

Provisional Translation (as of March 2010) *

PFSB (*Yakushoku*) Notification No. 0216002

February 16, 2005

To: Prefectural Governors

From: Director-General,
Pharmaceutical and Food Safety Bureau,
Ministry of Health, Labour and Welfare

Re: Applications for Marketing Approval for Medical Devices

The handling of applications for approval to manufacture or import medical devices has been provided in the PMSB (*Iyaku*) Notification No. 827 by the Director-General of Pharmaceutical and Medical Safety Bureau, Ministry of Health and Welfare, dated July 9, 1999, "Applications for Approval to Manufacture Medical Devices" and PMSB/ELD (*Iyakushin*) Notification No. 1043 by the Director of Evaluation and Licensing Division, Pharmaceutical and Medical Safety Bureau, Ministry of Health, Labour and Welfare, dated July 9, 1999, "Points to Consider in Applying for Approval to Manufacture Medical Devices."

The Pharmaceutical Affairs Law (Law No. 145 of 1960; hereinafter referred to as the "Law") as amended in Article 2 of the Law for Partial Revision of the Pharmaceutical Affairs Law and Blood Collection and Donation Services Control Law (Law No. 96 of 2002) will come into force on April 1, 2005 in accordance with the Cabinet Order That Specifies the Enforcement Date of the Law for Partial Revision of the Pharmaceutical Affairs Law and Blood Collection and Donation Services Control Law (Cabinet Order No. 534 of 2003). With the Law revised, the regulatory system for medical devices will be substantially changed.

Consequently, the Ministry has decided to review the handling applications for marketing approval of medical devices based on the document prepared by the Global Harmonization Task Force (GHTF). You are requested to check the information below, and to fully notify relevant organizations and business parties under your jurisdiction of such information.

* 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.

Please note that copies of this Notification will be sent to the Chief Executive of the Pharmaceuticals and Medical Devices Agency; the Chairperson of the Japan Federation of Medical Devices Associations; the Chairperson of Medical Devices and Diagnostics Subcommittee, the American Chamber of Commerce in Japan; and the Chairperson of Medical Equipment Committee, European Business Council in Japan.

I. General Provisions

1. When an application for marketing approval of a medical device is submitted by an applicant who intends to market the medical device or who intends to have an designated marketing authorization holder market the medical device according to the provisions of Article 14 and Article 19-2 of the Law, the Minister of Health, Labour and Welfare shall grant approval on a per-product basis, upon the required evaluation of the medical device in terms of intended use, indications, structure, principle, raw materials, components, product specifications, operation methods, usage methods, malfunctions, etc., except for general medical devices as stipulated in Article 2, Paragraph 7 of the Law or medical devices designated by the Minister of Health, Labour and Welfare, in accordance with specified standards, based on the provisions of Article 23-2, Paragraph 1 of the Law. The application for marketing approval must be accompanied by the data of which ethics, scientific soundness, and reliability is assured based on the current academic standards of medicine, pharmacology, or engineering at that point in time to fully demonstrate the quality, efficacy, and safety of the medical device for which approval is sought.

2. The terms used in this Notification shall have the following meanings:
 - (1) The term “Enforcement Ordinance” refers to the Ordinance for Enforcement of the Pharmaceutical Affairs Law (Ministry of Health and Welfare Ordinance No.1 of 1961) as revised by the Ministerial Ordinance on the Partial Revision of the Ordinance for Enforcement of the Pharmaceutical Affairs Law (Ministry of Health, Labour and Welfare Ordinance No.112 of 2004). The term “Essential Principles” refers to the standards for medical devices that are defined by the Minister of Health, Labour and Welfare under the provisions of Article 41, Paragraph 3 of the Pharmaceutical Affairs Law.

 - (2) The term “new medical device” refers to a medical device of which structure, principle, usage method, indications, performance, etc. is clearly different from those of medical devices already approved or certified for marketing.

 - (3) The term “approval standards” refers to standards for medical devices of which regulatory review is conducted by confirming their conformity to the standards. In principle, “approval

standards” are based on relevant international standards and specify the scope of products for which clinical trial data are not required to be submitted.

II. Data to Be Submitted in Support of Application for Marketing Approval

1. The tests for preparing data to be submitted in support of the application for marketing approval must properly be conducted in compliance with the Ministerial Ordinance on Good Laboratory Practice for Medical Devices and the Ministerial Ordinance on Good Clinical Practice for Medical Devices that will be promulgated in the future. At the same time, the tests must be conducted in a well-equipped facility, by experienced researchers, and based on the most current academic standards in medicine, pharmacology, engineering, etc. at the time. The data to be submitted in support of the application for marketing approval, which are prepared based on the results of the tests, must be collected and prepared according to the provisions of Article 43 of the Enforcement Ordinance.

2. The data to be submitted in support of the application for marketing approval must, in principle, be in Japanese.

If the submitted data are not in Japanese, its summary in Japanese should be submitted. In this case, the data in the original language, along with its summary in Japanese, may also be submitted.

3. The guideline and handling of tests that are conducted for preparing the data to be submitted in support of the application for marketing approval will be provided separately, as necessary.

4. Article 40, Paragraph 1, Item 5 of the Enforcement Ordinance shall basically provide the data as stipulated in the middle column of the Appendix Table 1.

5. The scope of the data to be submitted of the application for marketing approval is as stipulated in the top row of the Appendix Table 2. In principle, different data are required for different devices according to the application categories shown in the left column of the same table.

If the tests for preparing the data are technically infeasible or the tests are deemed unnecessary in terms of the structure, principle, usage method, etc. of the medical device, the data are not required to be submitted.

In addition, the specific content of the data to be submitted corresponding to the type of medical device will be provided separately.

6. In addition to the data to be submitted, when applying for marketing approval, submit the summary technical documentation (STED) that accurately and concisely summarizes the content of the data to be submitted, including intended use, indications, structure, principle, product specifications, operation or usage method, draft instructions for use, information on why the foregoing items were determined, and information on conformity to the Essential Principles. Instructions on preparing the summary technical documentation will be provided separately. The summary technical documentation must be written in Japanese.
7. When an application for approval is submitted for a medical device deemed to be equivalent to an already-approved new medical device during the re-examination period of the new medical device, data equivalent to or greater than those for the new medical device must be submitted.
8. Even if the above item 7 applies, when an application is submitted for partial change of approved information pursuant to Article 14, Paragraph 9 of the Law (including cases that the said provision applies *mutatis mutandis* to under Article 19-2, Paragraph 5), some of the data are not required to be submitted for the reason of the partial changes.

III. Miscellaneous

1. When an applicant files an application for approval of a new medical device for which there is no applicable generic name at the time of regulatory submission, the applicant must create a new generic name and determine the medical device class (e.g., specially controlled medical device) based on the opinion of the Pharmaceutical Affairs and Food Sanitation Council to submit such information before regulatory review.

[Appendix Table 1.]

Contents of Submitted Data and Summary Technical Documentation

Submitted data	Contents of submitted data	Summary technical documentation
a. Origin or history of discovery and usage conditions in foreign countries, etc.	<ol style="list-style-type: none"> 1. Origin or history of development 2. Usage conditions in foreign countries 3. Comparison with similar medical devices 	<ol style="list-style-type: none"> 1. Summary of the product 3. Information on the device 3.5 Comparison with similar medical devices
b. Setting of specifications	<ol style="list-style-type: none"> 1. Specifications and setting of the specifications 	<ol style="list-style-type: none"> 3. Device description 3.3 Product specifications
c. Stability and durability	<ol style="list-style-type: none"> 1. Stability and durability 	<ol style="list-style-type: none"> 4. Summary of design verification and validation documents
d. Conformity to the standards stipulated in Article 41, Paragraph 3 of the Pharmaceutical Affairs Law	<ol style="list-style-type: none"> 1. Declaration of conformity to the Essential Principles 2. Conformity to the Essential Principles 	<ol style="list-style-type: none"> 2. Essential Principles and conformity to the Essential Principles
e. Performance	<ol style="list-style-type: none"> 1. Tests to support performance and safety 2. Tests to support efficacy 3. Tests to support usage method 	<ol style="list-style-type: none"> 4. Summary of design verification and validation documents
		<ol style="list-style-type: none"> 5. Labeling
f. Risk analysis	<ol style="list-style-type: none"> 1. Risk analysis system 2. Important hazards 	<ol style="list-style-type: none"> 6. Risk analysis
g. Manufacturing method	<ol style="list-style-type: none"> 1. Manufacturing process and manufacturing site 2. Sterilization method 3. Quality control 	<ol style="list-style-type: none"> 7. Manufacturing information
h. Clinical evidence	<ol style="list-style-type: none"> 1. Clinical evidence 2. Survey plan (draft) for usage results of the new medical device 	<ol style="list-style-type: none"> 4. Summary of design verification and validation documents

[Appendix Table 2.]

Scope of Data to Be Submitted in Support of
the Application for Marketing Approval

Application category	a. Development			b. Specifications	c. Stability	d. Conformity to standards		e. Performance			f. Risk analysis		g. Manufacturing			h. Clinical evidence	
	1	2	3	1	1	1	2	1	2	3	1	2	1	2	3	1	2
(1) With clinical data (new medical devices)	○	○	○	○	△	○	○	○	△	△	○	○	○	△	○	○	○
(2) With clinical data	○	○	○	○	△	○	○	○	△	△	○	○	○	△	○	○	×
(3) Without approval standards, without clinical data	○	○	○	○	△	○	○	○	△	△	○	○	○	△	○	×	×
(4) With approval standards, without clinical data	×	△	○	○	△	○	○	○	△	△	○	○	○	△	○	×	×
(5) Controlled medical devices without approval standards or certification standards	△*	△	○	○	△	○	○	○	△	△	○	○	○	△	○	△	△

The items in the top row and the numbers in the second row correspond to the items in the left and middle columns, respectively, in the Appendix Table 1. The symbol “○” indicates that the data must be submitted, the symbol “×” indicates that the data need not be submitted, and the symbol “△” indicates that the data to be submitted is determined on a per-product basis.

* Limited to medical devices for which an application for approval is submitted due to nonconformity to certification standards and those that are especially innovative.

Note: For specially controlled medical devices with approval standards that do not conform to the standards, the Ministry will decide whether each device belongs to the “With clinical data” or “Without approval standards, without clinical data” category on a case-by-case basis.

Controlled medical devices for which approval standards are presented belong to the “With approval standards, without clinical data” category, and products that do not conform to certification standards belong to the “controlled medical devices without approval standards or certification standards” category.