Provisional Translation (as of March 16, 2009) [*]

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: Application for Marketing Approval for Medical Devices

The handling of application for approval for manufacture or import of 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, "Application for Approval forManufacture of 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 for Manufacture of 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 be implemented 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 approval system for medical devices will be substantially changed.

Consequently, the Ministry has decided to review the handling of marketing approval applications 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 Japanese text 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 for a medical device is submitted by an applicant who intends to market a medical device or who intends to have an appointed marketing authorization holder market a medical device according to the provisions of Article 14 and Article 19-2 of the Law, the Minister of Health, Labour and Welfare shall, for every item, grant his approval for its marketing 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., excluding general medical devices as stipulated in Article 2, Paragraph 7 of the Law or medical devices with specified standards designated by the Minister of Health, Labour and Welfare based on the provisions of Article 23-2, Paragraph 1 of the Law. The application for marketing approval must be accompanied by technical documents possible to ensure the ethics, scientific soundness, and reliability of the medical device based on the current academic standards of medicine, pharmacology, or engineering at that point in time to fully verify the quality, efficacy, and safety of the medical device for which the application is submitted.

2. The terms used in this Notification shall have the following meanings:

(1) “Enforcement Regulations” refers to the Regulations for Enforcement of the Pharmaceutical Affairs Law (Ministry of Health and Welfare Ministerial Ordinance No.1 of 1961) that has been revised in accordance with the Ministerial Ordinance to Partially Revise the Enforcement Regulations of the Pharmaceutical Affairs Law (Ministry of Health, Labour and Welfare Ministerial Ordinance No.112 of 2004). “Essential principles” refer 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) “New medical device” refers to a medical device whose structure, principle, usage method, indications, performance, etc. is clearly different from those of medical devices already approved for marketing or certified.

(3) “Approval standards” refer to standards for medical devices of which approval evaluation is

conducted by validating their conformity to the standards. In principle, “approval standards” are based on international standards and specify the scope of products that do not require the attachment of technical documents on clinical trial results.

II. Technical Documents to Be Attached to Marketing Approval Application Form

1. The tests for preparing technical documents to be attached to the marketing approval application form must properly be conducted in compliance with the Ministerial Ordinance concerning the standards for conducting non-clinical safety studies of medical devices and the Ministerial Ordinance concerning the standards for clinical trials on 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 technical documents attached to the marketing approval application are prepared based on the results of the tests and must be collected and prepared according to the provisions of Article 43 of the Enforcement Regulations.

2. The technical documents to be attached to the marketing approval application form must, in principle, be written in Japanese.
   If the attached technical document is not written in Japanese, its summary written in Japanese should be attached. In this case, the technical document written in the original language, along with its Japanese summary, may also be submitted.

3. The guideline and handling of tests that are conducted for preparing the technical documents to be attached to the marketing approval application form will be provided separately, as necessary.

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

5. The scope of the technical documents to be attached to the marketing approval application form is as stipulated in the top row of Table 2 of the Appendix. In principle, different technical documents 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 technical documents are technically infeasible or the tests are deemed unnecessary in terms of the structure, principle, usage method, etc. of the medical device, the technical documents need not be attached.
   In addition, the specific contents of the technical documents to be attached corresponding to

the type of medical device will be provided separately.

6. In addition to the attached technical documents, when applying for marketing approval, submit the summary technical documentation that accurately and concisely summarizes the contents of the attached technical documents, including intended use, indications, structure, principle, product specifications, operation method or usage method, draft package insert, 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 is submitted for a medical device deemed to be equivalent to a new medical device during the re-examination period of the new medical device, technical documents equivalent to or greater than those for the new medical device must be attached.

8. Even if the above item 7 applies, if the application is submitted for partial changes in approved information according to Article 14, Paragraph 9 of the Pharmaceutical Affairs Law (including cases where applied *mutatis mutandis* to Article 19-2, Paragraph 5), then some of the technical documents need not be attached for the reason of the partial changes .

III. Miscellaneous

1. When the application is made for a new medical device for which there exists no applicable generic name at the time of application for marketing approval, then the applicant must create a new generic name and define the medical device category (e.g., specially controlled medical device) based on the opinion of the Pharmaceutical Affairs and Food Sanitation Council, in addition to the result of the approval review.

[Appendix]

Table 1.

Contents of Attached Technical Documents and Summary Technical Documentation

Attached technical documents	Contents of attached technical documents	Summary technical documentation
a. Technical documents on the origin or course of discovery and usage status overseas	1. Technical documents on the origin or course of the development 2. Usage status overseas 3. Comparison with similar medical devices	1. Summary of the product 3. Information on the device 3.5 Comparison with similar medical devices
b. Technical documents on establishment of the specifications	1. Technical documents on the specifications and establishment of the specifications	3. Information on the device 3.3 Product specifications
c. Technical documents on stability and durability	1. Technical documents on stability and durability	4. Summary of design verification and validation documents
d. Technical documents on conformity to the standards stipulated in Article 41, Paragraph 3 of the Law	1. Technical documents on declaration of conformity to the essential principles 2. Technical documents on conformity to the essential principles	2. Essential principles and conformity to the essential principles
e. Technical documents on performance	1. Technical documents on the tests to support the performance and safety 2. Technical documents on the tests that support the indications 3. Technical documents on the tests that support the usage method	4. Summary of design verification and validation documents
		5. Labeling
f. Technical documents on risk analysis	1. Technical documents on the system to execute risk analysis 2. Technical documents on important hazards	6. Risk analysis
g. Technical documents on manufacturing method	1. Technical documents on the manufacturing process and the manufacturing facility 2. Technical documents on sterilization method 3. Technical documents on quality control	7. Information on the manufacturing
h. Technical documents on clinical trial results	1. Technical documents on clinical trial results 2. Investigation plan (draft) for the usage results of the new medical device	4. Summary of design verification and validation documents

[Appendix]

Table 2.

Scope of Technical Documents to Be Attached to

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	
	1	2	3	1	1	1	2	1	2	3	1	2	1	2	3	1	2
(1) Clinical trial required (new medical devices)	○	○	○	○	△	○	○	○	△	△	○	○	○	△	○	○	○
(2) Clinical trial required	○	○	○	○	△	○	○	○	△	△	○	○	○	△	○	○	×
(3) No approval standards established, no clinical trial required	○	○	○	○	△	○	○	○	△	△	○	○	○	△	○	×	×
(4) Approval standards established, no clinical trial required	×	△	○	○	△	○	○	○	△	△	○	○	○	△	○	×	×
(5) No approval standards and no certification standards established for controlled medical devices	△*	△	○	○	△	○	○	○	△	△	○	○	○	△	○	△	△

The symbols and numbers indicate the symbols and numbers of technical documents stipulated in Table 1 of the Appendix. "○" indicates that the documents must be attached, "×" indicates that the documents need not be attached, and "△" indicates whether to attach the documents is determined for each medical device.

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

Note: For specially controlled medical devices with established approval standards that do not meet the standards, the Ministry will decide which of the following categories the each device belongs to, "Clinical trial required" or "No Approval standards established, no clinical trial required."

Controlled medical devices for which approval standards are presented belong to "Approval standards established, no clinical trial required" ,and items that do not conform to certification standards belong to “No approval standards and no certification standards established for controlled medical devices.”