

Tentative translation ver. 3.1 (as of 5 September 2005)¹

MHLW Ministerial Ordinance No. 169, 2004

In accordance with the provisions of Item (4) of Paragraph 2 of Article 14 and Item (4) of Paragraph 2 of Article 14 applied *mutatis mutandis* under Paragraph 5 of Article 19-2 of Pharmaceutical Affairs Law (Law No. 145, 1960), MHLW Ministerial Ordinance on Standards for Manufacturing Control and Quality Control for Medical Devices and In-vitro Diagnostic Reagents is established as follows.

17 December 2004

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Ministerial Ordinance on Standards for Manufacturing Control and Quality Control for Medical Devices and In-vitro Diagnostic Reagents

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Supplementary Provisions

¹ Note/ This is a tentative translation of afore-mentioned Ordinance in English which is not an authentic and not formally authorised by Ministry of Health, Labour and Welfare of Japan.

Chapter 1 General Provisions

Section 1 General Rules

(Purpose)

Article 1 This Ministerial Ordinance shall provide the standards in accordance with the provision of Item (4) of Paragraph 2 of Article 14 (including the case where it is applied *mutatis mutandis* under Paragraph 5 of Article 19-2, and hereinafter referred to as such) of Pharmaceutical Affairs Law (Law No. 145, 1960) (hereinafter referred to as “Law”) which provides that such standards shall be provided by MHLW Ministerial Ordinances.

(Definitions)

Article 2 “**Product**” throughout this Ministerial Ordinance means the object (including those which have undergone the intermediate process and need to undergo subsequent process to be the (final) products (hereinafter referred to as “intermediate products”)) that has undergone the manufacturing process in the manufacturing site.

2. “**Constituent parts, etc.**” throughout this Ministerial Ordinance mean the parts, assemblies (limited to those which are used in the products), raw materials, materials, containers, wrappers, labellings (including the package inserts, and hereinafter referred to as such), etc. used in the manufacturing process that constitute parts of the products, as well as the software of the products.
3. “**Process agent**” throughout this Ministerial Ordinance means the object that is used for the intermediate products in the manufacturing process (excluding those that constitute parts of the products).
4. “**Packaging and labelling material**” throughout this Ministerial Ordinance means the container, wrapper and labelling among the constituent parts, etc.
5. “**Lot**” throughout this Ministerial Ordinance means a grouping of the products, process agents or constituent parts, etc. (hereinafter collectively referred to as “products, etc.”) that are manufactured so as to have a uniform quality in a series of the manufacturing process for a certain manufacturing period.
6. “**Batch for testing**” throughout this Ministerial Ordinance means a lot or another grouping equivalent thereto of the products with a uniform quality.
7. “**Controlled unit**” throughout this Ministerial Ordinance means a grouping of the packaging and labelling materials that have been verified to be same.
8. “**Sterile medical device**” throughout this Ministerial Ordinance means a medical device that is sterilised in the manufacturing process.
9. “**Validation**” throughout this Ministerial Ordinance means to verify and document that the buildings and facilities of the manufacturing site, procedures, processes and other procedures of the manufacturing control and quality control (hereinafter referred to as “manufacturing procedure, etc.”) provide the anticipated results.

10. “**Clean area**” throughout this Ministerial Ordinance means the place, among those areas where the manufacturing operations are conducted (hereinafter referred to as “work areas”), where the weighing operations for the constituent parts, etc. or the formulating operations are conducted or where the cleaned containers are exposed to the air in the work areas.
11. “**Aseptic area**” throughout this Ministerial Ordinance means the place, among the work areas, where the aseptic products or constituent parts, etc. or sterilised containers are exposed to the air in the work areas, where the sealing operations for the containers are conducted, or where the aseptic operations including the sterility tests are conducted.
12. “**Cell/tissue-based medical device**” throughout this Ministerial Ordinance means the medical device composed of human or animal cells or tissue.
13. “**Donor**” throughout this Ministerial Ordinance means the person who donates the cells or tissue that serves as the materials for the cell/tissue-based medical devices (excluding those concerned with the body of a brain-dead person specified in Paragraph 2 of Article 6 of Law on Organ Transplantation (Law No. 104, 1997)).
14. “**Donor animal**” throughout this Ministerial Ordinance means the animal which provides the cells or tissue that serves as the materials for the cell/tissue-based medical devices.
15. “**Input**” throughout this Ministerial Ordinance means the information, etc. necessary for the manufacturing control and quality control when conducting a certain process.
16. “**Output**” throughout this Ministerial Ordinance means the information, etc., that is obtained as a result of a certain process conducted.
17. “**Top management**” throughout this Ministerial Ordinance means the person or the group of people, including the executive officer who conducts the duties concerned with the manufacturing site, who directs and controls the manufacturing site.
18. “**Quality policy**” throughout this Ministerial Ordinance means the overall intentions and direction of the manufacturing site related to the quality as formally provided and expressed by the top management in order to ensure the quality of the products.
19. “**Quality management system**” throughout this Ministerial Ordinance means the management system that the manufacturer and the foreign manufacturer specified in Paragraph 1 of Article 13-3 of Law (hereinafter simply referred to as “foreign manufacturer”) (hereinafter collectively referred to as “manufacturer, etc.”) direct and control the manufacturing site with regard to quality.
20. “**Review**” throughout this Ministerial Ordinance means the activity undertaken to determine the suitability, adequacy and effectiveness of the subject matter to achieve the established objectives.
21. “**Resource**” throughout this Ministerial Ordinance means the personal knowledge and skills and technology, facilities and other resource that is utilised for the operations of the manufacturing site.

22. “**Infrastructure**” throughout this Ministerial Ordinance means the system of the facilities, equipment and services that are necessary for the operations of the manufacturing site.
23. “**Traceability**” throughout this Ministerial Ordinance means the ability to trace the history, application or location of that which is under consideration.
24. “**Advisory notice**” throughout this Ministerial Ordinance means the document that is issued subsequent to the delivery of the products to provide supplement any information or to advise what actions should be taken in use, modification, return or destruction of the products.

(Scope)

Article 3 The marketing authorisation holder of the medical devices or in-vitro diagnostic reagents specified in Paragraph 1 of Article 14 of Law, the appointed marketing authorisation holder of medical devices or in-vitro diagnostic reagents specified in Paragraph 4 of Article 19-2 of Law or the marketing authorisation holder of the designated controlled medical devices specified, etc. in Paragraph 1 of Article 23-2 of Law (hereinafter collectively referred to as “marketing authorisation holder, etc.”) shall, in accordance with the provision of Chapter 2 or the provision of Chapter 2 applied *mutatis mutandis* under Chapter 5, have the manufacturer, etc. conduct the manufacturing control and quality control of the products in the manufacturing site, with the proviso that the manufacturing control and quality control in the manufacturing site of the manufacturer in the category specified in Item (4) of Paragraph 5 of Article 26 of Pharmaceutical Affairs Law Enforcement Regulations (MHW Ministerial Ordinance No. 1, 1961) (hereinafter referred to as “Enforcement Regulations”) (hereinafter referred to as “labelling, etc.-category medical device manufacturer”) or the foreign manufacturer in the category specified in Item (4) of Paragraph 4 of Article 36 of Enforcement Regulations (hereinafter referred to as “foreign labelling, etc.-category medical device manufacturer”) (hereinafter collectively referred to as “labelling, etc.-category medical device manufacturer, etc.”), or the manufacturer in the category specified in Item (3) of Paragraph 2 of Article 26 of Enforcement Regulations (hereinafter referred to as “labelling, etc.-category in-vitro diagnostic reagents manufacturer”) or the foreign manufacturer in the category specified in Item (3) of Paragraph 2 of Article 36 of Enforcement Regulations (hereinafter referred to as “foreign labelling, etc.-category in-vitro diagnostic reagents manufacturer”) (hereinafter collectively referred to as “labelling, etc.-category in-vitro diagnostic reagents manufacturer, etc.”) are conducted in accordance with the provision of Chapter 3 or the provision of Chapter 3 applied *mutatis mutandis* under Chapter 5 may be applied, instead of the provision of Chapter 2 or the provision of Chapter 2 applied *mutatis mutandis* under Chapter 5.

2. The marketing authorisation holder, etc. of medical devices shall have the manufacturer of the products concerned with the medical devices which correspond to the biological-origin products specified in Paragraph 9 of Article 2 of Law (hereinafter referred to as “biological-origin medical devices”), the medical devices designated by Minister of Health, Labour and Welfare in accordance with the provision of Paragraph 2 of Article 43 of Law, or the cell/tissue-based medical devices (hereinafter collectively referred to as “biological-origin medical devices, etc.”) (hereinafter referred to as

“biological-origin medical devices, etc. manufacturer”), and the foreign manufacturer of the products concerned with the biological-origin medical devices, etc. (hereinafter collectively referred to as “biological-origin medical devices, etc. manufacturer, etc.”) conduct the manufacturing control and quality control of the products in the manufacturing site in accordance with the provision of Chapter 4 (limited to Articles 78 and 79 for the manufacturing site that conducts only the labelling, packaging or storing operations) in addition to the provision of Chapter 2.

3. The manufacturer, etc. of medical devices or in-vitro diagnostic reagents shall conduct the manufacturing control and quality control of the products in the manufacturing site specified in Article 96 of Enforcement Regulations in accordance with the provision of Chapter 2 or the provision of Chapter 2 applied *mutatis mutandis* under Chapter 5, with the proviso that the manufacturing control and quality control in the manufacturing site of the labelling, etc.-category medical device manufacturer, etc. or the labelling, etc.-category in-vitro diagnostic reagents manufacturer, etc. are conducted in accordance with the provision of Chapter 3 or the provision of Chapter 3 applied *mutatis mutandis* under Chapter 5, instead of the provision of Chapter 2 or the provision of Chapter 2 applied *mutatis mutandis* under Chapter 5. In addition, the manufacturing control and quality control of the products in the manufacturing site of the biological-origin medical device, etc. manufacturer, etc. shall be conducted in accordance with the provision of Chapter 4 (limited to Articles 78 and 79 for the manufacturing site that conducts only the labelling, packaging or storing operations) in addition to the provision of Chapter 2.
4. The manufacturer of the products concerned with the medical devices or drugs (limited to in-vitro diagnostic reagents, and referred to as such in this Paragraph 4) for the export specified in Paragraph 1 of Article 80 of Law shall conduct the manufacturing control and quality control of the products in the manufacturing site in accordance with the provision of Chapter 2 or the provision of Chapter 2 applied *mutatis mutandis* under Chapter 5, with the proviso that the labelling, etc.-category medical device manufacturer or the labelling, etc.-category in-vitro diagnostic reagents manufacturer conducts the manufacturing control and quality control of the products concerned with the medical devices or in-vitro diagnostic reagents for the export in accordance with the provision of Chapter 3 or the provision of Chapter 3 applied *mutatis mutandis* under Chapter 5, instead of the provision of Chapter 2 or the provision of Chapter 2 applied *mutatis mutandis* under Chapter 5. In addition, the manufacturing control and quality control of the products concerned with the medical devices for the export specified in same Article of Law in the manufacturing site of the biological-origin medical devices, etc. manufacturer shall be conducted in accordance with the provision of Chapter 4 (limited to Articles 78 and 79 for the manufacturing site that conducts only the labelling, packaging or storing operations) in addition to the provision of Chapter 2.

Chapter 2 Manufacturing Control and Quality Control in Manufacturing Sites of Medical Device Manufacturers, etc.

Section 1 General Rules

(Application)

Article 4 The provisions of Articles 30 to 36 shall not apply to the products concerned

with the medical devices other than both the specially designated medical devices specified in Paragraph 1 of Article 77-5 of Law and the medical devices designated by Minister of Health, Labour and Welfare as those of which design and development (hereinafter referred to as “**design and development**”) are necessary to be controlled to ensure that the manufacturing control and quality control are conducted appropriately.

2. The manufacturer, etc., in case where any provisions of Section 5 of this Chapter are not applicable to their products due to the nature of the medical devices concerned with the products, may not apply such provisions to their quality management system.
3. The manufacturer, etc. shall, in case where either of the provisions specified in preceding two Paragraphs 1 and 2 is applied to, describe the details of such application in the documents which specify the quality management system concerned with the manufacturing site (hereinafter referred to as “quality manual”).

Section 2 Quality Management System

(General Requirements for Quality Management System)

Article 5 The manufacturer, etc. shall establish, document, implement and maintain a quality management system and maintain its effectiveness in accordance with the provision of this Chapter.

2. The manufacturer, etc. shall conduct the following duties.
 - (1) To identify the processes needed for the quality management system (including the results to be achieved by the processes) (hereinafter simply referred to as “processes” in this Chapter) and their application throughout the manufacturing site,
 - (2) To determine the sequence and interaction of the processes,
 - (3) To determine the criteria and methods needed to ensure that both the operation and control of the processes are effective,
 - (4) To ensure the availability of the resources and information necessary to support the operation and monitoring of the processes,
 - (5) To monitor, measure and analyse these processes, and
 - (6) To implement the actions necessary to achieve the planned results specified in preceding Item (1) and maintain the effectiveness of these processes.
3. The manufacturer, etc. shall manage the processes in accordance with the provision of this Chapter.
4. Where the manufacturer, etc. choose to outsource any process (excluding those which are subject to the authorisation specified in Paragraph 1 of Article 13 of Law or the recognition specified in Paragraph 1 of Article 13-3 of Law) that affects the conformity

with the product requirements (including the laws, orders and ordinances which are relevant to the pharmaceutical affairs or the orders or official actions based on the laws, orders and ordinances (hereinafter simply referred to as “regulatory requirements” in this Chapter)) (hereinafter referred to as “product requirements” in this Chapter), the manufacturer, etc. shall ensure the control over such processes.

5. The manufacturer, etc. shall ensure that the control of such outsourced processes is identified within the quality management system.

(Documentation of Quality Management System)

Article 6 The manufacturer, etc. shall ensure that the quality management system documentation includes the following documents and that the documented requirement, procedure, activity or special arrangement is implemented and maintained.

- (1) The documented statements of the quality policy and quality objectives,
 - (2) The quality manual,
 - (3) The documents needed by the manufacturer, etc. to ensure the effective planning, operation and control of their processes in the manufacturing site,
 - (4) The documented procedure and records specified in this Chapter, and
 - (5) Any other documentation specified by the laws, orders and ordinances related to the pharmaceutical affairs.
2. For each type or model of the medical devices, the manufacturer, etc. shall establish and maintain the document defining the product specifications and quality management system requirements (hereinafter referred to as “*Seihin Hyojun Sho*” in this Chapter), or a file identifying *Seihin Hyojun Sho*.
 3. The manufacturer, etc. shall ensure that *Seihin Hyojun Sho* defines the complete manufacturing process concerned with the products of the manufacturing site and, if applicable, the installation specified in Paragraph 1 of Article 42 and the servicing specified in Paragraph 1 of Article 43.

(Quality Manual)

Article 7 The manufacturer, etc. shall establish and maintain the quality manual that includes the following items.

- (1) The scope of the quality management system, including the details of and justification for any exclusion and/or non-application,
- (2) The documented procedure established for the quality management system, or reference to them, and
- (3) The description of the interaction between the processes of the quality management system.

2. The manufacturer, etc. shall ensure that the quality manual outlines the structure of the documentation used in the quality management system.

(Control of Documents)

Article 8 The manufacturer, etc. shall ensure that the documents (excluding the records), including those specified in preceding two Articles and other Articles in this Chapter, required by the quality management system (hereinafter referred to as “QMS documents”) are controlled.

2. The manufacturer, etc. shall ensure that the documented procedure is established to define the controls needed for the following duties.
 - (1) To review and approve the QMS documents for adequacy prior to the issue,
 - (2) To review and update as necessary and re-approve the QMS documents,
 - (3) To ensure that the changes and current revision status of the QMS documents are identified,
 - (4) To ensure that the relevant versions of the applicable QMS documents are available at the points of the use,
 - (5) To ensure that the QMS documents remain legible and readily identifiable,
 - (6) To ensure that the QMS documents of external origin are identified and their distribution is controlled, and
 - (7) To prevent the unintended use of the obsolete QMS documents, and to apply suitable identification to them if they are retained for any purpose.
3. The manufacturer, etc. shall ensure that the changes to the QMS documents are reviewed and approved either by the original approving department or another designated department which has access to pertinent background information upon which to base its decisions.
4. The manufacturer, etc. shall retain at least one copy of the obsolete QMS documents for the following period (5 years for the QMS documents concerned with the training) from the date of obsolescence, with the proviso that this provision shall not apply to the documents used for the manufacturing or testing of the products in case where they are maintained to be available for the retention period of the records of the products specified in next Article.
 - (1) 15 years for the products concerned with the specially designated maintenance-control-required medical devices specified in Paragraph 8 of Article 2 of Law (1 year plus the shelf life or the period until the expiry date (hereinafter simply referred to as “shelf life”), for the products concerned with the medical devices of which shelf life shall be displayed and of which shelf life plus 1 year exceeds 15 years), or

- (2) 5 years for the products concerned with the medical devices other than the specially designated maintenance-control-required medical devices (1 year plus the shelf life, for the products of which shelf life shall be displayed and of which shelf life plus 1 year exceeds 5 years).

(Control of Records)

Article 9 The manufacturer, etc. shall ensure that the records are established and maintained to provide the evidence of the conformity to the requirements, including those for the records, specified in this Chapter and of the effective operation of the quality management system and that the records remain legible, readily identifiable and retrievable.

2. The manufacturer, etc. shall ensure that the documented procedure is established to define the controls needed for the identification, storage, protection, retrieval, retention time and disposition of the records specified in preceding Paragraph 1.
3. The manufacturer, etc. shall retain the records specified in preceding Paragraph 1 for the following period (5 years for the records concerned with the training) from the date of the establishment.
 - (1) 15 years for the products concerned with the specially designated maintenance-control-required medical devices (1 year plus the shelf life, for the products concerned with the medical devices of which shelf life shall be displayed and of which shelf life plus 1 year exceeds 15 years), or
 - (2) 5 years for the products concerned with the medical devices other than the specially designated maintenance-control-required medical devices (1 year plus the shelf life, for the products concerned with the medical devices of which shelf life shall be displayed and of which shelf life plus 1 year exceeds 5 years).

Section 3 Management Responsibility

(Management Commitment)

Article 10 The top management shall provide evidence of its commitment to the development and implementation of the quality management system and maintaining its effectiveness by conducting the following duties.

- (1) To establish the quality policy,
- (2) To ensure that the quality objectives are established,
- (3) To conduct the management reviews specified in Paragraph 1 of Article 18,
- (4) To ensure the availability of the resources, and
- (5) To communicate to the manufacturing site the importance of meeting the

requirements of the marketing authorisation holder and other bodies receiving the products (hereinafter referred to as “customers”) (hereinafter referred to as “customer requirements”) as well as the regulatory requirements.

(Customer Focus)

Article 11 The top management shall ensure that the customer requirements are determined and are met.

(Quality Policy)

Article 12 The top management shall ensure that the quality policy meets the following requirements.

- (1) To be appropriate to the purpose of the manufacturer, etc.,
- (2) To include the commitment to comply with the requirements and to maintain the effectiveness of the quality management system,
- (3) To provide the framework for establishing and reviewing the quality objectives,
- (4) To be communicated and understood within the manufacturing site, and
- (5) To be reviewed for continuing suitability.

(Quality Objectives)

Article 13 The top management shall ensure that the quality objectives, including those needed to meet the requirements for the products, are established at relevant departments within the manufacturing site.

2. The top management shall ensure that the quality objectives are measurable and consistent with the quality policy.

(Quality Management System Planning)

Article 14 The top management shall ensure that the planning of the quality management system is carried out in order to meet the requirements specified in Article 5, as well as the quality objectives.

2. The top management shall ensure that the integrity of the quality management system is maintained when changes to the quality management system are planned and implemented.

(Responsibility and Authority)

Article 15 The top management shall ensure that the responsibilities and authorities of the departments and personnel engaged in the duties are defined, documented and communicated within the manufacturing site.

2. The top management shall establish the interrelation of all personnel who manage, perform and verify the work affecting the quality, and shall ensure the independence and authority necessary to perform these tasks.

(Responsible Engineering Manager)

Article 16 The top management shall ensure that the responsible engineering manager specified in Paragraph 5 of Article 17 of Law and the manager controlling the manufacturing of the biological-origin products (the biological-origin products specified in Paragraph 9 of Article 2 of Law, and hereinafter referred to as such) specified in Paragraph 1 of Article 68-2 of Law (in case of a foreign manufacturer, the person responsible for the manufacturing site which has been recognised in accordance with the provision of Paragraph 1 of Article 13-3 of Law or the person designated beforehand by such a foreign manufacturer) (hereinafter collectively and simply referred to as “responsible engineering manager”) have the responsibility and authority for the following duties.

- (1) To ensure that the processes needed for the quality management system are established, implemented and maintained,
- (2) To report to the top management on the performance of the quality management system and any need for improvement, and
- (3) To ensure the promotion of the awareness of the regulatory and customer requirements throughout the manufacturing site.

(Internal Communication)

Article 17 The top management shall ensure that appropriate communication processes are established within the manufacturing site and that communication takes place regarding the effectiveness of the quality management system.

(Management Review)

Article 18 The top management shall review the manufacturing site's quality management system, at the interval defined in the plan specified in Paragraph 1 of Article 14, to ensure its continuing suitability, adequacy and effectiveness. This review (hereinafter referred to as “management review”) shall include assessing the opportunities for improvement and the need for changes to the quality management system, including the quality policy and quality objectives.

2. The manufacturer, etc. shall ensure that the records from the management reviews are maintained.

(Review Input)

Article 19 The manufacturer, etc. shall ensure that the input to the management review includes the information on the following items.

- (1) The results of the audits,
- (2) The customer feedback,
- (3) The process performance and product conformity to the product requirements,
- (4) The status of the corrective actions (the actions taken to eliminate the cause of the detected non-conformity or other undesirable situation, and hereinafter referred to as such) and the preventive actions (the actions to eliminate the cause of the potential non-conformity or other undesirable potential situation, and hereinafter referred to as such),
- (5) The follow-up actions from the previous management reviews,
- (6) The changes that could affect the quality management system,
- (7) The recommendations for improvement, and
- (8) New or revised regulatory requirements.

(Review Output)

Article 20 The manufacturer, etc. shall ensure that the output from the management review includes any decisions and actions related to the following items.

- (1) The improvements needed to maintain the effectiveness of the quality management system and its processes,
- (2) The improvement of the products related to the customer requirements, and
- (3) The resource needs to ensure continuing suitability, adequacy and effectiveness of the quality management system.

Section 4 Resource Management

(Provision of Resources)

Article 21 The manufacturer, etc. shall determine and provide the resources needed for the following duties.

- (1) To implement the quality management system and to maintain its effectiveness, and
- (2) To meet the regulatory and customer requirements.

(Personnel)

Article 22 The manufacturer, etc. shall ensure that the personnel performing the work

affecting the product quality are competent on the basis of the following requirements.

- (1) The appropriate training, and
- (2) The appropriate skills and experience.

(Competence, Awareness and Training)

Article 23 The manufacturer, etc. shall conduct the following duties.

- (1) To determine the necessary competence for the personnel performing the work affecting the product quality,
- (2) To establish the documented procedure for identifying the training needs,
- (3) To provide training or take other actions to satisfy the needs determined by the documented procedure specified in preceding Item (2),
- (4) To evaluate the effectiveness of the actions specified in preceding Item (3),
- (5) To ensure that the personnel are aware of the relevance and importance of their activities and how they contribute to the achievement of the quality objectives, and
- (6) To maintain appropriate records of the training, skills and experience.

(Infrastructure)

Article 24 The manufacturer, etc. shall determine, provide and maintain the following infrastructure, as applicable, needed to achieve the conformity to the product requirements.

- (1) The buildings, workspace and associated utilities,
 - (2) The process equipment (both hardware and software), and
 - (3) The supporting services (such as transport or communication).
2. The manufacturer, etc. shall provide and maintain the following infrastructure in case where they manufacture the following products.
- (1) For the products which need the control of dust, humidity, insects and rodents, the buildings or facilities for controlling dust, humidity, insects and rodents,
 - (2) For the products of which manufacturing process the poisonous gases are handled, the facilities necessary for disposing of such poisonous gases,
 - (3) For the products in a form of liquid, sol, gel or powder (excluding those concerned with the sterilised medical devices), the work rooms that meet the following requirements,

- a. Being the buildings which do not allow passage of the personnel other than those conducting operations in such work rooms, with the proviso that this provision shall not apply in case where the products, etc. could not be contaminated by the personnel other than those conducting operations in such work rooms,
 - b. Not being provided with the entrances directly leading to the outside (except those for emergency), with the proviso that this provision shall not apply in case where the work rooms are provided with the buildings and facilities necessary for preventing contamination due to the outside,
 - c. Being provided with the entrances and windows that can be closed,
 - d. Being provided with the buildings and facilities necessary for preventing contamination by dust or microorganisms according to the type and manufacturing process of the products, with the proviso that this provision shall not apply in case where the manufacturing facilities, etc. provide equivalent functions,
 - e. Being provided the effluent facilities, in case where they are provided in the work rooms, with the buildings necessary for preventing contamination of the work rooms, and
 - f. Being provided with the facilities for supplying water of the quality and quantity necessary for the manufacturing, according to the type and the manufacturing process of the products.
3. The manufacturer, etc. shall establish the documented requirements for the maintenance activities, including their frequency, when such activities or lack thereof can affect the product quality.
 4. The manufacturer, etc. shall ensure that the records of such maintenance are maintained.

(Work Environment)

Article 25 The manufacturer, etc. shall determine and manage the work environment needed to achieve the conformity to the product requirements.

2. The manufacturer, etc. shall establish the documented requirements for health, cleanliness and clothing of the personnel if contact between such personnel and the products, etc. or work environment could adversely affect the quality of the products, with the proviso that this provision shall not apply to the process in case where the products are cleaned in the subsequent process in accordance with the provision of Item (1) or (2) of Paragraph 1 of Article 41.
3. If the work environment conditions can have an adverse effect on the product quality, the manufacturer, etc. shall establish the documented requirements for the work environment conditions and the documented procedure or work instructions to monitor and control these work environment conditions, with the proviso that this provision

shall not apply to the process in case where the products are cleaned in the subsequent process in accordance with the provision of Item (1) or (2) of Paragraph 1 of Article 41.

4. The manufacturer, etc. shall ensure that all personnel who are required to work temporarily under special environmental conditions within the work environment are appropriately trained as specified in Item (3) of Article 23, with the proviso that this provision shall not apply in case where the personnel are supervised by a trained person.
5. The manufacturer, etc. shall ensure, if appropriate, that the special arrangements are established and documented for the control (including identification specified in Paragraph 3 of Article 47) of the contaminated or potentially contaminated products in order to prevent the contamination of other products, the work environment or personnel.

Section 5 Product Realisation

(Planning of Product Realisation)

Article 26 The manufacturer, etc. shall plan and develop the processes needed for the product realisation (the duties of the manufacturer, etc. for realisation of the products).

2. The manufacturer, etc. shall ensure that the planning of the product realisation specified in preceding Paragraph 1 (hereinafter referred to as “planning of product realisation”) is consistent with the requirements of the other processes of the quality management system.
3. The manufacturer, etc. in case where they conduct planning of product realisation, shall determine the following items, as appropriate.
 - (1) The quality objectives and requirements for the products,
 - (2) The need to establish the processes, QMS documents, and provide resources specific to the products,
 - (3) The required verification, validation, monitoring, inspection and test activities specific to the products and the criteria for the product acceptance (hereinafter referred to as the “manufacturing site release criteria”),
 - (4) The records needed to provide evidence that the realisation processes and resulting products meet the product requirements.
4. The manufacturer, etc. shall ensure that the output of the planning of product realisation is in a form suitable for the manufacturing site's method of the operations.
5. The manufacturer, etc. shall establish the documented requirements for the risk management throughout the product realisation.
6. The manufacturer, etc. shall ensure that the records arising from the risk management are maintained.

(Determination of Requirements Related to the Products)

Article 27 The manufacturer, etc. shall determine the following items as the product requirements.

- (1) The requirements specified by the customer, including the requirements for delivery and post-delivery activities,
- (2) The requirements not stated by the customer but necessary for the specified or intended use, where known,
- (3) The regulatory requirements related to the products, and
- (4) Any additional requirements determined by the manufacturer, etc.

(Review of Requirements Related to Products)

Article 28 The manufacturer, etc. shall review the product requirements, prior to their commitment to supply the products to the customer.

2. The manufacturer, etc. shall, in case where they conduct the review specified in preceding Paragraph 1, ensure the following items.
 - (1) To be ensured that the product requirements are defined and documented,
 - (2) To be ensured that the contract or order requirements of the customer differing from those previously expressed are resolved, and
 - (3) To be ensured that the manufacturing site has the ability to meet the defined requirements.
3. The manufacturer, etc. shall ensure that the records of the results of the review specified in preceding Paragraph 1 and the actions arising from the review are maintained.
4. Where the customer provides no documented statement of the requirement, the manufacturer, etc. shall confirm the customer requirements before the acceptance.
5. Where the product requirements are changed, the manufacturer, etc. shall ensure that the relevant documents are amended and that relevant personnel are made aware of the changed requirements.

(Customer Communication)

Article 29 The manufacturer, etc. shall determine and implement the effective arrangements for communicating with the customers in relation to the following items.

- (1) The product information,
- (2) The enquiries, contracts or order handling, including the amendments,
- (3) The customer feedback, including the customer complaints, and

- (4) The issuance and implementation of the advisory notices specified in Paragraph 2 of Article 62.

(Design and Development Planning)

Article 30 The manufacturer, etc. shall establish the documented procedure for the design and development.

2. The manufacturer, etc. shall establish the plan of the design and development of the products (hereinafter referred to as the “design and development plan”) and control the design and development of the products.
3. The manufacturer, etc. when they establish the design and development plan, shall determine the following items.
 - (1) The design and development stages,
 - (2) The review, verification, validation and design transfer activities (the duties, during the design and development process, to ensure that the design and development outputs are verified as suitable for the manufacturing before becoming the final production specifications) that are appropriate at each design and development stage, and
 - (3) The responsibilities and authorities of the departments and personnel concerned with the design and development.
4. The manufacturer, etc. shall manage the interfaces between different groups involved in the design and development to ensure effective communication and clear assignment of the responsibility.
5. The manufacturer, etc. shall ensure that the design and development plan are documented, and updated as appropriate, as the design and development progresses.

(Design and Development Inputs)

Article 31 The manufacturer, etc. shall ensure that the following inputs relating to the product requirements are determined and the records are maintained.

- (1) The functional, performance and safety requirements, according to the intended use,
- (2) Where applicable, the information derived from the previous similar designs,
- (3) The outputs of the risk management specified in Paragraph 5 of Article 26,
- (4) The applicable regulatory requirements, and
- (5) Other requirements essential for the design and development.

2. The manufacturer, etc. shall ensure that these inputs are reviewed for adequacy and approved.

(Design and Development Outputs)

Article 32 The manufacturer, etc. shall ensure that the outputs of the design and development are provided in a form that enables the verification against the design and development input.

2. The manufacturer, etc. shall ensure that the outputs of the design and development are approved prior to the release to the next process.
3. The manufacturer, etc. shall ensure that the design and development outputs meet the following requirements.
 - (1) To meet the input requirements for the design and development,
 - (2) To provide appropriate information for the purchasing, production and for the service provision,
 - (3) To contain or reference the product acceptance criteria, and
 - (4) To specify the characteristics of the products that are essential for their safe and proper use.
4. The manufacturer, etc. shall ensure that the records of the design and development outputs are maintained.

(Design and Development Review)

Article 33 The manufacturer, etc. shall ensure that, at suitable stages, the systematic reviews of the design and development (hereinafter referred to as “design and development review”) are performed for the purpose of the following items in accordance with the arrangements defined in the design and development plan.

- (1) To evaluate the ability of the results of the design and development to meet the requirements, and
- (2) To identify any problems and propose necessary actions.
2. The manufacturer, etc. shall ensure that the participants in such reviews include the representatives of the departments concerned with the design and development stages being reviewed, as well as other specialist personnel.
3. The manufacturer, etc. shall ensure that the records of the results of the reviews and any necessary actions are maintained.

(Design and Development Verification)

Article 34 The manufacturer, etc. shall ensure that the verification is performed in accordance with the arrangements defined in the design and development plan to ensure that the design and development outputs have met the design and development input requirements.

2. The manufacturer, etc. shall ensure that the records of the results of the verification specified in preceding Paragraph 1 and any necessary actions taken are maintained.

(Design and Development Validation)

Article 35 The manufacturer, etc. shall ensure that the design and development validation (hereinafter referred to as “design and development validation”) is performed in accordance with the arrangements defined in the design and development plan to ensure that the resulting products are capable of meeting the requirements for the specified application or intended use.

2. The manufacturer, etc. shall ensure that the design and development validation is completed prior to the delivery or implementation of the products. In case where the design and development validation can only be conducted following the assembly and installation at the point of the use, the validation shall be completed prior to the delivery of the medical devices to their user.
3. The manufacturer, etc. shall ensure that the records of the results of the design and development validation and any necessary actions are maintained.

(Control of Design and Development Changes)

Article 36 The manufacturer, etc. shall ensure that the design and development changes are identified and records thereof are maintained.

2. The manufacturer, etc. shall ensure that the changes are reviewed, verified and validated, as appropriate, and approved before the implementation.
3. The manufacturer, etc. shall ensure that the review of the design and development changes includes the evaluation of the effect of the changes on the constituent parts and products already delivered.
4. The manufacturer, etc. shall ensure that the records of the results of the review of the changes specified in preceding Paragraph 2 and any necessary actions are maintained.

(Purchasing Process)

Article 37 The manufacturer, etc. shall establish the documented procedure to ensure that the purchased products conform to the requirements that they specify for the purchased products (hereinafter referred to as “purchased product requirements”).

2. The manufacturer, etc. shall ensure that the type and extent of the control applied to the supplier and the purchased products are dependent upon the effect of the purchased products on subsequent product realisation or the final products.

3. The manufacturer, etc. shall evaluate and select the suppliers based on their ability to supply the products in accordance with the purchased product requirements.
4. The manufacturer, etc. shall ensure that the criteria for the selection, evaluation and re-evaluation are established.
5. The manufacturer, etc. shall ensure that the records of the results of the evaluations specified in preceding Paragraph 3 and any necessary actions arising from the evaluation are maintained.

(Purchasing Information)

Article 38 The manufacturer, etc. shall ensure that the information on the purchased products (hereinafter referred to as “purchasing information”) describes the products to be purchased, including the following items where appropriate.

- (1) The requirements for the approval of the purchased products, procedures, processes and equipment,
 - (2) The requirements for the qualification of the personnel,
 - (3) The quality management system requirements, and
 - (4) Other information necessary for the purchased products.
2. The manufacturer, etc. shall ensure the adequacy of the purchased product requirements prior to their communication to the supplier.
 3. The manufacturer, etc. shall maintain, to the extent required for the traceability given in the documented procedure in accordance with the provision of Paragraph 2 of Article 48, relevant purchasing information, i.e. documents and records.

(Verification of Purchased Products)

Article 39 The manufacturer, etc. shall establish and implement the inspection or other activities necessary for ensuring that the purchased products meet the specified purchase requirements.

2. Where the manufacturer, etc. or their customer intends to perform the verification at the supplier's premises, the manufacturer, etc. shall state the intended verification arrangements and method of the product release in the purchasing information specified in preceding Article.
3. The manufacturer, etc. shall maintain the records of the verification specified in preceding Paragraph 2.

(Control of Production and Service Provision)

Article 40 The manufacturer, etc. shall plan and carry out the production and service

provision under the controlled conditions including the following, as applicable.

- (1) The availability of the information that describes the characteristics of the products,
 - (2) The availability of the documented procedure, documented requirements, work instructions, and reference materials and reference measurement procedures as necessary,
 - (3) The use of the suitable equipment,
 - (4) The availability and use of the monitoring and measuring devices,
 - (5) The implementation of the monitoring and measurement in accordance with the provisions of Articles 57 to 59,
 - (6) The implementation of the release, delivery and post-delivery activities, and
 - (7) The implementation of the defined operations for labelling and packaging defined in the documented procedure, etc.
2. The manufacturer, etc. shall establish and maintain records for each batch of the products that provides traceability to the extent defined in the documented procedure in accordance with the provision of Paragraph 2 of Article 48 and identifies the amount manufactured and amount approved for distribution.
 3. The batch record established in accordance with the provision of preceding Paragraph 2 shall be verified and approved.

(Cleanliness of Products and Contamination Control)

Article 41 The manufacturer, etc. shall establish the documented requirements for the cleanliness of the products in case where they correspond to the following cases.

- (1) The products are cleaned by the manufacturer, etc. prior to the sterilisation and/or their use,
- (2) The products are supplied non-sterile to be subjected to the cleaning process prior to the sterilisation and/or their use,
- (3) The products are supplied to be used non-sterile and their cleanliness is of significance in use, or
- (4) The process agents are to be removed from the products during the manufacture.

(Installation Activities)

Article 42 If appropriate, the manufacturer, etc. shall, in case where they manufacture the products concerned with the installation-control-required medical devices specified in Paragraph 1 of Article 93 of Enforcement Regulations, establish the documented

requirements which contain the acceptance criteria for installing and verifying the installation of the medical devices.

2. The manufacturer, etc. shall provide the documented requirements for the installation and verification specified in preceding Paragraph 1 to the marketing authorisation holder.

(Servicing Activities)

Article 43 If the servicing is the specified requirement, the manufacturer, etc. shall establish the documented procedure, work instructions and reference materials and reference measurement procedures, as necessary, for performing the servicing activities (hereinafter referred to as “servicing activities”) and verifying that they meet the specified requirements.

2. The manufacturer, etc. shall ensure that the records of the servicing activities carried out by them are maintained.

(Manufacturing Control of Sterile Medical Devices)

Article 44 The manufacturer in the category specified in Item (2) of Paragraph 5 of Article 26 of Enforcement Regulations or the foreign manufacturer in the category specified in Item (2) of Paragraph 4 of Article 36 of Enforcement Regulations (hereinafter collectively referred to as “sterile-medical-device-category manufacturer, etc.”) shall maintain the records of the process parameters for the sterilisation process which was used for each sterilisation lot.

2. The sterile-medical-device-category manufacturer, etc. shall ensure that the sterilisation records specified in preceding Paragraph 1 are traceable to each production lot of the products.
3. The sterile-medical-device-category manufacturer, etc. shall provide and maintain the following infrastructure in addition to those specified in Paragraphs 1 and 2 of Article 24.
 - (1) The buildings and facilities necessary for preventing contamination with dust or microorganisms, according to the manufacturing process of the products, with the proviso that this provision shall not apply in case where the manufacturing facilities, etc. provide equivalent functions,
 - (2) The buildings and facilities for maintaining the degree of cleanliness according to the manufacturing process of the products in the work rooms or controlled work areas (the areas consisting of the work rooms, corridors, etc. that are controlled so as to maintain a uniform quality of cleanliness, and hereinafter referred to as such) where the assembling or packaging operations for the products are conducted,
 - (3) The facilities for supplying water of the quality and quantity necessary for the manufacturing, according to the type of the products and manufacturing process in the work rooms or controlled work areas where the assembling or packaging operations for the products are conducted,

- (4) The sterilisation apparatuses necessary for the manufacturing according to the type of the products, and
- (5) The facilities and equipment necessary for controlling the sterilisation process according to the type of the products.

(Validation of Processes for Production and Service Provision)

Article 45 The manufacturer, etc. shall validate any process for the production and service provision where the resulting output cannot be verified by the subsequent monitoring or measurement. This includes any processes where deficiencies become apparent only after the products are in use or the service has been delivered.

2. The manufacturer, etc. shall ensure that the validation demonstrates the ability of the processes specified in preceding Paragraph 1 to achieve the planned results specified in Paragraph 1 of Article 14.
3. The manufacturer, etc. shall establish the arrangements for the processes which should be validated in accordance with the provision of preceding Paragraph 1 including the following items, as applicable
 - (1) The defined criteria for the review and approval of the processes,
 - (2) The approval of the equipment and the qualification of the personnel,
 - (3) The use of the specific methods and procedures,
 - (4) The requirements for the records specified in Article 9, and
 - (5) The revalidation (conducting the validation again in case where the manufacturing procedure has been changed, etc.).
4. The manufacturer, etc. shall establish the documented procedure for the validation of the application of computer software (and changes to such software and/or its application) for the production and service provision that affect the ability of the products to conform to the specified requirements.
5. The manufacturer, etc. shall ensure that such software applications are validated prior to the initial use.
6. The manufacturer, etc. shall ensure that the records of the validation specified in preceding Paragraphs 1 to 5 are maintained.

(Validation of Sterilisation Process)

Article 46 The sterile-medical-device-category manufacturer, etc. shall establish the documented procedure for the validation of the sterilisation process.

2. The sterile-medical-device-category manufacturer, etc. shall ensure that the sterilisation

processes are validated prior to the initial use.

3. The sterile-medical-device-category manufacturer, etc. shall ensure that the records of the validation of each sterilisation process are maintained.

(Identification)

Article 47 The manufacturer, etc. shall identify the products by suitable means throughout the product realisation.

2. The manufacturer, etc. shall establish the documented procedure for the product identification specified in preceding Paragraph 1.
3. The manufacturer, etc. shall establish the documented procedure to ensure that the products returned to the manufacturer, etc. are identified and distinguished from the conforming products.

(Traceability)

Article 48 The manufacturer, etc. shall establish the documented procedure for the traceability.

2. The manufacturer, etc. shall ensure that the documented procedure specified in preceding Paragraph 1 define the extent of the product traceability and the records required.
3. Where the traceability is the requirement, the manufacturer, etc. shall control and record the unique identification of the products.

(Traceability of Specially Designated Medical Devices)

Article 49 In defining the records required for the traceability, the manufacturer, etc. shall include the records of all the constituent parts, etc. and work environment conditions, if these could cause the products concerned with the specially designated medical devices not to satisfy their specified requirements.

2. The manufacturer, etc. shall ensure that the records of the name and address of the shipping package consignee of the products concerned with the specially designated medical devices are maintained.

(Status Identification)

Article 50 The manufacturer, etc. shall identify the product status with respect to the monitoring and measurement requirements.

2. The manufacturer, etc. shall ensure that the identification of the product status is maintained throughout the production, storage, installation and servicing of the products to ensure that only products that have passed the required inspections and tests (or released under an authorised concession (the permission to use or release the products

that do not conform to the specified requirements after the appropriate verification of the manufacturing control and quality control of the products)) are dispatched, used, or installed.

(Customer Property)

Article 51 The manufacturer, etc. shall identify, verify, protect and safeguard the customer property provided for the use or incorporation into the products.

2. The manufacturer, etc. shall ensure that, if any property of the customer is lost or otherwise found to be unsuitable for use, the details are reported to the customer and records thereof are maintained.

(Preservation of Products)

Article 52 The manufacturer, etc. shall establish the documented procedure or documented work instructions for preserving the conformity of the products (including the identification, handling, packaging, storage and protection) during the internal processing and delivery to the intended destination. The preservation shall also apply to the constituent parts of the products.

2. The manufacturer, etc. shall establish the documented procedure or documented work instructions for the control of the products with the limited shelf life or requiring the special storage conditions.
3. The manufacturer, etc. shall ensure that the special storage conditions specified in preceding Paragraph 2 are controlled and recorded.

(Control of Monitoring and Measuring Devices)

Article 53 The manufacturer, etc. shall determine the monitoring and measurement to be undertaken and the monitoring and measuring devices needed to provide the evidence of the conformity of the products to the determined requirements.

2. The manufacturer, etc. shall establish the documented procedure to ensure that the monitoring and measurement specified in preceding Paragraph 1 can be carried out and are carried out in a manner that is consistent with the monitoring and measurement requirements.
3. Where necessary to ensure valid results, the manufacturer, etc. shall ensure that the measuring equipment meets the following requirements.
 - (1) To be calibrated or verified at the specified intervals, or prior to the use, against the measurement standards traceable to the measurement standards (in case where no such standards exist, the basis used for the calibration or verification shall be recorded),
 - (2) To be adjusted or re-adjusted as necessary,

- (3) To be identified to enable the calibration status to be determined,
 - (4) To be safeguarded from the adjustments that would invalidate the measurement result, and
 - (5) To be protected from damage and deterioration during the handling, maintenance and storage.
4. The manufacturer, etc. shall assess and record the validity of the previous measuring results when the equipment is found not to conform to the requirements.
 5. The manufacturer, etc., in case where they correspond to the case specified in preceding Paragraph 4, shall take appropriate action on the equipment and for any of the products affected.
 6. The manufacturer, etc. shall ensure that the records of the results of the calibration and verification are maintained.
 7. The manufacturer, etc. shall ensure that, when used in the monitoring and measurement of the specified requirements, the ability of the computer software to satisfy the intended application is confirmed prior to the initial use and reconfirmed as necessary.

Section 6 Measurement, Analysis and Improvement

(Measurement, Analysis and Improvement)

Article 54 The manufacturer, etc. shall establish a plan (including determination of the applicable testing procedure, such as the statistical techniques, and the extent of the application) and implement the monitoring, measurement, analysis and improvement processes needed for the following duties.

- (1) To demonstrate the conformity of the products, and
- (2) To ensure the conformity of the quality management system, and to maintain the effectiveness of the quality management system.

(Feedback)

Article 55 As one of the measurements of the performance of the quality management system, the manufacturer, etc. shall monitor the information relating to whether the manufacturer, etc. have met the customer requirements.

2. The manufacturer, etc. shall ensure that the methods for obtaining and using the information specified in preceding Paragraph 1 are determined.
3. The manufacturer, etc. shall establish the documented procedure for the feedback system to provide early warning of the quality problems and for the input into the corrective and preventive action processes.

4. The manufacturer, etc. shall ensure that the review of the experience gained from the post-production phase forms part of the feedback system specified in preceding Paragraph 3.

(Internal Audit)

Article 56 The manufacturer, etc. shall conduct the internal audits at planned intervals to determine whether the quality management system meets the following requirements.

- (1) To conform to the arrangements defined in the product realisation plan, to the requirements of this Ministerial Ordinance and to the quality management system requirements established by the manufacturer, etc., and
 - (2) To be effectively implemented and maintained.
2. The manufacturer, etc. shall ensure that the audit programme is planned, taking into consideration the status and importance of the processes and areas to be audited, as well as the results of the previous audits.
 3. The manufacturer, etc. shall ensure that the audit criteria, scope, frequency and methods are defined.
 4. The manufacturer, etc. shall ensure that the selection of the personnel who conduct the audits (hereinafter referred to as “auditors”) and the conduct of the audits ensures objectivity and impartiality of the audit process.
 5. The manufacturer, etc. shall ensure that the auditors do not audit their own work.
 6. The manufacturer, etc. shall ensure that the responsibilities and requirements for planning and conducting the audits, and for reporting the results and maintaining the records are defined in the documented procedure.
 7. The manufacturer, etc. shall ensure that the management responsible for the area being audited ensures that the actions are taken without undue delay to eliminate the detected nonconformities and their causes and the follow-up activities include the verification of the actions taken and the reporting of the verification results.

(Monitoring and Measurement of Processes)

Article 57 The manufacturer, etc. shall apply suitable methods for monitoring and, where applicable, measurement of the quality management system processes.

2. The manufacturer, etc. shall ensure that the methods specified in preceding Paragraph 1 demonstrate the ability of the processes to achieve the results defined in the plan specified in Paragraph 1 of Article 14.
3. The manufacturer, etc. shall ensure that, when the planned results specified in Paragraph 1 of Article 14 are not achieved, the correction and corrective action shall be taken, as appropriate, to ensure the conformity of the products.

(Monitoring and Measurement of Products)

Article 58 The manufacturer, etc. shall monitor and measure the characteristics of the products to verify that the product requirements have been met.

2. The manufacturer, etc. shall ensure that the monitoring and measurement specified in preceding Paragraph 1 should be carried out at appropriate stages of the product realisation process in accordance with the planned arrangements and documented procedure specified in Item (2) of Paragraph 1 of Article 41.
3. The manufacturer, etc. shall ensure that the evidence of the conformity with the acceptance criteria is maintained.
4. The manufacturer, etc. shall ensure that the records indicate the personnel authorising the release of the products.
5. The manufacturer, etc. shall ensure that the product release and service delivery do not proceed until the arrangements defined in the product realisation plan have been satisfactorily completed.

(Monitoring and Measurement of Specially Designated Medical Devices)

Article 59 The manufacturer, etc. shall record the identity of the personnel performing any inspection or testing specified in preceding Article of the products concerned with the specially designated medical devices.

(Control of Nonconforming Products)

Article 60 The manufacturer, etc. shall ensure that the products which do not conform to the product requirements (hereinafter referred to as “nonconforming products”) are identified and controlled to prevent their unintended use or delivery.

2. The manufacturer, etc. shall ensure that the controls and related responsibilities and authorities for dealing with the nonconforming products are defined in the documented procedure.
3. The manufacturer, etc. shall deal with the nonconforming products by one or more of the following ways.
 - (1) To take actions to eliminate the detected nonconformity,
 - (2) To authorise their use, release or acceptance under the concession, or
 - (3) To take actions to preclude their original intended use or application.
4. The manufacturer, etc. shall ensure that the nonconforming products are accepted by the concession only if the regulatory requirements are met.

5. The manufacturer, etc. shall ensure that the records of the identity of the personnel authorising the concession are maintained.
6. The manufacturer, etc. shall ensure that the records of the nature of the nonconformities and any subsequent actions taken, including the concessions obtained, are maintained.
7. The manufacturer, etc. shall ensure, when the nonconforming products are corrected, that they are subject to re-verification to demonstrate the conformity to the requirements.
8. When the nonconforming products are detected after the delivery or use has started, the manufacturer, etc. shall take actions appropriate to the effects, or potential effects, of the nonconformity.
9. If the products need to be reworked (one or more times), the manufacturer, etc. shall document the rework process in the work instructions that has undergone the same authorisation and approval procedure as the original work instructions.
10. The manufacturer, etc. shall ensure that, prior to the authorisation and approval of the work instructions, a determination of any adverse effect of the rework upon the products is made and documented.

(Analysis of Data)

Article 61 The manufacturer, etc. shall establish the documented procedure to determine, collect and analyse appropriate data (including the data generated as the result of the monitoring and measurement and from other relevant sources) to demonstrate the suitability and effectiveness of the quality management system and to evaluate if improvement of the effectiveness of the quality management system can be made.

2. The manufacturer, etc. shall ensure that the analysis of the data specified in preceding Paragraph 1 provides the information relating to the following items.
 - (1) The feedback collected in accordance with the documented procedure specified in Paragraph 3 of Article 55,
 - (2) The conformity to the product requirements,
 - (3) The characteristics and trends of the processes and products including the opportunities for the preventive actions, and
 - (4) The suppliers.
3. The manufacturer, etc. shall ensure that the records of the results of the analysis of the data specified in preceding two Paragraphs 1 and 2 are maintained.

(Improvement)

Article 62 The manufacturer, etc. shall identify and implement any changes necessary

to ensure and maintain the continued suitability and effectiveness of the quality management system through the use of the quality policy, quality objectives, audit results, analysis of the data, corrective and preventive actions and management review.

2. The manufacturer, etc. shall establish the documented procedure for the issue and implementation of the advisory notices, and shall ensure that such a procedure is capable of being implemented at any time, with the proviso that this provision shall not apply in case where the customer issues and implements the advisory notices, and the manufacturer, etc. shall provide the customer with the information necessary for issuing the advisory notices).
3. The manufacturer, etc. shall ensure that the records of all the customer compliant investigations are maintained.
4. If the investigation specified in preceding Paragraph 3 determines that the activities outside the manufacturer, etc. contributed to the customer compliant, the manufacturer, etc. shall ensure that the relevant information is exchanged between the organisations involved.
5. The manufacturer, etc. shall ensure, if any customer compliant is not followed by the corrective and/or preventive action, that the reason is authorised and recorded.
6. The manufacturer, etc. shall, in case where they become aware of the information on the products specified in Paragraph 2 of Article 253 of Enforcement Regulations, establish the documented procedure to notify such information to the customers.

(Corrective Actions)

Article 63 The manufacturer, etc. shall take the corrective actions which are appropriate to the effects of the nonconformities encountered to eliminate the cause of the nonconformities in order to prevent the recurrence.

2. The manufacturer, etc. shall ensure that the documented procedure is established to define the following requirements.
 - (1) To review the nonconformities (including the customer complaints),
 - (2) To determine the causes of the nonconformities,
 - (3) To evaluate the need for the actions to ensure that the nonconformities do not recur,
 - (4) To determine and implement the actions needed, including, if appropriate, updating the documentation,
 - (5) To record the results of any investigation and of the actions taken , and
 - (6) To review the corrective actions taken and their effectiveness.

(Preventive Actions)

Article 64 The manufacturer, etc. shall determine the preventive actions which are appropriate to the effects of the potential problems to eliminate the causes of the potential nonconformities in order to prevent their occurrence.

2. The manufacturer, etc. shall ensure that the documented procedure is established to define the following requirements.
 - (1) To determine the potential nonconformities and their causes,
 - (2) To evaluate the need for the actions to prevent the occurrence of the nonconformities,
 - (3) To determine and implement the actions needed,
 - (4) To record the results of any investigations and of the actions taken, and
 - (5) To review the preventive actions taken and their effectiveness.

Chapter 3 Manufacturing Control and Quality Control in Manufacturing Sites of Labelling, etc.-Category Medical Device Manufacturers, etc.

(Responsible Engineering Manager)

Article 65 The responsible engineering manager shall conduct the following duties.

- (1) To supervise the duties of the manufacturing control and quality control, to evaluate properly the results of the manufacturing control and quality control, and to decide whether or not releasing the products from the manufacturing site.
 - (2) To conduct the duties specified in Articles 68 and 71
 - (3) To verify that the internal audits have been conducted appropriately based on the documents reported in accordance with the provision of Item (2) Paragraph 1 of Article 70.
2. The labelling, etc.-category medical device manufacturer, etc. shall ensure that the responsible engineering manager can conduct his/her duties without hindrance.

(Documents Concerned with Manufacturing Control and Quality Control)

Article 66 The labelling, etc.-category medical device manufacturer, etc. shall, for each of the products, establish *Seihin Hyojun Sho*, concerned with their duties, describing the following items in each of the manufacturing sites.

- (1) The items concerned with the storing,
- (2) The items concerned with the packaging and labelling,

- (3) The items concerned with the testing, and
 - (4) Other necessary items.
2. The labelling, etc.-category medical device manufacturer, etc. shall, in order to conduct appropriately the duties specified in next Article to Article 72, establish the documented procedure concerned with the manufacturing control and quality control, control of the nonconforming products, corrective actions, internal audits, training, and document and record control in each of the manufacturing sites.

(Manufacturing Control and Quality Control)

Article 67 The labelling, etc.-category medical device manufacturer shall conduct appropriately the following duties in accordance with *Seihin Hyojun Sho* and the documented procedure concerned with manufacturing control and quality control.

- (1) To establish documented work instructions describing the instructions, precautions and other matters necessary for the manufacturing control,
- (2) To conduct the operations in accordance with the documented work instructions specified in preceding Item (1),
- (3) To establish records concerned with manufacturing of the products for each batch for testing,
- (4) To verify, for each batch for testing, that the packaging and labelling materials of the products are proper, and to establish and maintain records concerned with the results of the verification.
- (5) To properly store the products for each batch for testing, and the packaging and labelling materials for each controlled unit to control their receipt and delivery, and to establish and maintain records thereof,
- (6) To properly conduct the testing of the packaging and labelling materials for each controlled unit, and to establish and maintain the records of the testing,
- (7) To conduct the periodical maintenance of the buildings and facilities (including the calibration of the measuring equipment) and to establish and maintain the records of the maintenance,
- (8) To verify that the manufacturing control and quality control are properly conducted as evidenced by the records of the testing, storing and receiving and delivering, and to report in writing the results of the verification to the responsible engineering manager,
- (9) To establish and maintain the records of the manufacturing, testing, storing and receiving and delivering, and
- (10) To conduct other duties necessary for the manufacturing control and quality control.

(Control of Nonconforming Products)

Article 68 The labelling, etc.-category medical device manufacturer, etc. shall ensure that the controls and the responsibilities and authorities of the related departments and personnel for dealing with the nonconforming products are defined in the documented procedure specified in Paragraph 2 of Article 66.

2. The labelling, etc.-category medical device manufacturer, etc. shall have the responsible engineering manager conduct appropriately the following duties in accordance with the documented procedure, etc.
 - (1) To identify and control the nonconforming products to prevent their unintended use or delivery,
 - (2) To deal with the nonconforming products appropriately,
 - (3) To establish and maintain records of the nature of the nonconformities and any subsequent actions taken, and
 - (4) To take actions, when the nonconforming products are detected after the shipment or use has started, appropriate to the effects or potential effects of the nonconformity.

(Corrective Actions)

Article 69 The labelling, etc.-category medical device manufacturer, etc. shall take the corrective actions which are appropriate to the effects of the nonconformities encountered to eliminate the cause of the nonconformities in order to prevent recurrence.

2. The labelling, etc.-category medical device manufacturer, etc. shall define the following matters in the documented procedure for the corrective actions specified in Paragraph 2 of Article 66.
 - (1) To review the nonconformities (including the customer complaints),
 - (2) To determine the causes of the nonconformities,
 - (3) To evaluate the need for the actions to ensure that the nonconformities do not recur,
 - (4) To determine and implement the actions needed, including, if appropriate, updating the documentation,
 - (5) To record the results of any investigation and of the actions taken, and
 - (6) To review the corrective actions taken and their effectiveness.

(Internal Audit)

Article 70. The labelling, etc.-category medical device manufacturer, etc. shall have the person designated beforehand conduct the following duties in accordance with the documented procedure.

- (1) To conduct periodic internal audits on the manufacturing control and quality control of the products in the manufacturing site,
 - (2) To report in writing the results of the internal audits to the responsible engineering manager, and
 - (3) To establish and maintain records on the results of the internal audits.
2. The labelling, etc.-category medical device manufacturer, etc. shall take necessary actions in case where any improvement is needed for the manufacturing control and quality control in accordance with the results of the internal audits specified in preceding Paragraph 1, and establish and maintain records of the actions taken.

(Training)

Article 71 The labelling, etc.-category medical device manufacturer, etc. shall have the person designated beforehand conduct the following duties in accordance with the documented procedure.

- (1) To implement as planned the training concerned with the manufacturing control and quality control for the personnel,
- (2) To report in writing the results of the training to the responsible engineering manager, and
- (3) To establish and maintain records of the implementation of the training.

(Control of Documents and Records)

Article 72 The labelling, etc.-category medical device manufacturer, etc. shall retain at least one copy of the documents specified in this Chapter for the following period (5 years for the documents concerned with the training) from the date of obsolescence, with the proviso that this provision shall not apply to the documents used for the manufacturing or testing of the products in case where they are maintained to be available for the retention period of the records of the products specified in next Paragraph 2.

- (1) 15 years for the products concerned with the specially designated maintenance-control-required medical devices (1 year plus the shelf life, for the products concerned with the medical devices of which shelf life shall be displayed and of which shelf life plus 1 year exceeds 15 years), or
- (2) 5 years for the products concerned with the medical devices other than the specially designated maintenance-control-required medical devices (1 year plus the shelf life, for the products of which shelf life shall be displayed and of which shelf life plus 1 year exceeds 5 years).

2. The labelling, etc.-category medical device manufacturer, etc. shall retain the records specified in this Chapter for the following period (5 years for the records concerned with the training) from the date of the establishment.
 - (1) 15 years for the products concerned with the specially designated maintenance-control-required medical devices (1 year plus the shelf life, for the products concerned with the medical devices of which shelf life shall be displayed and of which shelf life plus 1 year exceeds 15 years), or
 - (2) 5 years for the products concerned with the medical devices other than the specially designated maintenance-control-required medical devices (1 year plus the shelf life, for the products concerned with the medical devices of which shelf life shall be displayed and of which shelf life plus 1 year exceeds 5 years).

Chapter 4 Manufacturing Control and Quality Control in Manufacturing Sites of Biological-origin Medical Device, etc. Manufacturers, etc.

(Infrastructure of Manufacturing Sites of Manufacturers, etc. of Specified Biological-origin Medical Devices, etc.)

Article 73 The manufacturer, etc. of the products concerned with the medical devices which correspond to the specified biological-origin products specified in Paragraph 10 of Article 2 of Law (hereinafter referred to as “specified biological-origin medical devices, etc.”), the medical devices designated by Minister of Health, Labour and Welfare in accordance with the provision of Paragraph 2 of Article 43 of Law, or the cell/tissue-based medical devices (hereinafter collectively referred to as “specified biological-origin medical devices, etc.”) (hereinafter collectively referred to as “specified biological-origin medical device, etc. manufacturers, etc.”) shall meet the following requirements in addition to those specified in Paragraphs 1 and 2 of Article 24 and Paragraph 3 of Article 44.

- (1) To be ensured that the facilities for supplying the distilled water, etc. necessary for manufacturing the products are provided with the structure necessary for preventing contamination of the distilled water, etc. with foreign particulate matter or microorganisms,
- (2) To be ensured that the work areas meet the following requirements,
 - a. Being ensured that the work rooms or controlled work areas, among the work areas, are provided with the buildings and facilities for maintaining the degree of cleanliness according to the manufacturing process,
 - b. Being ensured that the work rooms for the drying operations or sterilising operations for the cleaned containers are exclusively used for such operations, with the proviso that this provision shall not apply in case where

the cleaned containers could not be contaminated,

- c. Being provided with the following facilities in the rooms distinctly segregated from other rooms, with the proviso that this provision shall not apply in case where such facilities are verified not to be necessary for the manufacturing of the products according to the type, manufacturing procedure, etc. of such products,
 - (i) The facilities for storing the microorganisms,
 - (ii) The facilities for keeping the animals for utilising in the manufacturing or testing after inoculation with the microorganisms,
 - (iii) The facilities for treating the animals for utilising in the manufacturing or testing,
 - (iv) The facilities for inoculating the microorganisms into the culture media, etc.,
 - (v) The facilities for cultivating the microorganisms,
 - (vi) The facilities for collecting, inactivating, sterilising, etc., the cultured microorganisms, and
 - (vii) The facilities for disinfecting the equipment and instruments used in the manufacturing and testing.
 - d. Being ensured that the surfaces of the ceilings, walls and floors of the rooms provided with the facilities specified in preceding c.(ii) to (iv) and (vi) are the structure which can be easily cleaned and allow disinfection, and
 - e. Being ensured that the rooms provided with the facilities specified in preceding c. (iv) and (vi) meet the following requirements.
 - (i) Being aseptic rooms, with the proviso that this provision shall not apply in case where such work rooms are provided with the facilities which have functions to allow that the aseptic operations are conducted without hindrance according to the type, manufacturing procedure, etc. of the products, and
 - (ii) Being ensured that the aseptic rooms specified in preceding (i) are provided with the adjoining anterooms exclusively used for the rooms so that the rooms are routinely accessible only through such anterooms, and not being placed the entrances of the anterooms, and not being placed the entrances of the anterooms directly leading to the outside.
- (3) To be ensured that the work areas for the products concerned with the cell/tissue-based medical devices meet the following requirements, and
- a. Being ensured that the areas for receiving and processing the materials, storing the products, etc. are segregated from other areas for manufacturing the products, and
 - b. Being provided the areas for receiving and processing the materials, storing the products, etc. with the buildings and facilities necessary for conducting such operations.
- (4) To be ensured that the areas for manufacturing the products using human blood or

plasma as the materials are distinctly segregated from other areas and provided with the facilities and equipment exclusively used for such manufacturing, with the proviso that this provision shall not apply to the manufacturing process subsequent to the process of inactivating or removing viruses.

(Documents concerned with Manufacturing Control and Quality Control)

Article 74 The biological-origin medical device, etc. manufacturer, etc. shall, in case where they manufacture the products concerned with the biological-origin medical devices, etc., for each of the products, establish *Seihin Hyojun Sho* describing the following items in each of the manufacturing sites.

- (1) The name, essence and property of the objects obtained from humans, animals, plants or microorganisms using as the constituent parts, etc. and their quantities therein, and other specifications,
- (2) The specifications (including the keeping control methods) of the animals utilised in the manufacturing or testing (including the donor animals, and hereinafter referred to as “utilised animals”), and
- (3) Other necessary items.

(Process Control)

Article 75 The biological-origin medical device, etc. manufacturer, etc. shall, in case where they manufacture the products concerned with the biological-origin medical devices, etc., control appropriately the following duties concerned with the process control for such products in accordance with *Seihin Hyojun Sho* and documented procedure, in addition to the duties specified in preceding Article.

- (1) To have the person designated beforehand conduct the following duties according to the details of such duties,
 - a. Taking necessary actions, in case where the materials or products are inactivated or where microorganisms, etc. contained in the materials or products are inactivated or eliminated, for preventing contamination by the materials or products which have not undergone inactivation or elimination,
 - b. Conducting continuous measurement of the items necessary for controlling the manufacturing process such as temperature, hydrogen ion index, etc., in case where biochemical technology such as fermentation, etc. is applied to the manufacturing process,
 - c. Taking necessary actions, in case where the column chromatography apparatuses, etc. are used in the manufacturing process, for preventing contamination of such apparatuses with microorganisms, and to measure endotoxins, where necessary,
 - d. Taking necessary actions, in case where the culture media are continuously supplied to and the cultured broth is continuously discharged from the tanks,

for maintaining the incubation conditions in such incubation tanks during the incubating,

- e. Conducting the validation in the following cases and establishing and maintaining records thereof,
 - (i) The case where the manufacturing of the products concerned with the biological-origin medical device, etc. will newly start at such manufacturing site,
 - (ii) The case where any change will be made in the manufacturing procedure, etc. which seriously affect the quality of the products, or
 - (iii) Other cases where it is deemed to be necessary to conduct the validation for appropriate conduct of the manufacturing control and quality control of the products concerned with the biological-origin medical devices, etc.
- f. Placing as much restriction as possible on the personnel other than those engaged in the manufacturing operations entering the work areas,
- g. Conducting sanitation control of the personnel in accordance with the following requirements,
 - (i) Placing as much restriction as possible on the personnel entering the clean areas or aseptic areas under operation, and
 - (ii) Not allowing the personnel engaged in the manufacturing operations to conduct the duties concerned with the control of the utilised animals (excluding those actually utilised in the manufacturing process).
- h. Conducting sanitation control of the personnel conducting the duties in the clean areas or aseptic areas in accordance with the following requirements,
 - (i) Having the personnel engaged in the manufacturing operations wear clothes, work shoes, caps and masks, which have been disinfected,
 - (ii) Having the personnel undergo medical checkups at intervals not exceeding 6 months in order to verify that they do not suffer from the diseases which could contaminate, with microorganisms, etc., the materials or products, and
 - (iii) Having the personnel declare of any health condition that could contaminate the products or materials with microorganisms, etc. (including when suffering from a skin or hair infectious disease or a cold, when injured, when showing such symptoms as fever or diarrhoea of unknown cause, and hereinafter referred to as such).
- i. Constantly keeping the utilised animals (limited to those which are utilised in the manufacturing, and hereinafter referred to as such in this Item (1)) under proper control, and to physically examine the animals when utilising them so as not to utilise those suffering from communicable diseases nor those otherwise unsuitable for being utilised,
- j. Disposing of all the objects contaminated with microorganisms (limited to those contaminated in the manufacturing process) and the animal carcasses so as not jeopardise the public health and hygiene,

- k. Establishing and maintaining records of the following items concerned with the handling of the strains of the microorganisms for use in the manufacturing,
 - (i) The name of the microorganisms and the number assigned to each of containers thereof;
 - (ii) The date of receipt, and name and address of the person (in case of a corporation, its name and address) who transferred the strains,
 - (iii) The biological property and date of testing, and
 - (iv) The status of the passage.

 - l. Verifying that the raw materials or materials originated in organisms (except plants) that are used in the manufacturing of the products concerned with the biological-origin drugs (hereinafter referred to as “biological-origin raw materials”) are appropriate based on *Seihin Hyojun Sho* of such products, and to establish and maintain records of the results of the verification, and

 - m. Maintaining the information that is provided to be recorded under the rules set forth by Minister of Health, Labour and Welfare, or to conclude a contract with the business that collects the origins of the biological-origin raw materials (hereinafter referred to as “biological-origin raw material origins collectors, etc.”) and to ensure that the information is appropriately maintained by such biological-origin raw materials origins collectors, etc., for the period specified in Items (2) and (3) of Article 30, in case where the biological-origin raw materials are used in the manufacturing of the products concerned with the biological-origin drugs, and
- (2) To establish and maintain records specified in preceding Item (1) **e.**, **l.** and **m.** for each lot.
2. The biological-origin medical device, etc. manufacturers, etc. shall, in case where they manufacture the products concerned with the cell/tissue-based medical devices, control appropriately the following duties concerned with the process control for the products concerned with the cell/tissue-based medical devices in accordance with *Seihin Hyojun Sho* and documented procedure, in addition to the duties specified in preceding Paragraph 1.
- (1) To have the person designated beforehand conduct the following duties according to the details of the duties, and
 - a. Taking actions necessary, in case where they handle the cells or tissue collected from the different donors or donor animals, for preventing such cells or tissue from being mixed up or cross-contaminated,
 - b. Verifying, upon receipt, that the cells or tissue that serve as the raw materials or materials are appropriate, referring to the records of the following items, based on *Seihin Hyojun Sho* of such products, and establishing and maintaining records of the results of the verification,
 - (i) The premises where such cells or tissue was collected,
 - (ii) The date when such cells or tissue was collected,

- (iii) In case where such cells or tissue is originated in humans, the conditions of diagnosing by questioning, testing, etc. the donors for the purpose of donor screening (the process to diagnose the donors by questioning, testing, etc. and to judge whether they are sufficiently qualified for donating cells or tissue as the materials of the products concerned with the cell/tissue-based medical devices),
 - (iv) In case where such cells or tissue is originated in animals, the conditions of receiving the donor animals and the conditions of the testing and keeping control for the donor animals for the purpose of donor screening (the process to test the donor animals and control keeping thereof and to judge whether they are sufficiently qualified for providing cells or tissue as the materials of the products concerned with the cell/tissue-based medical devices),
 - (v) The course of the collecting operations for such cells or tissue, and
 - (vi) Other items necessary for ensuring the quality of the products concerned with the cell/tissue-based medical devices, in addition to the items specified in preceding (i) to (v).
 - c. Taking actions necessary for preventing contamination with microorganisms, etc. in the course of the collection, and to establish records of such actions, in case where the cells or tissue used as the materials are collected from the donor animals,
 - d. Not allowing the personnel, in case where they are applicable to any of the following cases, to conduct the operations in the clean areas or aseptic areas,
 - (i) The case where they are in those health conditions which could contaminate the products or materials with microorganisms, etc., or
 - (ii) The case where they handle the microorganisms, etc. which could contaminate the cells or tissue right before the collecting or processing the cells or tissue.
 - e. Comprehending the names of the shipping consignee premises, shipping date and lot number, and to establish records thereof,
 - f. Taking actions necessary for ensuring the quality of the products during the delivery and to establish records of such actions, and
 - g. To establish records of the keeping control for the donor animals after receipt.
 - (2) To establish and maintain records specified in preceding Item (1) **b.**, **c.**, **f.** and **g.** for each lot, and to establish and maintain records specified in preceding Item (1) **e.** for each product.
3. The biological-origin medical device, etc. manufacturer, etc. shall maintain the records specified in preceding two Paragraphs 1 and 2 in the manner which allows that the series of the records including those of biological-origin raw materials used in the manufacturing and those of the products manufactured using such biological-origin raw materials are verified appropriately.

(Testing)

Article 76 The biological-origin medical device, etc. manufacturer, etc. shall, in case where they manufacture the products concerned with the biological-origin medical devices, etc., control appropriately the duties concerned with the testing of the products concerned with the biological-origin medical devices, etc. in accordance with *Seihin Hyojun Sho* and the documented procedure, in addition to the duties specified in preceding Article.

- (1) To identify appropriately the samples in order to prevent them from being mixed up or cross-contaminated,
- (2) To conduct the testing which is important for the quality control and inapplicable to the final products at the appropriate stage of the manufacturing process,
- (3) To constantly keep the utilised animals (limited to those utilised in testing, and hereinafter referred to as such in this Item(3)) under proper control, and to physically examine the animals when utilising them, so as not to utilise those animals suffering from communicable diseases nor those otherwise unsuitable for being utilised,
- (4) To dispose of all the objects contaminated with microorganisms (limited to those contaminated in the testing processes) and the animal carcasses so as not to jeopardise the public health and hygiene,
- (5) To establish and maintain records of the following items concerned with the handling of the strains of the microorganisms for use in the testing, and
 - a. The name of the microorganisms and the number assigned to each of containers thereof,
 - b. The date of receipt, and the name and address of the person (in case of a corporation, its name and address) who transferred the strains,
 - c. The biological property and the date of the testing, and
 - d. The status of the passage.
- (6) To store a reserve sample in an amount of at least twice of the quantity necessary for the required testing from the products concerned with the specified biological-origin medical devices, etc. specified in Paragraph 10 of Article 10 of Law for each lot (in case where the products are those concerned with the specified biological-origin medical devices which do not constitute a lot, the biological-origin raw materials used in the manufacturing of the products for each manufacturing number of such products corresponding to or for each lot of such biological-origin raw materials) under appropriate conditions for the appropriate period from the date of the manufacturing (in case where the medical devices concerned with the products are the specified biological-origin medical devices, for 10 years plus the shelf life), with the proviso that this provision shall not apply to those products concerned with the specified biological-origin medical devices

which do not constitute a lot and of which reserve sample is stored for such period by the biological-origin raw material origins collectors, etc. under a contract concluded between the manufacturer, etc. and such biological-origin raw material origins collectors, etc. For the products concerned with the specified biological-origin medical devices which constitute a lot, after 3 years (for the products of which shelf life shall be displayed and of which shelf life plus 1 year exceeds 3 years, the shelf life of such products plus 1 year) have passed, storage of the biological-origin raw materials used in the manufacturing of such products may be substituted for storage of the products.

2. The biological-origin medical device, etc. manufacturer, etc. shall, in case where they manufacture the products concerned with the cell/tissue-based medical devices, control appropriately the following duties concerned with the testing of the products concerned with the cell/tissue-based medical devices in accordance with *Seihin Hyojun Sho* and documented procedure, in addition to the duties specified in preceding Paragraph 1.
 - (1) To have the person designated beforehand conduct the testing of the donor animals upon and after receipt and other necessary duties according to the details of such duties, and
 - (2) To establish and maintain records of the duties specified in preceding Item (1).
3. The biological-origin medical device, etc. manufacturer, etc. shall maintain the records specified in preceding two Paragraphs 1 and 2 in the manner which allows the series of the records including those of biological-origin raw materials used in the manufacturing and those of the products manufactured using such biological-origin raw materials are verified appropriately.

(Training)

Article 77 The biological-origin medical device, etc. manufactures, etc. shall, in case where they manufacture the products concerned with the biological-origin medical devices, etc., conduct the following duties in accordance with the documented procedure in addition to the duties specified elsewhere.

- (1) To provide the personnel engaged in the manufacturing or testing of the products concerned with the biological-origin medical devices, etc. with the training in microbiology, medicine, veterinary medicine, etc., and
- (2) To provide the personnel engaged in the operations in the aseptic areas or the areas, etc. where the pathogenic microorganisms are handled, with training for taking actions necessary for preventing contamination with microorganisms.

(Control of Documents and Records)

Article 78 The biological-origin medical device, etc. manufacturers, etc. shall retain at least one copy of the documents specified in this Chapter for the following period (5 years for the documents concerned with the training) from the date of obsolescence, with the proviso that this provision shall not apply to the documents used for the manufacturing or testing of the products in case where they are maintained to be

available for the retention period of the records of the products specified in next Paragraph 2.

- (1) 30 years plus the shelf life of the products concerned with the specified biological-origin medical devices or the biological-origin medical devices manufactured using human blood as the origins of the biological-origin raw materials (the origins of the raw materials or materials used in the manufacturing (including those used in the manufacturing process, and hereinafter referred to as such)), or
 - (2) 10 years plus the shelf life for the products concerned with the biological-origin medical devices (excluding those specified in preceding Item (1)) or the cell/tissue-based medical devices (excluding those specified in preceding Item (1)).
2. The biological medical device, etc. manufacturer, etc. shall retain the records specified in this Chapter for the period specified in preceding Item (1) or (2) of preceding Paragraph 1 (5 years for the records concerned with the training) from the date of the establishment.

(Exceptions to Retention of Records)

Article 79 The biological-origin medical device, etc. manufacturer, etc. shall, for the products concerned with the biological-origin medical devices designated by Minister of Health, Labour and Welfare, notwithstanding the provision of this Chapter, retain the records specified in this Chapter for the period designated by Minister of Health, Labour and Welfare, with the proviso that this provision shall not apply in case where the record are maintained appropriately by the biological-origin raw material origins collectors, etc. for such period under a contract concluded between the manufacturer, etc. and such biological-origin raw material origins collectors, etc.

Chapter 5 Manufacturing Control and Quality Control in Manufacturing Sites of In-Vitro Diagnostic Reagents Manufacturers, etc.

(Provisions to be Applied *Mutatis Mutandis*)

Article 80 For the manufacturing control and quality control in the manufacturing site of the in-vitro diagnostic reagents manufacturer, etc., the provisions of Chapter 2 and Chapter 3 (excluding Items (1) and (2) of Paragraph 4 of Article 8, Items (1) and (2) of Paragraph 3 of Article 9, Paragraph 2 of Article 24, Article 42, Article 44, Article 46, Article 49, Article 59, Items (1) and (2) of Paragraph 1 of Article 72 and Items (1) and (2) of Paragraph 2 of article 72) shall be applied *mutatis mutandis*. In this case, “other than both the specially designated medical devices specified in Paragraph 1 of Article 77-5 of Law and the medical devices designated by Minister of Health, Labour and Welfare as those of which design and development (hereinafter referred to as “design and development”)” in Paragraph 1 of Article 4 shall read “designated by Minister of Health, Labour and Welfare as those of which design and development”, “defines the complete manufacturing process concerned with the products of the manufacturing site and, if applicable, the installation specified in Paragraph 1 of Article 42 and the

servicing specified in Paragraph 1 of Article 43” in Paragraph 3 of Article 6 shall read “defines the complete manufacturing process concerned with the products of the manufacturing site”, “for the following period (5 years for the QMS documents concerned with the training)” in Paragraph 4 of Article 8 shall read “for 5 years (1 year plus the shelf life, for the products concerned with the in-vitro diagnostic reagents of which shelf life shall be displayed and of which shelf life plus 1 year exceeds 5 years, except those concerned with the training)”, “for the following period (5 years for the records concerned with the training)” in Paragraph 3 of Article 9 shall read “for 5 years (1 year plus the shelf life, for the products concerned with the in-vitro diagnostic reagents of which shelf life shall be displayed and of which shelf life plus 1 year exceeds 5 years, except those concerned with the training)”, “responsible engineering manager specified in Paragraph 5 of Article 17 of Law” in Article 16 shall read “drug manufacturing manager specified in Paragraph 3 of Article 17 of Law”, “responsible engineering manager” in same Article shall read “manufacturing manager”, “Paragraph 2” in Paragraph 6 of Article 62 shall read “Paragraph 1”, “responsible engineering manager” in Article 65 shall read “manufacturing manager”, “responsible engineering manager” in Article 67 shall read “manufacturing manager”, “responsible engineering manager” in Article 68 shall read “manufacturing manager”, “responsible engineering manager” in Article 70 shall read “manufacturing manager”, “responsible engineering manager” in Article 71 shall read “manufacturing manager”, “for the following period (5 years for the documents concerned with the training)” in Paragraph 1 of Article 72 shall read “for 5 years (1 year plus the shelf life, for the products concerned with the in-vitro diagnostic reagents of which shelf life shall be displayed and of which shelf life plus 1 year exceeds 5 years, except those concerned with the training)”, “for the following period (5 years for the records concerned with the training)” in Paragraph 2 of Article 72 shall read “for 5 years (1 year plus the shelf life, for the products concerned with the in-vitro diagnostic reagents of which shelf life shall be displayed and of which shelf life plus 1 year exceeds 5 years, except those concerned with the training)”.

Supplementary Provisions

(Enforcement Date)

Article 1 This Ministerial Ordinance shall come into effect on 1 April 2005.

(Transitional Measures)

Article 2 Medical Device Manufacturing Control and Quality Control Regulations (MHW Ministerial Ordinance No. 40, 1995) shall expire on 31 March 2005, with the proviso that this provision shall not apply to the case which the authorisation specified in Article 13, the approval specified in Article 14, or the certification specified in Paragraph 1 of Article 23-2 of Law is deemed to be given in accordance with the provisions of the supplementary provisions of Law to Revise the Pharmaceutical Affairs Law and Bleeding and Blood Donor Supply Service Control Law (Law No. 96, 2002) or the supplemental provisions of Cabinet Order Concerning the Organisation of Related Cabinet Order Pursuant to Implementation of Law to Revise Pharmaceutical Affairs Law and Bleeding and Blood Donor Supply Service Control Law (Cabinet Order No. 535, 2003).

Article 3 Medical Device Import and Distribution Control and Quality Control Regulations (MHW Ministerial Ordinance No. 63, 1999) shall expire on 31 March

2005.

Article 4 For 2 years from the date of enforcement of this Ministerial Ordinance, the provisions of Section 3 of Chapter 2 (excluding Article 15), Section 5 of Chapter 2 (limited to Paragraphs 5 and 6 of Article 26, Articles 27 to 36, Paragraphs 4 and 5 of Article 37, Article 41, Article 45 (excluding those concerned with the sterilisation process), Article 47, Article 50 and Article 51), and Section 6 of Chapter 2 (limited to Articles 57, 61 and 64) (including the case where these provisions are applied *mutatis mutandis* under Chapter 5).