Provisional Translation (as of March 2020)*

PFSB Notification No. 1121-15

November 21, 2014

To: Prefectural Governors

Director of the Pharmaceutical and Food Safety Bureau,
Ministry of Health, Labour and Welfare
(Official seal omitted)

Applications for Marketing Approval of *In Vitro* Diagnostics

The handling of applications for marketing approval of *in vitro* diagnostics is described in the "Applications for Marketing Approval of *In Vitro* Diagnostics" (PFSB Notification No. 0216004, dated February 16, 2005, issued by the Director of the Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare [MHLW]), etc.

The Act for Partial Amendment of the Pharmaceutical Affairs Act (Act No. 84 of 2013; hereinafter referred to as the "Revised Act") was promulgated on November 27, 2013. Subsequently, the following Cabinet Orders and Ministerial Ordinance were promulgated on July 30, 2014: the "Cabinet Order to Specify the Enforcement Date of the Act for Partial Amendment of the Pharmaceutical Affairs Act" (Cabinet Order No. 268 of 2014), "Cabinet Order on Arrangement etc. of Relevant Cabinet Orders and Interim Measures Incidental to Enforcement of the Act for Partial Amendment of the Pharmaceutical Affairs Act" (Cabinet Order No. 269 of 2014), and "Ministerial Ordinance on Arrangement of Relevant Ministerial Ordinances Incidental to Enforcement of the Act for Partial Amendment of the Pharmaceutical Affairs Act and to Enforcement of Cabinet Order on Arrangement etc. of Relevant Cabinet Orders and Interim Measures Incidental to Enforcement of the Act for Partial Amendment of the Pharmaceutical Affairs Act" (MHLW Ordinance No. 87 of 2014; hereinafter referred to as the Revised Ministerial Ordinance). The Revised Act, Cabinet Orders, and Ministerial Ordinance will come into force on November 25, 2014.

The MHLW previously notified in the "Enforcement of the Act for Partial Amendment of the Pharmaceutical Affairs Act etc." (PFSB Notification No. 0806-3, dated August 6,

*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.

2014, by the Director of the Pharmaceutical and Food Safety Bureau, MHLW) that the application form for marketing approval of *in vitro* diagnostics and the details of data to be attached to the application form would be notified at a later date. We have decided on the handling as provided below. You are therefore requested to review the information below, and notify all relevant associations, organizations and other parties under your jurisdiction of the information.

This Notification shall come into force as of November 25, 2014, and the former notification will be abolished upon application of this Notification.

Copies of this Notification will be sent to the Chief Executive of the Pharmaceuticals and Medical Devices Agency (PMDA); the President of the Federation of Pharmaceutical Manufacturers' Associations of Japan; the President of the Japan Association of Clinical Reagents Industries; the Chairman of the American Medical Devices and Diagnostics Manufacturers' Association; the Chairman of the Medical Equipment & Diagnostics Committee of the European Business Council in Japan; and the Chairman of the Association of Registered Certification Bodies under the Pharmaceutical Affairs Act.

Chapter I General Provisions

1 When an application for marketing approval of an *in vitro* diagnostics product is submitted by an applicant who intends to market the product or who intends to have a designated marketing authorization holder market the product, in accordance with the provisions in Article 23-2-5 and Article 23-2-17, Paragraph 1 of the "Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics" (Act No. 145 of 1960; hereinafter referred to as the Act) as revised by the Revised Act, the Minister of Health, Labour and Welfare shall approve the product on a per-product basis after a required regulatory review of the product in terms of its intended use, shape, structure, principle, product specifications, method of use, etc., unless the product falls under "specified *in vitro* diagnostics" designated by the Minister of Health, Labour and Welfare, in accordance with the standards established by the Minister, based on the provisions of Article 23-2-5, Paragraph 1 and Article 23-2-23, Paragraph 1 of the Act. The application for marketing approval must be accompanied by data (which must be ethical, scientific, and reliable according to the latest academic standards of medicine, pharmacology, etc.) that

provide adequate evidence to demonstrate the quality, efficacy, and safety of the proposed *in vitro* diagnostic product.

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

(1) The term "Enforcement Ordinance" refers to the "Ministerial Ordinance for Enforcement of the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics" (Ministry of Health and Welfare [MHW] Ordinance No. 1 of 1961) as revised pursuant to the provisions in the Revised Ministerial Ordinance. The term "Essential Standards" refer to the "Standards of *In Vitro* Diagnostics Defined by the Minister of Health, Labour and Welfare pursuant to the Provisions in Article 41, Paragraph 3 of the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics" (MHLW Ministerial Announcement No. 126 of 2005).

(2) The term "novel analytes or parameters" refer to target analytes or parameters that have never been detected or measured by any *in vitro* diagnostics already approved or certified in Japan.

(3) The term "approval standards" refer to the standards of *in vitro* diagnostics required to undergo a regulatory review that evaluates their conformity to the standards stipulated in the "Establishment of Approval Standards of *In Vitro* Diagnostics" (PFSB Notification No. 0622006, dated June 22, 2005, by the Director of the Pharmaceutical and Food Safety Bureau, MHLW).

Chapter II Categories of Application for Marketing Approval

Listed below are the application categories of marketing approval of *in vitro* diagnostics. Figure 1 shows the categories and subcategories of data to be submitted with application for marketing approval. Table 2 shows the scope of data that must be submitted with the application, shown separately for each application category.

(1) Novel products

Products intended to detect or measure novel target properties.

(2) Products without approval standards

A product falls into this category if its generic name does not have applicable approval standards.

(3) Products with approval standards

A product falls into this category if its generic name has applicable approval standards.

(4) Products without conformity to standards

A product falls into this category if its generic name has applicable approval and certification standards (standards pursuant to Article 23-2-23, Paragraph 1 of the Act) and applicable standards for waiver of approval or certification (standards pursuant to Article 23-2-5, Paragraph 1 of the Act) but the product does not meet these standards.

Chapter III Others

If no applicable generic name is available for an *in vitro* diagnostic product proposed for marketing approval, a new generic name should be established during the regulatory review of the product.

Table 1

Categories and Subcategories of Data to Be Submitted with Application

Categories	Subcategories
A. History of Development and Status of Use in Foreign Countries, etc.	1. History of development and Status of use in foreign countries, etc.
	2. Description of the product submitted for registration
B. Specifications	1. Method of quality control
	2. Measurements range, etc.
	3. Reference materials for calibration
C. Stability	Storage conditions and shelf life
D. Conformity to the Standards Stipulated in Article 41, Paragraph 3 of the Act	Conformity to Essential Principles
E. Performance	1. Performance
	2. Method of operation
	3. Specimens
	4. Correlation with approved *in vitro* diagnostics
	5. Studies using seroconversion panels, etc.
F. Risk Management	Risk management
G. Manufacturing Method	Manufacturing process and manufacturing sites
H. Clinical Performance Data	Clinical performance data

Table 2

Scope of Data Submitted with Application for Marketing Approval

	A. History of Discovery		**B.** Specifications			**C.** Stability and Durability	**D** Conformity to Standards	**E.** Performance					**F.** Risk Management	**G.** Manufacturing Method	**H.** Clinical Performance Data
	1	2	1	2	3			1	2	3	4	5			
Novel products	○	○	○	○	○	○	○	△	○	○	–	△	○	○	○
Products without approval standards	○	○	○	○	○	○	○	△	△	○	○	△	○	○	△
Products with approval standards	×	○	△	×	△	○	○	×	×	×	○	△	○	○	△
Products without conformity to standards	○	○	○	○	○	○	○	△	△	○	○	△	○	○	△

The alphabets and numbers correspond to those in “Categories” and “Subcategories,” respectively, in Table 1.

“○” indicates data that must be submitted.

“×” indicates data that need not be submitted.

“△” indicates data that may be, or may not be, submitted, as determined on a per-product basis.