Ordinance of the Ministry of Health, Labour and Welfare No. 135 of 2004 Ministerial Ordinance on Standards for Post-Marketing Safety Management of Pharmaceuticals, Quasi-Drugs, Cosmetics, Medical Devices and Regenerative Medicine Products

Pursuant to Article 12-2, item (ii) of the Pharmaceutical Affairs Act (Act No. 145 of 1960), the Ministerial Ordinance on Standards for Post-Marketing Safety Management of Pharmaceuticals, Quasi-Drugs, Cosmetics and Medical Devices is established as follows

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Chapter I General Provisions

(Purpose)

Article 1 This Ministerial Ordinance shall apply mutatis mutandis to the provisions of the Act on Quality, Efficacy and Safety Assurance of Pharmaceuticals, Medical Devices, etc. (Act No. 145 of 1960, hereinafter referred to as the "Act"). Hereinafter referred to as the "Act"). Article 12-2, paragraph (1), item (ii), Article 23-2-2, paragraph (1), item (ii), and Article 23-21, paragraph (1), item (ii) (hereinafter referred to as "post-marketing safety management") Article 23-2-2, paragraph (1), item (ii) and Article 23-21, paragraph (1), item (ii) (hereinafter referred to as "post-marketing safety management") shall be established by an Ordinance of the Ministry of Health, Labour and Welfare.

(Definition)

Article 2 The term "safety management information" as used in this Ministerial Ordinance means information concerning the quality, efficacy and safety of pharmaceutical products, quasi-drugs, cosmetics, medical devices or regenerative medical products (hereinafter referred to as "pharmaceutical products, etc.") and other information necessary for the proper use of pharmaceutical products, etc. Article 2 The term "safety management information" as used in this Ministerial Ordinance means matters concerning the quality, efficacy and safety of pharmaceutical products, quasi-drugs, cosmetics, medical devices or regenerative medical products (hereinafter referred to as "drugs, etc.") and other information necessary for the proper use of drugs, etc.

2 The term "safety assurance operations" as used in this Ministerial Ordinance means operations related to the collection and examination of safety management information and necessary measures based on the results thereof (hereinafter referred to as "safety assurance measures"), among operations related to post-marketing safety management.

3 The term "drug risk management" as used in this Ministerial Ordinance shall mean, among the safety assurance operations, the management of the risks associated with pharmaceutical products (excluding in vitro diagnostic products). The same shall apply hereinafter). 3. The term "drug risk management" as used in this Ministerial Ordinance means, among the services for ensuring safety, the services for ensuring safety of a pharmaceutical product (excluding in vitro diagnostic products; the same shall apply hereinafter) by a manufacturer and distributor of a pharmaceutical product (excluding in vitro diagnostic products) that has matters to be specifically considered concerning its safety and efficacy, by collecting information, conducting surveys, testing and other activities to minimize risks associated with the use of the pharmaceutical product, and evaluating and taking necessary measures based on the results thereof. (2) The term "drug product" means a drug product for which appropriate risk management pertaining to the safety and efficacy of said drug product is conducted by taking measures, and which is attached as a condition to approval under Article 14, paragraph (1) or Article 19-2, paragraph (1) of the Act, pursuant to the provisions of Article 79, paragraph (1) of the Act.

4 The term "risk management of medical devices, etc." as used in this Ministerial Ordinance means, as part of safety assurance activities, activities by a manufacturer and seller of a medical device or in vitro diagnostic drug, with respect to a medical device or in vitro diagnostic drug that has particular safety and efficacy issues to be considered, to collect information, conduct surveys and tests related to the safety and efficacy of the medical device or in vitro diagnostic drug, and conduct other activities to minimize risks associated with the use of the medical device or in vitro diagnostic drug, as well as to evaluate the results of such activities and take necessary measures based on such evaluation. (2) The manufacturer or distributor shall implement appropriate risk management concerning the safety and efficacy of the medical device or in vitro diagnostic product by conducting activities to minimize risks associated with the use of the medical device or in vitro diagnostic product, and by conducting evaluations based on the results of such activities and taking necessary measures based on such evaluations. Article 23-2-5, paragraph (12) of the Act (including the cases where it is applied mutatis mutandis pursuant to Article 23-2-17, paragraph (5) of the Act) (iii) "Approval" means an approval which is attached as a condition to the approval pursuant to the provision of Article 23-2-5, paragraph (1) or Article 23-2-17, paragraph (1) of the Act pursuant to the provision of Article 23-2-5, paragraph (1) or Article 23-2-17, paragraph (1) of the Act or Article 79, paragraph (1) of the Act.

5 The term "person in charge of drug information" as used in this Ministerial Ordinance means a person whose main duty is to collect and provide safety management information by visiting medical personnel, etc. in order to contribute to the proper use of pharmaceutical products.

6 The term "person in charge of information on medical devices, etc." as used in this Ministerial Ordinance means a person whose main duty is to collect and provide safety management information by visiting medical personnel, etc. in order to contribute to the proper use of medical devices or in vitro diagnostic products.

7 The term "person in charge of information on regenerative medical products" as used in this Ministerial Ordinance means a person whose main duty is to collect and provide safety management information by visiting medical personnel, etc. in order to contribute to the proper use of regenerative medical products.

8 The term "Class I Manufacturer and Distributor" as used in this Ministerial Ordinance means a manufacturer and distributor of pharmaceutical products designated by the Minister of Health, Labour and Welfare as prescribed in Article 49, paragraph (1) of the Act (hereinafter referred to as "prescription pharmaceutical products"). (2) The term "manufacturer and distributor" as used in this Ministerial Ordinance means a manufacturer and distributor of pharmaceutical products (hereinafter referred to as "prescription pharmaceutical products"), highly controlled medical devices or regenerative medical products as prescribed in Article 49, paragraph (1) of the Act.

9 The term "Class II manufacturer and distributor" as used in this Ministerial Ordinance means a manufacturer and distributor of pharmaceutical products, controlled medical devices or in vitro diagnostic products other than prescription pharmaceutical products.

10 The term "Class III manufacturer and seller" as used in this Ministerial Ordinance means a manufacturer and seller of quasi-drugs, cosmetics, or general medical devices.

Chapter II Post-Marketing Safety Management Standards for Class I Manufacturers and Distributors

(Duties of the Chief Manufacturing and Marketing Officer)

Article 3 A Class I manufacturing and marketing business operator shall perform the duties listed in the following items in accordance with the provisions of Article 17, paragraph (2) of the Act, Article 23-2-14, paragraph (2) of the Act, or Article 23-34, paragraph (2) of the Act (hereinafter collectively referred to as a "Chief Marketing Authorization Holder") (2) The same shall apply hereinafter.

(i) Supervise the person responsible for safety management prescribed in paragraph (2) of the following Article.

(ii) Respect the opinion of the person responsible for safety management set forth in the preceding item.

(iii) A person responsible for safety management set forth in item (i) and a person responsible for quality assurance, etc. (meaning a person responsible for quality

assurance prescribed in Article 4, paragraph (3) (including the cases where it is applied mutatis mutandis pursuant to Article 21 of the Ministerial Ordinance Concerning Standards for Quality Management of Pharmaceuticals, Quasi-drugs, Cosmetics and Regenerative Medicine Products (Ministerial Ordinance of the Ministry of Health, Labour and Welfare No. 136 of 2004)) and Article 17, paragraph (3) (including the cases where it is applied mutatis mutandis pursuant to Article 21 of the same Ordinance) (iii) A person responsible for quality assurance prescribed in Article 4, paragraph 3 (including the cases where it is applied mutatis mutandis pursuant to Article 21 of the same Ordinance) and Article 17 of the Ministerial Ordinance Concerning Standards for Manufacturing Control and Quality Control of Medical Devices and In Vitro Diagnostic Drugs (Ministerial Ordinance No. 169 of the Ministry of Health, Labour and Welfare of 2004), and (2) The term "domestic quality business operation manager" means a person in charge of domestic quality business operation prescribed in Article 72, paragraph 1 (including the cases where it is applied mutatis mutandis pursuant to Article 72-3, paragraph 3 of the same Ordinance). The same shall apply hereinafter). (iii) to promote close coordination with other persons responsible for operations pertaining to the manufacture and sale of prescription drugs, highly controlled medical devices, or regenerative medical products.

(iv) Where a Class I Marketing Authority conducts pharmaceuticals risk management or medical devices risk management (hereinafter referred to as "pharmaceuticals risk management") (iii) Where a Class I manufacturing and marketing distributor conducts pharmaceutical risk management or medical device risk management (hereinafter referred to as "pharmaceutical risk management"), a person responsible for post-marketing surveillance, etc. (as prescribed in Article 4, paragraph (1) of the Ministerial Ordinance Concerning Standards for Implementation of Post-Marketing Surveillance and Testing of Pharmaceuticals (Ministerial Ordinance of the Ministry of Health, Labour and Welfare No. 171 of 2004) or Article 4, paragraph (1) of the (A person responsible for post-marketing surveillance, etc. as prescribed in Article 4, paragraph (1) of the Ministerial Ordinance Concerning Standards for Implementation of Post-Marketing Surveillance and Testing of Medical Devices (Ministerial Ordinance of the Ministry of Health, Labour and Welfare No. 171 of 2004) (hereinafter the same shall apply) (The same shall apply hereinafter.) (iii) to ensure close mutual coordination with the person in charge of post-marketing surveillance, etc. (hereinafter the same shall apply).

(Organization and staff related to safety assurance operations)

Article 4 A Class I manufacturing and marketing business operator shall establish a department (hereinafter in this Chapter referred to as the "Safety Management Control Department") pertaining to the control of safety assurance operations that satisfies the following requirements Article 4 A Class I manufacturing and marketing business operator shall establish a department (hereinafter in this chapter referred to as the "Safety Management Control Department") pertaining to the control of safety assurance operations that meets the following requirements

(i) Under the supervision of a general manufacturing and marketing manager.

(ii) Have sufficient personnel who are capable of performing safety assurance work (excluding work to be performed by persons other than the person in charge of safety management pursuant to the provision of paragraph (4)) in a proper and smooth manner. (iii) The applicant shall have sufficient number of personnel who are capable of properly and smoothly performing safety assurance work (excluding work to be performed by a person other than a safety manager pursuant to paragraph (4)).

(iii) independent from divisions related to the sale of pharmaceutical products and other divisions that may hinder the proper and smooth performance of safety assurance operations; and

2 A Class I manufacturing and marketing business operator must appoint a person in charge of safety assurance operations (hereinafter in this Chapter referred to as a "safety management representative") who satisfies the following requirements (i) A person in charge of safety management who satisfies the following requirements (hereinafter in this chapter referred to as "Safety Management Manager")

(i) The person in charge of the Safety Management Control Division.

(ii) A person who has been engaged in safety assurance work or other similar work for at least three years.

(**iii) The applicant** must have the ability to properly and smoothly perform the safety assurance services.

(iv) the person is not a member of a department pertaining to the sale of pharmaceuticals, etc., and is not otherwise likely to hinder the proper and smooth performance of the services for ensuring safety.

(3) Except in the cases prescribed in the following paragraph, a Class I manufacturing and marketing business operator must have a person responsible for safety management perform safety assurance duties.

4 A Class I manufacturing and marketing business operator shall perform safety

assurance operations, which are defined in the Ordinance for Enforcement of the Act on Quality, Efficacy and Safety Assurance of Pharmaceuticals, Medical Devices, etc. (Ordinance of the Ministry of Health and Welfare No. 1 of 1961, hereinafter referred to as the "Ordinance"). (hereinafter referred to as the "Regulations"). (2) In the case of having a person other than a person responsible for safety management perform all or part of the tasks listed in each item of Article 97, each item of Article 114-59, or each item of Article 137-59, a person responsible for implementation of said tasks (hereinafter referred to as "person responsible for safety management implementation") who is capable of performing said tasks appropriately and smoothly shall be appointed.

(Post-marketing safety management operational procedures, etc.)

Article 5 A Class I manufacturing and marketing business operator shall prepare a post-manufacturing and marketing safety management operational procedure document that describes the following procedures in order to properly and smoothly conduct post-manufacturing and marketing safety management.

(i) Procedures for collecting safety management information

(ii) Procedures for reviewing safety management information and formulating safety assurance measures based on the results of such review

(iii) Procedures for implementation of safety assurance measures

(iv) Procedures for reporting from the Safety Management Manager to the General Manufacturing and Marketing Manager

(v) Procedures for reporting from the Safety Management Implementation Manager to the Safety Management Manager

(vi) In the case where a Class I manufacturer or distributor conducts risk management of pharmaceuticals, etc., procedures concerning risk management of pharmaceuticals, etc. (in the case where a drug risk management plan as prescribed in Article 9-2(1)(i) is based on a drug risk management plan as prescribed in Article 10(1), including procedures concerning said immediate post-marketing surveillance)

(vii) in the case where a Class I manufacturing and marketing agent conducts a post-marketing surveillance prescribed in Article 10, paragraph (1) as applied mutatis mutandis pursuant to Article 10-2, the procedure concerning the post-marketing surveillance

(viii) Procedures for self-inspection

(ix) Procedures for education and training for persons engaged in operations related to post-marketing safety management

(x) Procedures for the preservation of records pertaining to operations related to post-marketing safety management

(xi) Procedures for mutual coordination with quality assurance managers, etc. and other persons responsible for operations pertaining to the manufacture and sale of prescription drugs, highly controlled medical devices, or regenerative medical products

(xii) In cases where a Class I manufacturer/distributor conducts risk management of pharmaceutical products, procedures for mutual coordination with the person responsible for post-marketing surveillance, etc.

(xiii) Other procedures necessary to properly and smoothly conduct operations related to post-marketing safety management

2 A Class I manufacturing and marketing distributor must appropriately establish in writing the responsibilities and management system of persons engaged in work related to post-marketing safety management.

(3) A Class I manufacturing and marketing distributor must have a person responsible for general manufacturing and marketing or a person responsible for safety management establish in writing the matters necessary for proper and smooth implementation of safety ensuring operations.

(4) When a Class I manufacturer/distributor has prepared or revised the procedure manual referred to in paragraph (1) or the document referred to in paragraph (2), he/she shall record the date in said procedure manual or document and preserve it.

(5) A Class I manufacturer or distributor shall, when the person in charge of general manufacturing and marketing or the person in charge of safety management prepares or revises the document set forth in Paragraph 3, have the date recorded on said document and have it preserved.

(6) A Class I manufacturing and marketing distributor shall have the procedure manuals set forth in Paragraph 1, documents set forth in Paragraphs 2 and 3, documents concerning the safety of prescription drugs, highly controlled medical devices, or regenerative medical products handled by the marketing manager, and other documents necessary for safety assurance operations (hereinafter in this chapter referred to as "post-marketing safety management procedure manuals, etc.") at the office where the marketing manager performs his/her duties. (hereinafter in this chapter referred to as "post-marketing safety management procedure manuals, etc.").

(Duties of the Safety Manager)

Article 6 A Class I manufacturing and marketing business operator shall have a person responsible for safety management perform the following duties in accordance with the Post-Marketing Safety Management Operational Procedures, etc.

(i) Supervise safety assurance operations.

(ii) Confirm that safety assurance operations are being performed properly and smoothly, and prepare and preserve records of such operations.

(**iii)** When it is deemed necessary for safety assurance operations, to state its opinions in writing to the Chief Marketing Authority and retain a copy of such opinion.

(iv) When a Class I manufacturer/distributor conducts risk management of pharmaceutical products, etc., it shall cooperate closely with the person responsible for post-marketing surveillance, etc. so that said risk management of pharmaceutical products, etc. is conducted appropriately.

(Collection of safety management information)

Article 7 A Class I manufacturing and marketing business operator shall have a person responsible for safety management or a person responsible for safety management implementation collect the following safety management information in accordance with the Post-Marketing Safety Management Operational Procedures, etc. and have the person responsible for safety management prepare records thereof.

(i) Information from medical professionals

(ii) Information on conference reports, literature reports, and other research reports

(iii) Information from the Ministry of Health, Labour and Welfare and other government agencies, prefectures and the Pharmaceuticals and Medical Devices Agency

(iv) Information from foreign governments, foreign corporations, etc.

(v) Information from other manufacturers and distributors, etc.

(vi) Other safety management information

(2) When having the Safety Management Implementation Manager perform the duties prescribed in the preceding paragraph, the Class I Manufacturer/Distributor must have the Safety Management Implementation Manager report the records of the preceding paragraph to the Safety Management Manager in writing.

(3) A Class I manufacturer or distributor must have the safety manager retain the records collected or reported pursuant to the preceding two paragraphs.

(Examination of safety management information and planning of measures to ensure safety based on the results of such examination)

Article 8 A Class I manufacturing and marketing business operator must have a person responsible for safety management perform the following duties in accordance with the Post-Marketing Safety Management Operational Procedures, etc.

(i) review without delay the safety management information collected pursuant to the preceding Article and Article 10, and record the results of such review

(ii) In cases where the safety management information set forth in the preceding item is deemed necessary to be understood by the Quality Assurance Manager, etc., the safety management information shall be provided in writing to the Quality Assurance Manager, etc. without delay.

(iii) if it is found necessary as a result of the review under item (i), to formulate safety assurance measures such as discarding, recalling, suspending sales, changing the attached documents or information on precautions, etc., providing information to medical personnel by a person in charge of drug information, a person in charge of information on medical devices, etc. or a person in charge of information on regenerative medicine products, or reporting to the Minister of Health, Labor and Welfare under the Act; and (2) Planning of safety assurance measures

(iv) Report in writing to the Chief Marketing Authorities on the proposed safety assurance measures (hereinafter referred to as "proposed safety assurance measures" in this chapter) developed pursuant to the provisions of the preceding item, and keep a copy of the report. (iv) Report in writing to the Chief Marketing Authority on the proposed safety assurance measures (hereinafter referred to as "proposed safety assurance measures" in this chapter) developed pursuant to the preceding item, and retain a copy of the report.

(2) In cases where a Class I manufacturer or distributor has its Safety Management Implementation Manager perform the analysis necessary for the examination set forth in item (i) of the preceding paragraph in accordance with the Post-Marketing Safety Management Operational Procedures, etc., the Class I manufacturer or distributor must have its Safety Management Implementation Manager perform the following tasks.

(i) Instruct the person responsible for safety management implementation in writing and retain a copy of the instructions.

(ii) Have the person in charge of safety management implementation prepare the records, report them in writing to the person in charge of safety management, and preserve them.

(Implementation of safety assurance measures)

Article 9 A Class I manufacturing and marketing business operator must have a general manufacturing and marketing manager perform the following duties in accordance with the Post-Marketing Safety Management Operational Procedures, etc.

(i) Properly evaluate proposed safety assurance measures, determine safety assurance measures, and prepare and preserve records of these measures.

(ii) When having the person in charge of safety management implement the safety assurance measures, give written instructions on the implementation of the measures and have the instructions preserved.

(**iii)** When having the person in charge of safety management implementation take safety assurance measures, to instruct the person in writing on the implementation of the measures and to have the person in charge of safety management retain a copy of the instructions.

(iv) When having the person in charge of safety management implementation take safety assurance measures, have said person in charge of safety management implementation prepare a record of such measures, report it in writing, and have a copy of the record delivered to the person in charge of safety management implementation.

(v) Confirming the report pursuant to the preceding item and item (iv) of the following paragraph, and deciding on necessary measures.

2 A Class I manufacturing and marketing business operator must have a person responsible for safety management perform the following duties in accordance with the Post-Marketing Safety Management Operational Procedures, etc.

(i) take safety assurance measures based on the instructions of the marketing authorization holder as prescribed in the preceding paragraph, and prepare and preserve records of such measures; and

(ii) In the case of having the person responsible for safety management implementation take safety assurance measures, instructions for implementation shall be given in writing and a copy of the instructions shall be retained.

(**iii**) When having the person in charge of safety management implementation take safety assurance measures, have said person in charge of safety management implementation prepare a record of such measures, report it in writing, and preserve it.

(iv) Report the results of the implementation of safety assurance measures, etc., in writing to the Chief Marketing Authority, and retain a copy of the report.

(v) preserve a copy of item (iv) of the preceding paragraph.

(3) A Class I manufacturer and seller may have a safety manager perform the duties prescribed in paragraph (1) item (i) with regard to proposed safety assurance measures that are specified in advance in the Operational Procedures for Post-Marketing Safety Management, etc. in place of a general manufacturing and marketing manager. In this case, the necessary matters for the duties prescribed in the preceding two paragraphs shall be specified in advance in the Post-Marketing Safety Management Operational Procedures, etc.

(Drug Risk Management)

Article 9-2 A manufacturer and distributor of a prescription drug shall, when conducting drug risk management, have a general manufacturing and marketing manager or a safety manager perform the following duties

(i) For each drug risk management it conducts, a written plan (hereinafter referred to as a "drug risk management plan") that describes the following matters (i) A written plan (hereinafter referred to as the "Pharmaceutical Risk Management Plan") shall be prepared for each pharmaceutical risk management to be conducted.

(a) Matters to be particularly considered with respect to the safety and efficacy of pharmaceutical products

(b) A summary of information collection, investigations or tests on the safety and efficacy of a pharmaceutical product (including a summary of the information that a manufacturer and seller of a prescription pharmaceutical product has obtained from a post-marketing surveillance, etc. (meaning post-marketing surveillance, etc. prescribed in Article 2, paragraph 1 of the Ministerial Ordinance on Standards for the Implementation of Post-Marketing Surveillance and Testing of Pharmaceutical Products; the same shall apply hereinafter in this paragraph b). The same shall apply hereinafter in this paragraph (b)).

(c) Outline of activities to minimize risks associated with the use of pharmaceutical products

(d) Status of implementation and timing of evaluation of pharmaceutical risk management

(e) Other necessary matters

(ii) revise the drug risk management plan when it is deemed necessary for the implementation of drug risk management.

(**iii) When a** drug risk management plan is prepared or revised in accordance with the preceding item, the date of the revision shall be noted in the drug risk management plan and the plan shall be preserved.

(2) A manufacturer and distributor of a prescription drug shall keep a copy of the drug risk management plan at the office where the chief marketing authorization holder performs his/her duties and shall keep a copy of the items described in the drug risk management plan pertaining to the items for which he/she is responsible at other offices where drug risk management is performed. (2) The office shall not be responsible for the following

(3) The manufacturer and seller of a prescription drug shall, in accordance with the Post-Marketing Safety Management Operational Procedures, etc. and the Drug Risk Management Plan, have the person responsible for safety management conduct drug risk management (excluding the conduct of investigations and tests pertaining to the safety and efficacy of the drug). (3) A manufacturer and distributor of a prescription drug shall have the safety management representative perform the following duties in addition to the duties prescribed in paragraph (1).

(i) Confirming that pharmaceutical risk management is being carried out properly and smoothly.

(ii) Prepare and maintain records related to the implementation of pharmaceutical risk management.

4 In cases where a manufacturer and seller of a prescription drug has a safety management supervisor perform the tasks listed in each item of Article 97 of the Regulations in drug risk management in accordance with the Post-Marketing Safety Management Operational Procedures, etc. and the drug risk management plan, the manufacturer and seller of the prescription drug shall have the safety management supervisor make a record of such tasks, report it in writing to the safety management supervisor, and have the safety management supervisor retain the record. (2) When having the Safety Management Executives perform the duties listed in each item of Article 97 of the Regulations, the Safety Management Executives

shall have the Safety Management Executives prepare the records, report them in writing to the Safety Management Executives, and have the Safety Management Executives retain them.

(Risk Management of Medical Devices)

Article 9-3 A manufacturer and seller of an Advanced Controlled Medical Device shall, when conducting risk management of medical devices, etc., have a Chief Marketing Authorization Holder or a Safety Management Officer perform the following duties

(i) A written plan (hereinafter referred to as ″medical device risk management plan″) that describes the following matters for each medical device risk management to be conducted (i) A written plan that describes the following matters (hereinafter referred to as the ″Medical Device Risk Management Plan″) for each risk management of medical devices, etc. to be conducted

(a) Matters to be specifically considered with respect to the safety and efficacy of medical devices

(b) An outline of information collection, investigations or tests on the safety and efficacy of the medical device (including a summary of the information that the manufacturer or seller of the highly controlled medical device has obtained through post-marketing surveillance, etc. (meaning post-marketing surveillance, etc. prescribed in Article 2, paragraph 1 of the Ministerial Ordinance on Standards for Implementation of Post-Marketing Surveillance and Testing of Medical Devices; the same shall apply hereinafter in this b). The same shall apply hereinafter in this paragraph (b)).

(c) Outline of activities to minimize risks associated with the use of medical devices

(d) Status of implementation and timing of evaluation of risk management of medical devices, etc.

(e) Other necessary matters

(ii) revise the risk management plan for medical devices, etc., when it is deemed necessary for the implementation of risk management of medical devices, etc.

(**iii) When a** risk management plan for medical devices, etc. is prepared or revised pursuant to the preceding item, the date of the revision shall be noted on the risk management plan for medical devices, etc. and the plan shall be preserved.

(2) A manufacturer and seller of an advanced controlled medical device shall keep a copy of the risk management plan for medical devices, etc. at the office where the Chief Manufacturing and Marketing Officer performs his/her duties, and shall also

keep a copy of the matters described in the risk management plan for medical devices, etc. at other offices where he/she performs risk management for medical devices, etc. that the office is responsible for. (2) A copy of the risk management plan for medical devices, etc. shall be kept at the office in which the person responsible for the business is located.

(3) A manufacturer and seller of an advanced controlled medical device shall, in accordance with the post-marketing safety management operational procedures, etc. and the risk management plan for medical devices, etc., have the person in charge of safety management perform risk management for medical devices, etc. (excluding the implementation of investigations and tests pertaining to the safety and efficacy of medical devices or in vitro diagnostic products). (3) The Minister of Health, Labour and Welfare shall have the chief safety management officers perform the following duties in addition to the duties prescribed in paragraph (1).

(i) Confirming that risk management of medical devices, etc. is conducted properly and smoothly.

(ii) Prepare and preserve records related to the implementation of risk management of medical devices, etc.

(4) A manufacturer and seller of an advanced controlled medical device shall, when having the person responsible for safety management implement the tasks listed in each item of Article 114-59 of the Rules among the risk management of medical devices, etc., based on the post-marketing safety management operational procedures, etc. and the medical device risk management plan, have the person responsible for safety management implement the tasks, prepare records thereof, (2) When having the Safety Management Executor perform the duties listed in each item of Article 114-59 of the Regulations, the Safety Management Executor shall have the Safety Management Execution Manager prepare a record of the duties, report it in writing to the Safety Management Manager, and have the Safety Management Executor retain it.

(Post-marketing surveillance)

Article 10 A manufacturer and seller of a prescription drug shall conduct a post-marketing surveillance (which is conducted for a period of six months after the drug is put on the market to promote the proper use of the drug in medical practice and to promptly identify the occurrence of cases, etc. listed in Article 228-20, paragraph (1), item (i) a, c (1) through (5) and g and item (ii) a of the Regulations). (iii) ″Drug

risk management" means the management of the risk of a drug as a part of drug risk management. (2) In the case where the Minister of Health, Labour and Welfare conducts the following activities (hereinafter the same shall apply in this Article) (2) In cases where the Chief Marketing Authorization Holder or the Safety Management Officer (hereinafter the same shall apply in this Article) performs the following duties, the Chief Marketing Authorization Holder or the Safety Management Officer shall be required to perform the following duties.

(i) For each post-marketing surveillance to be conducted, a written implementation plan (hereinafter referred to as "post-marketing surveillance implementation plan") that describes the following matters based on the drug risk management plan (i) For each post-marketing surveillance to be conducted, a written implementation plan (hereinafter referred to as "post-marketing surveillance implementation plan") shall be prepared based on the drug risk management plan, which shall include the following

(a) Purpose of the post-marketing surveillance

(b) Methods of post-marketing surveillance

(c) Period of conducting post-marketing surveillance

(d) Other necessary matters

(ii) Revise the post-marketing surveillance protocol when deemed necessary for the implementation of the post-marketing surveillance.

(**iii) When a** post-marketing surveillance protocol is prepared or revised pursuant to the preceding item, the date shall be noted on the post-marketing surveillance protocol and it shall be preserved.

(2) The manufacturer and distributor of a prescription drug shall keep a copy of the post-marketing surveillance implementation plan at the office where the Chief Marketing Authority conducts its business and at other offices where the post-marketing surveillance is conducted.

(3) The manufacturer and seller of a prescription drug shall, in accordance with the post-marketing safety management operational procedures, etc., the drug risk management plan, and the post-marketing surveillance implementation plan, have the person responsible for safety management conduct the post-marketing surveillance and shall have the person responsible for safety management perform the following duties in addition to the duties prescribed in paragraph 1

(i) Ensure that the post-marketing surveillance is conducted properly and smoothly.

(ii) Prepare and preserve records related to the implementation of the post-marketing surveillance.

4 In cases where a manufacturer or distributor of a prescription drug has the Safety Administration Manager perform the tasks listed in each item of Article 97 of the Regulations in the immediate post-marketing surveillance in accordance with the Post-Marketing Safety Management Operational Procedures, etc., the drug risk management plan and the post-marketing surveillance implementation plan, the manufacturer or distributor shall have the Safety Administration Manager prepare records thereof, (2) In cases where the Safety Management Execution Manager is requested to perform the tasks listed in each item of Article 97 of the Regulations, the Safety Management Execution Manager shall have the Safety Management Execution Manager prepare the records, report them in writing to the Safety Management Executives, and have the Safety Management Executives preserve them.

(as applied mutatis mutandis)

Article 10-2 The provisions of the preceding Article shall apply mutatis mutandis to a manufacturer and seller of a regenerative medicine product. In this case, the term "Article 228-20(1)(i)(a), (c)(1) to (5) and (g) and (ii)(a) of the Regulations" in paragraph (1) of the preceding Article shall be deemed to be replaced with "Article 228-20(1)(i)(c)(1) to (5) and (4)(i)(a) and (f) and (ii)(a) of the Regulations" and "conducted as drug risk management (2) In the same paragraph, the term "in accordance with Article 23-25, paragraph (1) or Article 23-37, paragraph (1) of the Act" in item (i) shall be deemed to be replaced with "in accordance with a drug risk management plan for each post-marketing surveillance" and the term "in accordance with a drug risk management plan for each post-marketing surveillance" in item (i) of the same paragraph shall be deemed to be replaced with "in accordance with a drug risk management plan for each post-marketing surveillance", in paragraph (3) of the same Article shall be read as "Post-Marketing Safety Management Operational Procedures, etc., Drug Risk Management Plan", "Post-Marketing Safety Management Operational Procedures, etc., Drug Risk Management Plan" in paragraph (4) of the same Article shall be read as "Post-Marketing Safety Management Operational Procedures, etc.", "each item of Article 97 of the Regulations" in paragraph (3) of the same Article shall be read as "Article 137 of the Regulations", and Article 137-59," and "each item of Article 97 of the Regulations" shall be read as "each item of Article 137-59 of the Regulations" in paragraph (4) of the same Article.

(Self-inspection)

Article 11 A Class I manufacturing and marketing business operator must have a person designated in advance conduct periodic self-inspections of the operations related to post-marketing safety management in accordance with the post-marketing safety management operational procedure manual, etc.

(2) When the person designated in advance in the preceding paragraph is the person in charge of safety management, the Class I manufacturing and marketing supplier must have the person in charge of safety management prepare and preserve a record of the self-inspection set forth in the preceding paragraph.

(3) When the person designated in advance in Paragraph 1 is other than the person responsible for safety management, the Class I manufacturer or distributor shall have said person prepare a record of the self-inspection set forth in Paragraph 1, report it in writing to the person responsible for safety management, and have the person responsible for safety management preserve it.

4 The Class I manufacturer or distributor must have the safety manager report the results of the self-inspection in writing to the Class I manufacturer or distributor and the general manufacturing and marketing manager, and retain a copy of the report.

(5) A Class I manufacturing and marketing manager shall have the Chief Manufacturing and Marketing Officer consider the necessity of improving post-marketing safety management based on the results of the self-inspection set forth in Paragraph 1, and if necessary, have him or her take the necessary measures and prepare a record thereof.

6 The Class I manufacturer or distributor must have the person responsible for safety management preserve the records set forth in the preceding paragraph.

(Education and training for those engaged in work related to post-marketing safety management)

Article 12 A Class I manufacturer or distributor must have a general manufacturing and marketing manager prepare and keep an education and training plan.

2 A Class I manufacturer or distributor must have a person designated in advance systematically provide education and training on post-marketing safety management to persons engaged in work related to post-marketing safety management, in accordance with the Operational Procedures for Post-Marketing Safety

Management, etc. and the education and training plan set forth in the preceding paragraph.

(3) When the person designated in advance in the preceding paragraph is the person in charge of safety management, the Class I manufacturer or distributor must have the person in charge of safety management prepare and preserve records of the education and training set forth in the preceding paragraph.

(4) When the person designated in advance in Paragraph 2 is other than the person responsible for safety management, the Class I manufacturer or distributor shall have said person prepare a record of the education and training in Paragraph 2, report it in writing to the person responsible for safety management, and have the person responsible for safety management retain the record.

5 The Class I manufacturer or distributor must have the safety manager report the results of the education and training to the general manufacturing and marketing manager in writing and retain a copy of the report.

Chapter 3 Post-Marketing Safety Management Standards for Class II Manufacturers and Distributors

(Organization and staff related to safety assurance operations)

Article 13 A Type II manufacturer and seller must have sufficient personnel with the ability to properly and smoothly perform safety assurance services.

(2) A Class II manufacturing and marketing business operator must appoint a person in charge of safety assurance operations (hereinafter in this Chapter referred to as a "safety management representative") who satisfies the following requirements (1) A person who is responsible for safety management

(i) The applicant shall have the ability to perform safety assurance services properly and smoothly.

(ii) the person is not a member of a department pertaining to the sale of pharmaceuticals, etc., and is not otherwise likely to hinder the proper and smooth performance of the services for ensuring safety.

3 The department that performs safety assurance tasks (excluding tasks to be performed by persons other than the Safety Management Officer) must be independent from the departments related to the sale of drugs and other departments that may interfere with the proper and smooth performance of safety assurance tasks. (3) The department that performs safety assurance tasks

(excluding tasks to be performed by persons other than the safety management representative) must be independent from the department related to the sale of pharmaceutical products and other departments that may hinder the proper and smooth performance of the safety assurance tasks.

(as applied mutatis mutandis)

Article 14 The provisions of Article 3, Articles 5 to 10 (excluding Article 5 paragraph (1) items (v) and (vii), Article 7 paragraph (2), Article 8 paragraph (2), Article 9 paragraph (2) items (ii) and (iii), Article 9-2 paragraph (4), Article 9-3 paragraph (4) and Article 10 paragraph (4)), Article 11 and Article 12 shall apply mutatis mutandis to a Class II manufacturing and marketing agent. (2) The provisions of Article 3, Article 4, Article 5, Article 6, Article 7, Article 8, Article 9, Article 10, Article 11 and Article 12 shall apply mutatis mutandis. In this case, the term "the Chief Marketing Authorization Holder for Medical Devices, etc. prescribed in Article 23-2-14(2) of the Act or the Chief Marketing Authorization Holder for Regenerative Medicine, etc. prescribed in Article 23-34(2) of the Act" in Article 3 shall be deemed to be replaced with "or the Chief Marketing Authorization Holder for Medical Devices, etc. prescribed in Article 23-2-14(2) of the Act" and the same shall apply to Article 11 and Article 12. The term "Article 9-2, paragraph (1), item (i)" in Article 5, paragraph (1), item (vi) shall be deemed to be replaced with "Article 9-2, paragraph (1), item (i) as applied mutatis mutandis pursuant to Article 14," the term "Article 10, paragraph (1)" shall be deemed to be replaced with "Article 10, paragraph (1) as applied mutatis mutandis pursuant to Article 14," and the term "the Safety Management Manager or the Safety Management Execution Manager" in Article 7, paragraph (1) shall be deemed to be replaced with "the Safety Management Manager or the Safety Management Execution Manager. The term "safety of medical devices" in Article 9-3 paragraph (1) items (a) and (b) shall be deemed to be replaced with "safety of medical devices or in vitro diagnostic drugs," the term "medical devices" in item (c) of the same paragraph shall be deemed to be replaced with "medical devices or in vitro diagnostic drugs," and the term "safety of medical devices" in paragraph (3) of the same Article shall be deemed to be replaced with "safety of medical devices or in vitro diagnostic drugs.

Chapter IV Post-Marketing Safety Management Standards for Class III Manufacturers and Distributors

(as applied mutatis mutandis)

Article 15 The provisions of Article 3, Articles 6 through 9 and Article 13 (excluding Article 7, paragraph (2), Article 8, paragraph (2) and Article 9, paragraph (2), items (ii) and (iii)) shall apply mutatis mutandis to a Class III manufacturing and marketing agent.
(2) The provisions of Article 3 (excluding Article 7, paragraph 2, Article 8, paragraph 2, and Article 9, paragraph 2, items 2 and 3) shall apply mutatis mutandis. In this case, the term "the Chief Marketing Authorization Holder for Medical Devices, etc. prescribed in Article 23-2-14(2) of the Act or the Chief Marketing Authorization Holder for Regenerative Medical Products prescribed in Article 23-34(2) of the Act" in Article 3 shall be deemed to be replaced with "or the Chief Marketing Authorization Holder for Medical Devices, etc. prescribed in Article 23-2-14(2) of the Act," and the term "Article 23-2-14(2) of the Act" in the same Article shall be deemed to be replaced with "Article 23-2-14(2) of the Act. (2) The term "Article 13 paragraph (2) as applied mutatis mutandis pursuant to Article 15" in Article 13 paragraph (2) of the Act shall be deemed to be replaced with "Article 13 paragraph (2) as applied mutatis mutandis pursuant to Article 15," the term "following based on the Post-Marketing Safety Administration Operational Procedures, etc." in Article 6 paragraph (1) shall be deemed to be replaced with "following," the term "following based on the Post-Marketing Safety Administration Operational Procedures, etc." in Article 7 paragraph (1) shall be deemed to be replaced with "following" and the term "a Safety Management Manager or Safety Management Implementation Manager" in Article 7 paragraph (1) shall be deemed to be replaced with "following. In the same paragraph, in item (i), the term "the preceding Article and Article 10" shall be deemed to be replaced with "the preceding Article as applied mutatis mutandis pursuant to Article 15", the term "the person in charge of information on medical devices, etc. or on regenerative medical products" in item (iii) of the same paragraph shall be deemed to be replaced with "the person in charge of information on medical devices, etc.", the term "in accordance with Post-Marketing Safety Management Operation Procedures, etc. and then" in Article 9 paragraph (1) shall be deemed to be replaced with "then" and the term "in accordance with the Post-Marketing Safety Management Operation Procedures, etc." in the same paragraph shall be deemed to be replaced with "then.
(2) The term "a person in charge of safety management implementation" in Article 9, paragraph (1) shall be deemed to be replaced with "a person other than a person in charge of safety management," the term "based on the Post-Marketing Safety

Management Operational Procedures, etc., then" in Article 9, paragraph (2) shall be deemed to be replaced with "then," and the term "Post-Marketing Safety Management Operational Procedures, etc." in paragraph (3) of the same Article shall be deemed to be replaced with "documents".

Chapter V Miscellaneous Provisions

(Preservation of records pertaining to safety assurance operations)

Article 16 The retention period for documents and other records that are to be retained pursuant to the provisions of this Ministerial Ordinance shall be five years from the date on which said records are no longer used. However, the retention period for the following records shall be the periods specified in the respective items.

(i) records pertaining to biological products and regenerative medical products (excluding those listed in the following item and item (iii)) (ii) Records pertaining to biological products and regenerative medical products (excluding those listed in the following item and item (iii)): Ten years from the date of ceasing to be used

(ii) Records pertaining to specified biological products and designated regenerative medical products prescribed in Article 68-7(3) of the Act: 30 years from the date on which they are no longer used

(iii) Records pertaining to Specified Maintenance Managed Medical Equipment and Installed Controlled Medical Equipment prescribed in Article 114-55 paragraph (1) of the Ordinance (excluding those listed in the preceding item) (iii) Records pertaining to specified maintenance management medical devices and installation management medical devices prescribed in Article 114-55 paragraph (1) of the Rules (excluding those listed in the preceding item)

(iv) Self-inspection prescribed in Article 11 (including the cases where it is applied mutatis mutandis pursuant to Article 14) (iv) Records pertaining to self-inspection prescribed in Article 11 (including the cases where it is applied mutatis mutandis in Article 14) and education and training prescribed in Article 12 (including the cases where it is applied mutatis mutandis in Article 14) (v) Records pertaining to self-inspection prescribed in Article 11 (including the cases where it is applied mutatis mutandis in Article 14) and education and training prescribed in Article 12 (including the cases where it is applied mutatis mutandis in Article 14)

(2) Notwithstanding the provisions of this Ministerial Ordinance, a manufacturer and distributor shall not distribute the post-marketing safety management procedure, etc. prescribed in Article 5 (including the cases where it is applied mutatis mutandis pursuant to Article 14) (hereinafter referred to as "post-marketing safety management procedure, etc." in this chapter). 2 Notwithstanding the provisions of this Ministerial Ordinance, a manufacturing and marketing distributor shall preserve records in accordance with the post-manufacturing and marketing safety management operational procedures, etc. prescribed in Article 5 (including cases where it is applied mutatis mutandis pursuant to Article 14) (hereinafter in this chapter referred to as "post-manufacturing and marketing safety management operational procedures, etc."). (2) A manufacturer and seller may have a person designated by the manufacturer and seller preserve said records in place of the person who is required to preserve the records pursuant to this Ministerial Ordinance in accordance with the post-manufacturing and sales safety management operation procedures, etc. prescribed in Article 5 (including cases where it is applied mutatis mutandis pursuant to Article 14).

Supplementary Provisions

This Ministerial Ordinance shall come into effect as from April 1, 2005.

Supplementary Provisions (Ordinance of the Ministry of Health, Labour and Welfare No. 26 of March 11, 2013) (Extract)

(Effective date)

1 This Ministerial Ordinance shall come into effect as from October 1, 2006.

(Transitional measures)

2 The provisions then in force shall remain applicable to the post-marketing surveillance of drugs approved prior to the enforcement of this Ministerial Ordinance.

Supplementary Provisions (Ordinance of the Ministry of Health, Labour and Welfare No. 13 of February 26, 2006)

This Ministerial Ordinance shall come into effect as from April 1, 2006.

Supplementary Provisions (Ordinance of the Ministry of Health, Labour and Welfare No. 87 of July 30, 2006) (Extract)

(Effective date)

Article 1 This Ministerial Ordinance shall come into force as from the date of enforcement of the Act for Partial Revision of the Pharmaceutical Affairs Act, etc. (hereinafter referred to as the "Revised Act"). Article 1 This Ministerial Ordinance shall come into effect as from the date of enforcement of the Act for Partial Revision of the Pharmaceutical Affairs Act, etc. (hereinafter referred to as the "Revised Act") (November 25, 2006).

(Transitional measures in accordance with the partial revision of the Ministerial Ordinance on Standards for Post-Marketing Safety Control of Pharmaceuticals, Quasi-Drugs, Cosmetics and Medical Devices)

Article 9 A programmed highly controlled medical device (meaning a medical device that is a highly controlled medical device program or a recording medium on which the programmed highly controlled medical device program is recorded. The same shall apply hereinafter in this Article).

Supplementary Provisions (Ordinance of the Ministry of Health, Labour and Welfare No. 28 of November 21, 2006)

This Ministerial Ordinance shall come into effect as from the date of promulgation.

Supplementary Provisions (Ordinance of the Ministry of Health, Labour and Welfare No. 44 of March 26, 2007) (Extract)

(Effective date)

Article 1 This Ministerial Ordinance shall come into effect as from the date of promulgation.

Supplementary Provisions (Ordinance of the Ministry of Health, Labour and Welfare No. 80 of July 31, 2007) (Extract)

(Effective date)

Article 1 This Ministerial Ordinance shall come into effect as from the date of promulgation.

Supplementary Provisions (Ordinance of the Ministry of Health, Labour and Welfare No. 124 of November 24, 2007)

This Ministerial Ordinance shall come into effect as from the date of promulgation.

Supplementary Provisions (Ordinance of the Ministry of Health, Labour and Welfare No. 155 of August 31, 2020) (Extract)

(Effective date)

Article 1 This Ministerial Ordinance shall come into effect as from the date of enforcement (September 1, 2020) of the Act for Partial Revision of the Act on Quality, Efficacy and Safety Assurance, etc. of Pharmaceuticals and Medical Devices (Act No. 63 of 2027).

Supplementary Provisions (Ordinance of the Ministry of Health, Labour and Welfare No. 15 of January 29, 2021) (Extract)

(Effective date)

Article 1 This Ministerial Ordinance shall come into force as from the date of enforcement (August 1, 2021) of the provisions of Article 1, item (ii) of the Act for Partial Revision of the Act on Quality, Efficacy and Safety Assurance, etc. of Pharmaceuticals and Medical Devices (hereinafter referred to as "Revised Act"). This Ministerial Ordinance shall come into force as from the date of enforcement of the provisions prescribed in Article 1, item (ii) of the Supplementary Provisions (August 1, 2021).