独立行政法人 医薬品医療機器総合機構
Pharmaceuticals and Medical Devices Agency

Administrative Liaison
May 31, 2022

To each Prefectural Health Management Bureau

Division of Pharmaceutical Safety and Health Sciences,
the Ministry of Health, Labour and Welfare

医療用医薬品の市販直後調査に関するＱ＆Ａについて
Q&A on Early post-marketing phase vigilance (EPPV) of Medicinal Products

Methods of conducting Early post-marketing phase vigilance for Medicinal Products have been presented in the sections entitled "Methods of conducting Early post-marketing phase vigilance for Medicinal Products" (PFSB/SD Notification No. 0324001 of Director, Safety Division, Pharmaceutical and Food Safety Bureau, the Ministry of Health, Labour and Welfare, dated March 24, 2006. Hereafter referred to as the "Old Notice".) and "Q&A on Early post-marketing phase vigilance for Medicinal Products" (Administrative notice from the Division of Pharmaceutical Safety and Health Sciences, the Ministry of Health, Labour and Welfare, dated August 8, 2019. Hereafter referred to as "Old Office Liaison".), respectively.

In light of the recent abolishment of the old notification and the issuance of the "Methods of conducting Early post-marketing phase vigilance for Medicinal Products" (PFSB/SD Notification No. 0531-1, by the Director of the Pharmaceutical Safety Division, Pharmaceutical and Consumer Affairs Bureau, the Ministry of Health, Labour and Welfare, dated May 31, 2022. Hereafter referred to as the "New Notice".), the content of the old administrative communication has been reviewed and the "Q&A on Early post-marketing phase vigilance for Medicinal Products" has been compiled as attached.

With the issuance of this administrative communication, the old administrative communication will be abolished, but the separate forms referred to in Q28 may be used in the form attached to the old administrative communication only for those to be submitted to the Agency by May 31, 2023.

In addition, the e-mail submissions referred to in Q29 and 30 may be submitted by mail until July 31, 2022.

(Attachment)

Q&A on Early post-marketing phase vigilance (PMS) of Medicinal Products

(Abbreviations used)

Act	: Relating to ensuring the quality, efficacy and safety of pharmaceuticals, medical devices, etc. Act (Act No. 145 of 1960)
Regulations	: Relating to ensuring the quality, efficacy and safety of pharmaceuticals, medical devices, etc. Ordinance for Enforcement of the Act (Ordinance of the Ministry of Health and Welfare No. 1 of 1961)
GVP Ordinance	: Ordinance of the Ministry of Health, Labour and Welfare No. 135 of 2004 concerning standards for post-marketing safety control of pharmaceuticals, quasi-drugs, cosmetics, medical devices and regenerative medicine products
MR	: Medical Representative
PMDA（機構）	: Pharmaceuticals and Medical Devices Agency. For matters related to pre-approval: For matters related to the New Drug Evaluation Department, post-approval and Early post-marketing phase vigilance means the Drug Safety Division.

(Purpose of Early post-marketing phase vigilance - Products covered)

Q1

What kind of surveillance is Early post-marketing phase vigilance? And what kind of drugs are targeted?

A1

Early post-marketing phase vigilance is a survey conducted during the first six months of marketing by the MAH with the primary objectives of providing reliable information and reminding medical institutions of the proper use of the drug to promote understanding of the proper use of the drug, promptly collecting cases suspected to be caused by the adverse reactions of the drug (Cases 20, etc. set forth in Article 228, Paragraph 1, Item 1 “イ”, “ハ” (1) to (5) and “ト” of the Regulation and Item 2 (a) of the same paragraph), and implementing necessary safety measures to minimize the damage caused by the adverse reactions.

The target is new drugs specified in Article 14, 4, Paragraph 1, Item 1 of the Law. However, the target may not be applied if there is a reasonable reason not to do so.

(Reference) Ordinance for Enforcement of the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, etc. (Ordinance of the Ministry of Health and Welfare No. 1 of 1961) (Extract)

(Reporting of adverse reactions, etc.)

Article 228. 20 When a marketing authorization holder or a person with special foreign approval for pharmaceuticals becomes aware of the matters listed in the following items with regard to the marketed or approved pharmaceuticals:

he/she shall report to that effect to the Minister of Health, Labour and Welfare within the period specified in the respective items.

(一) The following matters: 15 days

"イ" Death occurrences suspected to be caused by the side effects of the pharmaceuticals.

"ロ" (omission)

"ハ" The following occurrences of cases, etc., due to adverse reactions of the pharmaceutical or foreign pharmaceutical.

that are suspected to be caused by and cannot be predicted from the precautions required for use of the pharmaceutical or can be predicted from the precautions required for use of the pharmaceutical and whose occurrence trend cannot be predicted or whose change in occurrence trend indicates the risk of occurrence or spread of hazards to public health and hygiene (Excluding matters listed in "ニ" and "ホ").

(1) Disability

(2) Death or Life-threatening (Fatal)

(3) A case that requires inpatient hospitalization or prolongation of existing hospitalization (excluding case in (2).)

(4) Cases that are fatal or serious according to cases listed in (1) through (3)

(5) Congenital disease or anomaly in future generations

"ニ" Among the occurrences of cases, etc. listed in "ハ" (1) to (5) pertaining to drugs approved under Article 14, paragraph (1) of the Act as drugs with different active ingredients from approved drugs prescribed in Article 7, paragraph (1), item "イ", (a) (1) of the Order on Fees Related to the Act on Securing Quality, Efficacy and Safety of Drugs, Medical Devices, etc., for which two years have not passed since the date of approval, those suspected to be caused by the side effects of the drugs.

"ホ" Incidences of cases, etc. listed in "ハ" (1) through (5) that are suspected to be caused by adverse reactions to the pharmaceuticals and that were obtained through Early post-marketing phase vigilance (Excluding matters listed in "ニ").

"ヘ" Incidences of cases, etc. due to infectious diseases suspected to be caused by the use of the pharmaceuticals that cannot be predicted from precautions required for use of the pharmaceuticals.

"ト" Incidences of deaths from infectious diseases suspected to be caused by the use of the pharmaceuticals or foreign pharmaceuticals or cases, etc. listed in "ハ" (1) through (5) (Excluding the matters listed in "ヘ".).

"チ" (omission)

(二) The following matters: 30 days

"イ" The occurrence of cases, etc. listed in "ハ" (1) through (5) of the preceding item that are suspected to be caused by the adverse reactions of the pharmaceuticals (Excluding matters listed in "ハ", "ニ" and "ホ" of the preceding item.).

(三) (omission)

2～5 (omission)

Q2

In what specific cases does the statement "If there is a reasonable reason for not implementing the measure, the measure may not be applicable" in A1 apply?

A2

For example, an application for partial change of approval for an additional indication (Hereafter referred to as the "application for transformation".) or an application for approval for a combination product consisting solely of an approved drug for which there is a sufficient track record of co-administration between single-agent products, and both of the following two requirements are met.

① Adequate accumulation of safety information on the drug or the approved drug

② No change in clinical use is expected, such as no change in the existing indication, dosage and administration, or department used, and no special safety reminders will be added

Q3

What should be done if the MAH considers that there is a reasonable reason not to conduct Early post-marketing phase vigilance for a new drug that requires Early post-marketing phase vigilance?

A3

A written rationale for not conducting Early post-marketing phase vigilance should be attached to Module 1.11 of the Common Technical Document (CTD) at the time of application, separately from the draft RMP(Drug Risk Management Plan), and submitted to the PMDA.

Q4

What is the relationship between Early post-marketing phase vigilance and the Adverse Drug Reaction and Infectious Disease Reporting System in accordance with Article 68, 10, Paragraph 1 of the “Medicinal Products Safety Information Reporting System”?

A4

Early post-marketing phase vigilance is conducted by MAHs on a regular basis to physicians, etc., who use the marketed drugs.

(1) The drug is a new drug and efforts should be made for its proper use.

(2) Use the safety management information provided to ensure proper use.

(3) Request prompt reporting of any serious adverse reactions or infections.

If serious adverse reactions or infections occur, prompt reporting of such information should be made without going unreported. Therefore, if a medical institution notifies the MAH that a serious adverse reaction or infection has occurred during Early post-marketing phase vigilance, the MAH is required to report it to the PMDA in accordance with the provisions of Article 68, 10, Paragraph 1 of the Act.

Note that Article 228, 20 Paragraph 1, Item 1 “ホ” of the Regulations stipulates that serious cases suspected to be caused by adverse reactions of drugs obtained through Early post-marketing phase vigilance should be reported to the Pharmaceuticals and Medical Devices Agency within 15 days regardless of the predictability of the Precautions.

(Reference) Act on Securing Quality, Efficacy and Safety of Drugs and Medical Devices (Act No. 145 of 1960)
(Extract)

(Reporting of adverse reactions)

Article 68 -10: MAHs of pharmaceuticals, quasi-drugs, cosmetics or medical devices, or When a Foreign Special Approval Holder becomes aware of the occurrence of disease, disability or death suspected to be caused by adverse reactions to the item or other causes, the occurrence of infectious diseases suspected to be caused by the use of the item, or other matters related to the efficacy and safety of drugs, quasi-drugs, cosmetics, medical devices, or regenerative medicine products that are marketed or approved pursuant to Article 19 “二”, Article 23 “二” - “十七”, or Article 23 “三十七” and that are specified by an Ordinance of the Ministry of Health, Labour and Welfare, he/she shall report to that effect to the Minister of Health, Labour and Welfare as specified by an Ordinance of the Ministry of Health, Labour and Welfare.

2・3 (omission)

(Early post-marketing phase vigilance Plan)

Q5
Is a Early post-marketing phase vigilance protocol required to be submitted before Early post-marketing phase vigilance is initiated?

A5

Although advance submission is not uniformly required, if there are any matters to be discussed in preparing the Early post-marketing phase vigilance, consult with the PMDA.

Q6
When does the date of "Commencement of marketing" as specified in Article 10 of the GVP Ordinance refer to?

A6

In principle, the date of launch should be determined by the MAH.

Q7
In the case of an additional indication or an additional dosage and administration, when is the "date of launch"?

A7

For marketing approval of principle, indication, or dosage and administration the date of partial change approval (Hereafter referred to as "partial change approval".) should be changed to the date on which the product was launched. In this case,

explanations and requests for cooperation regarding Early post-marketing phase vigilance, which is supposed to be conducted prior to delivery, may be made within two weeks of the approval of the Partial change.

However, if a new drug is to be delivered to a medical institution that has not received the drug in question, efforts should be made to provide explanations and requests for cooperation prior to delivery.

Q8

How is the end date for Early post-marketing phase vigilance determined?

A8

The " Early post-marketing phase vigilance end date" is, in principle, the date six months after the start of the survey, but may be the end of the month to which the end date belongs. In such cases, the Early post-marketing phase vigilance implementation report should be submitted within two

Q9

How should a Early post-marketing phase vigilance be conducted at a medical institution with a past record of delivery (Only at medical institutions where the drug has been unused and returned in full after delivery.) if the product is delivered again?

A9

A Early post-marketing phase vigilance should be conducted starting from the date of redelivery. If a pre-delivery explanation and request for cooperation were made at the time of first delivery, the explanation may be omission.

However, even if a periodic request for cooperation and a reminder were made after the first delivery, a periodic request for cooperation should be made starting from the redelivery date.

Q10

In the new notification, a standard method is indicated as "Methods for conducting Early post-marketing phase vigilance should be considered for each drug, but (omission) the standard methods for conducting Early post-marketing phase vigilance are as follows:" However, what should be done if a method that takes into account product characteristics, safety profile, etc. (e.g., changing the frequency of face-to-face or online interviews, etc.) is used?

A10

When conducting the survey in a manner that takes into account the product characteristics, safety profile, etc., such as changing the frequency of face-to-face or online interviews according to the drug, the indicated disease, the population to be treated, and the issues to be addressed, the applicant should consult with the PMDA at the stage of preparing the draft Early post-marketing phase vigilance.

Q11
Regarding Early post-marketing phase vigilance, is a contract with a medical institution required before starting the survey?

A11

Not necessary.

Unlike use-results surveys, etc., Early post-marketing phase vigilance is not an investigation of individual cases, but is part of the safety management information provision, collection and reporting activities conducted in accordance with Article 68 (2)−1) and Article 68 (10) -1) of the Act.

(Facilities subject to Early post-marketing phase vigilance)

Q12
Are pharmacies subject to Early post-marketing phase vigilance?

A12

We believe that Early post-marketing phase vigilance is generally conducted at hospitals and clinics and not at pharmacies. However, any necessary information should be provided to pharmacies.

Q13
For Medicinal Products with additional indications (additional indications, etc.) to be used in a different department from the conventional department by a univariate application, is it correct that Early post-marketing phase vigilance is conducted only at institutions that have a department where the drug may be prescribed for the additional indications, etc.?

A13

In principle, it is acceptable to consult with the PMDA.

(Explanation of Early post-marketing phase vigilance and request for cooperation)

Q14
As a general rule, MRs should visit medical institutions directly to explain and request for cooperation, but what other methods are possible?

A14

Implementation methods such as online interviews and phone calls can be used to communicate in real time.

Q15

What are the explanations and written requests for cooperation provided by MRs, etc. prior to drug delivery when such explanations and requests for cooperation cannot be implemented due to face-to-face or online interviews? Also, how will they be implemented specifically?

A15

For example, a request form prepared by the MAH stating the purpose of the Early post-marketing phase vigilance and a request for cooperation. However, the "Explanation of "Precautions" for new drugs" or the "Prescription Drug Product Information Summary" may not be substituted for the explanatory document.

As for the communication method, it is acceptable to provide the document by mail, facsimile, e-mail or by using a wholesaler. In such a case, explanations and requests for cooperation should be made in person by MRs, etc., or in online interviews, within two weeks after the start of delivery, in principle.

Q16

If an MR, etc. held a product briefing for multiple medical institutions and provided explanations and requests for cooperation related to Early post-marketing phase vigilance, is it correct that by providing the explanation and requests for cooperation, pre-delivery explanations and requests for cooperation were provided to individual medical institutions that participated in the briefing?

A16

It is acceptable if the medical institutions that participated in the briefing can be confirmed. However, it should be explained at the briefing that the briefing was conducted as an explanation of Early post-marketing phase vigilance and a request for cooperation.

Q17

If a medical institution does not receive cooperation even after providing an explanation and a request for cooperation before the delivery of a drug, can it not supply the drug?

A17

Although Early post-marketing phase vigilance does not restrict the supply of the drug to a medical institution, please explain the purpose of this system after the start of delivery and continue to request cooperation.

Q18

In the case of medical institutions with out-of-hospital prescriptions, at what point does delivery refer?

A18

In the case of medical institutions with out-of-hospital prescriptions, as a general rule, the date on which the prescription is started (or the date on which the prescription is found to have been started) or the date of adoption by the medical institution is earlier than

the date of delivery to conduct a Early post-marketing phase vigilance. If the patient becomes aware that a prescription has been made for the first time based on spontaneous reports of adverse drug reactions or information from the dispensing pharmacy, an explanation by the MR etc. and request for cooperation should be provided within 2 weeks from the date of delivery.

Q19

If the product is found to have been delivered to a medical institution that has not provided the explanation and request for cooperation that should be provided before delivery, how should the explanation and request for cooperation be provided?

A19

Efforts should be made to ascertain the delivery destination before delivery, but if it is found after delivery, the explanation and request for cooperation should be provided by the MRs, etc. within 2 weeks as a guideline after knowing that the product has been delivered.

Q20

Is it necessary to keep records of the implementation of pre-delivery (post-delivery) explanations, requests for cooperation, regular post-delivery requests for cooperation and reminders?

A20

Records concerning the conduct of early post-marketing phase vigilance should be prepared and appropriately managed for each medical institution as described in Section 2. (9) "エ" of the section titled "Enforcement of Ministerial Ordinance on Standards for Post-Marketing Safety Management of Pharmaceuticals, Quasi-drugs, Cosmetics, Medical Devices, and Regenerative Medicine Products" in PFSB Notification No. 0812 No. 4 of the Director General of the Ministry of Health, Labour and Welfare, dated August 12, 26.

Reference: PFSB Notification No. 0812-4 of the Director General of the Pharmaceutical and Food Safety Bureau, the Ministry of Health, Labour and Welfare, dated August 12, 2014 (Extract)

Section 2-2. (9) Early post-marketing phase vigilance (Re: Articles 10 and 10 (2))

“ア” – “ウ” (omission)

“エ” Type 1 marketing authorization holder shall collect and review safety control information pertaining to Early post-marketing phase vigilance and take necessary measures based on the results of such collection and review in accordance with the provisions of Articles 7, 8 and 9 of the GVP Ministerial Ordinance, respectively. Records concerning the conduct of Early post-marketing phase vigilance should be prepared for each medical institution and managed appropriately.

Q21
How should regular requests for cooperation and reminders be made after delivery?

A21

In view of the purpose of Early post-marketing phase vigilance, it is desirable to provide information and collect information reliably and promptly through face-to-face meetings with MRs, etc., or online interviews, etc. However, to the extent that the purpose of Early post-marketing phase vigilance can be achieved, it may be done by letter, facsimile, e-mail, etc., or by communication with wholesalers, etc. Note that if a serious adverse reaction or infection occurs, MRs, etc. are required to collect information in accordance with the operating procedures for post-marketing safety control of each MAH.

Q22
What are alternatives to conducting Early post-marketing phase vigilance, such as face-to-face or online interviews with MRs? Also, what should be noted when using alternatives?

A22

Alternatives include letters, facsimiles, e-mail and direct mail (Hereafter referred to as "DM".). When communicating by these alternative means, it should be explained to the medical institution that the communication means is a reliable and prompt way to provide and collect information so that the purpose of Early post-marketing phase vigilance can be achieved, instead of responding only by sending unsolicited communications.

Q23
In the case of multi-company sales of one product and one name, are requests for Early post-marketing phase vigilance cooperation made by multiple distributors respectively?

A23

These are performed responsibly by the MAH and not by individual distributors. To the extent specified, consignment may be accepted.

Q24
When requesting a wholesaler to provide information such as periodic alerts to medical institutions, is a contract with the wholesaler necessary?

A24

When entrusting activities specified in Article 97 of the Regulations (to the extent that post-marketing safety control activities may be entrusted), a contract with a trustee is required in accordance with the provisions of Article 98 (2) of the Regulations (method of entrusting post-marketing safety control activities for Medicinal Products) or Article 98 (3) of the Regulations (method of entrusting post-marketing safety control activities for drugs other than Medicinal Products).

(Evaluation of Early post-marketing phase vigilance Results)

Q25

Is it necessary to provide safety management information obtained through Early post-marketing phase vigilance to medical institutions?

A25

Safety management information obtained through Early post-marketing phase vigilance should be provided to medical institutions at an appropriate frequency, for example, if many serious adverse reactions are reported, such information should be compiled monthly and provided along with safety measures.

Q26

If safety measures such as revision of Precautions are to be taken based on Early post-marketing phase vigilance, is it appropriate to consult the first or second part of the pharmacovigilance section of the PMDA regarding consultation with the PMDA?

A26

No problem (Acceptable).

(Early post-marketing phase vigilance Implementation Report)

Q27

What are the "safety assurance measures" described in the Early post-marketing phase vigilance Implementation Report?

A27

These include, for example, revisions of electronic package inserts and information provision activities to ensure safety when the MAH receives information from a medical institution that a serious adverse reaction or infection has occurred.

Q28

What data should be attached when submitting a Early post-marketing phase vigilance protocol and Early post-marketing phase vigilance report?

A28

The following data should be attached to confirm the implementation status of Early post-marketing phase vigilance and the appropriateness of safety measures.

① Data provided to medical institutions during and/or after Early post-marketing phase vigilance.

② Data on the status of Early post-marketing phase vigilance conducted by medical institutions, etc. prepared using the format specified in the Appendix. Such data should include at least the following:

- Number of facilities where requests for cooperation, etc. prior to drug delivery were made in person by MRs, etc., through online interviews, etc., or through briefings, and the percentage of such facilities to the number of facilities covered. Facilities where neither in-person or online interviews, etc. nor e-mail, DM, etc., were made are counted as not implemented.
- The number of facilities that made regular requests for cooperation after the delivery of drugs and the percentage of such facilities in the number of facilities covered by the survey were calculated by means of requests for cooperation and the number of times they were made.
- If there are facilities where face-to-face or online interviews with MRs, etc. have not been conducted before or after the delivery of drugs, the reason and the status of response to such facilities (including an explanation of whether the purpose of Early post-marketing phase vigilance has been achieved). In addition, if it is determined that the implementation method needs to be improved, improvement measures should be included.

Q29
Do Early post-marketing phase vigilance implementation reports and periodic safety reports be submitted separately?

A29

Submission separately. Companies intending to report on EPPV should consult with the PMDA with sufficient leeway to meet the Early post-marketing phase vigilance reporting deadline.

For such consultations, the consultation application form and electronic files of the materials (Early Early post-marketing phase vigilance Plan, Early post-marketing phase vigilance Phase Vigilance Report, and Attached Materials) should be submitted via e-mail to the "Visiting Consultation Form Reception (anzen2-menkai@pmda.go.jp)," which is the dedicated address for consultations pertaining to the first part of the PMDA and the second part of the PMDA.

If the size of the file is too large to send in a single mail because the receivable capacity of each mail is about 10 MB, the file should be divided into multiple files and listed in such a way that the order and the total number sent are known, such as "1/3," "2/3" and "3/3." If submission by email is not possible, consult with the Institute about the submission method.

Q30
Are there rules on how to submit electronic files (Mail title, file name, etc.)?

A30

The title of the e-mail should include the name of the document (including "Submission of Early post-marketing phase vigilance Reports" as【市販直後調査報告書関係提出】), the name of the manufacturer, and the brand name.

At this time, there are no specific rules for file names, but Early post-marketing phase vigilance protocols and Early post-marketing phase vigilance implementation reports should be one electronic file each, and other materials to be attached should be prepared in an appropriate electronic format with a file name that can identify the content of the materials.

(Dissemination of Products Subject to Early post-marketing phase vigilance)

Q31

Is it necessary to include the conditions for approval in the electronic package insert of a drug subject to the conditions for Early post-marketing phase vigilance as specified in Article 10 of the GVP Ordinance?

A31

It is not necessary to include such conditions.

Q32

In what way do you specify that a new drug is subject to Early post-marketing phase vigilance?

A32

Prescription drug product information summaries, "Explanation of "Precautions" for new drugs" and interview forms should clearly indicate that the drug is subject to Early post-marketing phase vigilance during the first six months of marketing.

(Exhibit form)

	Number of facilities covered	Before delivery 1)	Week 2 2)	Week 4	Week 6	Week 8	Month 3	Month 4	Month 5	Month 6
Number of facilities covered	●	●	●	●	●	●	●	●	●	●
Number of institutions 3, 4)	-	● (●)	● (●)	● (●)	● (●)	● (●)	● (●)	● (●)	● (●)	● (●)
(Breakdown of means of implementation) Face-to-face and online interviews, etc. 3)	-	● (●)	● (●)	● (●)	● (●)	● (●)	● (●)	● (●)	● (●)	● (●)
E-mail, DM, etc. 3, 5)	-	● (●)	● (●)	● (●)	● (●)	● (●)	● (●)	● (●)	● (●)	● (●)
Number of non-implementation sites 3, 6)	-	● (●)	● (●)	● (●)	● (●)	● (●)	● (●)	● (●)	● (●)	● (●)

1) Summary of pre-delivery activities

The number of facilities with pre-delivery activities includes:

•Face-to-face or online interviews or briefings prior to delivery (aggregated as "face-to-face or online interviews, etc.")

•E-mail or DM prior to delivery and face-to-face or online interviews or briefings with MRs, etc., within two weeks (approximately) of delivery (aggregated as "face-to-face or online interviews, etc.")

•E-mail or DM prior to delivery but unavoidably unable to conduct face-to-face or online interviews or briefings with MRs, etc., within two weeks (approximately) of delivery (Aggregated as "E-mail, DM, etc.")

The following facilities should be excluded from the tabulation of the number of facilities covered and the number of facilities implemented, and should be explained in an explanatory note along with the number of facilities listed in a and b below. With regard to a), it should also be explained whether face-to-face or online interviews, etc. or information sessions were held within two weeks (approximately) of the finding. In addition, if some facilities were excluded for reasons other than the following, the reason should be explained in the commentary.

a, Explanation to be given before delivery and facilities found to have been delivered to medical institutions that did not request cooperation

b, Delivery facilities from before the date of partial change approval when the date of partial change approval is the start date of the Early post-marketing phase vigilance (because they are not subject to the pre-delivery explanation)

In addition to face-to-face or online interviews, non-delivery facilities are those for which explanations and requests for cooperation could not be provided by e-mail, DM, or any other means.

2) The frequency of delivery in the form (from Week 2 to Month 6) should be modified as appropriate based on the Early post-marketing phase vigilance.

3) The number of facilities (percentage) should be indicated. The percentage should be calculated as a percentage of the number of facilities covered.
4) If it is determined that the method of conducting Early post-marketing phase vigilance needs to be improved, the improvement measures should be explained in the form of commentary.
5) Details of the alternative measures (E-mail, DM, etc.), their reasons, and the status of compliance (including whether the objectives of Early post-marketing phase vigilance were achieved) should be included in the commentary.
6) Reasons for non-implementation and the status of compliance should be explained in the commentary.

Exhibits, etc. may be used to explain 1, 4 ~ 6) above.