordinance prescribes the following matters. Facilities, systems, devices, manufacturing process, and cleaning that require validation shall be specified by the manufacturer under its responsibility with the consideration of quality risk judging from the results of development research and manufacturing status of similar products, such as structure and quality property.

(a) Overall validation policy of the manufacturers

(b) Persons predesignated by manufacturers (hereinafter referred to as the "responsible person for validations" in this criteria) prescribed in Article 14, Paragraph 1 of the GCTP Ordinance, and other matters regarding responsibilities of relevant organizations

(c) Matters regarding the timing of conducting the validations indicated in section "(5)"

(d) Matters regarding creation, modification, and approval of protocol for validations specified in section "(4) A."

(e) Matters regarding creation, evaluation, and approval (including recording method) of the protocol for validations specified in section "(4) D."

(f) Matters regarding storage of documents and records on validations

(g) Other necessary matters

B. The procedure for validations shall be created on subject items specified in section "(2)" so as to meet the requirements specified in section "(4)".

(4) Responsibility of the responsible person for validations

The responsible person for validations shall execute the following operation based on the procedure for validations.

A. A protocol for validations (hereinafter referred to as the "protocol" in this criterion) shall be created on the subject items specified in section "(2)" for the product intended to be manufactured based on the procedure for validations. The validation shall have the following matters stipulate with the consideration

of the content of the validations. In cases where the scope of the validations is wide and there are multiple individual protocols, as in large-scale projects, use of a master plan summarizing the entire validations shall be put into consideration.

(a) Items

(b) Purpose of the validations for the relevant items (including the purpose of the entire validation)

(c) Subject facility, system, device, manufacturing process, or cleaning, and their outline

(d) Expected outcome of the manufacturing procedures

(e) Method of verification or confirmation (including evaluation criteria and method of verification or confirmation results)

(f) Timing of conducting verification or confirmation

(g) The name of person who conducts the validations and his/her responsibility

(h) Author of the plan, date of creation, reviser, date and content of revision, and reason for the revision

(i) Other necessary matters

B. Validation specified in section "(5)" shall each be conducted in accordance to the plans described in section "A."

C. Any changes in deviation or instruction shall be recorded and shall be examined for their influence on the validation results.

D. Validation report shall be created on its results.

E. Other operations prescribed in Article 14 of the GCTP Ordinance shall be appropriately conducted.

(5) Conduct of validation

This section prescribes the basic requirements for when conducting validations, etc.

A. Qualification

Generally, the following qualifications shall be conducted individually or in combination on newly installed or improved facilities, systems, or devices.

In principle, qualification at each stage shall be followed by the next qualification stage.

(a) Design qualification (DQ)

Facilities, systems, or devices shall be confirmed that they are appropriate for their intended use, and this shall be documented.

(b) Installation qualification (IQ)

Facilities, systems, or devices shall be confirmed that they conform to the approved requirements of the design and manufacturer, and this shall be documented. Calibrated measuring equipment shall be used.

(c) Operational qualification (OQ)

Facilities, systems, or devices shall be confirmed that they operate in the expected operating range in an intended manner, and this shall be documented. Calibrated measuring equipment shall be used.

(d) Performance qualification (PQ)

Facilities, systems, or devices shall be confirmed that they function in an effective and reproducible manner based on their approved manufacturing methods and specifications, and this shall be documented. Calibrated measuring equipment shall be used.

B. Process validation (PV)

The processes expected to operate under permissible condition that was established with the consideration of variable factors (e.g., physical property of raw materials and packaging and labeling materials, operational conditions) with possibility of influencing product quality that were prespecified based on the results of development research and manufacturing status of similar products shall be confirmed that they are appropriate for constant manufacturing of products that conform to the intended quality, and this shall be documented.

Process validation shall be conducted with the consideration of at least the following points.

(a) Before initiating process validation, confirm that the facilities, systems, or devices intended to be used for the validation have completed their qualifications.

(b) Before initiation process validation, confirm the appropriateness of the testing method intended to be used for the validation.

(c) Verification method shall, in principle, be conducted at the manufacturing scale of the actual production and shall be conducted on 3 lots or manufacturing number repeatedly or using other method of at least equivalent to this.

(d) Generally complete before release acceptance from the manufacturing site.

If the product whose process is subject to process validation is expected to be released into the market, their manufacturing conditions shall thoroughly conform to the requirements of GCTP Ordinance and marketing approval, including the results that are required in the validation operation.

C. Verification

For manufacturing processes (excluding manufacturing processes whose process validation can be appropriately conducted via use of experimental samples) with difficulty in conducting process validations because of quantitative or technical limitations due to ethical reasons, such as products pertaining to human (auto) cell processed products, confirm the products according to each lot or manufacturing number that expected outcome has been obtained from the manufacturing procedure whose prespecified variable factors that influence product quality are within the permissible conditions, and this shall be documented.

Verification shall be conducted with the consideration of at least the following points.

(a) Before initiating verification, confirm that the qualification of the facilities, systems, or devices that compose the manufacturing process of the product subject to verification has been completed, as well as their cleaning validation of the cleaning operation pertaining to the manufacturing process.

(b) Before initiating verification, evaluate the appropriateness of the study method intended to be used in the verification.

D. Cleaning validation

Cleaning operation shall be confirmed for their effectiveness against elimination of component cells or transgenes and detergents, and this shall be documented. Residual limits shall be set based on logical evidence of product safety and safety of the material quality used in the manufacturing facility. The study method of cleaning validation shall be an appropriate one with specificity and sensitivity that thoroughly detects the residues. Note that even if the cleaning operations pertaining to product manufacturing process are subject to verification, cleaning validation shall also be applicable in principle.

E. Re-validation

Qualification, process validation, or cleaning validation shall be conducted periodically to re-confirm that the subject facilities, systems, devices, manufacturing processes, or cleaning operations are maintained in a validated state, and to verify that they are appropriate for constant manufacturing of products so that the products will continue to be conforming to the intended quality. A product manufacturing process that will be subject to verification, shall, in principle, be required to have their verification conducted but shall not be subject to re-validation (excluding qualification of facilities, systems, and devices that compose the manufacturing process, and cleaning validation of cleaning operation pertaining to the manufacturing process).

The necessity, timing, and items shall be determined with the consideration of manufacturing frequency and review results of product quality. Re-validation shall be periodically conducted for manufacturing procedures that largely influence product quality, such as facilities, systems, devices, and manufacturing processes pertaining to sterility assurance, regardless of review results of product quality.

F. Validation at modifications

Validation shall be conducted when modifications are made on the raw materials, packaging and labeling materials, manufacturing process, buildings and felicities, and cleaning operation. If there is a possibility of product quality or reproducibility of manufacturing process being influenced, process validation or verification and qualification and cleaning validation shall be considered for their necessity based on quality risk as a part of modification control, and the extent of their conduct shall be determined.

Section 4 Qualification Criteria

1. Conformity status to each of the Articles prescribed in the GCTP Ordinance shall be evaluated according to each manufacturing site and each product based on the "Qualification Criteria for Each GCTP Ordinance Article" (hereinafter referred to as the "GCTP Ordinance Qualification Criteria") of Attachment 2. In this evaluation, items that are considered necessary regardless of product item shall also be evaluated as matters pertaining to the product item.

2. GCTP Ordinance Qualification Criteria shall have the evaluation items indicated 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 GCTP 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 of a problem regarding influence on 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 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 23-25, Paragraph 2, Item 4 of the Act (including mutatis mutandis application of Article 23-37, Paragraph 5 of the Act, and reference of Article 80, Paragraph 3 of the Act and Article 137-58 of the Ordinance for Enforcement; the same shall apply hereinafter) is as follows:

(1) Manufacturing sites corresponding to "conforming": Manufacturing control and quality control methods do not correspond to Article 23-25, Paragraph 2, Item 4 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 (in case of new license application, before disposition upon such application), and may be handled according to the above section "(1)". However, if there is no submission of detailed report on improvement results or a specific improvement plan within the period until the next renewal of licensing, 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 when necessary if the confirmation of improvement status is required on-site.

(3) Manufacturing sites corresponding to "improvement required": The provision of section "(2)" shall apply mutatis mutandis to items in which the evaluation results of conformity status for each Article were categorized as B to. 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 improvement is completed during the period until the next renewal of licensing (in case of new license application, before disposition upon such application), and the manufacturing site 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 the manufacturing site shall be handled according to the below section "(4)".

(4) Manufacturing site corresponding to "not conforming": Manufacturing control or quality control method shall be corresponding to Article 23-25, Paragraph 2, Item 4 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.

Chapter 4 GQP Ordinance (Cellular and Tissue-based Products)

Section 1 Summary

1. Article 3 through Article 16 (excluding Article 15, Item 3 (c) and Article 16, Item 3 (c)) of the GQP Ordinance as applied mutatis mutandis to Article 1, Article 2, and Article 21 of the GQP Ordinance shall be prescribed as the quality control standard code of cellular and tissue-based products prescribed in Article 23-21, Item 1 of the Act.

Section 2 Commentary

1. Purport (related to Article 1)

   (1) Standards for quality control of cellular and tissue-based products shall be established based on the provisions prescribed in Article 12-2, Item 1 and Article 23-21, Item 1 of the Act after partial revision of GQP Ordinance.

   (2) Although the GQP Ordinance is a licensing requirement for a marketing authorization holder, a new licensing application is expected to be submitted before training and self-inspection, for example, has been actually conducted. The requirement shall be considered satisfied if a system has been established by the applicant for immediate conduct of these requirements after licensing, such as of having established their procedures and protocols.

2. Definitions (related to Article 2)

   (1) The definitions of "quality control operation," "release to the market" and "lot" shall be prescribed.

   (2) Quality control operation shall be the operation regarding the marketing authorization holders to ensure necessary product quality for marketing. This operation shall include not only be the operations of the quality assurance division but also the operations of other divisions.

   (3) "Other persons who conduct operations relevant to manufacturing (including testing operations)" indicated in Paragraph 1 shall include those indicated in the manufacturing method column in the marketing approval of those who conduct the

testing operations. Others shall be judged by the marketing authorization holder with consideration of their necessity for supervision of quality control.

(4) Release to the market shall be the act to release for marketing, leasing, or granting the cellular and tissue-based products for marketing, the final product (including transfer of the final product to the distributor of the same corporation as the marketing authorization holder). That is to say that cellular and tissue-based products that completed their release acceptance can be controlled at the distributor.

3. Operations of the cellular and tissue-based products marketing supervisor-general (related to Article 3 that apply mutatis mutandis to Article 21)

(1) Operations pertaining to quality control required in cellular and tissue-based products marketing supervisor-generals, other than operations prescribed in the Ordinance and the GVP Ordinance. Other specific operations individually pertaining to quality control required in cellular and tissue-based products marketing supervisor-generals shall be prescribed in Article 11, Paragraph 2, Item 2 as applied mutatis mutandis to Article 21.

(2) Item 2 requires cellular and tissue-based products marketing supervisor-generals to decide necessary measures based on reports from responsible person for quality assurance and to provide instruction to the quality assurance division, etc. on those measures, and marketing authorization holders shall not impede the operations of the marketing supervisor-general and the responsible person for quality assurance as applied mutatis mutandis to Article 21.

4. Organization and personnel pertaining to quality control operation (related to Article 4 as applied mutatis mutandis to Article 21)

(1) Matters regarding organizations and personnel pertaining to quality assurance division, responsible person for quality assurance, and quality control operation.

(2) Paragraph 1 shall stipulate that all divisions of quality control operation are required to have sufficient number of qualified personnel.

(3) The phrase "have the capacity to appropriately and smoothly execute operations" indicated in Paragraph 1 and Paragraph 2, Item 2 shall be to determine as a marketing authorization holder that the person has capacity considering the content of the operation, and experience and training.

(4) Paragraph 2, Item 3 shall be a provision established for the operations of the quality assurance division in order eliminate as much influence as possible from the viewpoint of sales, such as of profitability. From this perspective, divisions that promote sales, for example, shall be regarded as corresponding to the "other divisions that influence appropriate and smooth quality control operation".

(5) Paragraph 3, Item 2 shall be a provision established with the consideration of product risk for the necessity of requiring persons responsible for quality control operation regarding cellular and tissue-based product to be persons with thorough knowledge of relevant operations, such as of having sufficient experience in the quality control operation. "Other persons who have been engaging in similar operations for 3 or more years" shall be marketing supervisor-generals of drugs, quasi-drugs, cosmetics, medical devices, or cellular and tissue-based products (hereinafter referred to as "drugs"); manufacturing supervisor or responsible engineering supervisor of drugs; persons who have been engaging in operations pertaining to manufacturing control or quality control at manufacturer of drugs; persons who have been engaging in operations pertaining to manufacturing control or quality control at cell culture processing facility prescribed in Article 2, Paragraph 4 of the Act on Safety Assurance of Cellular and Tissue-based Products (Act No. 85 of 2013). "Three or more years" can be the total number of years engaged in the relevant operations regardless of his/her company or other companies.

(6) "Persons with capacity to appropriately execute quality control operations", indicated in Paragraph 3, Item 3, shall be persons entrusted under the responsibility of the marketing authorization holder comprehensively considering his/her work experience, years of experience, training status, and educational background.

(7) Paragraph 3, Item 4 shall be a provision established for the operations of the responsible person for quality assurance in order eliminate as much influence as possible from the viewpoint of sales, such as of profitability. From this perspective, divisions that promote sales, for example, shall be regarded as corresponding to the "other divisions that influence appropriate and smooth quality control operation".

(8) "Via document", indicated in Paragraph 4, shall include an organization chart if the responsibility and authority of the personnel engaged in quality control operation and the control system are appropriately indicated. The date of documentation, and

when revised, the date, revised matters, and the reason for revision shall also be indicated.

5. Quality standards (related to Article 5 as applied mutatis mutandis to Article 21)

(1) This Article shall prescribe that quality standards are required to be created for each product item of the cellular and tissue-based products that is to be marketed.

(2) "Approved product information and other necessary matters pertaining to quality" shall, for example, be matters that reflect the content of agreements with the manufacturer on the product master formula required by the GCTP Ordinance. From the perspective of supervising the manufacturing site relevant to the product, conformity is required between those product master formulas. However, manufacturing methods and manufacturing procedures are not necessarily required to be as detailed as in the product master formula, but shall be included at least the information necessary for supervising the manufacturing site.

6. Documents on procedures for quality control operation (related to Article 6 as applied mutatis mutandis to Article 21)

(1) This Article shall prescribe matters on procedures for quality control operation for their appropriate and smooth conduct.

(2) Procedures indicated in Paragraph 1, Item 9, shall include necessary matters such as mutual allocation of operations, contact person, and contact method.

(3) The procedure indicated in Paragraph 1, Item 10 shall be procedures expected to be created separately from the procedures prescribed in Item 1 to Item 9, such as procedures for outsourcing on-site conformity inspections to confirm the GCTP compliance status at the manufacturing sites.

(4) When providing a copy at other manufacturing sites that conduct quality control operations specified in the provisions of Paragraph 2, the necessary sections of the quality standards and quality control operation procedures (hereinafter referred to as "procedures for quality control operations") shall suffice for appropriate and smooth quality control operation at the site.

7. Agreements with the manufacturers (related to Article 7 as applied mutatis mutandis to Article 21)

(1) This Article shall prescribe matters regarding agreements with manufacturers for those necessary in ensuring appropriate and smooth conduct of manufacturing control and quality control at manufacturers.

(2) The method for concluding agreements can be prescribed as a format that clearly indicates the content of the agreement in the contract itself or as a format that clearly and externally indicates the content of the agreement.

(3) If the marketing authorization holder and the manufacturer are of the same corporation, their relationship as a marketing authorization holder and manufacturer shall suffice if appropriately indicated in the control provision of the corporation.

(4) Although agreements are to be concluded basically between the two parties, i.e., with the manufacturers, the agreement between manufacturers can stipulate that the agreement shall be concluded among three parties including the marketing authorization holder.

(5) "Manufacturers" indicated in Item 1 shall include those indicated in the manufacturing methods column of the marketing approval document, such as manufacturers, foreign manufacturers of cellular and tissue-based products, and those who conduct testing. Others shall be judged by the marketing authorization holder with consideration of their necessity for supervision of quality control.

(6) "Scope" and "procedures" indicated in Item 1 shall require being reflected in manufacturing operations via specification in the product master formula required by the GCTP Ordinance.

(7) "Technical conditions" indicated in Item 2 shall require being reflected in manufacturing operations via specification in the product master formula required by the GCTP Ordinance.

(8) "Periodic confirmation" indicated in Item 3 shall be the confirmation prior to initiating manufacturing and the periodic confirmations that follow.

(9) "Quality control methods for shipping and receipt" indicated in Item 4 shall be require to be reflected in the manufacturing operations via specification in the product master formula required by the GCTP Ordinance.

(10) Prior contact methods pertaining to manufacturing methods, and testing methods indicated in Item 5 shall be required to be reflected in the manufacturing operations via specification in the product master formula required by the GCTP Ordinance.

(11) "Other information on quality of the product" indicated in Item 6 (b) shall include information with doubt or possibility of being quality information. Any deviation control at manufacturing sites shall also be included.

(12) "Other necessary matters" indicated in Item 7 shall include matters on storage of reserve samples required by the GCTP Ordinance.

8. Operations of the responsible person for quality assurance (related to Article 8 as applied mutatis mutandis to Article 21)

(1) This Article prescribes matters regarding operations of the responsible person for quality assurances.

(2) Specific operations individually required for the responsible person for quality assurance other than those prescribed in this Article shall be prescribed in the Articles of GQP Ordinance.

(3) Item 4 prescribes that recalls, marketing suspension, and other quality information are required to be provided to medical institutions when necessary.

9. Release acceptance (related to Article 9 as applied mutatis mutandis to Article 21)

(1) This Article shall prescribe matters regarding control of release acceptance.

(2) "Results of manufacturing control and quality control" indicated in Paragraph 1 and Paragraph 2 shall be prescribed for the purpose of evaluating whether manufacturing control and quality control are appropriately conducted at all manufacturing sites pertaining to manufacturing of a single product item.

(3) Based on the provisions of Paragraph 2, release acceptance shall be determined by the marketing authorization holder itself or shall be able to be determined by a domestic manufacturer under the responsibility of the marketing authorization

holder. Manufacturers that are accepted by the marketing authorization holder to determine release acceptance shall be manufacturers that handle cellular and tissue-based products in which release acceptance pertaining to manufacturing has been completed. Release acceptance shall not be impeded if determined via cooperation regarding the manufacturer and the marketing authorization holder.

(4) "Those results and records on release such as records on the destination of shipping" indicated in Paragraph 2 shall possibly be the following:

A. Records on shipping and receipt of cellular and tissue-based products (brand name, lot number (or manufacturing number for products that do not compose a lot; the same shall apply hereinafter) quantity of shipping and receipt, destination of shipping, etc.)

B. Records pertaining to evaluation of manufacturing control and quality control results

C. Records provided based on the provisions in Paragraph 6 that pertain to evaluation of information on quality, efficacy, and safety by which release acceptance may be influenced.

D. Records on release acceptance (brand name, lot number, person who determined the release acceptance, date for determination, etc.)

(5) "Persons with capacity to appropriately and smoothly execute the operation" indicated in Paragraph 3 shall be persons that satisfy requirements equivalent to those of the responsible person for quality assurance prescribed in Article 4, Paragraph 3 as applied mutatis mutandis to Article 21.

(6) "Results of determining release acceptance" indicated in Paragraph 4 shall be the records prescribed in Paragraph 2.

(7) Reporting prescribed in Paragraph 4 is prescribed with the intention of ensuring that information pertaining to determination of release acceptance is collected and controlled by the responsible person for quality assurance, and shall not necessarily require reporting of each determination of release acceptance as long as the operations are appropriately executed.

(8) Paragraph 5, Item 1 (c) is prescribed with the intention of requiring prompt instructions to be sought from the responsible person for quality assurance in case of deviations from the procedure, and "deviations" shall include those with doubt or

possibility of being a deviation. Matters agreed regarding (a) to (c) of the same item shall be required to be reflected in the manufacturing operations via specification in the product master formula required by the GCTP Ordinance.

(9) "A person, designated beforehand" indicated in Paragraph 5, Item 2 shall mean a personnel with thorough knowledge of the operation who has been predesignated as the person responsible for this operation.

(10) Paragraph 5, Item 3 (a) and (b) shall be required to be reflected in the manufacturing operations via specification in the product master formula required by the GCTP Ordinance.

10. Appropriate manufacturing control and quality control assurance (related to Article 10 as applied mutatis mutandis to Article 21)

(1) This Article prescribes matters on appropriate manufacturing control and quality control assurance.

(2) The provisions of Paragraph 1 require for manufacturing control and quality control to be periodically confirmed on whether they are appropriately and smoothly conducted at the manufacturers based on the agreement with marketing authorization holders as prescribed in Article 7 as applied mutatis mutandis to the GCTP Ordinance and Article 21 which is a requirement for marketing approval and a compliance requirement of the manufacturer.

(3) The phrase "to periodically confirm" indicated in Paragraph 1 shall be the confirmation prior to initiating manufacturing and the periodic confirmations that follow.

(4) "A person, designated beforehand" indicated in Paragraph 1 and Paragraph 3 shall mean a personnel with thorough knowledge of the operation who has been predesignated as the person responsible for this operation.

(5) Any instructions provided pursuant to the provision in Paragraph 2, Item 1 after periodic confirmations according to Paragraph 1, Item 1 shall be required to be reflected in the manufacturing operations via specification in the product master formula required by the GCTP Ordinance.

(6) Any instructions provided pursuant to the provision in Paragraph 4 after evaluation according to Paragraph 3, Item 1 shall be required to be reflected in the manufacturing operations via specification in the product master formula required by the GCTP Ordinance.

(7) Paragraph 5 shall prescribe that marketing authorization holders are required to provide manufacturers quality information necessary for the manufacturers to appropriately and smoothly conduct manufacturing control and quality control. This information shall be required to be reflected in the manufacturing operations via specification in the product master formula required by the GCTP Ordinance.

11. Quality information and management of quality defect (related to Article 11 as applied mutatis mutandis to Article 21)

(1) This Article shall prescribe matters on quality information and management of quality defect.

(2) Upon receiving quality information, operations shall be conducted based on the provisions in Paragraph 1, and if quality defect or possibility of quality defect have been found, operations based on the provision in Paragraph 2 shall be promptly and concurrently conducted.

(3) "Quality pertaining to cellular and tissue-based products" indicated in Paragraph 1 shall include quality pertaining to containers, packages, and labelings.

(4) Paragraph 1, Item 3 and Item 5 shall require being reflected in manufacturing operations via specification in the product master formula required by the GCTP Ordinance.

(5) Paragraph 1, Item 6 prescribes that quality information regarding safety assurance measures are required to be provided to the safety control supervisory division via document without delay. Note that quality information is required to be provided from the safety control supervisory division as prescribed in Article 8, Paragraph 1, Item 2 of the GVP Ordinance (including mutatis mutandis application of Article 14 of the GVP Ordinance).

(6) "Quality defect" indicated in Paragraph 2 shall mean that details of the marketing approval document or other necessary quality is not being complied.

12. Management of recalls (related to Article 12 as applied mutatis mutandis to Article 21)

(1) This Article prescribes matters on management of recalls. Recalls shall be managed with the cooperation regarding manufacturers, distributors, founders of hospitals and clinics, and other relevant persons.

(2) "Certain period" indicated in Item 1 shall be the period until measures for the recalled cellular and tissue-based products have been determined.

13. Self-inspection (related to Article 13 as applied mutatis mutandis to Article 21)

(1) This Article prescribes matters on self-inspection.

(2) "A person, designated beforehand" indicated in Paragraph 1 shall mean a personnel with thorough knowledge of the operation who has been predesignated as the person responsible for this operation.

(3) In principle, persons shall not conduct self-inspections on operations that they are engaged in.

14. Training (related to Article 14 as applied mutatis mutandis to Article 21)

(1) This Article prescribes matters on training.

(2) "A person, designated beforehand" indicated in Paragraph 1 shall mean a personnel with thorough knowledge of the operation who has been predesignated as the person responsible for this operation.

15. Storage control of cellular and tissue-based products (related to Article 15 as applied mutatis mutandis to Article 21)

(1) This Article prescribes matters regarding control of cellular and tissue-based products in which release pertaining to manufacturing has been determined, for when they are stored or displayed at the office of the marketing authorization holder for the purpose of marketing after release acceptance.

(2) This Article shall not be applied if the products will not be stored or displayed.

(3) If prior to release acceptance cellular and tissue-based products are stored or displayed at a place other than the place where the office at which the cellular and tissue-based products marketing supervisor-general conducts operations, a license