



PMDA/OSI Notification No. 1031001

PMDA/OSII Notification No. 1031001

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 separately listed)

Points to Consider regarding the Notification and Publication 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”), revised pursuant to the Act for Partial Amendment of the Pharmaceutical Affairs Act etc. (Act No. 84 of 2013), marketing authorization holders of pharmaceuticals, medical devices, and regenerative medicine products (hereinafter, “MAHs”) are required to notify and publish the information 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” .)

Accordingly, points to consider related to the notification, etc. of Package Insert Language have now been made available in 2-I-2 (2) of “Enforcement of the Act for Partial Amendment of the Pharmaceutical Affairs Act etc.” (Notification No. 0806-3, by the Director of the Pharmaceutical and Food Safety Bureau [PFSB], Ministry of Health, Labour and Welfare [MHLW], dated August 6, 2014) and in “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”).

Based on these Notifications, we have specified points to consider regarding the notification, etc. of Package Insert Language, as follows. We request that you circulate this Notification among the relevant parties under your supervision.

1. Method of notification and publication

A. Ethical drugs (excluding *in vitro* diagnostics and drugs not requiring approval; the same shall

apply hereinafter.)

Notification of Package Insert Language and publication of the same on the website of the Pharmaceuticals and Medical Devices Agency (hereinafter, “PMDA”) should be done on the designated page of the PMDA website. For further details concerning methods of notification and publication of Package Insert Language as well as how to prepare this information for publication, please refer to the “Website for marketing authorization holders of drugs” (hereinafter, the “SKW website”), as necessary.

Notification is not mandatory for revisions outside the scope of Package Insert Language requiring notification as specified in the Director Notification, provided, that such revisions are not made contemporaneously with revisions requiring notification. However, information contained in package inserts, etc. should be published on the designated page of the PMDA website as mentioned above. When entering information on this page, please select “Mandatory notification: No” as the reason for revision.

B. Specially controlled medical devices (hereinafter, “Class IV medical devices”)

Notification of Package Insert Language and publication of the same on the PMDA website should be done on the designated page described previously. For further details concerning methods of notification, publication, and the preparation of information for publication, please refer to the “Website for marketing authorization holders of medical devices, *in vitro* diagnostics, and regenerative medicine products” (hereinafter, the “IKW website”) as necessary.

At the time of notification, a table comparing new and old Package Insert Language must accompany any revisions made. This comparative table should be submitted in renderable text PDF format. If revisions outside the scope of Package Insert Language are intended contemporaneously with revisions to Package Insert Language, all revisions should be reflected in the same comparative table.

For products subject to the transitional measures described in “Revisions of Instructions for Package Inserts of Medical Devices” (Notification No. 1002-(8) by the Director, PFSB, MHLW, dated October 02, 2014), the following dates should be included in the comments column when providing the required information.

- If the product was approved prior to November 25, 2014 and the date of the new notification falls on or after November 25, 2014: The product approval date
- If the product was pending approval on November 25, 2014: The product application submission date

No notification is required for revisions outside the scope of Package Insert Language. However, the information contained in the package inserts, etc. should be published on the designated page of the PMDA website as mentioned above. When entering information on this page, please select “Mandatory notification: No” as the reason for revision.

C. Pharmacist Intervention Required Medicines (hereinafter, “PIRMs”)

When issuing notifications of Package Insert Language, the required information should be

provided on the specified form. The completed form should be delivered in person or via postal mail to the Risk Communication Promotion Division, Office of Safety I, PMDA.

When preparing notifications, the appropriate “Consultation Number” as described in Section 4 herein, in addition to the name of the responsible party, their department, and contact information (telephone number, e-mail address) should be included in the comments column of the form. Inclusion of a “Consultation Number” is not required with respect to consultations for which no “Consultation Number” has been issued.

Information regarding package inserts, etc. should be published on the designated page of the PMDA website.

For further details concerning methods of notification, publication, and the preparation of information for publication, please refer to the SKW site, as necessary.

D. Regenerative medicine products

When notifying Package Insert Language, the required information should be provided on the specified form. The completed form should be delivered in person or via postal mail to the Risk Communication Promotion Division, Office of Safety I, PMDA. When submitting notifications, one (1) CD-R or DVD-R containing the revised package insert information as well as a table comparing the old content against the intended revisions in renderable text PDF format should be included with your submission. Refer to the IKW website as necessary for guidance regarding the proper naming of PDF files.

When preparing notifications, the appropriate “Consultation Number” as described in Section 4 herein, in addition to the name of the responsible party, their department, and contact information (telephone number, e-mail address) should be included in the comments column of the form. Inclusion of a “Consultation Number” is not required with respect to consultations for which no “Consultation Number” has been issued.

2. Preliminary consultation for revision

For revisions to Package Insert Language requiring notification, with the exception of the cases specified in items A through G in Section 3 below, requests for consultation should be made in advance to the Office of Safety II, PMDA for ethical drugs and PIRMs, and to the Medical Devices Safety Division, Office of Safety I, PMDA for Class VI medical devices and regenerative medicine products. If PMDA decides that discussion of safety measures is necessary and sends an inquiry to the relevant MAHs regarding such, such inquiry should be treated as a preliminary consultation.

3. Cases not requiring preliminary consultation

- A. When a revision is made in accordance with instructions or guidance set forth in the Director Notification and the applicable “Consultation Number” is shared with other companies that have already consulted with PMDA.
- B. When a revision is made voluntarily and the applicable “Consultation Number” is shared with other companies that have already consulted with PMDA.

C. When Package Insert Language is newly prepared or revised in connection with product approval (including approvals of partial amendments).

Application of this exemption is limited to cases where the package insert (draft) already accepted by the applicable review division of PMDA contains no changes to Package Insert Language requiring notification. In cases involving approvals of substitute products, the name of the drug (former brand name) should be included in the comments column.

D. When Package Insert Language is newly prepared in connection with the transfer of approval status

Application of this exemption is limited to cases where there have been no changes in Package Insert Language that requires notification from the package insert submitted by the original approval holder.

E. When revisions were made as a result of a change in a product name due to revision of the Japanese Pharmacopoeia

F. When any of the following revisions related to the instructions for package inserts of medical devices;

- revises the description of the “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 “Questions and Answers for Instructions for Package Inserts of Medical Devices” (Administrative Notice, Safety Division, PFSB, MHLW, dated October 31, 2014; hereinafter, the “Administrative Notice”).

- revises the content related to the “Precautions to be Included in Package Insert of Electrical Medical Device” (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 designated as not requiring inclusion in package inserts pursuant to an Administrative Notice.

G. Does not affect the substantive meaning of the content, such as corrections of typographical errors.

A table comparing old contents against new revisions should be included in the notification. Alternatively, an explanation of the revisions and their rationale should be included in the comments column.

4. Consultation Numbers

If PMDA decides that revision to Package Insert Language is necessary or valid as a result of a preliminary consultation with a MAH, PMDA will issue a “Consultation Number” to such MAH to be used for notification purposes. The MAH receiving this number must share the number with related MAHs when necessary. In all other instances, the Consultation Number should be kept secure internally. When submitting notifications, the Consultation Number must be typed or

written correctly.

Contemporaneous voluntary revisions corresponding to multiple “Consultation Numbers” should be notified together. Prepare a single comparative table of new and old contents, and consult with the Medical Devices Safety Division, Office of Safety I, PMDA or the Office of Safety II, PMDA for additional guidance.

Additionally, when revision in response to instructions for revision to precautions in package insert, etc. and voluntary revision are notified contemporaneously, the respective “Consultation Numbers” for these types of revisions should each be typed or written in the form, and numbers should be separated by commas.

When providing notifications concerning ethical drugs and Class IV medical devices on the designated webpage, an error will occur if the “Consultation Number” column is left blank. Accordingly, please enter “9999” in this column when submitting notifications with no corresponding “Consultation Number” issued by PMDA (as in items C through G in Section 3 above).

5. Timing of notification

A. Notification based on approval

Notification should be submitted well in advance; submit notification either before the start of marketing or before providing information on the Package Insert Language, whichever is earlier.

Notifications regarding ethical drugs, PIRMs, or regenerative medicine products may be provided prior to approval if the applicable review division of PMDA has already accepted the draft package insert. Notifications concerning Class IV medical devices should be made following approval.

B. Notification based on the transfer of approval

Notification should be submitted well in advance; submit notification either before the start of marketing or before providing information on Package Insert Language, whichever is earlier. Notification may be submitted even before the transfer of approval is effected.

C. Notification based on the notification of revision instructions, etc. or voluntary revision

Notifications should be submitted well in advance, before the start of information provision.

D. Notification based on the distribution of the Dear Healthcare Professional Letters of Emergent Safety Communications (Yellow Letters) or Dear Healthcare Professional Letters of Rapid Safety Communications (Blue Letters)

Please cooperate fully with PMDA and promptly submit notifications. Prompt submissions allow this important information to be disseminated more quickly.

6. Notice of receipt

Once a notification is received, PMDA will notify the submitting MAH of such fact and will provide a registration number, etc. via e-mail. For notifications concerning ethical drugs

and Class IV medical devices, PMDA will provide confirmation of its receipt of the notification to the contact address previously registered on the webpage designated. For notifications concerning PIRMs and regenerative medicine products, PMDA will provide confirmation of its receipt of the notification to the contact address provided in the form. The registration number provided should be used when making inquiries to PMDA. Please note that notifications will be formally deemed as received through this e-mail confirmation of receipt from PMDA.

7. Notice of acceptance

After the content submitted is confirmed by PMDA, PMDA will confirm via e-mail that the content of notification has been accepted. For ethical drugs and Class IV medical devices, this confirmation will be provided to the contact address pre-registered on the website designated. For PIRMs and regenerative medicine products, this confirmation will be provided to the contact address provided in the form.

The confirmation process by PMDA typically requires approximately 5 business days. However, please recognize that during periods where PMDA receives large numbers of notifications, including notifications involving generic drugs included in the National Health Insurance Drug Price Standard Listing, a greater amount of time may be required for confirmation. Accordingly, notifications should be submitted well in advance.

Package Insert Language for ethical drugs, Class IV medical devices, and regenerative medicine products will be published on the PMDA website on either the date of acceptance or on the planned publication date set by the MAH, whichever is later.

8. How to respond to a request for correction from PMDA

In the event that any deficiencies, etc. are discovered by PMDA during its review of submitted content, PMDA will notify the submitting MAH via e-mail of any necessary corrections. For ethical drugs and Class IV medical devices, this notification will be provided to the contact address pre-registered on the website designated. For PIRMs and regenerative medicine products, this notification will be provided to the contact address provided in the form. If you receive a correction request from PMDA, applicable procedure for correction etc. should be adopted.

9. Others

- A. Requests for further information regarding how to access the SKW and IKW sites should be directed to the Risk Communication Promotion Division, Office of Safety 1, PMDA.
- B. Notification is not required with respect to over-the-counter drugs and Class I-III medical devices. However, because the information contained in the package inserts etc. for these products (renderable text PDF format for class I-III medical devices) can be posted on the same designated page on the PMDA website, the SKW and IKW sites should be referred to

as appropriate.

10. Effective date

This Notification will come into effect on November 25, 2014.

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