

Provisional Translation (as of March 2010)*

PFSB/ELD/OMDE (*Yakushokuki*) Notification No. 0216001

February 16, 2005

To: Directors of Health Departments (Bureaus),
Prefectural Governments

From: Director of Office of Medical Devices Evaluation,
Evaluation and Licensing Division,
Pharmaceutical and Food Safety Bureau,
Ministry of Health, Labour and Welfare

Re: Points to Consider When Applying for Marketing Approval for Medical Devices

Handling of applications for approval to market medical devices pursuant to Article 14 and Article 19-2 of the Pharmaceutical Affairs Law (Law No. 145 of 1960; hereinafter referred to as the “Law”) was provided in the PFSB (*Yakushoku*) Notification No. 0216002 of the Director-General of Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare (MHLW), dated February 16, 2005, “Application for Marketing Approval for Medical Devices” (hereinafter referred to as the “Director-General Notification”). You are requested to review detailed information described below on the handling of applications, and to provide the information and give appropriate guidance to relevant organizations and business parties under your jurisdiction.

Please note that copies of this Notification will be sent to the Chief Executive of the Pharmaceuticals and Medical Devices Agency (hereinafter referred to as “PMDA”), the Chairperson of the Japan Federation of Medical Devices Associations, the Chairperson of Medical Devices and Diagnostics Subcommittee of the American Chamber of Commerce in Japan, and the Chairperson of Medical Equipment Committee of Business Conference in Europe.

I. Scope

This Notification applies to medical devices other than those that require a preliminary

* This English version of the Japanese Notification is provided for reference purposes only. In the event of any inconsistency between the Japanese original and the English translation, the former shall prevail.

evaluation for confirmation of the quality and safety of a medical device before proceeding with clinical trials according to the Guidelines for Assurance of Quality and Safety of Drugs and Medical Devices Processed from Cells and Tissues of Human Origin (PMSB [*Iyaku*] Notification No. 1314 of the Director-General of Pharmaceutical and Medical Safety Bureau, dated December 26, 2000).

II. Information on Application Form for Marketing Approval for Medical Devices

Other than those stipulated separately, the following information must be provided in the relevant columns of the application form for marketing approval for medical devices.

1. Category

State the type by referring to Appendix Table 1 of the Cabinet Order for Enforcement of the Law (Cabinet Order No. 11 of 1961; hereinafter referred to as the "Enforcement Order"). When determining which category a medical device belongs to, refer to the Appendix to the Notification issued by the Director-General of Pharmaceutical and Food Safety Bureau, dated July 20, 2004 (Implementation of Specially Controlled Medical Devices, Controlled Medical Devices, and General Medical Devices Designated by the Minister of Health, Labour and Welfare Pursuant to Article 2, Paragraphs 5 through 7 of the Law (Ministerial Notification), and Specially Designated Maintenance and Management Required Medical Devices Designated by the Minister of Health, Labour and Welfare Pursuant to Article 2, Paragraph 8 of the Law [Ministerial Notification]) (hereinafter referred to as the "Classification Notification"). When a single product belongs to multiple categories, select the category of the medical device that is classified into the highest risk class. If the product consists of more than one medical device that is classified into the highest risk class, choose the category based on its primary performance.

2. Name

(1) Provide the generic name of the medical device as defined in the Appendix to Classification Notification. If no generic name applicable to the medical device is found at the time of regulatory submission, leave the column blank. An appropriate generic name to identify the medical device and its classification (e.g., specially controlled medical device) will be established when the medical device for which approval is being sought is actually approved. In this case, provide a summary of the medical device (approximately 300 characters) in the "Remarks" column, and indicate which classification rule, as stipulated in the Classification Notification, is deemed to apply to the medical device.

When more than one generic name is found for a single product, and if there is no single generic name that refers to a multi-purpose device, then state the generic name of the medical device that belongs to the highest risk class. If the product consists of more than one medical device that is classified into the highest risk class, then state the generic name based on its primary performance. In this case, state all the relevant generic names in the “Remarks” column.

- (2) The applicant should not use a brand name that may cause misunderstanding of the performance of the medical device, leading to potential health damage. The applicant should also not use a brand name that may degrade the medical device. Any name that may conjure up other uses is not acceptable.

In principle, only one name should be given per product, but if the applicant intends to apply for approval for a product to be marketed under more than one brand name for a valid reason, documents explaining the reason must be attached to the application form. In this case, the application for marketing approval of the product must be submitted for each brand name.

3. Intended Use and Indications

Properly describe the intended use of the product, including the target patient population and disease, usage conditions, and anticipated results. In addition, state the indications of the product as necessary.

4. Shape, Structure, and Principle

Provide a concrete and detailed description to identify the product, such as by explaining external appearance, structure, principle, components, electrical rating, and function of each component of the medical device. If the medical device represents medical electrical equipment, use a block diagram etc. to explain the principle of how the medical device meets its intended use. If the medical device has auxiliary functions, then explain these functions. If the medical device is in a powder or liquid state, then specify the state for explaining its shape.

If the medical device is used in combination with another medical device that has already been approved or certified, or with a medical device for which a notification has been submitted as stipulated in Article 14-9, Paragraph 1 of the Law (hereinafter referred to as “marketing notification”), then its approval number or certification

number, or marketing notification number and brand name may, in principle, be provided in lieu of the description of the medical device that has already been approved or certified, or for which the marketing notification has already been submitted, provided that the intended use does not deviate from the approved or certified intended use of the medical device or the definition of the generic name applicable to the medical device for which the marketing notification has been submitted.

5. Raw Materials or Components

Accurately describe the raw materials so that their relations with the information provided in the “Shape, Structure, and Principle” column may be clarified, and state their specifications. If any component or material does not come into contact with blood, body fluid, mucosa, etc. (regardless of whether directly or indirectly) and does not have a significant impact on the performance, then concise information will suffice. It is desirable to state the raw materials by reference to the Administrative Notice, dated November 15, 2004 (PFSB/ELD/OMDE No. 19).

If the medical device is used in combination with another medical device that has been approved or certified or with a medical device for which marketing notification has been submitted, then its approval number or certification number, or marketing notification number may, in principle, be provided in lieu of the description of the medical device that has been approved or certified, or for which the marketing notification has been submitted, provided that the intended use does not deviate from the approved or certified intended use of the medical device or the definition of the generic name applicable to the medical device for which the marketing notification has been submitted.

If the raw materials include human or animal tissues or a product derived from these tissues, establish the necessary raw material specifications by taking into account the possibility of infection with pathogens. In particular, specify donor or animal selection method, virus tests, and inactivation method.

In addition, if a bovine-derived material is used, state the country of origin of the raw material, the body part, processing method, and, if necessary, information on TSE data, and other information that is necessary to ensure the quality and safety of the medical device.

If a human- or animal-derived material is used, then describe the source of the raw

material, details of donor screening, and other information that is necessary to ensure the quality and safety of the medical device.

6. Product Specifications

Of the design specifications that are requirements for the product in terms of quality, safety and efficacy, state the information that does not fall under the scope of Shape, Structure, and Principle. This information is specifications to ensure the quality, safety, and efficacy of the relevant product that are obtained primarily from verification at the designing stages. Therefore, specify standards etc. that are required in terms of quality, safety (including physical, chemical, and biological safety), and efficacy (performance and functions). In the case of medical devices for which a standard is separately notified by MHLW per generic name, the devices are evaluated by confirming their conformity to the applicable standard (hereinafter referred to as "approval standard"). If the product for which approval is sought falls under one of those medical devices, then state the product specifications corresponding to the requirements and the order of the approval standard. If there are specifications that do not conform to the approval standards or those that are not established in the approval standards, clearly state these specifications.

If there are no standards or criteria applicable to a medical device, then also specify the testing method. In this case, also include important standards, specifications, etc. to which conformity must be verified during the manufacturing process. For example, if a medical device is released to the market after sterilization, then the sterilization validation standards for sterility assurance must be included.

7. Operation or Usage Method

Describe the operation or usage method in sequence to facilitate understanding, for example, by using illustrations as necessary. If the product is non-sterilized and requires sterilization before use, make a note to that effect, and describe the sterilization method and conditions (including chemicals and gases).

If the product is used in combination with another product, then explain how the two products are operated together.

If the medical device is intended to be used repeatedly after re-sterilization, then make a note to that effect, and provide the re-sterilization method.

8. Manufacturing Method

- a. State the processes from the acceptance to the market release inspection of the components etc. (refers to the “components etc.” as stipulated in Article 2, Paragraph 2 of the Quality Management System for Medical Devices and *In Vitro* Diagnostics [MHLW Ordinance No. 169 of 2004; hereinafter referred to as “QMS Ministerial Ordinance on Medical Devices”]). If procedures have been established to ensure the conformity of the components etc. to the requirements of purchased components but the purchased components are not verified based on such procedures, or when the components etc. fall under Appendix Table 5 of the Ordinance of Enforcement of the Law (MHLW Ordinance No. 1 of 1961; hereinafter referred to as the “Enforcement Ordinance”), then also provide the manufacturing process of the components etc. When the components etc. have been registered pursuant to Article 14-11, Paragraph 1 of the Law (hereinafter referred to as “Master File registration”), then the name of the manufacturing site of the components etc. may be provided in lieu of the manufacturing process.
- b. Describe the manufacturing process at each manufacturing site by using flowcharts as shown in Attachment 4 to facilitate understanding of the process.
- c. If the quality, property, etc. of the product differs according to manufacturing conditions, then state the manufacturing conditions for any process that has a significant impact on the quality or safety of the medical device for which approval is sought.
- d. If the medical device is a sterile medical device, then state the sterilization method, etc.
- e. If a material of human or animal origin is used to manufacture the medical device, then state the inactivation/removal methods of bacteria, fungi, viruses, etc., in the manufacturing process, and other information that is necessary to ensure the quality and safety of the medical device.
- f. If in-process inspections are outsourced to an external testing/inspection laboratory, then state the name and address of the external testing/inspection laboratory for each applicable process step. In this case, make sure that it is easy to identify manufacturing process steps where in-process inspections are commissioned to external testing/inspection laboratories.
- g. State the name of the business establishment that conducted the primary design of the product.
- h. If the applicant intends to obtain a marketing approval for the medical device whose component might be distributed as a single product, provide the information specified in “a” through “g” above for the manufacturing process of the component.

- i. When incorporating into the medical device a component that has been approved or certified or for which a marketing notification has been submitted as a single medical device, state the name of the marketing authorization holder of the component, address of the principal place of business, license number of the marketing authorization holder, approval (or certification or marketing notification) number or accreditation number, brand name, and component name in the section where the component is indicated.
- j. If a raw material is registered in the Master File as the material for medical devices, then state the name and address of the raw material manufacturer, the name and address of the manufacturing site, Master File registration number, and registration date in the section where the raw material is indicated. If the manufacturing site is required to have the license for manufacturer of medical devices, then state the license category, license number, and license date.

9. Storage Method and Expiration Date

When it is difficult to ensure the quality of the medical device unless stored in a certain way, or when an expiration date must be designated for maintaining the quality of the medical device due to deterioration with time, provide such information. No expiration date is necessary if the expiration period exceeds three years.

When the medical device, unless stored under certain conditions, such as in a cool, dark place, is susceptible to deformation, degradation, etc., state the storage method and conditions.

10. Manufacturing Site of Marketed Product

State the name and address of a manufacturing site, license or accreditation number of the manufacturer, license or accreditation category of the site where the manufacturing process stated in the "Manufacturing Method" column is conducted. If an application has been submitted to obtain the license for or accreditation of the manufacturer that operates the manufacturing site, then make a note to that effect.

11. Manufacturing Site of Raw Materials

For the manufacturing site of the materials that are registered in the Master File as the materials for medical devices (only if a license for manufacturer or accreditation of manufacturer is necessary for manufacturing the registered materials), state the address of the manufacturing site. If an application has been submitted to obtain the license for or accreditation of the manufacturer that operates the manufacturing site, then make a

note to that effect.

12. Remarks

- (1) Indicate whether the medical device is a specially controlled medical device or a controlled medical device.
- (2) State the classification according to the Classification Notification.
- (3) If the medical device is a specially designated maintenance and management required medical device, then make a note to that effect.
- (4) If the medical device contains a biologically derived material or an equivalent thereto, state that it contains biologically derived material.
- (5) If the medical device is manufactured by using genetical recombination technology, then state it is a “medical device manufactured by genetical recombination technology.”
- (6) If the medical device is a disposable, single-use medical device, then make a note to that effect.
- (7) If the medical device contains a new raw material, then make a note to that effect.
- (8) If more than one generic name is included, state all applicable generic names.
- (9) If a marketing application is filed for a kit product as stipulated in PAB/ERD-2 (*Yakushin 2*) Notification No. 98 issued jointly by the Director of First Evaluation and Registration Division, the Director of Second Evaluation and Registration Division, and the Director of Biologics and Antibiotics Division, Pharmaceutical Affairs Bureau, “Handling of Kit Products Combining Injections with Reconstitution Solutions, etc.,” dated March 12, 1986, or if a marketing application is filed for a product with priority review status as stipulated in PAB/NDD (*Yakushinyaku*) Notification No. 92 issued jointly by the Director of New Drug Division, the Director of Medical Device Development Division, and the Director of Safety Division, Pharmaceutical Affairs Bureau, “Enforcement of the Law for Partial Revision of the Pharmaceutical Affairs Law, and the Law for Adverse Drug Reaction Sufferings Relief and Research Promotion Fund,” dated October 1, 1993, then make a note to that effect. If more than one applicant submits a marketing application for a jointly developed product, then make a note to that effect, and state the names of the joint applicants.
- (10) Attach the instructions for use (draft).
- (11) State the clinical trial notification number and, if the applicant used the clinical trial consultation service at the Pharmaceuticals and Medical Devices Agency, then make a note to that effect.
- (12) State the marketing authorization holder license number of the applicant, license

category, and address of the principal place of business. If the applicant has applied for license for marketing authorization holder, then make a note to that effect (including the address of the principal place of business).

- (13) State the application category as stipulated in Appendix Table 2 of the Director-General Notification.
- (14) If a medical device marketing application is filed for a product that does not conform to the standards for designated controlled medical devices as stipulated in Article 23-2, Paragraph 1 of the Law (hereinafter referred to as the “certification standards”), then make a note to that effect, and submit data that demonstrate its non-conformity to the standards.
- (15) If there is no applicable generic name for the medical device at the time of regulatory submission, provide a summary of the medical device (approximately 300 characters), and indicate which classification rule, as stipulated in the Classification Notification, is deemed to apply to the medical device.
- (16) If the product for which approval is sought is used in the manufacturing process of another product as part of another medical device, then state that it is a “medical device that can be used exclusively for manufacturing.”
- (17) Affix a photograph that shows the external appearance of the product.

III. Points to Consider in Handling and Preparation of Data to Be Submitted in Support of Marketing Application

Provided below are guidance on handling and preparation of the data/information that should be submitted in support of a marketing application as stipulated in Article 40, Paragraph 1, Item 5 of the Enforcement Ordinance (hereinafter referred to as the “data”) and the points to consider in preparing the data. For a medical device that conforms to the applicable approval standard, however, it is necessary to prepare the data according to the separately notified guidance for preparing the data submitted in support of an application for marketing approval of a medical device that conforms to its approval standard.

The data must be prepared in strict compliance with Article 43 of the Enforcement Ordinance and be based on precise and objective considerations.

Test results that are submitted as the data must meet the requirements of test reports specified in the General Requirements for the Competence of Testing and Calibration Laboratories (ISO 17025) established by the International Organization for Standardization (ISO) or the General Requirements for the Competence of Testing and Calibration Laboratories (Q17025) established by the Japan Industrial Standards (JIS).

(1) Origin or History of Discovery and Usage Conditions in Foreign Countries

- a. For the data on the origin or history of discovery of the medical device, concisely show in chronological order the course of events leading from the initial idea for the development of the medical device to its clinical use, to aid in understanding the history and evolution of the technology. Describe the history of development of the medical device while referring to the associated technology.
- b. For the data on usage in foreign countries, state the usage conditions (e.g., names of countries where the medical device is used, year of starting use in each country, year of approval in countries with approval systems, and approximate number of annual use by country) in foreign countries (if the medical device is manufactured overseas, then include the name of the country in which it is manufactured).

If a partial change approval application for the product that has already been approved is submitted, then state the actual use and occurrence of malfunctions in Japan.

If a marketing application is filed for a medical device that has been used in foreign countries, then state any malfunctions that have been reported in its use in foreign countries (indicate the type and incidence of malfunction).

- c. For the data on comparison with other similar medical devices in terms of principle, properties, etc., state the new features and improvements of the medical device and study results on the differences from or equivalences to the similar medical devices already on the market. Use a comparison chart to aid in understanding the medical positioning of the medical device and other treatment options, if any.

(2) Setting of Specifications

- a. For "product specifications," set the design specifications that are required in terms of the quality, safety (including physical, chemical, and biological safety), and efficacy (performance and function) of the product for which approval is sought.
- b. Prepare the data to explain the reason for selecting tests included in the product specifications. In this case, explain why the product specifications are sufficient to ensure the efficacy, safety, and quality of the product for which approval is

sought.

When adopting any Japanese or foreign standards, explain why it is appropriate to adopt the standards. The Ministry may require the applicant to submit the full text of such standards.

- c. If the medical device uses a dental material, polymeric material, absorbent material, etc., and when these materials or composition affect the performance or safety of the medical device, then establish specifications concerning physical and chemical properties such as the chemical structure of the materials or composition.

(3) Safety and Durability

For a medical device other than those whose stability has already been sufficiently confirmed, conduct stability testing, such as tests on chronological changes of the medical device that is stored under actual storage conditions and stress conditions, and establish the appropriate storage method and expiration period based on the test results. When establishing the storage method and expiration date based on the results from accelerated tests, the use of the testing method to evaluate stability must be justified by sufficient scientific evidence. If there is no appropriate accelerated testing method, it is necessary to obtain test results based on the actual measurements obtained under actual storage conditions.

If the medical device undergoes radiation sterilization, then submit the data on deterioration of materials such as results of changes in properties and strength tests conducted immediately after sterilization and at least six months after sterilization (excluding medical devices whose expiration period is less than six months) under the condition of maximum radiation dose as specified in the information on manufacturing method (the dose equivalent to that of the worst case) or under sterile conditions with twice the effect (e.g., dose or duration). The foregoing shall not apply, however, if deterioration of the materials is already known.

If the medical device is intended to be resterilized and reused, then also explain the durability of the medical device that has repeatedly been sterilized under sterile conditions while taking into account how the medical device is used.

(4) Conformity to the Standards Stipulated in Article 41, Paragraph 3 of the Law

a. General information

If the applicant intends to claim that the product conforms to the Essential Principles, that it is manufactured in conformity to QMS Ministerial Ordinance on Medical Devices, and that it conforms to the applicable approval standard, if any, then the applicant must attach a declaration stating that the medical device conforms to the approval standard. It is desirable to prepare the declaration of conformity in accordance with ISO 17050-1 (Conformity Assessment - Supplier's Declaration of Conformity Part 1: General Requirement).

b. Data that demonstrate conformity to Essential Principles

(i) Product that conforms to the applicable approval standard when applying for marketing approval

Submit the data that demonstrate conformity of the medical device to the Essential Principles and which have been prepared according to the Essential Principles conformity checklist that is presented as part of the approval standard.

(ii) Product for which there are no approval standards or product that does not conform to the applicable approval standard

Submit a list of the standards or criteria, and testing methods established by the applicant, which were adopted in the designing stage to demonstrate that the medical device conforms to the Essential Principles. Also explain why it was appropriate to adopt the standards, testing methods, etc.

In addition, even when there are no appropriate standards or criteria for the medical device, and if there are standards etc. that serve as reference, then such standards may be provided as reference. In this case, it is naturally necessary to explain why it was appropriate to use the standards etc. to prove that the medical device conforms to the essential principles.

(5) Performance

Submit the data on tests to support the performance, safety, efficacy, and usage method of the medical device and the results of the test. These tests should be conducted to verify and validate the conformity to the Essential Principles and design of the medical device. If the medical device's conformity to the standards ensures its performance, safety, etc., then the test results may be substituted with a certificate of conformity, provided, however, that such conformity to the standards has been

certified by a certification body which is accredited as conforming to ISO 17025 by an accreditation body belonging to the International Accreditation Forum (IAF), or by a certification body registered pursuant to Article 57, Paragraph 1 of the Industrial Standardization Law (Law No. 185 of 1949) (hereinafter referred to as “JNLA registration”).

If the medical device is a calibration medical device that is used for tests, diagnosis, etc., submit the data on calibration performance such as scope of measurement, sensitivity, specificity, and reproducibility (if an *in vitro* diagnostic is exclusively used in combination with the analytical instrument, then also take into account the performance of the *in vitro* diagnostic).

Points of consideration for primary tests are provided below for reference.

- A. For the data on electrical safety, explain conformity to each requirement of the standards adopted, such as JIST0601-1 “Medical Electrical Equipment Part 1: General Requirements for Safety,” for each item to demonstrate that the medical device conforms to the standards when explaining the electrical safety by conducting necessary tests.

When conducting a test on electromagnetic compatibility, refer to PFSB/ELD (*Iyakushin*) Notification No. 0830006 by the Director of Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau of MHLW, dated August 30, 2002, “Handling of Confirmation of Conformity of Medical Devices to Electromagnetic Compatibility Standards.”

- B. Biological safety testing is, in principle, required for medical devices that are implanted or inserted into the human body or that either directly or indirectly come into contact with the living body. Refer to PFSB/ELD (*Iyakushin*) Notification No. 0213001 of the Director of Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau dated February 13, 2003, “Basic Principles of Biological Safety Evaluation Required for Application for Approval to Manufacture (Import) Medical Devices” and separately notified “Basic Principles of Biological Tests Required for Application for Marketing Approval of Dental Materials,” and submit the necessary data.
- C. For the data on radiation safety, when explaining radiation safety by conducting necessary tests, submit the data on the test results that demonstrate conformity to

the standards adopted.

- D. For the data on mechanical safety, when explaining mechanical safety by conducting necessary tests, submit the data on the test results that demonstrate conformity to the standards adopted.

(6) Clinical Evidence

- a. The sample size should be large enough to perform statistical analysis to prove the efficacy and safety of the medical device. If the number of patients with target diseases is small, such as cases of medical devices for orphan diseases, prepare an appropriate clinical trial plan by taking into account the circumstances, and study the sample size that can practically be evaluated.
- b. When the medical device is classified into Class IV under the Classification Notification, clinical data must, in principle, be submitted for each product, excluding medical devices that can be proved to be equivalent to already approved medical devices and those falling under the scope of medical devices for which the approval standard is specified. The foregoing shall not apply, however, if due to a valid reason, the clinical efficacy and safety of the product can be evaluated based on the data other than clinical data of the product.
- c. When the medical device is classified into Class III, clinical data may be required, excluding medical devices that can be proved to be equivalent to already approved medical devices and those falling under the scope of medical devices for which the approval standard is specified. As of present, however, the data must be submitted, in principle, for the medical devices listed in Attachment 1.

Even if a medical device is listed in Attachment 1, the foregoing shall not apply if due to a valid reason, the clinical efficacy and safety of the product can be evaluated based on the data other than clinical data of the product. On the other hand, even for medical devices not listed in Attachment 1, clinical data may be required for the evaluation of the efficacy and safety of the medical device.

- d. When the medical device is classified into Class II, and if it is a new medical device for which the approval of the Minister of Health, Labour and Welfare is required (including a medical device for which a marketing application has been filed because its intended use and indications deviate from those stipulated in the

certification standards, or its performance, structure, etc. is clearly different from those of already approved medical devices), and falls under the scope of medical devices for which no approval standards are specified (limited to a medical device that cannot be proved to be equivalent to already approved medical devices), clinical data may be required for the evaluation of the efficacy and safety of the medical device.

- e. If the medical device, for which an approval standard has been specified, conforms to the standard, the applicant is not required to, in principle, submit clinical data. As an exception, however, clinical data may be required for some medical devices for the safety evaluation. In this case, the application category is naturally treated as that of medical devices that require clinical data.
- f. In the case of a new medical device, prepare and submit a survey plan (draft) on use results of the new medical device by referring to PAB/MDD (*Yakuki*) Notification No. 133 issued jointly by the Director of Medical Device Development Division and the Director of Safety Division, Pharmaceutical Affairs Bureau, dated July 26, 1995, "Use Results Survey of New Medical Devices."
- g. Because the need for clinical data is determined based on a wide range of factors including the features of each medical device and non-clinical study results, the applicant is advised to use the pre-application consultation service offered by PMDA to determine the need as necessary.

(7) Risk Analysis

Submit the data/information on the risk management system which the applicant has established for the medical device and the overview of implementation status of the system by referring to JIS T 14971 "Medical Devices - Application of Risk Management to Medical Devices."

In the risk analysis, explain that the foreseeable risks of the hazards described below are acceptable if the clinical benefit is expected to outweigh the risks.

- a. Among potential hazards from the medical device for which approval is sought, submit the data that summarize in a tabular format the risk analysis and risk mitigation measures for hazards (that are related to similar medical devices and include those having an association with the medical device for which approval is

sought), against which the applicant is requested by MHLW, etc. to take safety measures.

- b. If, as a result of risk management based on JIS T 14971, a serious hazard other than those provided in above “a” is found, submit the data that summarize in tabular format the risk analysis and risk mitigation measures for the hazard.

(8) Manufacturing Method

- a. State the processes from the acceptance to the market release inspection of the components etc. If procedures have been established to ensure the conformity of the components etc. to the requirements of purchased components but the purchased components are not verified based on such procedures, or when the components etc. fall under Appendix Table 5 of the Enforcement Ordinance, then also provide the manufacturing process of the components etc. If the components etc. have been registered in the Master File, then information on the manufacturing site of the components etc. may be provided in lieu of the manufacturing process.
- b. Use a process flowchart etc. as shown in Attachment 5 and describe the quality inspection that is conducted for each manufacturing process step.
- c. If the quality, property, etc. of the product vary depending on the manufacturing conditions, state the manufacturing conditions of any process that has a significant impact on the quality or safety of the medical device for which approval is sought.
- d. Provide information on manufacturing sites that conduct the process steps (names, addresses, and license or accreditation number, if obtained) by clearly associating the information with a flowchart. If the manufacturing process is divided between multiple manufacturing sites, describe the association of the process with the sites to facilitate understanding. If the test is outsourced to an external testing/inspection laboratory, state the name and address of the commissioned laboratory for each outsourced test.
- e. State the name and address of the business establishment that performed the primary design of the product, and explain the relationship with the applicant.

- f. When the applicant intends to obtain approval to market a component of the medical device as a single product, and if information on the manufacturing method or quality inspection for the component is different from that stated in “a” through “e” above, the information must be stated separately.
- g. When incorporating a component that by itself has been approved or certified as a medical device or for which marketing notification has been submitted, state the name of the marketing authorization holder of the component, address of its principle place of business, license number of the marketing authorization holder and approval number, accreditation number, or marketing notification number, brand name, and product name in the section where the component is indicated.
- h. If a raw material of the medical device has been registered in the Master File, state the name and address of the supplier of the material, and the name and address of the manufacturing site, Master File registration number, and, if the manufacturing site is required to obtain a medical device manufacturing license, then state the license category, license number, and license date in the section where the raw material is indicated.
- i. If the medical device is a sterile medical device, then submit a declaration on the sterilization validation period and parameters.
- j. If a bovine-derived material is used, state the country of origin of the raw material, the body part, processing method, and, as necessary, information on TSE data and other information that is necessary to ensure the quality and safety of the medical device. In addition, when using a human- or animal-derived material, state the origin of the raw material, details of donor screening, inactivation/removal methods of bacteria, fungi, viruses, etc. during the manufacturing process, and other information that is necessary to ensure the quality and safety of the medical device.
- k. For each quality inspection, explain the purpose and overview of the inspection, and relationship with product specifications.

IV. Miscellaneous

1. Handling of the Data in Joint Development

- (1) When more than one individual jointly develops a new medical device, and

conditions as stated in “a” and “b” below are met, all or some of the members of the group of individuals (hereinafter referred to as a “joint development group”) may use the data developed by other members when applying for marketing approval for the new medical device.

- a. A contract concluded between the members should include the following requirements: Every member of the joint development group can use all data developed by other members (including source data that served as the basis for the relevant data) and it is ensured that all members of the joint development group cooperate with each other in acting as the responsible manager for storing the data.
- b. A copy of the contract as specified in above “a” is submitted when applying for marketing approval.

(2) Whether or not each of the applicants must prepare the data when multiple individuals of the joint development group apply for marketing approval of a new medical device developed jointly is determined based on the content of the joint development and the equivalence of the product. The applicants should therefore consult with PMDA for each type of the data to be submitted.

(3) Even if some members of the joint development group do not file an application for marketing approval of the new medical device developed jointly, Article 43 of the Enforcement Ordinance shall apply to them.

(4) If more than one individual files an application for marketing approval of the same medical device at the same time, the individuals must clarify the relationship between the multiple applications and differences between the data packages submitted by them. In addition, submit the data proving that the applications are filed for the same medical device.

2. Compiling Method of the Data for Review

(1) Prepare the submission data package in accordance with Appendix Table 2 of the Director-General Notification, and attach a complete copy of the entire submission as the data for review at the time of regulatory submission. In this case, the data should, in principle, be compiled according to the following guideline. When compiling the data for an application for marketing approval of a medical device that conform to the applicable approval standard, follow the guidance for preparing the data for an application for marketing approval of a medical device that conforms

to the approval standard notified separately by MHLW.

- ① Cover letter for the data for review (refer to the Attached Form)
- ② Application form (copy)
- ③ “Summary Technical Documentation” as a summary of the data submitted in support of a medical device application as stipulated in the separately notified “Handbook for Preparation of Summary Technical Documentation Submitted in Applications for Marketing Approval of Medical Devices.”
- ④ List of the data submitted
- ⑤ The data submitted (the data as stipulated in Appendix Table 1 of the Director-General Notification)
- ⑥ Evidence (e.g., a copy of the contract on joint development)
- ⑦ Other data that serve as reference

(2) Pay attention to the following points when compiling the data.

- a. If photographs concerning test results, photographs of tissues, etc., are unclear, submit the photographs separately from the application as a photo album.
- b. Among other supporting documents, attach samples of the protocol and the case report form to the clinical study report that is submitted as part of clinical data. Although it is normally not necessary to include other supporting documents, prepare the documents beforehand for their prompt submission upon the request by the Office of Medical Devices Evaluation, Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau of MHLW or PMDA.

3. Application for Partial Change of Approved Information

- (1) Attach a copy of the certificate of marketing approval for the relevant product to the application for approval of partial change or the change notification of approved information.
- (2) When any change is made to an approved medical device, the decision on whether to submit an application for marketing approval of a new product or for partial change of the approved information should be made based on whether the change affects the equivalence between the pre-change and post-change products. Refer to Attachment 2 for cases in which an application for partial change of the approved information on the relevant medical device should be submitted, and those in which another marketing application should be submitted for the medical device.
- (3) If the sole purpose of the application for post-approval partial change is to extend the expiration period, then the application will promptly be handled. Write “*cho*” in kanji character in red ink on the application form, and attach the necessary test

results etc.

- (4) In the “Remarks” column of the application form for approval of partial change of approved information, provide the information that has been changed, among the information described under the aforementioned Section II-12. If the application for partial change of approved information is submitted pursuant to Article 14, Paragraph 9 of the Law (including cases where it applies *mutatis mutandis* in Article 19-2, Paragraph 5), describe the reason and details of these changes by using a comparison table. In addition, provide a table of the marketing approval process.

4. Change Notification

- (1) Attach a copy of the certificate of marketing approval for the relevant product when submitting a change notification of approved information.
- (2) Attachment 3 shows specific examples of the scope of change notifications of approved information on medical devices as stipulated in Article 14, Paragraph 10 of the Law.

V. Transitional Measures

The data submitted for marketing approval applications filed on or before March 31, 2008 shall be handled as follows:

(1) Stability and durability

Upon presentation of the data on the equivalence to a clinically proven medical device as shown in Attachment 6, the applicant is deemed to have demonstrated that the medical device has the equivalent stability, durability, and performance to those of the comparator. The data for this section can therefore be substituted with data showing that the medical device is equivalent to a clinically proven medical device.

(2) Conformity to the standards as stipulated in Article 41, Paragraph 3 of the Law

Upon presentation of the data on the equivalence to a clinically proven medical device as shown in Attachment 6, the applicant is deemed to have demonstrated that the medical device conforms to the Essential Principles. The data for this section can therefore be substituted with data showing that the medical device is equivalent to a clinically proven medical device.

(3) Performance

Upon presentation of the technical documents on the equivalence to a clinically proven medical device as shown in Attachment 6, the applicant is deemed to have demonstrated that the medical device has the comparable performance to that of a clinically proven

medical device. The data for this section can therefore be substituted with data showing that the medical device is equivalent to a clinically proven medical device.

(4) Risk analysis

The applicant may submit the data/information on the risk management system which the applicant has established and the overview of implementation status of the system. Also, among potential hazards from the medical device for which approval is sought, the applicant may present the data that explain the risk analysis and risk mitigation measures only for hazards (which are related to similar medical devices and include those associated with the medical device for which approval is sought), against which the applicant is requested by MHLW, etc. to take safety measures.

Attached Form

Cover Letter for Data for Review

Please find enclosed the data (indicated by the symbol “○” in the “The data submitted” column) for the product indicated below.

Product name	Generic name	
	Brand name	
Name of applicant		
Date of application		Date sent

Name of data		The data submitted		
1	Table of contents			
2	Application form (copy) (including a copy of the approval certificate)			
3	Summary Technical Documentation			
4	List of the data submitted			
5	The data submitted	a. Origin or history of discovery and usage conditions in foreign countries	1. Origin or history of development	
			2. Usage conditions in foreign countries	
			3. Comparison with similar medical devices	
		b. Setting of the specifications	1. Specifications and setting of the specifications	
		c. Stability and durability	1. Stability and durability	
		d. Conformity to the standards stipulated in Article 41, Paragraph 3 of the Law	1. Declaration of conformity to Essential Principles	
			2. Conformity to Essential Principles	
		e. Performance	1. Tests to support performance and safety	
			2. Tests to support efficacy	
			3. Tests to support usage method	
		f. Risk analysis	1. Risk analysis system	
			2. Important hazards	
		g. Manufacturing method	1. Manufacturing process and manufacturing site	
2. Sterilization method				
3. Quality control				
h. Clinical evidence	1. Clinical evidence			
	2. Survey plan (draft) for use results of the new medical device			
6	Evidence (e.g., copy of the contract on joint development)			
7	Other data that serve as reference			

Attachment 1

Examples of medical devices for which clinical data must, in principle, be submitted, out of medical devices that require regulatory approval pursuant to Article 14, Paragraph 1 of the Law

1. When no applicable generic name is established for the medical device for which approval is sought
2. The medical device that belongs to Class IV and whose risk assessment has not been determined (those with limited cases of approval) or the medical device that is included in those different from already approved medical devices.
3. The medical device that belongs to Class III and whose risk assessment has not been determined (those with limited cases of approval) or the medical device that is included in those different from already approved medical devices.

In addition, among the medical devices listed below, Class III medical devices whose risk assessment has not been determined or those that cannot be judged as being the same as already approved medical devices (if the scope of medical devices that require clinical data is specified separately, then refer thereto).

- (1) Wound dressing or protective material
- (2) Surgical adhesive
- (3) Artificial joint, artificial bone, or related devices that fall under any one of the following:
 - Those made of ceramics
 - Those which feature a special surface treatment to improve biocompatibility
 - Biological bone
 - Bone filler material
 - Bone cement
- (4) Sensory function supportive device (e.g., artificial ear drum, artificial inner ear, artificial middle ear, artificial vocal cord)
- (5) Dental implant material (refer to PMSB/MDD [*Yakuki*] Notification No. 59 of the Director of Medical Device Development Division, dated March 31, 1997, "Handling of Clinical Data to Be Submitted in Support of Application for Approval to Manufacture or Import Intraocular Lenses or Dental Materials)
- (6) Intrauterine contraceptive device
- (7) Any of the following artificial blood vessels:
 - Gelatin- or collagen-coated artificial blood vessel
 - Artificial blood vessel made of polytetrafluoroethylene (PTFE) or polyethylene

- terephthalate (PET) and whose diameter does not exceed 4 mm
- (8) Tissue repair materials, such as materials for vascular repair
 - (9) Any of the following stents:
 - Stent that is placed into an artery
 - Stent that is placed into a vein for the purpose of opening phlebostenosis
 - Stent that is placed into the urethra for a long period
 - Stent that is placed into large intestine or rectum
 - (10) Dialyzer
 - (11) Blood purifier
 - (12) Ascites filtration and reinfusion system
 - (13) Radioactive compound synthesis system
 - (14) Helium neon laser treatment system
 - (15) Semiconductor laser treatment system
 - (16) Microwave hypothermia system
 - (17) Short wave hypothermia system
 - (18) Intracorporeal lithotripter
 - (19) Extracorporeal shock wave lithotripter (refer to PMSB/MDD [*Yakuki*] Notification No. 418 of the Director of Medical Device Development Division, dated October 28, 1996, “Handling of Clinical Trials for Application for Marketing Approval for Extracorporeal Shock Wave Lithotriptors”)
 - (20) Laser surgical system or laser coagulation system (refer to Administrative Notice No. 91-7 from the Medical Device Development Division, Pharmaceutical Affairs Bureau dated August 6, 1991, “Exemption of Submission of Clinical Data on Laser Surgical Systems”)
 - (21) Intraocular lens
 - (22) Contact lens
 - (23) Any other medical device that falls under any one of the following:
 - Tubes and catheters made of antibacterial materials
 - Detachable balloon catheter
 - Thrombus filter
 - Embolectomy catheter
 - Periodontal guided tissue regeneration material
 - Penile prosthesis
 - Urethral sphincter prosthesis
 - Ligament prosthesis
 - Breast prosthesis
 - Spiral urethral catheter with function to assist emiction

Intravascular ultrasonic system (including probes)

Needle-less syringe

Embolectomy material

4. The medical device that belongs to Class II and that is a new medical device (including a medical device for which a marketing application has been submitted as the medical device whose intended use and indications clearly deviate from those established in the applicable certification standards or whose performance, structure, etc. are clearly different from those of already approved medical devices).

Attachment 2

Examples of Changes that Require Application for Partial Change of Approved Information on Medical Devices or New Marketing Application

1. General Cases

(1) In principle, an application for partial change of approved information is accepted for following changes that do not affect the essential nature of the medical device.

(a) Minor change in the structure, raw material, ingredient, quantity, performance, etc.

(Example)

(i) Addition of a component to a combination medical device falls under partial change.

(b) Change of name, shape, dimensions, intended use, indications or product specifications

(Examples)

(i) If the essential nature is not affected, a change of manufacturing method falls under partial change (excluding those which can be made by a change notification).

(ii) Addition to, change of intended use or indications

(iii) Change of sterilization method falls under partial change.

(2) In principle, the following changes require a new application for approval.

A change in the structure, raw material, ingredient, quantity, performance, etc. that does not fall under minor change requires a new marketing application.

(Example)

(i) A significant change of the maximum output rating of a laser treatment system requires a new marketing application.

2. Examples for Each Product Group (in the order described in Appendix Table 1 of the Enforcement Order)

Apparatus and Appliances 7. Internal Organ Substitutes

Dialyzers

(1) One product category for each different model (e.g., laminating type, coil type, hollow fiber type) or raw material of dialysis membrane

(2) Change in the area of hollow fiber membrane falls under partial change.

(3) If the performance is not affected, change in the thickness of hollow fiber

membrane falls under partial change.

Artificial vessels

- (1) One product category for each different raw material or manufacturing method (including weaving method)
- (2) Change in length or diameter falls under partial change.

Blood strainer and blood purifier

- (1) Change in the area of hollow fiber membrane falls under partial change.
- (2) If the performance is not affected, change in the thickness of hollow fiber membrane falls under partial change.

Artificial lungs

- (1) One product category for each different model or membrane raw material
- (2) Change in the area of membrane falls under partial change.
- (3) If the performance is not affected, change in the thickness of membrane falls under partial change.

Apparatus and Appliances 8. Incubators

One product category for each different type (e.g., plenum system, natural ventilation type, transportable type)

Apparatus and Appliances 9. Medical X-ray Systems

One product category for each different model

Apparatus and Appliances 12. Physical Diagnosis Apparatuses

Low-frequency therapy equipment

Addition of the number of connection terminals on professional low-frequency therapy equipment (a new marketing application is required for the equipment of household type).

Apparatus and Appliances 16. Clinical Thermometers

One product category for each different model (e.g., one-minute type, flat type, stick type)

Apparatus and Appliances 18. Blood Pressure Gauges

One product category for each different model

Apparatus and Appliances 47. Needles for Syringes

The same product category for products that are used for subcutaneous, intravenous, transfusion, and muscle injections but are of different sizes. One product category for each anesthesia, dental conduction anesthesia, and dental toponarcosis.

Apparatus and Appliances 48. Glass Syringes

One product category for each general medical, microinjection, and dental application. One product category for general medical syringes whose only difference is size. Likewise, one product category for microinjection syringes.

Apparatus and Appliances 49. Dental Units

Minor change of rating falls under partial change.

Apparatus and Appliances 60. Dental Engines

- (1) One product category for each dental pneumatic rotary drive device and dental electric rotary drive device
- (2) One product category for each different maximum revolution

Apparatus and Appliances 72. Vision Corrective Lenses

One product category for each different raw material, ingredient, or quantity

Medical Supplies 2. Sutures

One product category for each different raw material (e.g., small intestine of mammal, silk, cotton, steel, nylon, or Teflon)

Medical Supplies 4. Orthopedic Articles

Artificial joints

One product category for each different raw material, ingredient, or quantity

One product category for each major difference in structure or form

In principle, one product category for each applicable body part

A combination of series of products used at the same time may be deemed as one product category, but multiple combinations are not permitted.

Artificial bones

One product category for each different raw material, ingredient, or quantity

In principle, one product category for each applicable part

Wound dressings, protective materials, medical non-sticking tendency gauze

Minor change in the ingredient or composition of a part that does not come into direct contact with the skin or wound, provided the change does not affect performance

Dental Materials 1. Dental metals

One product category for each different raw material, ingredient, or quantity

Dental Materials 2. Dental crown materials

One product category for each different raw material, ingredient, or quantity (excluding color materials). In this case, if the only difference between products is color tone, then a marketing application may be submitted for one product encompassing a number of color tones.

Dental Materials 3. Denture base materials

One product category for each different raw material, ingredient, or quantity (excluding color materials). In this case, if the only difference between products is color tone, then a marketing application may be submitted for a single product encompassing multiple color tones.

Dental Materials 4. Dental root canal filling materials

One product category for each different raw material, ingredient, or quantity (excluding color materials). In this case, if the only difference between products is color tone, then a marketing application may be submitted for a single product encompassing multiple color tones.

Dental Materials 5. Dental adhesive filling materials

One product category for each different raw material, ingredient, or quantity (excluding color materials). In this case, if the only difference between products is color tone, then a marketing application may be submitted for a single product encompassing multiple color tones.

Dental Materials 6. Dental impression materials

One product category for each different raw material, ingredient, or quantity (excluding color materials). In this case, if the only difference between products is color tone, then a marketing application may be submitted for a single product

encompassing multiple color tones.

Sanitation Products 3. Contraceptive devices

Intrauterine contraceptive device (IUD)

One product category for each different structure, raw material, ingredient, or quantity

Attachment 3

Scope of Change Notification of Approved Information on Medical Devices as Stipulated in Article 14, Paragraph 10 of the Law

Name

- When a change must be made due to an unavoidable reason such as a change in a name related to the trademark or business name due to a merger or consolidation of corporation.

Shape, Structure, and Principle

- Name change of a component that is distributed independently, which falls within the scope of change notification specified in the “Name” section above
- Name change of a component that is distributed as a single medical device

Raw Materials or Components

- No change in the raw materials, but a change in the standards provided in the raw material standards (only when the receiving standards are based on JIS, ISO/IEC, etc., and the change follows revision of the standards)
- When the raw material is the same, but a change in the name of the supplier or change in the name of the raw material
- Change in the packaging material, thickness, or form as far as the quality of the product is assured by the sterilization validation standards
- Replacement of a raw material that comes into short-term contact with tissue or blood with a raw material that has been used in the company's product with the same level of biological safety risk (excluding biologically derived material)
- Deletion of a raw material when more than one raw material of the same body part is specified

Product Specifications

- Change of wording caused by revision of the referenced standards (only when no change has been made to the medical device)

Manufacturing Method

- Deletion of a sterilization method that will no longer be used when multiple sterilization methods are designated by case
- Change of the laboratory to which testing is outsourced (only when testing in the same process is outsourced)

- Deletion of one of the licensed manufacturers when multiple licensed manufacturers are designated for the same process
- Change of the name of the business establishment that performed design control
- When a component has been approved or certified independently as a medical device or a marketing notification has been submitted for a component, and the name or address of the marketing authorization holder of the component (i.e., medical device) is changed or the brand name of the component is changed
- Change of the manufacturing site that is licensed pursuant to Article 26, Paragraph 5, Item 4 of the Enforcement Ordinance

Licensed Manufacturer of Marketed Product

- Change of the manufacturing site that is licensed pursuant to Article 26, Paragraph 5, Item 4 of the Enforcement Ordinance

Attachment 4

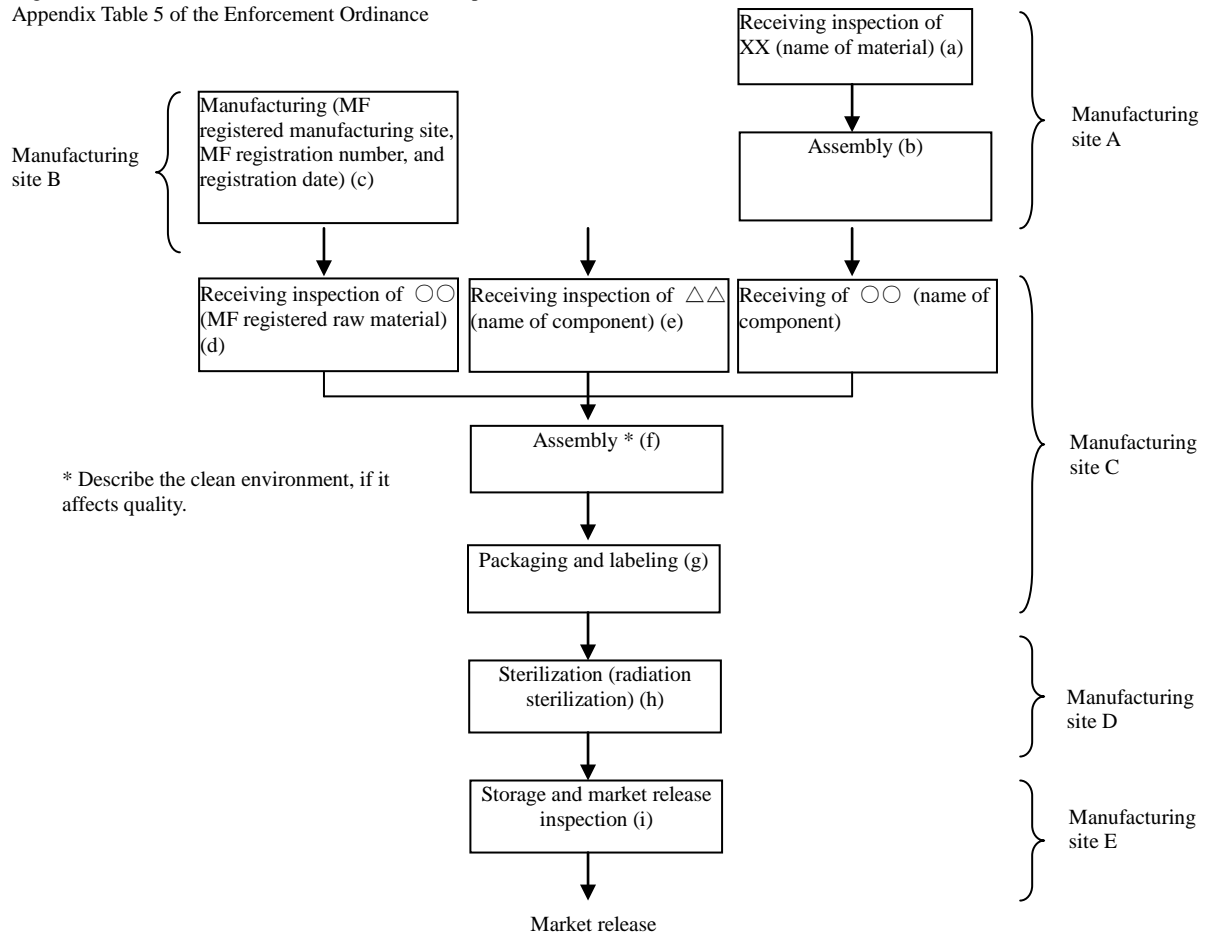
Example for Completing “Manufacturing Method” Column (1)

(Note)

Left: When the applicant receives a component that is registered in the Master File (MF)

Center: When manufacturing site C establishes the procedure for ensuring that the component conforms to the purchased article requirements, and verifies purchased articles according to the procedure

Right: Cases other than those above, or when the component falls under Appendix Table 5 of the Enforcement Ordinance



Company that performed design control and its business establishment

Name of Company:

Company to which quality inspection in the process step (e) is outsourced

Name and address of laboratory that performs testing:

(Licensed Manufacturers of Marketed Product)

Manufacturing site A

Name and address of licensed manufacturer:

Name and address of manufacturing site:

Manufacturer's license number: xxxxxxxxxx / License category: General

Manufacturing site B

Name and address of licensed manufacturer:

Name and address of manufacturing site:

Manufacturer's license number: xxxxxxxxxx / License category: General

(License number is not necessary if the product registered in the Master File does not require the manufacturer's license.)

Manufacturing site C

Name and address of licensed manufacturer:

Name and address of manufacturing site:

Manufacturer's license number: xxxxxxxxxx / License category: General

Manufacturing site D

Name and address of licensed manufacturer:

Name and address of manufacturing site:

Manufacturer's license number: xxxxxxxxxx / License category: Sterilization

Manufacturing site E

Name and address of licensed manufacturer:

Name and address of manufacturing site:

Manufacturer's license number: xxxxxxxxxx / License category: Storage

Attachment 5

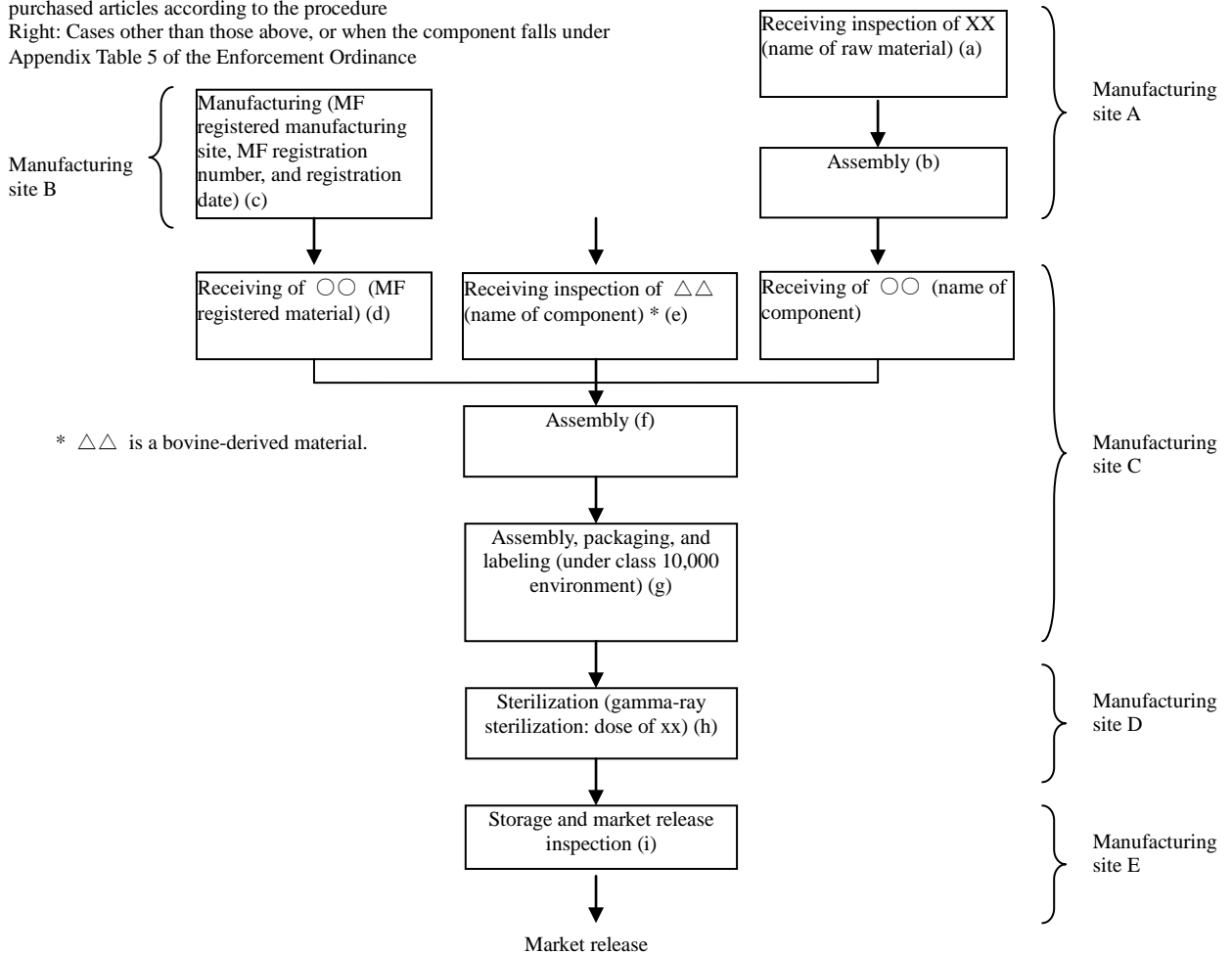
Example for Data on Manufacturing and Quality Controls

(Note)

Left: When the applicant receives a component that is registered in the Master File (MF)

Center: When manufacturing site C establishes the procedure for ensuring that the component conforms to the purchased article requirements, and verifies purchased articles according to the procedure

Right: Cases other than those above, or when the component falls under Appendix Table 5 of the Enforcement Ordinance



1. Information on manufacturing sites

Manufacturing site A

Name and address of licensed manufacturer:

Name and address of manufacturing site:

Manufacturer's license number: xxxxxxxxxx / License category: General

Manufacturing site B

Name and address of licensed manufacturer:

Name and address of manufacturing site:

Manufacturer's license number: xxxxxxxxxx / License category: General

(License number is not necessary if the product registered in the Master File does not require the manufacturer's license.)

Manufacturing site C

Name and address of licensed manufacturer:

Name and address of manufacturing site:

Manufacturer's license number: xxxxxxxxxx / License category: General

Manufacturing site D

Name and address of licensed manufacturer:

Name and address of manufacturing site:

Manufacturer's license number: xxxxxxxxxx / License category: Sterilization

Manufacturing site E

Name and address of licensed manufacturer:

Name and address of manufacturing site:

Manufacturer's license number: xxxxxxxxxx / License category: Storage

2. Information on company responsible for design control

Name and address of the company:

Name and address of the business establishment that performs design control:

Relationship with the company that performed design control:

3. Information on quality inspection

(1) Quality inspection (a separate table may be prepared for explanation)

- Quality inspection for the process step (a): dimensional measurement, visual inspection (color tone), ...

(Explain the relationship with the inspection shown in the "Performance" column.)

- Quality inspection for the process step (e): visual inspection (color tone), biological safety testing

(Explain the relationship with the inspection shown in the "Performance" column.)

(The remainder is omitted.)

(2) Company to which quality inspection is outsourced

Company to which quality inspection in the process step (e) is outsourced

Name and address of the company:

Name and address of the laboratory that performs testing:

4. Cases that manufacturing control method affects quality of the product

Process step: “Assembly, packaging, and labeling” shown in the process step (g) in the flowchart above.

Manufacturing control method: conduct the work under class 10,000 environment.

5. Information on sterilization process

(1) Sterilization validation period

From MM DD, YYYY to MM DD, YYYY

(2) Declaration on sterilization parameters

(Separate sheet attached: state the sterilization parameters.)

6. Miscellaneous

(Information on raw material, BBB, a bovine-derived material)

Country of origin:

Body part:

Processing method:

State in finished product: coated on ○○ of XX

(Information on TSE data: as shown on Appendix [])

<Indicates that it conforms to the conditions stipulated in PMSB (*Iyaku*) Notification No. 1471 of 2001, Section 2-(1)-② >

Attachment 6. Points to Consider in Preparing "Data on Equivalence"

1. Points to consider in general

"Data on equivalence" explain the applicant's view on the equivalence of the medical device for which approval is sought to the already approved (certified) medical devices. It is desirable to explain the concept of the medical device for which approval is sought and the bases for the decisions through the course of the development, including the concept in the initial development stage. The information should be provided accurately and concisely, including the applicant's evaluation of equivalence in terms of quality, efficacy, and safety, and clinical equivalence.

2. Points to consider in preparation

(1) For the product for which approval is sought as well as the approved, certified, or notified medical device to which the product is believed to be equivalent, prepare, by referring to the Appendix Table (example), a table that provides "Category," "Generic Name," "Classification," "Approval (Certification or Marketing Notification) Number," "Name of Marketing Authorization Holder," "Name of Licensed Manufacturer," "Brand Name," "Intended Use and Indications," "Shape, Structure, and Principle," "Raw Materials or Components," "Product Specifications," etc.

(2) For each item in the table, in principle, provide the applicant's view on equivalence. In addition, consider the following points when providing the applicant's view on equivalence:

- Are the indications for use (target diseases) same?
- If the indications for use (target diseases) are different, then is there a possibility that the intended clinical efficacy will be compromised?
- Is the usage method or operation method, such as whether the medical devices can be reused, same?
- Can the intended use be determined as being equivalent or being substantially equivalent?
- Are the designs, raw materials, and other technical elements* same?
- Is the description of technical elements* sufficient for determining equivalence?
- If there is any novelty in technical elements*, does it affect safety or efficacy?
- If there is any novelty in technical elements*, is there a scientific method for evaluating the novelty?
- Are there sufficient performance data that are necessary to evaluate equivalence?
- Can the medical devices be determined as being equivalent based on the performance data?

- * Technical elements: In the case of catheters, differences in technical elements refer to differences in elements such as shape, anti-kink property, marker position, material, shape and processing of tip, and coating. In the case of devices, differences in technical elements refer to differences in energy source, power level, battery design, etc., from already approved products.
- (3) When providing the applicant's view on equivalence of shape, structure, etc., it is desirable to attach, as necessary, color photographs or clear color printed matters for verification of external appearance and dimensions.
 - (4) When providing the information, clearly distinguish the fact based on the data from the applicant's view or interpretation.
 - (5) Avoid repetitive information whenever possible, and clearly specify the information provided as reference.
 - (6) When approval standards, guidelines, etc. are available, state whether or not the application for marketing approval for the product is submitted based on such standards or guidelines. If there is any non-conformity to such standards or guidelines, provide the applicant's view on the non-conformity and the reason why the medical devices are still deemed to be equivalent.
 - (7) Besides the points above, consider the following points:
 - (a) Use headings and subheadings wherever possible, and itemize the descriptions if possible. Also use appropriate heading numbering.
 - (b) Use legible fonts and font sizes.
 - (c) Insert a line break or page break where appropriate.
 - (d) Use fold-out pages only when necessary.
 - (e) Always clarify units of numerical values, such as measurements.
 - (f) Use appropriate academic terminology.
 - (g) When quoting other publications, provide a bibliography of the publications at the bottom of the page or at the end of each section.

Appendix Table (Example)

	Product for which approval is being sought	Already approved product 1	Already approved product 2	
Category	Medical Supply 4 Orthopedic article	Medical Supply 4 Orthopedic article	Medical Supply 4 Orthopedic article	
Generic Name	Artificial xxxxx joint	Artificial xxxxx joint	Artificial xxxxx joint	
Classification	Class III	Class III	Class III	
Approval Number		20800BZY.....	20900BZZ.....	
Name of Marketing Authorization Holder	ABC Corporation	XYZ Manufacturing Corporation	XXX Medical	
Name of Licensed Manufacturer	ABC Corporation	XYZ Manufacturing Co., XX Factory	YYY Seiki Corporation	
Brand Name	□△×○●	◎●□◇▼	◇■▲▽◎○	
Intended Use and Indications				
Shape and Structure, or Principle				
Raw Materials or Components				
:	:	:	:	
:	:	:	:	