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Pharmaceuticals and Medical Devices Agency

PSEHB/PED Notification No. 0318-2
PSEHB/PSD Notification No. 0318-1
March 18, 2022

To: Directors of Prefectural Health Departments (Bureaus)

Director of Pharmaceutical Evaluation Division,
Pharmaceutical Safety and Environmental
Health Bureau, Ministry of Health, Labour and
Welfare
(Official seal omitted)

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

Risk Management Plan templates, instructions and publication

The Ministry of Health, Labour and Welfare (herein after referred to as MHLW) previously issued notifications entitled "Risk Management Plan templates and instructions" (PFSB/ELD Notification No. 0426-2 and PFSB/SD Notification No. 0426-1 dated April 26, 2012, Joint Notification by the Director of Evaluation and Licensing Division and the Director of Safety Division, Pharmaceutical and Food Safety Bureau, MHLW), "Publication of Risk Management Plans (PFSB/ELD Notification No. 0304-1 and PFSB/SD Notification No. 0304-1 dated March 4, 2013, Joint Notification by the Director of Evaluation and Licensing Division and the Director of Safety Division, Pharmaceutical and Food Safety Bureau, MHLW), "Creation and Publication of RMP Outline Sheets" (PSEHB/ELD Notification No. 0331-13 and PSEHB/SD Notification No. 0331-13 dated March 31, 2016, Joint Notification by the Director of Evaluation and Licensing Division and the Director of Safety Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW), and "Application of the Risk Management Plan Guideline for Generic Drugs" (PFSB/ELD Notification No. 0826-3 and PFSB/SD Notification No. 0826-1 dated August 26, 2014, Joint Notification by the Director of the Evaluation and Licensing Division and the Director of the Safety Division, Pharmaceutical and Food Safety Bureau, MHLW) and described handling of templates submission, publication, and generic products for Risk Management Plan (hereinafter referred to as "RMP").

This time, concerning handling of Risk Management Plan templates and instructions and publication, the templates submission method, timing of submission, etc. have been reviewed in order to improve the efficiency of preparation and submission of the RMP by marketing authorization holders (hereinafter referred to as MAHs), and the previous notifications have been organized and integrated as shown in the Attachment. Please understand this matter and disseminate it to related organizations under your jurisdiction.

This notification will come into effect on May 1, 2022. However, for Appended Form 1, which is used for submission of the draft RMP at the time of making an approval application based on Attachment 2. in this notification and for submission of the RMP based on Attachment 3., 4. and 5. in this notification, it is acceptable to use the Appended Form of "Risk Management Plan templates and instructions" (PFSB/ELD Notification No. 0426-2 and PFSB/SD Notification No. 0426-1 dated April 26, 2012, Joint Notification by the Director of Evaluation and Licensing Division and the Director of Safety Division, Pharmaceutical and Food Safety Bureau, MHLW) for one year after the application of this notification as a transition period.

In association with the implementation of this notification, "Risk Management Plan templates and instructions" (PFSB/ELD Notification No. 0426-2 and PFSB/SD Notification No. 0426-1 dated April 26, 2012, Joint Notification by the Director of Evaluation and Licensing Division and the Director of Safety Division, Pharmaceutical and Food Safety Bureau, MHLW), "Publication of Risk Management Plans" (PFSB/ELD Notification No. 0304-1 and PFSB/SD Notification No. 0304-1 dated March 4, 2013 ,Joint Notification by the Director of Evaluation and Licensing Division and the Director of Safety Division, Pharmaceutical and Food Safety Bureau, MHLW), "Creation and Publication of RMP Outline Sheets" (PSEHB/ELD Notification No. 0331-13 and PSEHB/SD Notification No. 0331-13 dated March 31, 2016, Joint Notification by the Director of Evaluation and Licensing Division and the Director of Safety Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW), and "Application of the Risk Management Plan Guideline for Generic Drugs" (PFSB/ELD Notification No. 0826-3 and PFSB/SD Notification No. 0826-1 dated August 26, 2014, Joint Notification by the Director of the Evaluation and Licensing Division and the Director of the Safety Division, Pharmaceutical and Food Safety Bureau, MHLW) will be abolished.

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Attachment

Handling of Risk Management Plan templates, instructions and publication

1. Preparation of the RMP
   (1) A document of the RMP should be prepared using Appended Form 1.
   (2) A single document of the RMP for a drug with an active ingredient that has different indications, dosages and administrations, forms and routes of administration, etc. is acceptable.
   (3) A document of the RMP by joint names is acceptable as well, when multiple MAHs collaborate on their pharmacovigilance activities and risk minimization activities for their drug products. In this case, even in the cases that the information is different depending on the drug products, the information should be described in the same column clarifying the differences between the drug products.

2. Submission of a draft of the RMP at the time of the application for marketing authorization
   (1) When a new drug application is filed, the applicant for marketing authorization shall file a draft RMP prepared using Appended Form 1 instead of a draft of Post-Marketing Surveillance and Study Basic Plan shown in 3-1-1-(11) and Attachment 2-11 of the notification entitled "Points of preparation for the data to be attached for application form in the new drug application" (PMSB/ELD Notification No. 899 dated June 21, 2001 by the Director of Evaluation and Licensing Division, Pharmaceutical and Medical Safety Bureau, MHLW).
   (2) In terms of biosimilars/follow-on biologics, the applicants for marketing authorization shall file a draft RMP prepared using Appended Form 1, based on Attachment 7 to the "For 'the Guidelines for ensuring the quality, safety and efficacy of biosimilars/follow-on biologics'" (PSEHB/PED Notification No. 0204-1 dated February 4, 2020 by the Director of the Pharmaceutical Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW).
   (3) In terms of generic drug products, the applicants for marketing authorization shall file a draft RMP prepared using Appended Form 1 when the applicants submit an approval application for generic drug products with the same indication, etc. as those of the original drugs for which an RMP has been published based on below 6.

3. Submission of RMP
   (1) i) In the case of products for which a draft RMP has been submitted based on the above 2-(1) at the time of the new drug application, an RMP should be submitted with attachments instead of the Post-Marketing Surveillance and Study Basic Plan under Section 3 of the notification entitled “Basic plans including post-marketing surveillance and studies pertaining to the re-examination of new medicinal products” (PFSB/ELD Notification No. 1027007 dated October 27, 2005 by the Director of Evaluation and Licensing Division, Pharmaceutical and

Food Safety Bureau, MHLW). It is desirable to publish, promptly after approval, an RMP and materials to be prepared and provided for healthcare professionals and patients as additional risk minimization activities (hereinafter referred to as "materials"). Therefore, in consideration of the confirmation period at the Pharmaceuticals and Medical Devices Agency (hereinafter referred to as PMDA), submission should be made promptly after the completion of the First or Second Committee on New Drugs of the Pharmaceutical Affairs and Food Sanitation Council, which deliberates or reports on the approval of the target drug. Even if it takes time to submit the RMP and attachments for special reasons, they should be submitted no later than one month before the timing of the planned product market launch.

ii) In the case of products for which a draft RMP is submitted by the MAHs based on the above 2-(2) at the time of the application for approval, an RMP with attachments should be submitted. The timing of submission should be in accordance with i) above.

iii) In the case of products for which a draft RMP is submitted by the MAHs based on the above 2-(3) at the time of the application for approval, an RMP with attachments should be submitted. The submission should be made promptly after the completion of the review of the relevant product for the same reason as i) above. Even if it takes time to submit the RMP and attachments for special reasons, they should be submitted no later than one month before the timing of the planned product market launch.

iv) When submitting an RMP for i), ii), and iii) above, a cover page with a title of "Risk Management Plan for XXX (brand name)" and an outline of the RMP prepared using Appended Form 2 should be attached to the RMP prepared using Appended Form 1, and they should be submitted with a submission notification prepared using Appended Form 3. In the case of more than one brand name, each brand name should be identified by describing the title such as "Risk Management Plan for XXX (brand name)/ YYY (brand name)" on the cover page.

(2) Items in the Appendix should be described in the Post-Marketing Surveillance and Study Implementation Plan. As a general rule, the Post-Marketing Surveillance and Study Implementation Plan should be filed as an attachment of the RMP one month before the timing of the planned start of the surveillance or clinical studies.

(3) An RMP should be submitted by e-mail to the Administration Division Ⅰ of the Office of Review Administration, PMDA (ann-madoguchi@pmda.go.jp). Attachments to be submitted should be a text-based PDF file with no copy protection.

4. Submission of the RMP when new safety concerns have been identified in the post-marketing phase

When new safety concerns have been identified in the post-marketing phase and the MAHs want to develop or change the RMP, contact PMDA regarding the timing of submission and the contents of the RMP.

5. Changes in RMP

Including the case of the above 4, for a change in the RMP, except for a minor change, the latest RMP should be submitted to PMDA. At the time of submission, an outline of

the contents of the changes (name of the applicable items, an outline of the contents of the changes, the reason for the changes, etc.) should be described in the column of change history, and the changed part should be underlined. In addition, a series of documents specifying the details of the contents of the changes (old/new comparison tables including the contents before and after the changes, history of the amendments, etc.) should be submitted as a reference.

6. Publication of RMP

(1) The following RMPs should be included in the scope for publication:

i) RMPs of new drugs and biosimilars/follow-on biologics for which approval applications are submitted on or after April 1, 2013.

ii) RMPs for generic drugs.

iii) RMPs submitted to the PMDA on or after April 1, 2013 by MAHs because new safety concerns have been identified in the post-marketing phase.

iv) The latest RMPs submitted to the PMDA by the MAHs due to changing RMPs that have been submitted to the PMDA in accordance with i), ii) or iii).

(2) The scope of publication documents

The following i) and ii) (hereinafter referred to as "publication documents") should be a text-based PDF file with no copy protection.

i) RMP submitted to the PMDA (cover page with a title of "Risk Management Plan for XXX [brand name]," outline of the RMP prepared using Appended Form 2, and RMP itself prepared using Appended Form 1).

ii) Of attachments submitted with an RMP to the PMDA, materials to be prepared and provided for healthcare professionals and patients as additional risk minimization activities.

(3) Posting and deletion of the publication documents on the PMDA's website should be done according to the following procedures:

i) After an RMP is submitted based on 3, 4, and 5 above, the PMDA notifies the MAH to post the publication documents on the PMDA's website. After receiving the notification from the PMDA, the MAH should upload the publication documents described in (2) on the dedicated page of the PMDA's website to post them within five business days in principle. If there is a minor change, it is not necessary to submit the RMP or materials to the PMDA, but the publication documents should be changed promptly on the dedicated page of the PMDA's website.

ii) If it is judged that all additional activities are completed and the conditions for approval related to the RMP are satisfied as a result of the evaluation by the PMDA, the MAH should delete the publication documents from the PMDA's website within five business days in principle from the date of issuance of the Administrative Notice related to lifting of the conditions for approval.

iii) When additional risk minimization activities are partially completed, the MAH should delete the corresponding materials from the PMDA's website in association with updating the RMP.

7. Assessment reports based on implementation of an RMP for biosimilars/follow-on

biologics and generic drugs

Handling of reports of assessment results on biosimilars/follow-on biologics and generic drugs, for which reporting of assessment results of RMPs is required based on the "Risk Management Plan Guidance" (PFSB/SD Notification No. 0411-1 and PFSB/ELD Notification No. 0411-2 dated April 11, 2012, Joint Notification by the Director of Safety Division and the Director of Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, MHLW), should be in accordance with the "Partial Amendment of 'Assessment Report After the End of Re-examination Period Based on Implementation of Risk Management Plan" (PSEHB/SD Notification No. 0302-1 dated March 2, 2018 by the Director of Pharmaceutical Safety Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW).

(Appended Form 1)

Risk Management Plan

Company Name:

Outline of the product			
Date of market authorization		Therapeutic category	
Re-examination period		Approval number	
International birth date			
Brand name			
Active ingredient			
Strengths and dosage form			
Dosage and administration			
Indication			
Conditions for approval			
Remarks			

Change history
Date of previous submission
Summary of the changed contents:
Reasons for change:

1. Summary of the Risk Management Plan

1.1 Safety specifications

Important identified risks	
(Name of identified important risks)	
	The reasons why it is identified as an important identified risk:
	The contents of pharmacovigilance activities and the reasons why they are chosen:
	The contents of risk minimization activities and the reasons why they are chosen:
(Name of a safety specification)	
	The reasons why it is identified as an important identified risk:
	The contents of pharmacovigilance activities and the reasons why they are chosen:
	The contents of risk minimization activities and the reasons why they are chosen:
(Name of a safety specification)	
	The reasons why it is identified as an important identified risk:
	The contents of pharmacovigilance activities and the reasons why they are chosen:
	The contents of risk minimization activities and the reasons why they are chosen:
Important potential risks	

(Name of important potential risks)	
	The reasons why it is identified as an important potential risk:
	The contents of pharmacovigilance activities and the reasons why they are chosen:
	The contents of risk minimization activities and the reasons why they are chosen:
(Name of a safety specification)	
	The reasons why it is identified as an important potential risk:
	The contents of pharmacovigilance activities and the reasons why they are chosen:
	The contents of risk minimization activities and the reasons why they are chosen:
(Name of a safety specification)	
	The reasons why it is identified as an important potential risk:
	The contents of pharmacovigilance activities and the reasons why they are chosen:
	The contents of risk minimization activities and the reasons why they are chosen:
Important missing information	
(Name of important missing information)	

	The reasons why it is identified as important missing information:
	The contents of pharmacovigilance activities and the reasons why they are chosen:
	The contents of risk minimization activities and the reasons why they are chosen:
(Name of a safety specification)	
	The reasons why it is identified as important missing information:
	The contents of pharmacovigilance activities and the reasons why they are chosen:
	The contents of risk minimization activities and the reasons why they are chosen:
(Name of a safety specification)	
	The reasons why it is identified as important missing information:
	The contents of pharmacovigilance activities and the reasons why they are chosen:
	The contents of risk minimization activities and the reasons why they are chosen:

1.2 Efficacy specification

(Name of an efficacy specification)	
	The reasons why it is identified as an efficacy specification:
	Name of the surveillance and/or the studies related to the efficacy
	Objective, summary of the contents, and method of the surveillance and/or the studies, and the reasons why the surveillance and/or the studies are chosen

2. Summary of the pharmacovigilance activities

Routine pharmacovigilance activities	
Summary of the routine pharmacovigilance activities:	
Additional pharmacovigilance activities	
(Name of the pharmacovigilance activity)	
(Name of the pharmacovigilance activity)	
(Name of the pharmacovigilance activity)	

3. Summary of the plans for surveillance and studies for efficacy

(Name of surveillance or study for efficacy)	
(Name of surveillance or study for efficacy)	
(Name of surveillance or study for efficacy)	

4. Summary of the risk minimization plan

Routine risk minimization activities	
Summary of the routine risk minimization activities:	
Additional risk minimization activities	
(Name of the risk minimization activity)	
(Name of the risk minimization activity)	
(Name of the risk minimization activity)	

5. Lists of the pharmacovigilance plan, surveillance and studies for efficacy, and the risk minimization plan

5.1 A list of the pharmacovigilance plans

Routine pharmacovigilance activities				
Additional pharmacovigilance activities				
(Name of the additional pharmacovigilance activities)	Milestones for the number of cases/ Target number of cases	Timing to reach milestones	Implementation status	Due date for preparation of the report

5.2 A list of plans on surveillance and studies for efficacy

(Name of the surveillance and studies)	Milestones for the number of cases /Target number of cases	Timing to reach milestones	Implementation status	Due date for preparation of the report

5.3 A list of risk minimization plans

Routine risk minimization activities		
Additional risk minimization activities		
Name of additional risk minimization activities	Timing to reach milestones	Implementation status

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Guide for developing Appended Form 1

1. General
   - The text should be laid out for Japanese Industrial Standards A4 paper.
   - For all particular items in the RMP, if there is no statement to be included in the column, the author may put N/A in the space.
   - If a submitter files a draft RMP as a part of applications for new drugs, biosimilars/follow on biologics, generics and partial changes, it is recommended that the document should be submitted along with an outline of the draft of Post-Marketing Surveillance and Study Implementation Plans for additional pharmacovigilance activities and surveillance and studies for efficacy, and the draft of materials for additional risk minimization activities at the time.
   - If a submitter files a draft of an RMP other than a point of drug application, a draft of Post-Marketing Surveillance and Study Implementation Plans for additional pharmacovigilance activities and surveillance and studies for efficacy, and a draft of materials for additional risk minimization activities should be submitted at the time of submission.

2. Outline of the products
   - If a submitter files a draft of an RMP as a part of a drug application or files a draft of an RMP before approval (after completion of the Committee on Drugs, Pharmaceutical Affairs and Food Sanitation Council or after the completion of review), the submitter should leave the undecided items such as "approval date," "approval number" and "conditions for approval," etc., as blank. For the items of "therapeutic category," "dosage and administration" and "indication," etc., the author should describe the same contents as the marketing application form and put "planned" on each item.
   - In the remarks column, the following should be stated:
     - The distinction of generic drug, etc.
     - The name of the product and the company name in the case of a joint development product. If an RMP is submitted to PMDA by joint names of the relevant parties for their products, a description of a joint development product is not required.

3. Summary of Risk Management Plan
   - For the safety specification, if there are some important identified risks, important potential risks and important missing risks, the author should increase the number of columns based on user need.
   - For "The reasons why it is identified as an important identified risk," "The reasons why it is identified as an important potential risk," and "The reasons why it is identified as important missing information," based on the information from non-clinical data, clinical data and the situation of post marketing stage, the author should provide concise descriptions by attaching related information and literature and using citations from the documents, etc. If a submitter files a draft of the RMP

as a drug application, it should be considered whether the items in the document are consistent with the related items in the Common Technical Document.

- If there are some efficacy specifications, the author should increase the number of columns based on user need.

4. Summary of pharmacovigilance plans
   - For additional pharmacovigilance activities, the relevant safety specification, objectives and reasons, etc., should be described. If there are some additional Pharmacovigilance activities, the author should increase the number of columns based on user need.
   - If there are additional pharmacovigilance activities, the implementation plans should be submitted as Post-marketing Surveillance and Study Implementation Plans.

5. Summary of plans on surveillance and studies for efficacy
   - For the surveillance and studies for efficacy, the relevant specifications related to efficacy, objective and reasons, etc., should be described. If there are some surveillance and studies for efficacy, the author should increase the number of columns based on user need.
   - If there are surveillance and studies for efficacy, the implementation plans should be submitted as Post-marketing Surveillance and Study Implementation Plans.

6. Summary of the risk minimization plan
   - For additional risk minimization activities, the relevant safety specifications, objectives and reasons should be described. If there are some additional risk minimization plans, the author should increase the number of columns based on user need.

7. Lists of the pharmacovigilance plan, plan of surveillance and studies for efficacy and risk minimization plan
   - For each, the author should prepare each plan not only in practice but also under planning.
   - In the column for status of implementation, the author should describe the status of implementation of each activity at the time of the update of the RMP.

8. Other attached documents
   - Describe the attached documents to the RMP in the list in Appended Form 3.
   - The following documents should be prepared as attached.
     (1) The Post-Marketing Surveillance and Study Implementation Plans for additional pharmacovigilance activities and surveillance and studies for efficacy
     (2) The materials, etc. for additional risk minimization activities

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(Appended Form 2)

Summary of Risk Management Plan (RMP) for ○○○○○○ (brand name)

Brand name	○○○○○○	**Active ingredient**	○○○○○○
Marketing authorization holder	○○○○○ Co., Ltd.	**Therapeutic category**	○○○○○○
Date of submission		DD/MM/YY	

1.1 Safety specifications		
[Important identified risks]	**[Important potential risks]**	**[Important missing information]**
(Name of a safety specification)	(Name of a safety specification)	(Name of a safety specification)

1.2. Efficacy specifications	
(Name of an efficacy specification)	

↓ Pharmacovigilance activities based on the above

2. Summary of the pharmacovigilance activities
Routine pharmacovigilance activities
Additional pharmacovigilance activities
(Name of the pharmacovigilance activity)
3. Summary of the plans for surveillance and studies for efficacy
(Name of surveillance or study for efficacy)

↓ **Risk minimization activities based on the above**

4. Summary of the risk minimization plan
Routine risk minimization activities
Additional risk minimization activities
(Name of the risk minimization activity)

Please confirm the contents of each item in the text of the RMP.

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Guide for developing Appended Form 2

1. Appended Form 2 should be prepared using the link tool of Adobe Acrobat as a link for each specification, concern, and activity in the RMP when it is posted on the PMDA's website according to Attachment 6. (3) in this notification. At the time of submission of an RMP according to Attachment 3.,4. and 5. in this notification, it is not necessary to set the link.
2. The brand name, active ingredient, and therapeutic category should be excerpted from page 1 of Appended Form 1.
3. For "1.1. Safety specification," "1.2 Efficacy specification," "2. Summary of the pharmacovigilance activities," "3. Summary of the plans for surveillance and studies for efficacy," and "4. Summary of the risk minimization plan," names of all specifications and concerns and activities described in the RMP should be extracted and described for each one.
4. In principle, the form should be prepared within an A4-sized piece of paper. For "1.1. Safety specification," "1.2 Efficacy specifications," "2. Summary of the pharmacovigilance activities," "3. Summary of the plans for surveillance and studies for efficacy," and "4. Summary of the risk minimization plan," since the number of items differs among drugs, the layout can be changed so that this summary fits in an A4-sized piece of paper as the number of items differs depending on drugs.
5. Enter "None" if no item is set.

(Appended Form 3)
DD/MM/YY

Risk Management Plan Notification of Submission/ Request for Replacement

To: Chief Executive, Pharmaceuticals and Medical Devices Agency

I hereby notify the following Risk Management Plan as attached.

Submission category	New / Change / Replacement
Brand name	(* Describe the official name including the strength, etc.)
Assigned area	(* In the case of a new drug or follow-on biologics, describe the assigned area based on Attachment 9 of "Implementation guidelines for clinical trial consultation and confirmation of certification, etc., conducted by the Pharmaceuticals and Medical Devices Agency" (PMDA Notification No. 0302070 dated March 2, 2012). In the case of a generic drug, describe "Generic Department.")
Remarks	

Describe the following information only in the case of replacement.

Date of submission	(* Date of submission of the Risk Management Plan to be replaced)
Replacement part	
Reason for replacement	

Attachments

Document title	**Document No.**

Company name Address Name of representative
Contact information Name of affiliated department Name of person in charge TEL FAX E-MAIL

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(Appendix)

1. Drug use-results survey implementation plan (general drug use-results survey, specified drug use-results survey, drug use-results comparative survey)

   (1) Purpose of the survey
   (2) Safety and efficacy specifications
   (3) Survey implementation plan (draft)
      1) Number of subjects of the survey and rationale
      2) Scope of subjects of the survey
      3) Number of institutions for each clinical department scheduled for survey
      4) Method of the survey
      5) Survey period
      6) Items to be surveyed
      7) Items to be analyzed and methods
      8) Organizational structure for conducting the survey
      9) When a part of the duties related to the survey is outsourced, the name and address of the contractor and the scope of the duties outsourced
   (4) Additional measures that may be taken based on the results of the survey and the decision criteria for the initiation
   (5) Timing to reach milestones to evaluate the implementation status of the survey and the results obtained, or to report them to PMDA, and its rationale
   (6) Other necessary matters

   ○ Attachments
   1) Implementation guideline (draft)
   2) Registration form (draft)
   3) Survey form (draft)

2. Post-marketing database surveillance implementation plan

   (1) Purpose of the survey
   (2) Safety and efficacy specifications
   (3) Survey implementation plan (draft)
      1) Outline of the medical information database to be used in the survey
      2) Number of subjects of the survey and rationale
      3) Scope of subjects of the survey
      4) Method of the survey
      5) Period for the survey (data period)
      6) Items to be surveyed
      7) Items to be analyzed and methods
      8) Organizational structure for conducting the survey
      9) When a part of the duties related to the survey is outsourced, the name and address of the contractor and the scope of the duties outsourced
   (4) Additional measures that may be taken based on the results of the survey and the decision criteria for the initiation
   (5) Timing to reach milestones to evaluate the implementation status of the survey and the results obtained, or to report them to PMDA, and its rationale
   (6) Other necessary matters

   ○ Attachments
   1) Documents explaining the certainty of survey results

3. Post-marketing clinical study protocol

(1) Purpose of the study
(2) Concerns for safety, concerns for efficacy
(3) Study protocol (draft)
    1) Name and address of the person who intends to sponsor a post-marketing clinical study
    2) When a part of the duties related to the studies is outsourced, the name and address of the contractor and the scope of the duties outsourced
    3) Name and address of the medical institution (number of institutions for each clinical department where the study is scheduled)
    4) Name and title of the prospective investigator of the post-marketing clinical study
    5) Summary of the study drug
    6) Method of the study
    7) Matters related to selection of subjects (subjects of the study)
    8) Number of study subjects and rationale
    9) Items to be investigated such as follow-up items and evaluation items
    10) Study period
    11) Items to be analyzed and methods
    12) Matters concerning access to source documents
    13) Matters related to retention of records (including data)
    14) Name and title of the physician who is commissioned to a coordinating investigator for a post-marketing clinical study, if applicable
    15) Names and titles of physicians constituting the committee, if a post-marketing clinical study is commissioned
    16) If the Efficacy and Safety Evaluation Committee is established, describe it accordingly.
    17) The person who intends to sponsor a post-marketing clinical study shall, when the study drug is expected to have no effect on the subjects and when the study is expected to include subjects from whom it is difficult to obtain written informed consent in advance to participate in the study, describe as such and the following matters.
        i) Explanation that the post-marketing clinical study must include subjects from whom it is expected to be difficult to obtain written informed consent in advance for participation in the study
        ii) Explanation that the expected disadvantages to subjects in the post-marketing clinical study are the minimum necessary
    18) When a post-marketing clinical study involves subjects from whom, or from whose legally acceptable representatives, it is expected to be difficult to obtain written informed consent in advance to participate in the study, the person who intends to sponsor the post-marketing clinical study shall describe such a fact and the following matters:
        i) Explanation that the current treatment is not expected to be sufficiently

effective for the candidate subject.

ii) Explanation that the use of the study drug has the sufficient potential to avoid a life-threatening risk of the candidate subject.

iii) The fact that the Efficacy and Safety Evaluation Committee has been established.

19) Organizational structure for conducting the study

(4) Additional measures that may be taken based on the study results and the decision criteria for the initiation

(5) Timing to reach milestones to evaluate the implementation status of the survey and the results obtained, or to report them to PMDA, and its rationale

(6) Other necessary matters

○ Attachments

1) Subject information sheet (draft) and consent form (draft)

2) Case report form (draft)