



PMDA/OSI Notification No. 1031002

PMDA/OSII Notification No. 1031002

October 31, 2014

Director of Office of Safety I, Pharmaceutical and Medical Devices Agency

Director of Office of Safety II, Pharmaceutical and Medical Devices Agency

To: (Refer to the heads of organization as listed separately)

Points to Consider for Consultations Related to Revisions of Package Insert Language

In accordance with the Act on Securing Quality, Efficacy, and Safety of Pharmaceuticals, Medical Devices, etc. (Act No. 145 of 1960; hereinafter, the “Act”), which was revised pursuant to the Act for Partial Amendment of the Pharmaceutical Affairs Act etc.” (Act No. 84 of 2013), the legal category of regenerative medicine product was newly defined, and marketing authorization holders (hereinafter, “MAHs”) of ethical drugs (excluding *in vitro* diagnostics and drugs not requiring approval; the same shall apply hereinafter), Pharmacist Intervention Required Medicines (hereinafter, “PIRMs”), specially controlled medical devices (hereinafter, “Class IV medical devices”), and regenerative medicine products are required to publish and provide notifications regarding the contents set forth in each item of Article 52-1, Article 63-2-(i), and Article 65-3-(i) of the Act (hereinafter, “Package Insert Language”).

In addition, “Points to Consider when Providing Notification, etc. concerning Package Insert Language” (Notification No. 0901-1, by the Director, Safety Division, PFSB, MHLW, dated September 1, 2014; hereinafter, the “Director Notification”) specified that notification of Package Insert Language is mandatory as of November 25, 2014.

In accordance with these changes, the Offices of Safety I and II at the Pharmaceuticals and Medical Devices Agency (PMDA) have, in order to ensure the safety of ethical drugs, medical devices, regenerative medicine products, quasi-drugs, and cosmetics, set forth various points to

consider regarding consultations associated with revisions, etc. [Revision Consultations] to package inserts and patient information leaflets (including user manuals), consultations regarding amendments and guidance concerning other safety measures (including product improvement, etc.) [Other Consultations] with MAHs, which will become applicable from the date of issue of this Notification. We request that you circulate this Notification among the relevant parties under your supervision.

Regarding the enforcement of this notification, “Changes in face-to-face consultation application form and reception method associated with revisions of package inserts of pharmaceuticals and medical devices” (Joint Administrative Notice, Office of Safety I and Office of Safety II, PMDA, dated March 25, 2014) will be abolished.

1. General points to consider

If you apply for consultation, please fill out the Consultation Application Form and send it to PMDA via facsimile or e-mail. If you would like to have a face-to-face interview during consultation, please include the proposed interview date and time in the “Requested date of interview” column of the Consultation Application Form. Application for a preliminary consultation is required when preparing notification of revisions to Package Insert Language for ethical drugs, PIRMs, Class IV medical devices, or regenerative medicine products requiring notification as specified in the Director Notification. Accordingly, the “Consultation Application Form (for Revisions, etc. to Package Inserts)” should be used for such preliminary consultations (excluding cases where a preliminary consultation is not necessary, such as corrections of typographical errors, etc.) If you would like to discuss matters other than those listed in the “Consultation Application Form (for Revisions, etc. to Package Inserts)”, please use the “Consultation Application Form (for Other Safety Measures).”

2. Consultations for Class IV medical devices and regenerative medicine products

If revision to Package Insert Language is intended in conjunction with the submission of a malfunction report, a foreign corrective action report, or a research report, provision of the proposed revisions in such a report may be considered as a preliminary consultation. However, the Consultation Application Form should be submitted separately nonetheless as it is necessary to obtain a consultation number for notification purposes. In this regard, it is sufficient to indicate in the “Consultation items” column of the Consultation Application Form that a preliminary consultation has been completed by submitting such a malfunction, corrective action, or research report.

3. Consultations for Class I-III medical devices

“Questions and Answers for Instructions for Package Inserts of Medical Devices” (Administrative Notice, Safety Division, the Safety Division, PFSB, MHLW dated October 31, 2014; hereinafter, the “Administrative Notice”) states that for Class I-III medical devices, a preliminary consultation should be performed if any content that could have a significant impact (on the safety of patients) is revised. The following items require consultation:

- Class II-III medical devices:

Revisions to: “Warnings”, “Contraindications”, “Precautions for intended uses or indications”, “Precautions (device should be used carefully in the following patients)”, “Contraindications for concomitant use (non-concomitant use)”, or “Clinically significant malfunctions and adverse events”

- Class I medical devices:

Revisions to: “Warnings”, “Contraindications”, or “Contraindications for concomitant use (no concomitant use)”

However, in “cases where a revision is made in accordance with the instructions or guidance provided in the Director Notification and the Consultation Number described in Section 4 is shared with other companies that have already consulted with PMDA”, no preliminary consultation is required for notification, as stated in the “Points to Consider for Notification and Publication of Package Insert Language” (Joint PMDA/OSI Notification No. 1031001/ PMDA/OSII Notification No. 1031001 by the Directors of the Offices of Safety I and II, PMDA, dated October 31, 2014). Accordingly, consultations for Class I-III medical device products are also not required. In addition, consultation is not required in the following cases:

- (1) When content pertaining to “examples of matters considered to have already been acknowledged by healthcare professionals in the course of providing medical care” that has been specified as material not requiring inclusion in package inserts, etc. in accordance with Attachment 1 of the Administrative Notice is revised.
- (2) When content that relates to the “Precautions to be Included in Package Insert of Electrical Medical Devices” (Notification No. 495 by the Director, Pharmaceutical Affairs Bureau (PAB), MHLW, dated June 1, 1972)” (abolished in accordance with “Revisions of Instructions for Package Inserts of Medical Devices” [Notification No. 1002-(10) by the Director, PFSB, MHLW, dated October 2, 2014]) and was designated as not requiring inclusion in package inserts pursuant to an Administrative Notice, is revised.

In addition, if Package Insert Language is revised in conjunction with the submission of a malfunction report, a foreign corrective action report, or a research report, the proposed revisions may be provided in such report. The submitting MAH will then be deemed to have completed a preliminary consultation. However, the Consultation Application Form should be submitted separately nonetheless. In this regard, it is sufficient to indicate in the “Consultation items” column of the Consultation Application Form that a preliminary consultation has been completed by submitting such a malfunction, corrective action, or research report.

4. Consultation for combination products

For consultations for revision of Package Insert Language of drugs etc. that constitute combination products (a device or processed cells in combination products corresponding to drugs, the drugs or processed cells in combination products corresponding to medical devices, or the drugs or device in combination products corresponding to regenerative medicine products), please use the Consultation Application Form appropriate for the product classification of the approved final combination product.

End of Document

(Company names)

President of the Federation of Pharmaceutical Manufacturers' Associations of Japan
President of the Japan Pharmaceutical Manufacturers Association
President of the Japan Federation of Self-Medication Industries
Chairman of the Japan Self-Medication Industry
Chairman of the European Federation of Pharmaceutical Industries and Associations
Chairman of the Japan-Based Executive Committee (JBEC) of the Pharmaceutical Research and Manufacturers of America (PhRMA)
Chairman of the Japan Federation of Medical Devices Associations
President of the Japan Association of Clinical Reagents Industries
Chairman of the Medical Equipment Committee of European Business Council in Japan
Chairman of the Medical Diagnostics Committee of European Business Council in Japan
Chairman of the American Medical Devices and Diagnostics Manufacturers' Association
Chairman of the Forum for Innovative Regenerative Medicine
President of the Japan Cosmetic Industry Association
President of the Japan Soap and Detergent Association
Director of the Japan Hair Color Industry Association
Director of the Japan Permanent Waving Lotion Industry Association
Chairman of the Japan Dentifrice Manufacturers' Association
Chairman of the Household Pesticide Industry Association of Japan
Chairman of the Hygienic Insecticide Industrial Association of Japan
Chairman of the Japan Hygiene Products Industry Association
Chairman of the Japan Bath Additive Industry Association
Chairman of the Cosmetic Committee of the European Business Council in Japan
Chairman of the Cosmetic Committee of the American Chamber of Commerce in Japan
Chairman of the Japan Direct-Selling Pharmaceutical Manufacturers Association
Chairman of the Home Medical Association of Japan
Chairman of the Japan Kampo Medicines Manufacturers Association
Chairman of the Japanese Society-Drug Home Delivery
Chairperson of the Cosmetic Importers Association of Japan
Chairman of the Aerosol Industry Association of Japan
Chairman of the Aerosol Hair Lacquer Industry Association of Japan
Chairman of the Japan Industry Association of Cleaning Papers/Cottons
Chairman of the Japan Association of Contract Laboratories for Safety Evaluation

President of the Japan Blood Products Association
Chief Executive of the Japan Association of Vaccine Industries
Chairman of the Association of Registered Certification Bodies under PAL
President of the Osaka Pharmaceutical Manufacturers Association
President of the Pharmaceutical Manufacturers' Association of Tokyo
President of the SAMURAI Biotech Association
President of the Japan Generic Medicines Association
Chairman of the Japan Society of Quality Assurance