Administrative Liaison
June 24, 2022

To the Pharmaceutical Affairs Division of each Prefectural Health Management Division

Pharmaceutical Evaluation and Management Division, Pharmaceutical Division,
the Ministry of Health, Labour and Welfare

Medical Safety Division, Pharmaceutical and Consumer Affairs Division,
the Ministry of Health, Labour and Welfare

E2B(R3)実装ガイドに対応した市販後副作用等報告及び治験副作用等報告に関する Q&A について
Q&A on Post-marketing adverse reaction reports and Clinical trial adverse reaction reports in accordance with the E2B (R3) Implementation Guide

A question-and-answer sheet (Q&A) on (Joint Notification of the Evaluation and Licensing Division, PFSB Notification No. 0831 No. 12 and PFSB Notification No. 0831 No. 3, by the Director of the Evaluation and Licensing Division, Pharmaceutical and Medical Safety Division, the Ministry of Health, Labour and Welfare, dated August 31, 2020) has just been presented in "Revision of Q&As on Post-marketing and Clinical trials adverse reaction reports in accordance with the E2B (R3) Implementation Guide" (Joint Office Communication, Pharmaceutical Evaluation and Management Division and Pharmaceutical Safety Division, Pharmaceutical and Consumer Affairs Division, the Ministry of Health, Labour and Welfare, dated February 7, 2022. Hereafter referred to as "Old Admirative Liaison ".).

We have recently reviewed the content of the Q&A in conjunction with the publication of the "Partial Amendments to Postmarketing Adverse Reaction Reporting and Clinical Study Adverse Reaction Reporting in Response to E2B (R3) Implementation Guide" (Notification No. 0624 No. 4 of the Pharmaceutical and Pharmaceutical Safety Bureau and Notification No. 0624 of the Pharmaceutical and Pharmaceutical Safety Bureau dated June 24, 2022! Joint Notification of the Director of the Pharmaceutical Evaluation and Management Division and the Director of the Pharmaceutical Safety Division, Pharmaceutical and Community Health Agency, the Ministry of Health, Labour and Welfare) and have newly compiled the content as shown in the Attachment. We ask that you please understand this and give due consideration to disseminating this information to the relevant parties in your jurisdiction as a reference for your business.

This Administrative Liaison by MHLW is July 2022, it applies from the day.

Exhibit

Q&A on Post-marketing adverse reaction reports and Clinical trial adverse reaction reports in accordance with the E2B (R3) Implementation Guide

June 24, 2022

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(Abbreviations used)

Act: Act on Securing Quality, Efficacy and Safety of Pharmaceuticals and Medical Devices (Act No. 145 of 1960)

Ordinance for Enforcement: 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)

Postmarketing Director General's Notice: PFSB Notification No. 1002 No. 20 of the Director General of the the Ministry of Health, Labour and Welfare Pharmaceutical and Food Safety Bureau, dated October 2, 2014, "Reporting of Adverse Reactions to Drugs, etc."

Director of Investigations Notification: Yakuho Notification No. 0831 No. 8 of August 31, 2020, by the Director of the Pharmaceutical and Community Health Bureau of the the Ministry of Health, Labour and Welfare "Reporting of Adverse Drug Reactions to the Pharmaceuticals and Medical Devices Agency" E2B (R3) Second Director Notification: Yakuho Notification No. 0831 No. 12 and Yakuho Safety Notification No. 0831 of August 31, 2020

3 Joint Notification of the Director of the Evaluation and Licensing Division, Pharmaceutical Affairs and Consumer Affairs Bureau, and the Director of the Pharmaceutical Safety Division, the Ministry of Health, Labour and Welfare, entitled "Reporting of post-marketing adverse drug reactions and reports of investigational adverse drug reactions in accordance with the E2B (R3) Implementation Guide," E2B (R2) Joint Notification of the Director of the Evaluation and Licensing Division, PFSB No. 0331022 and the Ministry of Health, Labour and Welfare PFSB No. 0331009, dated March 31, 2006, entitled "Reporting of post-marketing adverse drug reactions and reports of investigational adverse drug reactions" (repealed)

E2B (R3) 5 Director General Notice: Joint Notification of E2B (R3) dated August 31, 2020, titled "Points to keep in mind for post-marketing adverse drug reaction reports and clinical trial adverse drug reaction reports in accordance with the E2B (R3) Implementation Guide"

ICH: International Conference on Harmonization of Drug Regulations

E2B (R3) Implementation Guide: Joint Notification of the Evaluation and Licensing Division, PFSB No. 0315-6 and PFSB No. 0315-1, by the Director of the Evaluation and Licensing Division, Pharmaceutical Affairs and Consumer Affairs Bureau, the Ministry of Health, Labour and Welfare and by the Director of the Safety Division, dated March 15, 2017, "Revision of the Implementation Guide for Electronic Transmission of Individual Case Safety Reports, etc."

E2B (R3) ICHQ&A: Joint Administrative Notice of the Pharmaceutical Evaluation and Management Division and the Pharmaceutical Safety Division, Pharmaceutical and Medical Safety Division, the Ministry of Health, Labour and Welfare, dated September 26, 2019, entitled "Questions and Answers on the Electronic Transmission of Individual Case Safety Reports (Q&A)"

E2D Guideline: PFSB/SD Notification No. 0328007 of the Director of Safety Division, Pharmaceutical and Food Safety Bureau, the Ministry of Health, Labour and Welfare, dated March 28, 2005, "Handling of post-approval safety information: Definition of terms for emergency reporting and criteria for reporting"

Reporting of post-marketing adverse reactions: Reporting of adverse reactions as specified in Article 68, 10, Paragraph 1 of the Law

Reporting of Adverse Drug Reactions in Clinical Trials: Reporting of Adverse Drug Reactions in Clinical Trials as specified in Article 80 (2) (6) of the Act

Pharmaceuticals and Medical Devices Agency

Electronic reporting: Reporting by electronic data processing system

Reports on CDs, etc.: Reports by submitting a CD-R (ROM) or DVD-R (ROM) that records the matters listed in the form attached to the Postmarketing Director's Notice or the form attached to the Director of the Investigator's Notice, and the name, address, date of report of the reporter and other necessary matters specified in the Postmarketing Director's Notice or the Director of the Investigator's Notice.

Paper report: Report by submitting a written report containing the necessary items specified in the form attached to the Postmarketing Director's Notice and the form attached to the Investigator's Notice, and CD-R (ROM) or DVD-R (ROM) in which the items listed in Exhibit 1 "the Ministry of Health, Labour and Welfare System Management Data Items" and Exhibit 2 "Individual Case Safety Report Data Items" of the E2B (R3) Director's Notice are recorded in an XML format corresponding to the E2B (R3) Implementation Guide.

Immediate report: Post-marketing Director's Notice Attachment 2 (1) Reports that fall under ②

ICSR file: Electronic file recording E2B and J items in XML format

Old reporting standards: provisions for reporting of adverse reactions, etc. in the Ordinance for Enforcement of the Pharmaceutical Affairs Act prior to revision by the Ministerial Ordinance for Partial Revision of the Ordinance for Enforcement of the Pharmaceutical Affairs Act (Ordinance of the Ministry of Health, Labour and Welfare No. 30 of 2001) or for reporting of adverse reactions, etc.

1) Reports of adverse reactions and infections

(1) **Subject of report**

Q1: (Post-marketing) and (Clinical trials)

What is the range of "suspected side effects"?

Are events for which a causal relationship cannot be ruled out and events for which a causal relationship is unknown subject to reporting?

A1: Post-marketing and Clinical trials

According to ICH etc., adverse drug reactions are defined as "adverse events for which a causal relationship to the drug cannot be ruled out," and information is collected to that extent in our country at present.

"Suspected adverse reactions" are those other than "events for which a causal relationship can be denied" and "events for which a causal relationship is unknown" are also subject to reporting.

Q2: (Post-marketing) and (Clinical trials)

Who makes decisions about "suspected side effects"?

A2: Post-marketing and Clinical trials

It is the sender's responsibility to make a judgment based on the causality assessment provided by the reporter. When reporting, report items other than those for which the sender and all reporters have determined that a causal relationship can be denied. If the reporter includes a "lawyer" or a "consumer or other non-medical professional" and there is another reporter who is a "physician," "pharmacist" or "other medical professional," it can be concluded that all the reporters denied a causal relationship when all the reporters who are "physicians," "pharmacists" or "other medical professionals" denied a causal relationship.

Q3: (Post-marketing)

Should cases of adverse drug reactions that are clearly judged by the reporter to be non-serious be considered serious if they require hospitalization for treatment of adverse drug reactions or prolonged hospitalization?

A3: Post marketing

Treat as a serious case.

Q4: (Post-marketing) and (Clinical trials)

If an infection is suspected to be caused by viral contamination that can only be detected by a test that is now not fully recognized, should any data negative for viral contamination by a currently recognized test be reported?

A4: Post-marketing and Clinical trials

Should be reported. Infections suspected to be caused by drug use must be reported regardless of whether a test is established.

Q5: (Post-marketing)
Is it necessary to report adverse reactions caused by defective products?

A5: Post marketing

Even if it is caused by a defective product, it is necessary to report adverse reactions, etc.

Q6: (Post-marketing)

Are cases of health hazards that occur in non-medical uses (off label use), such as suicide, crime, accidental ingestion by infants, etc., apparently to treat diseases, subject to reporting?

A6: Post marketing

Such cases are not subject to reporting under Article 228, 20 of the Enforcement Regulations.

Q7: (Post-marketing)

The Post-marketing Director's Notice states that "It should be reported at least for cases that need to be reported urgently to the government of the country where the case occurred." What specific points should be kept in mind?

A7: Post marketing

Note that if a pharmaceutical is sold in Japan by a Japanese corporation and in a foreign country by a partner company, etc., and the adverse reaction is reported urgently to the government of the country where the case occurred by the partner company, etc., and cannot be predicted from the necessary precautions for use in Japan, the Japanese corporation should consider the adverse reaction to be unknown and serious and report the case.

Q8: (Post-marketing)

What is a drug used in a foreign country whose ingredients are recognized to be identical to the drug in question (approved in Japan) and are subject to reporting?

A8: Post marketing

(1) If the ingredients are identical, even if the dosage and administration, indication or other active ingredients are not identical, they are subject to reporting.

(2) If the sender has obtained marketing approval for more than one drug product with identical ingredients in Japan and learns of a foreign adverse reaction or infectious disease case of the active ingredient, the sender should report the case as a drug product that the sender considers more appropriate among the products with marketing approval in Japan, in light of the reason for use of the drug in the case, dosage and administration, other active ingredients in the formulation, etc., to avoid omissions.

(3) If the ingredients are identical, in addition to the products of the foreign partner, information such as adverse reactions that are serious and not foreseeable due to precautions in use, even if the products are not those of the partner company, will be subject to reporting.

Q9: (Post-marketing) and (Clinical trials)

Is it necessary to report as a parent and child/fetus report when an abortion occurs due to malformations that are considered to be caused by the drug or investigational product?

A9: Post-marketing and Clinical trials

Report as parent and child/fetus report.

Q10: (Clinical trial)

Can a hospital admission (such as elective surgery or a test) that was scheduled before the trial only for the purpose of conducting the therapy or test during the trial be excluded from reporting?

A10: Clinical trial

May be excluded from reporting.

Q11: (Post-marketing)

Do we need to report an infection, if a doctor reports it

① Viral hepatitis caused by blood products
② Sepsis associated with agranulocytosis
③ mycosis as a result of antibiotic use
④ Aseptic meningitis associated with vaccine administration
⑤ MRSA (methicillin-resistant staphylococcus) infection during antibiotic use
⑥ Emerging infectious diseases during the use of pharmaceuticals, etc.

A11: (Post marketing)

(1) Infection reports are required for ①
(2) Reports of adverse reactions ② to ④ have been required for some time and should be continued in the future.
(3) should not be reported as a case report for ⑤. However, if knowledge of resistance mechanisms and changes in emergence trends of bacteria resistant to antibiotics associated with the use of antibiotics should be treated as a research report, individual consultation should be made with the first part or second part of the PMDA's pharmacovigilance program.
(4) Should be reported. Investigate detailed information such as symptoms of patients whether they are domestic or foreign cases, and clarify the basis of diagnosis for ⑥.

In the event of such an incident, individual consultation should be made with the first part or second part of the pharmacovigilance department of the PMDA (In the case of in-vitro diagnostics, Medical Device Safety Division, Medical Device Quality Control and Safety Division).

Q12: (Post-marketing)

We learned of the occurrence of adverse events through investigations using medical information databases such as MID-NET, but there is no correspondence table and it is not possible to trace back to the original medical information.

In this case, is it necessary to report adverse reactions and infections?

A12: Post marketing

If there is no correspondence table in the medical information database that enables the matching with the original medical information, the information is provided on the assumption that it does not go back to the original medical information, and there is no need to investigate additional information. For information obtained from medical information databases for which no correspondence tables exist, it is not necessary to report adverse reactions/infections for each individual case.

Q13: (Clinical trial)

For investigational products and investigational products other than investigational products, how should we consider the cases that need to be reported and the reporting deadlines (due date)?

A13: Clinical trial

For investigational and non-investigational drugs, the following are the cases that need to be reported and their reporting deadlines:

For a test drug, if the test drug is "Other than partial change" follows the "Other than partial change" table, and if the test drug is "Partial change," follow the "Partial change" table.

For investigational new drugs other than the investigational product, if the notification contains at least one investigational product that is not a "Partial change", Respond according to the "Other than Partial change" table, and if all the test drugs in the notification are "Partial change" respond according to the "Partial change" table.

Respond according to the

	Expectedness	Seriousness	Other than partial change	Partial Change *
Suspect Drug	Unknown (Un-Labelled)	Death or Life-threatening (Fatal)	7 days	7 days
		Other serious	15 days	15 days
	Known (Labeled)	Death or Life-threatening (Fatal)	15 days	15 days
		Other serious	Not required	Not required
Investigational drugs other than the Suspect Drug	Unknown (Un-Labelled)	Death or Life-threatening (Fatal)	7 days	7 days
		Other serious	15 days	15 days
	Known (Labeled)	Death or Life-threatening (Fatal)	15 days	15 days
		Other serious	Not required	Not required

Cases in clinical studies conducted in foreign countries >

	Expectedness	Seriousness	If the Suspect Drug is used in a clinical study conducted in a foreign country		If the Suspect Drug is not used in a clinical study conducted in a foreign country
			Other than partial change	Partial Change *	
Suspect Drug	Unknown (Un-Labelled)	Death or Life-threatening (Fatal)	7 days	Not required	—

		Other serious	15 days	Not required	—
	Known (Labeled)	Death or Life-threatening (Fatal)	15 days	Not required	—
		Other serious	Not required	Not required	—
investigational drugs other than the Suspect Drug	Unknown (Un-Labelled)	Death or Life-threatening (Fatal)	7 days	Not required	Not required
		Other serious	15 days	Not required	Not required
	Known (Labeled)	Death or Life-threatening (Fatal)	15 days	Not required	Not required
		Other serious	Not required	Not required	Not required

(Excluding use in clinical trials.) >

	Expectedness	Seriousness	Other than partial change	Partial Change *
Suspect Drug	Unknown (Un-Labelled)	Death or Life-threatening (Fatal)	7 days	Not required
		Other serious	15 days	Not required
	Known (Labeled)	Death or Life-threatening (Fatal)	15 days	Not required
		Other serious	Not required	Not required
investigational drugs other than the Suspect Drug	Unknown (Un-Labelled)	Death or Life-threatening (Fatal)	Not required	Not required
		Other serious	Not required	Not required
	Known (Labeled)	Death or Life-threatening (Fatal)	Not required	Not required
		Other serious	Not required	Not required

＊: Approval for additions, changes or deletions concerning dosage and administration or indication or effect
Limited to clinical trials used in new drug applications for partial changes in information.

Q14: (Clinical trial)

How do we report a case that has been unblinded (Key break) and is found not to have received the Suspect Drug?

A. The initial report was reported only for the blinded Suspect Drug, and additional information provided that:

A-1. Suspected drug only placebo

A-2. A control drug (a drug other than the investigational drug) that is not used by the suspect drug in a domestic clinical trial in a case from a foreign clinical trial

B. In a trial using multiple investigational drugs, the initial report is reported only with the investigational drug under blindness
and additional information indicates that if

B-1. Suspected drug is a placebo or investigational drug

C.The investigational product and other investigational products that are blinded to the initial report are reported for reporting purposes, and additional information indicates that:

C-1. The unlocked result is a placebo or a control drug in a case originating from a foreign clinical trial, which is not used in the domestic clinical trial (a drug other than the investigational drug), and the other investigational drug used as the suspected drug remains subject to reporting.

C-2. When the result of the unlocking: “Code broken is a placebo or a control drug in a case originating from a foreign clinical trial that has not been used in a domestic clinical trial (a drug other than the investigational drug) and the other investigational drug used as the suspected drug is no longer subject to reporting.

A14: Clinical trial

A-1. Withdrawal (Nullification) is reported because the investigational new drug to be reported has not been administered.

A-2: Withdrawal (Nullification) is reported because the investigational product has not been administered. (The suspected comparator is not subject to reporting because it is a comparator < non-investigational drug > that has not been used in a domestic clinical trial.)

B-1. An additional report is made because the investigational product to be reported remains as the suspected drug even though the Suspect Drug has not been administered.

C-1. An additional report is made because the investigational new drug to be reported remains as the suspected drug even though the Suspect Drug has not been administered.

C -2. An additional report is made as not subject to reporting because the investigational product to be reported was administered, although the Suspect Drug was not administered.

Q15: (Clinical trial)

The case does exist, but how can the adverse event be reported when the adverse event once reported by the investigator is deleted due to reconsideration, etc.?

A15: Clinical trial

If the event did not exist, the Withdrawal (Nullification) report should be filed in the same manner as if the case did not exist. However, this does not apply when other adverse events to be reported exist (Includes cases where a causal relationship to the reported adverse event was denied or where the severity of the event was changed).

Q16: (Clinical trial)

If a case in a clinical study conducted in a foreign country is suspected to be an investigational product other than the investigational product, is it subject to reporting even if a causal relationship to the investigational product is ruled out and not subject to reporting?

A16: Clinical trial

Cases for which information is available are reportable.

Q17: (Post-marketing) and (Clinical trials)

When a clinical trial is switched to a post-marketing clinical trial and is continued, the drug used as the investigational product during the clinical trial (In the post-marketing clinical study, the drug used in the post-marketing clinical study)

Therefore, is it correct to assume that the obligation to report adverse reactions, etc. that occur during the post-marketing clinical study period falls on the MAH: Marketing Authorizations holder of each drug, not the post-marketing clinical study sponsor?

A17: Post-marketing and Clinical trials

(Acceptable): The sender may report in the manner presented in the question. It should be kept in mind that the sponsor is required to report any adverse reactions that occurred during the pre-switch clinical trial if they are known during the post-marketing clinical trial period.

(2) Time limit for reporting, etc.

Q18: (Post-marketing)

Notification No. 25 of the Director of Safety Division, Pharmaceutical Safety Bureau, Ministry of Health and Welfare, dated March 11, 10, In Item 2. (2) of the article, it is stipulated that "Any adverse drug reaction newly included in the package insert as a result of the revision should be treated as an "unexpected adverse drug reaction based on the Precautions" and reported within 15 days if information similar to the adverse drug reaction is obtained during the period between the revision of the package insert and the completion of communication to medical institutions." At what point should it be considered until the communication to medical institutions is completed?

A18: Post marketing

The date of completion of communication by the MAH or the date of distribution of the Drug Safety Update (DRUG SAFETY UPDATE (DSU)) to medical institutions, whichever comes first.

Q19: (Post-marketing) and (Clinical trials)

What is the deadline for reporting post-marketing adverse drug reaction reports in cases where it was thought to be subject to reporting within 30 days, but before reporting the first report it was found to be subject to reporting within 15 days due to additional information?

Also, when is the deadline for reporting an adverse drug reaction in a clinical trial that was considered to be subject to reporting within 15 days, but was found to be subject to reporting within 7 days due to additional information before reporting the first report?

A19:

Post-marketing

Report within 15 days from the date on which it was found to be the subject of a report within 15 days. However, if this reporting deadline exceeds 30 days from the date on which information considered to be subject to reporting within 30 days was obtained, at least the information considered to be subject to reporting within 30 days from the date on which the information was obtained should be reported within 30 days from the date on which the information was obtained.

Clinical trials

Report within 7 days from the date on which it was found to be the subject of a report within 7 days. However, if this reporting deadline exceeds 15 days from the date on which information considered to be subject to reporting within 15 days was obtained, at least the information considered to be subject to reporting within 15 days from the date on which the information was obtained should be reported within 15 days from the date on which the information was obtained.

Q20: (Clinical trial)

For cases that have already been reported, can additional medically important information be obtained and, when submitting additional reports, can the statutory reporting deadline be considered from the date of receipt of additional information?

A20: Clinical trial

(Acceptable): The sender may report in the manner presented in the question. Additional reporting within the deadline, with the date of receipt of additional information as the starting date. For example, for cases that have already been reported within 15 days, if additional information to be reported within 7 days is obtained, additional reporting should be made within 7 days. If additional information to be reported is obtained for a case that has already been reported within 7 days, additional reports should be made within 7 days unless the deadline for reporting the case is changed to 15 days with additional information.

Q21: (Clinical trial)

How should reporting deadlines be set when the ICCC (In country Clinical Care-taker) of a clinical trial report adverse reaction?

A21: Clinical trial

The date of receipt of information to be reported by the sponsor or the ICCC (In country Clinical Care-taker) of the clinical trial, whichever comes first, who does not have an address in Japan, should be converted to Japanese time and used as the initial reporting date.

(3) Expectedness

Q22: (Post-marketing)

What are the items under "Precautions for Use" in the Cautionary Notes and Other Information that are used to determine whether they can be predicted?

A22: Post marketing

The following items apply to the "Precautions" described in accordance with the "Guidelines for Electronic Package insert of Prescription Drugs" (MHLW Notification No. 0611-1 dated June 11, 2021).

"1. Warning", "2. Contraindications", "5. Precautions Related to Indications", "7. Precautions on Dosage and Administration", "8. Important Precautions", "9. Notes on patients with specific backgrounds", "10. Interactions", "11. Side effects", “12. Effects on Laboratory Results", “13. Overdose", "14. Notes of Application".

In addition, the following items apply to the "Precautions" described in accordance with the "Guidelines for Inclusion of Prescription Drugs" (MHLW Notification No. 606 of the PMSB dated April 25, 1997) and the "Guidelines for Inclusion of Precautions in Prescription Drugs" (MHLW Notification No. 607 dated April 25, 1997).

“Warnings”, “Contraindications”, “General Contraindications”, “Precautions of Indications”, “Precautions of Dosage and Administration”, “Careful Administration”, “Important Precautions”, “Interactions”, “Adverse Reactions”, “Administration in the Elderly”, "Use in Pregnant”, “Parturient and Nursing Women (Female)”, "Administration in Children”, “Effects on Laboratory Results”, “Overdose”, “Precautions”.

Q23: (Post-marketing)

How are adverse reactions that cannot be predicted from the precautions required for use determined?

A23: Post-marketing

In accordance with "2.4 Unexpected Adverse Drug Reactions" in the E2D Guideline, Judgment should be made in light of the Precautions for Use.

Q24: (Post-marketing)

In the Post-marketing Director's Notice, it is stated that "Those that are not included in the Precautions section of the Precautions section (Warnings, Important Precautions, Interactions, Adverse Reactions, etc.), or those that are included but whose nature, severity of symptoms, specificity, etc. do not match the description." In what cases is "Products described in "PRECAUTIONS" but whose nature, severity of symptoms, specificity, etc. do not match the description"?

A24: Post marketing

For example, the following cases apply:

(1) Adverse reactions that are similar in name to those listed in the Precautions section but differ in severity or mechanism of onset ('Hepatitis' = > 'Fulminant Hepatitis' [If Hepatitis is listed in the Precautions section and Fulminant Hepatitis occurs], "Anemia" = > "Aplastic anemia"
"Leukopenia, erythrocytopenia, and thrombocytopenia" = > Pancytopenia, "Leukopenia" (granulocytopenia)" = > "agranulocytosis", "Diarrhea" = > "Diarrhea with dehydration and electrolyte abnormalities").

(2) In the event of a more specific (limited) adverse reaction than listed in the Precautions section (e.g., acute renal failure, interstitial nephritis)

(3) If abnormal laboratory values are described but are accompanied by other symptoms ("Low serum potassium with weakness, arrhythmia," etc.)

The symptoms and signs that usually accompany the listed adverse reactions can be predicted from the Precautions section. (For example, Shock "Decreased blood pressure, increased heart rate, and decreased urine output associated with shock," Aplastic Anemia "Paleness and fatigue associated with aplastic anemia," etc.)

Q25: (Post-marketing)

Is it correct to judge the predictability of adverse reactions reported in foreign countries based on the Precautions in the Precautions section of the Package insert in Japan?

A25: Post marketing

(Acceptable): The sender may report in the manner presented in the question.

Q26: (Clinical trial)

The Director of Investigations Notice states that "Information that is not predictable from the Investigator's Brochure of the investigational product or existing scientific knowledge about the investigational product other than the investigational product" refers to items that are not included in the documents used to make the latest predictive assessment at the time of evaluation of the adverse drug reaction (Investigator's Brochure, a document describing scientific findings (Package inserts, interview forms, academic papers, etc.). Hereafter referred to as the "Investigator's Brochure, etc.".) or items that are included but whose nature, the severity of symptoms, or trend of occurrence do not match the descriptions." What is "The nature, severity, or trend of occurrence of adverse drug reactions that are not consistent with the descriptions in the documents used to assess the latest predictability at the time of evaluation?"

A26: Clinical trial

As indicated in the Notice of the Director of the Evaluation and Licensing Division, Pharmaceutical Affairs Bureau, MHLW No. 227 dated March 20, 1995, "Handling of Safety Information Obtained during Clinical Trials," events that are more specific (limited) or severe than those listed in the Investigator's Brochure, etc. are those that cannot be predicted.

For example, if the Investigator's Brochure contains a description of "acute renal failure" and reports "interstitial nephritis," "interstitial nephritis" is judged to be unpredictable from the Investigator's Brochure.

The same applies to "fulminant hepatitis" for "hepatitis", "aplastic anemia for anemia", "pancytopenia for Leukopenia, erythropenia, and thrombocytopenia" "agranulocytosis for leukopenia (granulocytopenia)", and "Diarrhea with dehydration and electrolyte abnormalities for diarrhea”.

In addition, even if abnormal laboratory values are described, the same is true when abnormal laboratory values are accompanied by other symptoms (For example, "Low serum potassium with weakness, arrhythmia" for "low serum potassium").

Symptoms and signs usually associated with the listed adverse reactions can be predicted from the Investigator's Brochure, etc. (For example, "Decreased blood pressure, increased heart rate, and decreased urine output associated with shock" for "shock" and "Paleness and fatigue associated with aplastic anemia" for "aplastic anemia".)

Q27: (Clinical trial)

An adverse reaction that occurred during a double-blind controlled trial was reported as an "Investigational Adverse Reaction Report" with an unopened key, reflected in the Investigator's Brochure with an unopened key, and reported to the medical institution, but if the same adverse reaction subsequently occurs, can the adverse reaction be predicted from the Investigator's Brochure or not?

A27: Clinical trial

If an unopened key is reported as a "Report on Adverse Drug Reactions," reflected in the Investigator's Brochure, and communicated to the medical institution, it can be treated thereafter as predictable from the Investigator's Brochure.

Q28: (Clinical trial)

If an adverse drug reaction reported as unknown is found to be caused by an investigational product other than the Suspect Drug after the opening of the key of the double-blind controlled trial, and the information of the adverse drug reaction report by the Suspect Drug was not obtained outside of the case, the adverse drug reaction has not been reported from the Investigator's Brochure since the opening of the key. Treat them as unmeasurable?

A28: Clinical trial

Correct in that interpretation

Q29: (Clinical trial)

If, after unlocking: “Code broken” a double-blind controlled trial, it is determined that a placebo was administered, and the other investigational product is the suspected drug, and an additional report is to be made, is it correct to enter the information on the placebo or not enter the information on the placebo in the items included under "Drug identification (G.k.2)" after deleting the information on the Suspect Drug included in the previous report?

A29: Clinical trial

(Acceptable): The sender may report in the manner presented in the question.

Q30: (Clinical trial)

E2B (R3) 2 Section Chief's Notice Attachment 8. (1) “エ” and “カ” In cases where the sponsor and the marketing authorization holder applying for approval are different and the sponsor is unable to obtain a summary of application data, can the Investigator's Brochure be used as the basis for judging the Expectedness of adverse drug reaction reports from the sponsor?

A30: Clinical trial

(Acceptable): The sender may report in the manner presented in the question

Q31: (Clinical trial)

Is it acceptable for the sponsor to select "documents containing scientific findings" for each investigational product when reporting adverse reactions to investigational products other than the investigational product?

A31: Clinical trial

(Acceptable): The sender may report in the manner presented in the question.

Q32: (Clinical trials)

E2B (R3) Notice of Two Directors Attachment 8. (1) “イ” with respect to, it is stated that "The time point considered "predictable" should be the date of preparation or revision of the latest Investigator's Brochure or document containing the latest scientific findings." However, if the Package insert or interview form of another company's product is used as a document describing the latest scientific knowledge of investigational new drugs other than the Suspect Drug, how should the revision date be considered?

A32: Clinical trial

When a Package insert or interview form of another company's product is used as a document describing the latest scientific findings of investigational new drugs other than the Suspect Drug, the date of receipt of the revised information may be acceptable, but efforts should be made to obtain the revised information promptly.

(4) Criteria for determining seriousness

Q33: (Post-marketing)

If we receive information that an adverse reaction has occurred, but we do not have information to assess its severity, how should we deal with it?

A3 3: Post marketing

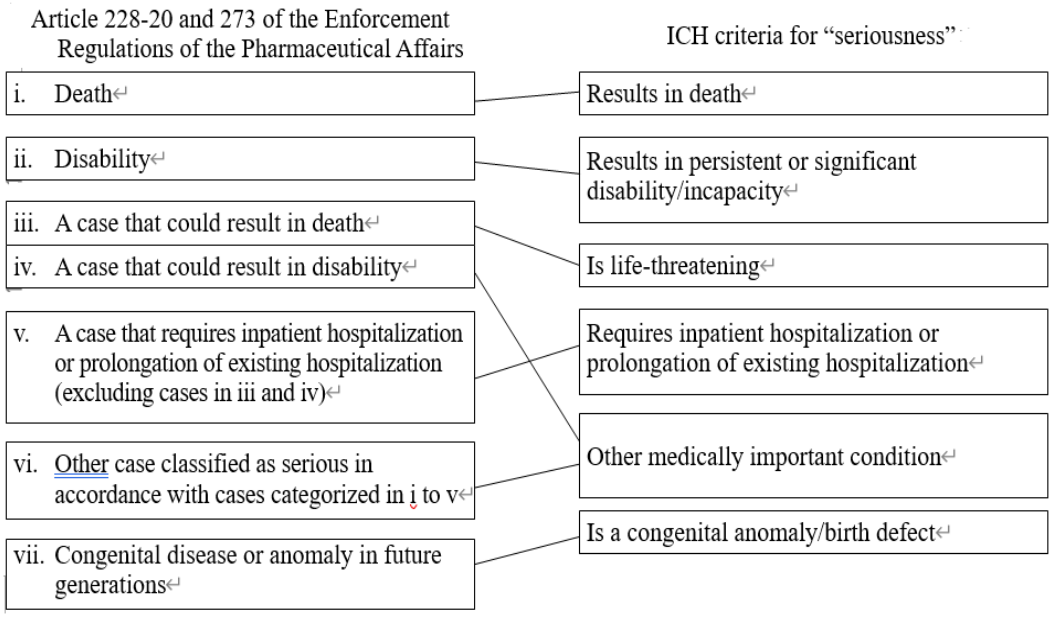
A33: Post-marketing

Efforts should be made to collect detailed information so that the severity can be evaluated, and the severity of each adverse reaction should be evaluated based on the available information.

Q34: (Post-marketing) and (Clinical trials)
How can we relate the definition of severity of adverse reactions in ICH?

A34: Post-marketing and Clinical trials

The following table should be used as a guide.



Q35: (Post marketing)
What should we think of "death" in Article 228, Section 20 of the Enforcement Regulations?

A35: Post marketing

This is a case of death suspected to be caused by an adverse reaction and falls under the definition of "fatal" in the ICH regulations (see E2D guideline). For example, a patient who developed an infection due to granulocytopenia, myelosuppression, etc., and died also naturally falls into the category of a fatal case subject to adverse reaction reports. Even if the reporter did not determine that the death was caused by an adverse reaction, the case that the sender determined to be caused by an adverse reaction should be treated as a case of death caused by an adverse reaction.

Q36: (Post-marketing)

What should we think of "disability" in Article 228, Section 20 of the Implementing Regulations?

A36: Post marketing

It indicates the development of dysfunction that interferes with daily activities and falls under the category of "permanent or significant disability/dysfunction" in the ICH regulations (see E2D guideline).

Q37: (Post marketing)

What should we think of "cases that may lead to death" in Article 228, Paragraph 20 of the Enforcement Regulations?

A37: Post marketing

This refers to cases that fall under the definition of "life-threatening" in the ICH regulations (see E2D guideline) and the patient is at risk of death at the time of the event. That doesn't mean it could have caused death if it had been more severe.

Q38: (Post-marketing)

How should we consider "cases that may lead to disability" in Article 228, paragraph 20 of the Enforcement Regulations?

A38: Post marketing

Refers to cases in which the patient was at risk of developing dysfunction that interfered with his or her daily life when the adverse reaction occurred. It falls under the category of "events or reactions considered to be other medically important conditions" in the ICH regulations (see E2D guideline). That doesn't mean he might have remained disabled if it had been more severe.

Q39: (Post-marketing)

What should we think of "cases requiring admission to a hospital or clinic for treatment or an extension of the period of hospitalization" in Article 228, paragraph 20 of the Enforcement Regulations?

A39: Post marketing

In the provisions of ICH (see E2D guideline), "those requiring hospitalization for treatment or extension of hospital stay" is applicable. Patients who were hospitalized for treatment of adverse drug reactions or whose hospital stay was extended, and those who were hospitalized for treatment of adverse drug reactions but did not take any specific measures (rest treatment) also fall into this category. For example, patients hospitalized for anaphylactic shock or pseudomembranous colitis fall into this category. It does not include hospitalization for testing or extension of the period or hospitalization for follow-up although the adverse reactions have been cured or improved.

Q40: (Post-marketing)

In Article 228, Paragraph 1, Item 1 “ﾊ“ (4) of the 20 Enforcement Regulations, what should be considered as "death or a case that is serious according to the cases listed in (1) to (3)"?

A40: Post marketing

"Events or reactions considered to be other medically important conditions" in the provisions of ICH (see E2D guideline), that is, events or reactions that do not immediately threaten life or result in death or hospitalization, may cause the patient to die.

This applies to critical medical events that are likely to be exposed or require treatment or treatment so as not to result in "death," "permanent or significant disability or dysfunction," "life-threatening," or "requiring hospitalization or prolonged hospitalization for treatment." For example, in the case of allergic monobronchial bronchospasm requiring intensive care in an emergency room or at home, or blood disorder or convulsion that does not result in hospitalization, drug addiction or drug tongue L use fall under this category.

Q41: (Post-marketing)
How to think of "congenital disease or abnormality in later generations" in Article 228, paragraph 20 of the Enforcement Regulations?

A41: Post marketing

According to the provisions of the ICH (see E2D guideline), the case falls under the category of "those causing birth defects or birth defects" and includes cases in which an abnormality is suspected to have occurred in the offspring due to exposure to drugs before or during pregnancy. Examples include thalidomide-induced organogenesis imperfecta in offspring and diethylstilbestrol induced vaginal cancer in female offspring.

(5) Description

Q42: (Post-marketing)
E2B (R3) For items that can be abbreviated in Exhibit 1 and Exhibit 2 of the Director's Notice, how should these items be described?

A42: Post marketing

E.i.1.1 a, E.i.1.1 b and E.i. With the exception of 1.2, these are items that must be included in the completion report, and if they are not included at all, an error report will result. Therefore, they should be described in simplified form, referring to the "Supplement" column under "Tolerance related" in the tables in Exhibits 1 and 2.

Q43: (Post-marketing) and (Clinical trials)
Are there any precautions when writing Time Zones?

A43: Post-marketing and Clinical trials

See Appendix II of the E2B (R3) Implementation Guide for how to enter dates/times. When conducting inter-item data checks, etc., caution should be exercised as the data is converted to Japanese time (+ 09: 00) if the time zone is not stated, and to Japanese time if the time zone is stated.

Q44: (Post-marketing) and (Clinical trials)
Is the use of full-width characters (Double bytes Character) permitted in the input types "NUM" and "Date (minimum precision)"?

A44: Post-marketing and Clinical trials

Enter "NUM" and "Date (minimum precision)" in half-width characters (Single byte Character).

Q45: (Post-marketing) and (Clinical trials)
Is the use of characters with “Umlauts”, etc. allowed in the input type TXT?

A45: Post-marketing and Clinical trials

Characters with “Umlauts”, etc., may be accepted as long as the character string can be used in UTF-8. However, it is recommended that characters with umlauts, etc. are not used in domestic cases. Also, characters such as "<" and ">" that are not allowed in XML messages are not allowed.

(6) J Item

Q46: (Post-marketing) and (Clinical trials)

When reporting post-marketing adverse drug reactions, etc., it was thought to be subject to reporting within 30 days, but before reporting the first report, it was discovered by additional information that it was subject to reporting within 15 days, and the content of the reports within 30 days and within 15 days is combined and reported at one time, which start date should be included in "J2.2.1 Start date of reporting"? Should "C.1.7 Does this case meet the criteria for emergency reporting in the country?" be a 15-day report?

In addition, when reporting an adverse drug reaction in a clinical trial, etc. was considered to be subject to reporting within 15 days, but before reporting the first report, additional information revealed that it was subject to reporting within 7 days, and the content of the report within 15 days and the report within 7 days is combined and reported at one time, which start date should be included in "J2.2.1 Start Date of Reporting"? Should "C.1.7 Does this case meet the criteria for emergency reporting in the country?" be a 7-day report?

A46:

(After the market)

"J2.2.1 Initial reporting date" is the date on which the information subject to reporting was obtained within 30 days.

J2.2.2 Comments on the reporting start date should explain the relationship between the reporting start date and the date of receipt of additional information and the reporting deadline date. Also, "C.1.7 Does the case meet the criteria for emergency reporting in the country?" should be reported on the 15th.

(Clinical trials)

"J2.2.1 Initial reporting date" is the date on which the information subject to reporting was obtained within 15 days.

J2.2.2 Comments on the reporting start date should explain the relationship between the reporting start date and the date of receipt of additional information and the reporting deadline date. Also, "C. 1.7 Does the case meet the criteria for emergency reporting in the country?" should be a 7-day report.

Q47: (Post-marketing)

During the reexamination period for drugs with new active ingredients, if an adverse reaction occurs after the completion of EPPV in a drug that is newly subject to EPPV due to an additional indication, should the "J2.4.k Status Classification of New Drugs, etc." be reported according to which category?

A47: Post marketing

Such cases should be reported as "within 2 years of approval" if they occur within 2 years of approval of an additional indication, or "not applicable" if they occur after 2 years of approval of an additional indication. However, if an approval for an additional indication, etc. is obtained after the expiration of the reexamination period, it should be reported as "not applicable" even within two years of the approval.

Q48: (Post-marketing) and (Clinical trials)

Why are the symbols indicating repetition in J items such as "J2.4.k Status Classification of New Drugs, etc." and "J2.14 i Unknown/Known (Expectedness)" used differently, such as "k" and "i"?

A48: Post-marketing and Clinical trials

The repetition symbols in the J items correspond to the repetition symbols in the E2B (R3) items as follows: In addition, the adverse drug reaction information management system acquires values using XPath, but the "J2.4 .k" belonging to the "G.k" acquired first by XPath falls under the first iteration.

J Item		E2B (R3) items	
J2.4.k	Status classification of new drugs, etc.	G.k	Drug Information
J2.5.k	Risk Categories, etc. for OTC: Over-the-Counter Drugs, etc.		
J2.6.k	Access to OTC drugs		
J2.14.i	Unknown/Known	E.i	Adverse reactions/events
J2.15.r	State of publication	C.4.r.1	"Publication Status" in Research/Action Reports
J2.17.r	Classification of tests/studies		

Q49: Clinical trial

What "J2.4.k Status Classification of New Drugs, etc." should be selected for investigational new drugs such as:?

① When a drug manufactured and sold in a foreign country with the same ingredients as a domestically approved drug (foreign drug) is used as a Suspect Drug
② When a drug (foreign drug) manufactured and sold in a foreign country with the same ingredients as a domestically approved drug is used as an investigational new drug (excluding Suspect Drug)

A49: Clinical trial

① Select "4 = investigational Partial change."
② Select "8 = Japan domestically approved (excluding Suspect Drugs)."

Depending on the status of the domestic approval of the active ingredient, the drug should be appropriately selected from "3 = Not approved" and "4 = In Partial change" for the Suspect Drug, and "8 = Japan Domestic approved (excluding Suspect Drug)" and "9 = Domestic unapproved (excluding Suspect Drug)" for the investigational drug excluding the Suspect Drug.

Q50: Clinical trial

Information on investigational new drugs is supposed to be entered in the "Presence or absence of cases on medication (J2.13.r.4)" but what information should be entered in the "Presence or absence of cases on medication (J2.13.r.4)"?

A50: Clinical trial

The status of all investigational products listed in the protocol notice or protocol change notice for the principal investigational product should be entered, regardless of whether they are administered in the report. In this case, it is acceptable to enter only the investigational product used in the primary investigational product trial.

Q51: Clinical trial

In a trial using multiple Suspect Drugs, if the primary Suspect Drug is approved or discontinued but no new notification is made regarding the change of the primary Suspect Drug, how should adverse reaction reports be made?

A51: Clinical trial

Even if the primary investigational product is approved or discontinued, the "Study Ingredient Symbol (J2.12)" and the "Japanese Clinical Trial Summary (J2.13)" should include information on the main investigational product that has been approved or discontinued.

For the main investigational product that has been approved or whose development has been discontinued, there is no obligation to report the adverse reactions in clinical trials.

Q52: Clinical trial

Even during the transitional period, are the code system versions of the J items used for reporting up to date?

A52: Clinical trial

It is recommended to use the latest code system version, but the available version should be checked on the PMDA's website for drug manufacturers (PMDA SKW site).

(7) ICSR Items

Q53: (Post-marketing) and (Clinical trials)

"N.1.5 Date of batch transmission" "N.2.r.4 Date of message creation" "C.1.2 Date of Creation" gives the year, date, time, minutes and seconds, but what if there is a time lag between the time when the ICSR etc. file is created and the time when the data is sent?

A53: Post-marketing and Clinical trials

If an ICSR etc. file is to be created, "N.2.r.4" and "C.1.2 J must match exactly. For N.1.5, enter the date (year, month, date, minute and second) so that the time is after the creation time of "N.2.r.4" etc. In the additional report, if the date of "C.1.2" is the same as the date of the previous report, it will be an error. Therefore, make sure that the date is after the time of the previous report.

When submitting by CD, etc., minutes and seconds may be entered as "0000."

Q54: Clinical trial

If the two companies that are co-developing the product each report adverse drug reactions, is it correct that the sponsor who reported the adverse drug reactions first should inform the other sponsor of the "C.1.1 Unique (case) safety report identifier for each sender"?

A54: Clinical trial

It is recommended that the sponsor who reported the adverse reactions first contact the co-development company in the ICSR file with "C.1.1", "C.1.8.1 Globally unique case identifier" etc. When preparing the ICSR file, the sponsor who has been contacted should write "C.1.8.1" in C.1.8.1, "C.1.9.1 Are there any other case identifiers described in past transmissions?" should be 'true' (= yes), the name of the other party's organization should be written in "C.1.9.1.r.1 Source of Case Identifiers," and "C. 1.9.1.r.2 Case identifier" should be written in C.1.1.

Q55: (Post-marketing) and (Clinical trials)

When reporting by mail, are "N.1.5 Date of batch transmission" "N.2.r.4 Date of message creation" and "C.1.2 Date of Creation" all on the day of mailing?

A55: Post-marketing and Clinical trials

(Acceptable): The sender may report in the manner presented in the question. When submitting a CD, etc., minutes and seconds may be entered as "0000."

Q56: (Post-marketing)

In the case of reports on proprietary Post-marketing drugs obtained from trials conducted by other companies, is it correct to set the "C.1.3 Types of Reports as “2 = reports from Clinical trials”?

A56: Post marketing

(Acceptable): The sender may report in the manner presented in the question.

Q57: (Post-marketing) and (Clinical trials)

If the reporter suspects the possibility of an infectious disease caused by the use of a drug or investigational product and informs the person in charge of drug information, etc., but the reporter wishes to make a final judgment based on the results of other tests (viral markers), may "C.1.4 Date of first receipt of report from source" be the date on which the reporter makes a final judgment based on the results of other tests?

A57: Post-marketing and Clinical trials

The date should be the date on which the reporter informed the medical information officer of the possibility of an infectious disease caused by the use of the drug or investigational product.

Q58: (Post-marketing)

If the MAH has partially outsourced post-marketing safety control, should the date on which the MAH obtained the information from the outsourcer be designated as "C.1.4 Date of first receipt of report from source"?

A58: Post marketing

The date on which the information was first received by either the MAH or the subcontractor should be treated as "C.1.4."

Q59: Clinical trial

When the ICCC (In country Clinical Care-taker) reports adverse reactions, etc. related to investigational products, at what point should the "C.1.4 Date of first receipt of report from source" be?

A59: Clinical trial

It should be the time when either the sponsor without an address in Japan (Hereafter referred to as "foreign sponsor") or ICCC (In country Clinical Care-taker) in Japan first obtained the information.

Q60: (Post-marketing) (Trial)

When the same case as the one reported in the Investigational Adverse Drug Reaction Report is reported as a Post-marketing Adverse Drug Reaction Report, the identifiers in each report must be included in "C.1.8.1 Globally unique case identifier" and "C.1.10.r Identifiers of this report and related reports."

A60: Post-marketing and Clinical trials

The "C.1.8.1" should be the same as the in the "Report of post-marketing adverse reactions, etc." section and, if possible, the identifier in each report should be included in the "C.1.10.r" section. In addition, in the section "J2.11 Other Reference Information, etc," the fact that it has been or will be submitted in the "Report on Adverse Drug Reactions in Clinical Trials" (or "Report on Adverse Drug Reactions in Post-marketing Phase") should be noted, and if it has already been submitted, the "J2.1 Identification Number" of the report should also be noted.

Q61: (Post-marketing) and (Clinical trials)

If the same case as the one reported in the Report on Adverse Drug Reactions is to be reported as the Report on Adverse Drug Reactions Post marketing, should the company-specific Case Report Numbers, etc. ("C.1.1 Unique (case) safety report identifier for each sender" and "N.2.r.1 message identifier") use the same or different values for reporting as the Report on Adverse Drug Reactions Post marketing?

A61: Post-marketing and Clinical trials

Use different values.

Q62: (Post-marketing) and (Clinical trials)

If part of the patient abbreviation is unknown, unlisted or not listed in its entirety, may "D.1 Patient (name or initials)" be listed as "X.X."?

A62: Post-marketing and Clinical trials

If the patient abbreviation is unknown or not described, use NullFlavor in "D.1 Patient (name or initials)." If you know the patient abbreviation but do not include it to protect your personal information, use Null Flavor's MSK.

See Attachments 1 and 2 of the E2B (R3) Implementation Guide and the E2B (R3) ICH Q&A on the use of Null Flavor.

Q63: (Post-marketing) and (Clinical trials)

Is the "E.i Adverse drug reactions/events (repeat as needed)" required to list all adverse reactions and infections reported by the reporter?

A63: Post-marketing and Clinical trials

All adverse reactions/infections reported by the reporter may be listed, but it may be acceptable to list only the names of adverse reactions/infections to be reported in accordance with the provisions of Articles 228 20 and 273 of the Enforcement Regulations.

Q64: (Post-marketing) and (Clinical trials)

When the name of an adverse reaction is listed, for example, can "Decreased blood pressure, increased heart rate, decreased urine output, etc." associated with "shock" only be listed?

A64: Post-marketing and Clinical trials

If the reinvestigation indicates that the reporter is a case of shock, it is acceptable to list only shock in the "E.i Adverse drug reactions/events (repeat as needed)" section. However, "H.1 Case descriptive information, including clinical course, treatment procedures, outcomes and other relevant information" should be accompanied by "Decreased blood pressure, increased heart rate, decreased urine output, etc."

For further details, please refer to "MedDRA TERM SELECTION: POINTS TOCONSIDER" (PTC).

Q65: (Post-marketing) and (Clinical trials)

"E.i.1.2 Translated and reported adverse reactions/events by primary source",

Is it correct not to write "E.i.1.1a Adverse reactions/events reported by the primary source, described in the mother tongue" when it is written in Japanese or English?

A65: Post-marketing and Clinical trials

(Acceptable): The sender may report in the manner presented in the question. If "E.i.1.1a" is written in a language other than Japanese or English,

"E.i.1.2" in Japanese or English.

Q66: (Post-marketing) and (Clinical trials)

If the reporter is not a health professional (For example, consumers or other non-medical professionals),

Can "E.i.3.1 Adverse drug reactions/events identified as important by the reporter" be interpreted as' not given importance by the reporter 'or should it be left blank as' unknown '?

A66: Post-marketing and Clinical trials

Regardless of the reporter's qualifications, it should be stated as judged by the reporter.

Q67: (Post-marketing) and (Clinical trials)

How should "E.i.7 Adverse drug reaction/event outcome at last observation" be described for the outcome of side effects that did not cause death?

A67: Post-marketing and Clinical trials

Appropriate outcomes other than "death" can be selected for each side effect.

Q68: (Post-marketing) and (Clinical trials)

In the "E.i.7 Adverse drug reaction/event outcome at last observation," if the mother has a miscarriage, should the outcome be described in relation to the fetus or the mother?

A6 8: Post-marketing and Clinical trials

In the case of fetal death or early spontaneous abortion, the parent's outcome relative to the adverse reaction name (fetal death, etc.) should be described. For example, "1 = recovery" may be used when a parent's physical condition has recovered.

Q69: (Post-marketing) and (Clinical trials)

Is it correct to assume that "E.i.8 MEDICAL CONFIRMATION BY MEDICAL PROFESSIONALS" does not need to be entered if "C.2.r.4: Qualifications" is "1 = physician," "2 = pharmacist," or "3 = other medical professional"?

A69: Post-marketing and Clinical trials

(Acceptable): The sender may report in the manner presented in the question. If C.2.r.4 is "4 = attorney" or "5 = consumer or other non-medical professional," the presence or absence of medical confirmation should be indicated in E.i.8.

Q70: (Post-marketing) and (Clinical trials)

When the results of a drug-induced lymphocyte stimulation test (DLST) are described, the MedDRA LLT code for DLST can be described in the "F.r.2.2b Test name (MedDRA code)" section.

A70: Post-marketing and Clinical trials

"F.r.2.2b Test name (MedDRA code)" should include the MedDRA LLT code indicating DLST, and "F.r.3.4 Unstructured data on test results" should include the name of the drug and test results.

Q71: (Post-marketing) and (Clinical trials)

Does "G.k.4.r.7 batch/lot number" need to list other suspected drugs?

A71:

Post-marketing

If another company's suspected drug is a vaccine, make efforts to obtain information on its batch/lot number and list it as much as possible.

(Clinical trials)

If the other suspected drug is a vaccine, make efforts to obtain information on its batch/lot number and list it as much as possible.

Q72: (Post-marketing)

Since "G.k.4.r Dose and related information (repeat as needed)" or "G.k.7.r Reasons for Use of Drugs" etc. are unknown, "G.k.2.1 Unique Identifiers of Drugs/Unique Identifiers of Formulations" etc. may not be identified, but if the sender has multiple drug products (different brand names), specifications (different contents), dosage forms (different dosage forms for the same route of administration) or route of administration approval for the same active ingredient, which drug should be reported?

A72: Post marketing

Investigate and try to identify drugs. Even if the drug could not be identified as a result, it should be reported as a drug that is considered more appropriate than the information obtained. If it is not possible to determine which drug is considered more appropriate, it can be reported as the most commonly used drug.

Q73: (Post-marketing)

When the dosing interval of the drug is three times a day, "G.k.4.r.2 Number of units between doses" and
How should "G.k.4.r.3 Definition of dosing intervals" be described?

A 73: Post marketing

In the case of three times a day, enter a UCUM code indicating "G.k.4.r.2" in and "time" in "G.k.4.r.3." Similarly, twice a day has a UCUM code for "12" and "hours" respectively, every other day has a UCUM code for "2" and "days" respectively, and once a week has a UCUM code for include the UCUM code indicating "1" and "week."

Q74: (Post-marketing) and (Clinical trials)

If an adverse reaction occurred during the administration of the suspected drug, but the drug was continued and the adverse reaction recovered during the administration period, how should the "G.k.9.i.3.2 Time interval from last dose of drug to onset of reaction/event" be described?

A74: Post-marketing and Clinical trials

"G.k.9.i.3.2." should be left blank and entered in "H.1 Case descriptive information, including clinical course, treatment procedures, outcomes and other relevant information."

Q75: (Post-marketing) and (Clinical trials)

Drugs with letters such as' 輸 ',' 東薬 ',' 愛薬 ', or' 阪'in the approval number

A75: Post-marketing and Clinical trials

Approval numbers should be changed in accordance with the Joint Notification of the Evaluation and Licensing Division, PFSB Notification No. 0216-1 and the Evaluation and Licensing Division, PFSB, by the Director of the Evaluation and Licensing Division, the Ministry of Health, Labour and Welfare, dated February 16, 2022, entitled "Handling of Flexible Disk Applications."

Q76: (Clinical trial)

In the Domestic Infectious Disease Case Reports (clinical trials) and the Domestic Adverse Drug Reaction Case Reports (clinical trials), if a Suspect Drug is being developed with the same active ingredient as an approved drug in a different dosage form and route of administration, is it correct to include the Clinical drug substance code in the "G.k.2.2 Drug names reported by primary sources"?

A7 6: Clinical trial

A Clinical drug substance code should be provided.

Q77: Clinical trial

In the case of investigational new drugs not yet approved in Japan, except for investigational new drugs, the foreign brand name should be written in half-width alphanumeric characters. What should be written if the brand name does not exist or is unknown?

A77: Clinical trial

Information obtained, such as general names, should be written in half-width alphanumeric characters.

Q78: Clinical trial

How should "G.k.2.2 Drug names reported by primary sources" be described for suspected drugs other than investigational products?

A78: Clinical trial

As much as possible, enter a 9- or 7-digit code (for prescription drugs) or a 12-digit code (for prescription drugs or over-the-counter drugs). Drugs for which a 9-digit reexamination code is missing or unknown, but a 7-digit reexamination code is known, should be included in the "G.k.2.3.r.1 Ingredient/Specific Ingredient Name" and always include a 7-digit reexamination code in the "G.k.2.2 Drug names reported by primary sources." If the code is unknown, enter the brand name, and if neither the code nor the brand name is known, enter the available information, such as the generic name, in Japanese or English.

Q79: Clinical trial

How should "G.k.2.3.r.1 Ingredient/Specific Ingredient Name" describe investigational new drugs that fall under the category of foreign drugs, excluding suspected drugs?

A79: Clinical trial

Enter a 7-digit code (for prescription drugs) or a 12-digit code (for guidance-required drugs or over-the-counter drugs) whenever possible. If the code is unknown, the generic name (brand name in the case of guidance-required drugs or OTC drugs) should be indicated. If neither the code nor the generic name is known, the available information should be provided in Japanese or English.

Q80: Clinical trial

How should "G.k.2.3.r.1 Ingredient/Specific Ingredient Name" be described for suspected drugs other than investigational products if the generic name can be identified?

A80: Clinical trial

Enter a 7-digit code (for prescription drugs) or a 12-digit code (for guidance-required drugs or over-the-counter drugs) whenever possible. If the code is unknown, the generic name (brand name in the case of guidance-required drugs or OTC drugs) should be indicated. If neither the code nor the generic name is known, the available information should be provided in Japanese or English.

Q81: Clinical trial

Different Clinical drug substance code (治験成分記号) are used for different routes of administration due to different routes of administration, although the active ingredients are identical. In addition, each trial protocol notification is submitted with each Clinical drug substance code as the primary Suspect Drug.

How do we report foreign adverse drug reaction cases of the active ingredient if I get them?

A81: Clinical trial

Report by one of the following methods:

(1) Report for each Clinical drug substance code of the main test drug.

(2) Describe items related to drug names in the following manner and report them in one report

Examples:

If the 2-Clinical drug substance code (治験成分記号) of the drug are ChikenA-Tab and ChikenA-INJ, the drug should be handled according to the circumstances described in (1) to (3) below, depending on the confirmation status of the generic name of the active ingredient, etc.

In addition, it is acceptable to use either "Chiken A-Tab" or "Chiken A-INJ" as the Clinical drug substance code in "J2.12 (Clinical drug substance code)."

① Non-approved active ingredients in Japan for which a generic name has not been established

J2.12 (Study ingredient symbol): 'ChikenA-Tab"

G.k.2.2 (name of drug as reported by primary source): "$ChikenA-Tab$$ChikenA-INJ$" (insert Clinical drug substance code with $mark, and list all Clinical drug substance codes subject to happy report)

G.k.2.3.r.1 (Ingredient/Specific Ingredient Name): Enter "ChikenA" (any name that indicates the active ingredient) or "general name undecided." As optional ingredient names, the trial ingredient code provided in the clinical trial notification shall not be used.

②Non-approved active ingredients in Japan with non-proprietary names (e.g., JAN: in the case of "チケンマブ")

J2.12 (Study ingredient symbol): 'ChikenA-Tab"

G.k.2.2 (name of drug reported by primary source): "$ChikenA-Tab$$ChikenA-INJ$" (insert Clinical drug substance code with $mark, and list all Clinical drug substance codes subject to congratulations)

G.k.2.3.r.1 (Ingredient/Specific Ingredient): "チケンマブ"

③ (For example, in the case of JAN: "チケンマブ" and reexamination codes: "1234567" < 7 digits reexamination code >, "123456789" < 9 digits reexamination code >), an active ingredient approved in Japan

(Correspondence 1)

J2.12 (Clinical drug substance code): "ChikenA-Tab"

G.k.2.2 (name of drug as reported by primary source): "$ChikenA-Tab $$ChikenA-INJ $" (Include all Clinical drug substance codes subject to reporting, with the Clinical drug substance code sandwiched by the $mark)

G.k.2.3.r.1 (Ingredient/Specific Ingredient): "チケンマブ"

(Response 2)

J2.12 (Clinical drug substance code): "ChikenA-Tab"

G.k.2.2 (Name of drug reported by primary source): "123456789"

G.k.2.3.r.1 (Ingredient/Specific Ingredient Name): "1234567"

If reporting by Response 2, an application stating that "Foreign study adverse reaction reports with "123456789" in "G.k.2.2" are reported with the Clinical drug substance codes "ChikenA-Tab" and "ChikenA-INJ". should be submitted prior to reporting. When submitting such an application, obtain confirmation of the contents of the application from the Review Planning Division of the Review Management Department

If a 9-digit reexamination code for generic drugs is not granted but a 7-digit reexamination code is known, enter the 7-digit reexamination code (e.g., "1234567") in "G.k.2.2(Name of drug reported by the source).

Q82: (Post-marketing)

For the "G.k.2.2 Drug names reported by primary sources" in foreign cases, should the brand name in the country where the adverse reaction occurred be listed, or should the brand name in Japan be listed in the Japanese section?

A82: Post marketing

Foreign brand names other than the company's own suspected drugs should be written in half-width alphanumeric characters.

In the case of an in-house suspect drug, the code of the drug product that the sender considers more appropriate from among the products approved for marketing in Japan should be provided in light of the reason for use of the drug in the case, dosage and administration, and other active ingredients in the drug.

Q83: (Post-marketing) and (Clinical trials)

If there are multiple reporters and the "C.2.r.4 Qualifications" includes both "1 = physician," "2 = pharmacist," or "3 = other medical professional" and "4 = attorney," or "5 = consumer or other non-medical professional," should the assessment of causality by "4 = attorney," or "5 = consumer or other non-medical professional" be included in the "G.k.9.i.2.r Causality between drug and reaction/event (repeat as needed)"?

A83: Post-marketing and Clinical trials

If the reporter includes "1 = physician," "2 = pharmacist," or "3 = other health care professional," the assessment of causality by "4 = attorney" or "5 = consumer or other non-health care professional" is It does not need to be stated in "G.k.9.i.2.r."

Q84: (Post-marketing) and (Clinical trials)

When conducting a clinical trial for partial changes in approved matters related to the addition, change, or deletion of the dosage and administration or indication of a drug that has already been approved for marketing in Japan, the person approved is required to enter in half-width alphabetic characters in the "G.K.11 Other Pharmaceutical Information" column, etc., when reporting a case report of a foreign infectious disease or a case report of a foreign adverse reaction in accordance with Article 228, 20 of the Enforcement Regulations. How do I enter this “TIKEN” when there are multiple suspected drugs other than the Suspect Drug in the clinical trial?

A84: Post-marketing and Clinical trials

Enter "TIKEN" in half-width (single byte) English letters only for the study drug.

Q85: (Post-marketing) and (Clinical trials)

In the case of fetal death or early spontaneous abortion, should the description of the gestational age at the time of fetal death or early spontaneous abortion be included in "D.2.2.1 Gestational age at onset of adverse reaction/event in fetus" or "H.1 Case descriptive information, including clinical course, treatment procedures, outcomes and other relevant information"?

A85: Post-marketing and Clinical trials

In the case of fetal death or early spontaneous abortion, the gestational period should be written in "H.1" instead of "D.2.2.1" because the patient is becoming a mother. "D.2.2.1" should be written when adverse reactions occur in the fetus and the fetus is the patient.

Q86: (Post-marketing) and (Clinical trials)

In foreign cases, if the opinion of the foreign company is written in English in "H.4 Sender's Comments," can it be reported in English?

A86: Post-marketing and Clinical trials

(Acceptable): The sender may report in the manner presented in the question. If the foreign company's opinion is written in a language other than English or Japanese, translate it into English or Japanese. In addition, the sender's opinion should be written in Japanese, separately from that of the foreign company.

Q87: Clinical trial

"H.4 Sender's Comments" is an essential item, but is it necessary to include it when the in-country controller of the study is the sender?

A87: Clinical trial

be unnecessary. However, the opinion of the foreign sponsor should be included in "H.4."

Q88: (Post-marketing) and (Clinical trials)

Although the E2B (R3) Implementation Guide states that "If more than one source exists, the person who first reports the fact to the sender is the "primary source for regulatory purposes"," in the case of cases obtained via authorities or partner companies, who is the primary source?

A88: Post-marketing and Clinical trials

When reports of adverse reactions, etc. are forwarded, the primary source of the report remains the same. Therefore, the primary source of information should be the person through whom the information passed and who was the primary source of information by the authority or the affiliated company.

Q89: (Post-marketing) and (Clinical trials)

If the CIOMS report form or MedWatch report form for the adverse drug reaction case report is used, and all the contents of the report are included in the adverse drug reaction report, is it not necessary to include them in the "C.1.6.1.r.1 List of materials held by the sender"?

A89:

Post-marketing

(Acceptable): The sender may report in the manner presented in the question. However, when reporting foreign infectious disease case reports (post-marketing) and foreign adverse drug reaction case reports post-marketing by simplifying the input by attaching materials with case information such as the CIOMS reporting form to the ICSR file, enter the name of the material corresponding to this item and attach the material to "C.1.6.1.r.2 Materials Contained" (C.4.r.1/C.4.r.2 for literature). In this case, it is permissible not to enter items other than those required to be entered according to the required items and the contents of other items. Materials that can be attached in this case must be in English or Japanese or translated into English or Japanese, but not handwritten materials.

Clinical trial

(Acceptable): The sender may report in the manner presented in the question.

Q90: (Post-marketing)

When a company's drug is reported using a provisional code, an additional report is supposed to be made immediately when a reexamination code is granted. Is it necessary to make an additional report only because a reexamination code has been granted?

A90: Post marketing

An additional report may be made only because a reexamination code has been granted for a domestic adverse reaction report. In the additional report, "C.1.11.1 Nullification/Correction Report" shall state "2 = correction" and "C.1.11.2 Reasons for Discarding/Revising the Report" should state that an additional report will be made because a reexamination code has been granted.

Foreign adverse reaction reports, research reports, or action reports may be reported using the reexamination code if they are additionally reported for other reasons after the reexamination code has been granted.

(8) Reception related

Q91: (Post-marketing)

If an adverse reaction occurs when a domestic pharmaceutical is used during an overseas trip or when an adverse reaction occurs when a privately imported pharmaceutical is used from overseas, should it be reported in the domestic adverse reaction report or the foreign adverse reaction report?

A91: Post marketing

Reports should be differentiated by the product used, regardless of where the reaction occurred.

(1) Any adverse reactions that occur as a result of the use of a pharmaceutical product taken overseas should be reported by the MAH as a domestic adverse reaction report. For example, a case in which a drug in Japan is used during an overseas trip and a side effect occurs is applicable.

(2) If a drug (foreign drug) manufactured and sold in a foreign country with the same ingredients as the company's own drug is brought into the country and the MAH becomes aware of any adverse reactions that may occur as a result of its use, It should be reported as a Foreign Adverse Drug Reaction Case Report. For example, a case in which adverse reactions occur from the use of pharmaceuticals imported by individuals from overseas.

Q92 Clinical trial

If a foreign sponsor appoints a ICCC (In country Clinical Care-taker) to conduct a clinical trial, is it possible for the ICCC (In country Clinical Care-taker) to report adverse reactions related to investigational products?

A92: To be reported by the ICCC (In country Clinical Care-taker)

Q93: (Post-marketing) and (Clinical trials)

Can multiple domestic companies jointly report individual cases that occur in foreign countries? (For example, companies A and B should report side effects of rooster mixture in joint names, and vice cases of the same case should be reported.

Sell reports of effects (case reports from foreign literature) under one product and two names (co-developed products) Is it possible for two companies or two companies developing jointly to report jointly?

A93: Post-marketing and Clinical trials

Because of electronic signatures, joint reports are not allowed in electronic reports, each company should report each adverse reaction. In addition, since joint reports are not allowed when reporting CDs, each company should report each adverse reaction. In each company's report, as far as possible "C.1.8.1 Globally unique case identifier" should be the same value.

Q94: (Post-marketing) and (Clinical trials)

How should Company A or Company B report a drug that Company B already has on the market as a control in a double-blind controlled trial of a new drug from Company A (before approval), if the drug is found to be an adverse reaction caused by the control as a result of unlocking: “Code broken?

A94: Post-marketing and Clinical trials

Company A should report this as a "Report on Adverse Drug Reactions in Clinical Trials." In addition, Company A should notify Company B of any adverse reaction caused by the control drug, and Company B should report the adverse reaction as a "post-marketing adverse reaction report" if it meets the reporting requirements.

Q95: (Post-marketing) and (Clinical trials)

While conducting clinical trials for a partial change in the indication, dosage and administration of drugs already on the market in Japan,

(1) Should adverse reactions/infections caused by the Suspect Drug be reported in a domestic clinical trial as a municipal post-marketing adverse reaction report or as a clinical trial adverse reaction report?

(2) How should adverse reactions/infections caused by drugs with the same ingredients as the drug be reported in foreign countries?

(3) How should research reports and foreign action reports be reported?

A95:

Post-marketing

(1) Adverse reactions/infections caused by the Suspect Drug during the domestic clinical trial do not fall under the provisions of Article 228, 20 of the Enforcement Regulations and therefore need not be reported as "post-marketing adverse reaction reports."

(2) Report pursuant to Article 228, paragraph 20 of the Enforcement Regulations.

(3) Report pursuant to Article 228, paragraph 20 of the Enforcement Regulations.

Clinical trials

(1) Adverse reactions/infections caused by the investigational product during the domestic clinical trial fall under the provisions of Article 273 of the Enforcement Regulations and should be reported as "Report on Adverse Drug Reactions in Clinical Trials."

(2) It does not need to be reported because it falls under Article 273 (3) of the Enforcement Regulations.

(3) Report pursuant to Article 273 of the Enforcement Regulations. In addition, similar measures in Japan should be reported as the "Report on Foreign Measures in Clinical Trials" and the fact that such measures are taken in Japan should be noted in "J2.11 Other Reference Information, etc."

Q96: (Post-marketing) and (Clinical trials)

What should I do if I receive new information after reporting completion?

A96: Post-marketing and Clinical trials

Any changes or additions that are determined to have an impact on the evaluation should be reported as a completion report.

Q97: (Post-marketing)

If a registration number or identification number has already been assigned to an adverse drug reaction report prior to October 26, 2003 (prior to the date on which electronic reporting is permitted) and an additional report is to be made on or after October 27, 2003, how should the registration number or identification number be entered?

A97: Post marketing

When additional reports are made after October 27, 2003, they should be treated as new reports and "J2.1b identification number (number)" should be left blank. For identification numbers granted before October 26, 2003, enter "C.1.9.1.r.2 Case identifier" and for registration numbers, enter "J2.11 Other References." When entering the identification number in "C.1.9.1.r.2," enter in "C.1.9.1 Are there any other case identifiers described in past transmissions?" and "C.1.9.1.r.1 Source of Case Identifiers" in “MHLW”.

Q98: (Post-marketing) and (Clinical trials)

In reporting the same case, the first report is a paper report, and subsequent reports are electronic. Can we change the reporting method, etc.?

A98: Post-marketing and Clinical trials

For the same case, the means of reporting additional reports may vary from time to time.

Q99: (Post-marketing) and (Clinical trials)

Should domestic adverse reactions occurring before or after the approval date be included in the Investigational Adverse Drug Reaction Report? How should we determine whether the term "post-marketing adverse reaction report" should be used?

A99: Post-marketing and Clinical trials

Judgment should be based on the approval status of the Suspect Drug in Japan for the product as of the onset date of the adverse reaction.

(1) Adverse reactions that occurred before the approval date should be reported as "Report on Adverse Drug Reactions in Clinical Trials" in accordance with Article 273 of the Enforcement Regulations.

(2) Additional information on adverse reactions that occurred before the approval date should be reported as "Report of study adverse reactions, etc." In doing so, in "J.2.13.r.3 Clinical Development Phase," enter "8 = other" and in "J2.11 Other References, etc," enter the words "after approval" and "brand name" respectively.
Enter.

(3) Adverse reactions that occurred after the approval date should be reported as post-marketing adverse reaction reports in accordance with Article 228, 20 of the Enforcement Regulations. In addition, information related to other adverse drug reactions that occurred after the approval date in patients who reported the adverse drug reaction reports prior to the approval date as "Investigational Adverse Drug Reaction Reports" will also be reported as "Post-marketing Adverse Drug Reaction Reports" in the first report.

and 6 3 should be used as reference. If an additional report in (2) and another report of an adverse reaction newly developed after the approval date are to be reported at the same time, they may be reported together as a "Post-marketing Adverse Drug Reaction Report."

Q100: (Post-marketing) (Clinical trial)

Should foreign adverse reactions occurring before or after the approval date be included in the "Report on Adverse Drug Reactions in Clinical Trials"? How should we determine whether the term post-marketing adverse reaction report should be used?

A100: Post-marketing and Clinical trials

Judgment should be based on the approval status of the product in Japan at the time of receipt of the information.

(1) If you received the first information before the approval date, Under the provisions of Article 273 of the Implementing Regulations

This report should be submitted as a "Report on Adverse Drug Reactions." If additional information is obtained after the approval date, the first report of the case should be newly reported as a "post-marketing adverse reaction report" in accordance with Article 228, 20 of the Enforcement Regulations. In doing so, please refer to Q&A 62 and 63 for necessary information.

(2) If the first information is obtained after the approval date, the first report should be reported as a "post-marketing adverse reaction report."

Q101: (Post-marketing) and (Clinical trials)

Is it necessary to include "C.1.11 Nullification/Correction Report" in the case of additional reports of adverse reactions?

A101: Post-marketing and Clinical trials

The E2B (R3) Implementation Guide states that "C.1.11" should be used to indicate that a previously transmitted report has been corrected, but additional reports may not necessarily include "C.1.11.1 Nullification/Correction" and "C.1.11.2 Reasons for Nullification/Correction Report."

When making a non-reportable report, do not include it in "C.1.11.1" or "C.1.11.2."

J2.8.1 non-reportable flag and J2.8.2 Reasons not reportable.

Q102: (Post-marketing) and (Clinical trials)

What should I do if I submitted the report with the name of the document, etc., with the intention of obtaining and sending the attached documents, etc., at a later date, but the documents, etc. were not available after that?

A102: Post-marketing and Clinical trials

If the fact that a document was not available is stated in "J2.11 Other References, etc." and there is no additional information to be reported, "C.1.11.1 Nullification/Correction Report" should be stated as "2 = correction" and an additional report should be made.

Q103: (Post-marketing)

If multiple in-house drugs are suspected drugs in the same case, multiple reports for each suspected drug should be provided. May I write and report?

A103: Post marketing

Report in one report instead of preparing a report for each suspected drug. If different events occur in the same case, depending on the suspected drug, and the time of occurrence of each event varies greatly, and it is considered appropriate to treat the case as a different case, multiple reports may be used.

Q104: Clinical trial

Multiple reports for each suspected drug when multiple investigational drugs are suspected drugs in the same case. May I write a letter and report it?

A104: Clinical trial

Report in one report instead of preparing a report for each suspected drug. If different events occur in the same case, depending on the suspected drug, and the time of occurrence of each event varies greatly, and it is considered appropriate to treat the case as a different case, multiple reports may be used.

Q105: Clinical trial

4. of the E2B (R3) Notice by the Director of the Division 2 states that "Handling of Notification of Clinical Trial Plans for Drugs by Persons Who Intend to Request Clinical Trials" For those who have submitted notification of their clinical trial plans in accordance with the previous rules in accordance with the (Notification No. 10 0831 of the Evaluation and Licensing Division, Pharmaceutical and Pharmacological Evaluation and Licensing Division, the Ministry of Health, Labour and Welfare, dated August 31, 2020), a clinical trial adverse reaction report should be submitted in accordance with the previous rules." For the same case, multiple investigational products are reporting adverse reactions, etc. for each investigational product because of the suspected drug, and if additional reporting is to be made on or after September 1, 2022, how should we respond?

A105: Clinical trial

For clinical trials for which notification of clinical trial protocol or notification of change of clinical trial protocol was submitted in the old format, it is permissible to continue reporting of adverse drug reactions on or after September 1, 2022 in accordance with the previous rules. However, it should be kept in mind that after September 1, 2022, if a change occurs in the notification form and a clinical trial protocol notification is submitted in the new form, a report of adverse reactions, etc. is required to be submitted based on the E2B (R3) Director's Notice.

In addition, a clinical trial for which a protocol notification or protocol change notification was submitted in the old format may be combined into a single report as an additional report to the main study drug adverse reaction report. In doing so, there is no need to withdraw previous reports of Suspect Drugs other than the main Suspect Drug.

Q106: Clinical trial

Regarding the section 4 of the E2B (R3) Notice by the two section chiefs, it says, ""Handling of Notification of Clinical Trial Plans for Drugs by Persons Who Intend to Request Clinical Trials" For those who have submitted notification of their clinical trial plans in accordance with the previous rules in accordance with the (Notification No. 10 0831 of the Evaluation and Licensing Division, Pharmaceutical and Pharmacological Evaluation and Licensing Division, the Ministry of Health, Labour and Welfare, dated August 31, 2020), a clinical trial adverse reaction report should be submitted in accordance with the previous rules." Is it possible to report adverse reactions, etc. based on the E2B (R3) Notice by the two section chiefs, although the clinical trial protocol notification has been submitted according to the previous examples?

A 10 6: Clinical trial

possible. Although the notification form is submitted in the old format, if reports of adverse reactions, etc. are made based on the E2B (R3) two section chief notification, the drugs to be reported are the Suspect Drugs.

Q107: Clinical trial

Do we need to report any adverse reactions, etc., that were obtained prior to the notification of the new form with respect to investigational new drugs other than the investigational products listed when switching from the old form of the protocol notification or protocol change notification to the new form?

A107: Clinical trial

No need to report.

Q108: Clinical trial

In a situation where the primary investigational product A and the non-primary investigational product B are notified in one notification, if the Cohort study for investigational product B has ended but the clinical trial for the other investigational product (primary investigational product A) is still ongoing, is it correct to assume that the submission of a change in the clinical trial protocol notification to the effect that the Cohort study for investigational product B has ended is considered to be the submission of the notification for completion of the clinical trial for investigational product B, and that the mandatory reporting period for adverse reactions of investigational products other than investigational products used in the Cohort study for investigational product B has ended?

A108: Clinical trial

(Acceptable): The sender may report in the manner presented in the question. When the Cohort study for the investigational drug B is completed, the note column of the notification will read:

The Cohort study ended. Drugs used in the study other than the study drug used in the Cohort study for study drug B should be described as "●●●," "▲▲," and "■■."

However, the quantity of investigational new drugs other than the investigational new drug used in the Cohort study for the investigational new drug B

Information should be included in the notification of completion or discontinuation of the study.

(9) Related to paper reporting

Q109: (Post-marketing)

When submitting the first report of an adverse reaction report in a paper report, what items need to be included in the form attached to the Post-marketing Director's Notice?

A109: Post marketing

E2B (R3) The "◎" shown in Exhibit 1 and Exhibit 2 of the Director's Notice should be entered at a minimum. The N items required for electronic reporting need not be included in the report.

Q110: (Post-marketing) and (Clinical trials)

In the case of paper reports, how should "E.i.3.2 Criteria for Seriousness for Each Adverse Event" be described?

A110: (Post-marketing) (Clinical trial)

The following a to f, as applicable, must be listed in alphabetical letters (multiple selections are allowed).

a = anything that results in death
b = Life-threatening
c = Requires hospitalization for treatment or extension of hospital stay
d = permanent or significant disability - resulting in dysfunction
e = those resulting in birth defects
f = other medically important conditions

Q111: (Post-marketing) and (Clinical trials)

In the case of paper reports, how should items other than "E.i.3.2 Criteria for each adverse event" listed in Q112 above, for which tolerance values are specified as "code values," "true" or "false," be described?

A111: Post-marketing and Clinical trials

"Code value," "true" or "false" should not be stated as is, but should be stated so that the content of the relevant item is clear from the report without referring to the code table, etc.

Q112: (Post-marketing) and (Clinical trials)

The MedDRA version is required for "D.7.1.r.1 a MedDRA version of relevant treatment history and, "accompanying symptoms D.8.r.7a" MedDRA version of adverse drug reactions, etc.

Where should it appear in the paper form attached to the Postmarketing Director's Notice or the Investigator's Notice?

A112: Post-marketing and Clinical trials

Enter the information in the "Remarks" column of Form 1.

Q113: (Post-marketing) and (Clinical trials)

According to Attachment 1 of the E2B (R3) Implementation Guide, "G.k.9.i.1 Adverse reactions/events to be evaluated" is a technical reference item and not an item entered by the user. However, in the case of paper reports, how should the information on "G.k.9.i.1 Adverse reactions/events to be evaluated" be included in the attached form of the City Post-Sales Director's Notice or the Director of Investigations Notice?

A113: Post-marketing and Clinical trials

The name of the reaction/event to be evaluated should be provided.

(10) Electronic reporting-related

Q114: (Post-marketing) and (Clinical trials)

Is the period (including the time) and the day of the week during which the confirmation of the connecting stone can be made when applying for the confirmation of the connection with the information management system for the reporting of adverse reactions, etc. to be done electronically?

A114: (Post-marketing) (Clinical trial)

The connection check shall be conducted during the business days and business hours of the PMDA.

The details of the schedule will be communicated by the Information Management Division of the Safety Information and Planning Department of the PMDA after application.

Q115: (Post-marketing) and (Clinical trials)

Must it be the same as the unique number in the file name and the company-specific tracking number in "N. 1.2 Batch No."?

A115: Post-marketing and Clinical trials

Anything else is fine.

Q116: (Post-marketing) and (Clinical trials)

The electronic certificate is supposed to be a representative of the company (such as the president and representative director), but can it be an electronic signature of a person in charge appointed by the president and representative director?

A116: Post-marketing and Clinical trials

No person other than a representative of a business is permitted to use an electronic certificate.

Q117: (Post-marketing)

The sender identifier must be the same as the sender identifier registered with the PMDA for reporting malfunctions, etc. of medical devices or reports of malfunctions, etc. of regenerative medicine products.

A117: Post marketing

Identical is desirable. However, it is acceptable to register a different sender identifier for each type of report only in a situation where, as a sender, it is administratively necessary to register a sender identifier for each type of report.

Q118: (Post-marketing) and (Clinical trials)

ED: When reporting using the tool (AS1 standard or AS2 standard), can the email address or URL already registered as the email address (AS1 standard) or ED: URL (AS2 standard) for reporting malfunctions of medical devices or regenerative medicine products be registered?

A118: Post-marketing and Clinical trials

Send/receive email addresses or ED: TURU URLs should be registered separately for reports of adverse reactions of drugs, quasi-drugs, and cosmetics, reports of malfunctions of medical devices, or reports of malfunctions of regenerative medicine products (Hereafter referred to as "reports of adverse reactions, etc."), except for reports of in-trial malfunctions of medical devices and regenerative medicine products. However, it is acceptable to register the same email address or URL if the ED: tool can receive and process ACK files of different types, such as reports of adverse drug reactions, without confusion due to the settings of the tool.

Q119: (Post-marketing) and (Clinical trials)

If electronic reporting is not possible due to a shutdown of the information management system for adverse drug reactions, and the system shutdown date is the reporting deadline date, what should be done when paper reporting is not available in time because the reporting company is located far away?

A119: Post-marketing and Clinical trials

Safety Information/Contact the Information Management Division, Planning and Management Department by phone.

Q120: (Post-marketing) (Clinical trial)

In an ACK file in an electronic report, in an acknowledgment message item

If the error code is listed for "ACK.A.4" as "AE," "ACK.B.r.6" as "CA," and "ACK.B.r.7," it is classified as "when additional report is required," but is the report acceptable?

A120: Post-marketing and Clinical trials

Yes, but correct the error and report it as an additional or revised report.

Q121: (Post-marketing) and (Clinical trials)

In the Post-marketing and Clinical trials registration forms for persons in charge of reporting adverse drug reactions (new/changed), are the primary and secondary persons in charge of reporting adverse drug reactions appropriate, or is the person in charge of electronic reporting appropriate?

A121: Post-marketing and Clinical trials

The registration form for persons in charge of reporting adverse reactions, etc. should be used when communicating instructions such as re-investigation of reported adverse reactions, consideration of revising the Precautions section, or submission of cumulative reported cases of specific adverse reactions. Therefore, the first and second persons in charge of reporting adverse reactions, etc. should be registered in the Information Management Division of the Safety Information and Planning Department of the PMDA. The persons in charge of reporting adverse drug reactions in Post-marketing and Clinical trials may overlap.

Q122: (Post-marketing) and (Clinical trials)

If the same case is retransmitted (or resubmitted) on the same day, is it necessary to change the file name?

A122: Post-marketing and Clinical trials

File names should be changed after each transmission (or submission).

When instructed by the PMDA, these instructions should be given priority.

Retransmissions should be made only after acknowledgement of receipt of the ACK for the original report.

Q123: (Post-marketing) and (Clinical trials)

What is the relationship between the expiration date of an electronic certificate and the expiration date of a public key?

A123: Post-marketing and Clinical trials

When an electronic certificate expires, the public key naturally becomes invalid.

Q124: (Post-marketing) and (Clinical trials)

What should be the file name when submitting the public key for reporter to the PMDA?

A124: Post-marketing and Clinical trials

The file should be named "Sender Identifier.cer."

Q125: (Post-marketing) and (Clinical trials)

What procedures should be followed when an authority's public key expires?

A125: Post-marketing and Clinical trials

About one month before the expiration date, the new public keys are scheduled to be distributed to companies reporting electronically by the PMDA, so each company should make a sequential switch.

Q126: (Post-marketing) and (Clinical trials)

What should be done if the creation of the XML file is not completed in time by the reporting deadline date because the internal system has stopped due to a natural disaster, other emergency, or serious system failure or other unavoidable reasons (For example, computer virus infection, etc.)?

A126: Post-marketing and Clinical trials

Since this will be handled on a case-by-case basis, contact the Information Management Division of the Safety Information and Planning Department of the PMDA for post-marketing, or the Review Planning Division of the Review Management Department of the PMDA for clinical trials.

Q127: (Post-marketing) and (Clinical trials)

When the adverse drug reaction information management system stops due to the occurrence of a natural disaster or other emergency, etc., the situation will be promptly notified by the registered post-marketing or clinical trial representative email address or the PMDA website. However, what should be done, such as the company being unable to check the situation because it is unable to connect to the Internet?

A127: Post-marketing and Clinical trials

Safety Information/Contact the Information Management Division, Planning and Management Department by phone.

Q128: (Post-marketing) and (Clinical trials)

If there are no problems with the xml Parse check, all the data listed on the XML is reported information
will be incorporated into the adverse drug reaction information management system as?

A128: Post-marketing and Clinical trials

In the adverse drug reaction information management system, only the items that match the XPath stated in the notification are regarded as the reported information. For J items, each item should be prepared in XML according to the XPath described in Exhibit 4 of the E2B (R3) two-section chief's notice. For E2B (R3) items, each item should be prepared in XML according to the XPath described in Attachment 3 of the E2B (R3) Implementation Guide.

Q129: (Post-marketing) and (Clinical trials)

In Exhibit 2 of the E2B (R3) Director's Notice, "F.r.3.3 Results (Units)" is stated in the standard UCUM format, but please provide a specific form of check.

A129: Post-marketing and Clinical trials

The adverse drug reaction information management system checks whether the UCUM format follows the syntax rules defined in UCUM. Details of the rules and acceptable UCUM code samples can be found at the following URL:

https://unitsofmeasure. org/trac/

Q130: Clinical trial

When additional reports of Saiwai, who reported "J.12.i.2 Clinical Development Phase" as "4 = bioequivalence study," "5 = clinical pharmacology study" and "6 = application in preparation" in accordance with the E2B (R2) Notice are reported in accordance with the E2B (R3) Notice, which code should be included in "J.2.13.r.3 Clinical Development Phase"?

A130: Clinical trial

E2B (R3) If the minister falls under the category of Clinical Development Phase in accordance with the Director's Notice, enter the corresponding code, and if not, enter "8 = other."

The development phase should include information on the main Suspect Drugs.

2) Immediate reporting

Q131: Post-marketing

If a "death" suspected to be caused by an adverse drug reaction is found based on additional information after an incomplete report of an adverse drug reaction that cannot be predicted from the precautions required for use, an immediate report is required at that time.

Report immediately and immediately. If an immediate report is made by FAX, the report shall be made separately as provided in Article 228, Paragraph 1, Item 1 of the 20 Enforcement Regulations.

Q132: Post-marketing

After an immediate report by FAX and before a report as provided in Article 228, 20 Paragraph 1, Item 1 of the Regulations is made, if a causal relationship with the suspected drug is denied or if it is found that the drug has not been administered, what should be done?

A132: Post marketing

This information should be sent to the first section or second section of the Pharmaceuticals and Medical Devices Agency (In the case of in-vitro diagnostics, Medical Device Safety Division, Medical Device Quality Control and Safety Division) by fax.

Q133: Post-marketing

The Post-marketing Director's Notice states that "Promptly report the first report by fax, etc., of cases of death in Japan that are suspected to be caused by unknown adverse reactions." On the other hand, the E2D guideline states that "Such an adverse reaction with a fatal outcome should be considered an unpredictable adverse reaction unless it is specified that it may result in a fatal outcome." How do you think about what to report immediately?

A133: Post marketing

As in the past, deaths suspected to be caused by adverse drug reactions for which the occurrence of the adverse drug reaction itself is unknown are subject to immediate reporting, and even adverse drug reactions described in sections such as "Clinically Significant Adverse Drug Reactions" are not specified in sections such as "Important Precautions" and "Clinically Significant Adverse Drug Reactions" to the effect that the adverse drug reaction can lead to a fatal outcome. Therefore, immediate reporting of deaths suspected to be caused by the adverse drug reaction is not required for those that are treated as "unknown" under the E2D guidelines.

Infectious disease cases should be reported immediately, regardless of whether they are unknown or known, as in the past.

3 - Research Report - Foreign Action Report

(1) Research Reports - Common Precautions for Reporting Foreign Measures

Q134: Post-marketing

In a research report or foreign action report, if there are multiple items in question and the report is to be made as a single report, is it correct to use the repetition of "G.k Drug Information (repeat as needed)" and list all the products in question?

A134: Post marketing

(Acceptable): The sender may report in the manner presented in the question.

Q135: (Post-marketing) and (Clinical trials)

Is it necessary to submit all of the materials held by the reporting company in a research report or foreign action report?

A135: Post-marketing and Clinical trials

You don't have to submit all the materials you have. However, such documents, CCDS, etc. need to be submitted regardless of whether they are published or not.

Q136: (Post-marketing) and (Clinical trials)

If information to be reported is obtained before or after the approval date, how should we determine whether it should be reported as "Investigational research/foreign action report" or "post-marketing research/foreign action report"?

A136: Post-marketing and Clinical trials

Judgment should be based on the approval status of the product in Japan at the time of receipt of the information.

(1) If initial information is obtained before the approval date, it should be reported as "Investigational Research/Foreign Action Report" under Article 273 of the Enforcement Regulations. If additional information is obtained on or after the approval date, the initial report shall be newly reported as a "post-marketing research/foreign action happy report" pursuant to Article 228, Paragraph 20 of the Enforcement Regulations. In doing so, please refer to Q&A 139 and 140 for necessary information.

Q137: (Post-marketing) and (Clinical trials)

When the content reported as the Investigational Research/Foreign Action Report is reported as the Post-marketing Research/Foreign Action Report, is it necessary to include the identifiers in each report in the "C.1.8.1, Globally unique case identifier" and "C.1.10.r Identifiers of this report and related reports"?

A137: Post-marketing and Clinical trials

The "C.1.8.1" should be the same identifier in the and the "C.1.10.r" sections, and if possible, the identifier in each report should be provided in the section. In addition, in the section "J2.11 Other Reference Information, etc," the fact that it has been or will be submitted in the "Investigational Research/Foreign Action Report" (or "Post-marketing Research/Foreign Action Report") should be indicated, and if it has already been submitted, the "J2.1 Identification Number" of the report should also be indicated.

Q138: (Post-marketing) and (Clinical trials)

If the content reported as "Institutional Research/Foreign Measures Report" is reported as "Post-marketing Research/Foreign Measures Report," should the firm-specific case report numbers, etc. ("C. 1.1 Unique (case) safety report identifier for each sender" and "N.2.r.1 message identifier") use the same or different values for reporting as "Institutional Research/Foreign Measures Report" and "Post-marketing Research/Foreign Measures Report"?

A138: Post-marketing and Clinical trials:
Different values should be used.

(2) Research Report

Q139: Post-marketing

What is a research report showing "Risk of causing cancer or other serious illness, disability or death as a result of side effects of the pharmaceutical or the foreign pharmaceutical or an infectious disease caused by the use of the pharmaceutical or the foreign pharmaceutical" in the Postmarketing Director's Notice?

A139: Post marketing

This includes research reports indicating that there is a risk of disability or death such as cancer, deafness, blindness, etc., due to ingredients contained in the drug.

A research report is a research report published in a Japanese or foreign academic journal or published/unpublished or conducted by the marketing authorisation holder of the drug or its affiliated companies, and specifically includes reports on epidemiological investigations (or tabulation/analysis of adverse reactions), test results on animals, physical or chemical tests, etc.

Q140: (Post-marketing) and (Clinical trials)
"Research report indicating no approved indication" (for clinical trials)

"Research report indicating no indication for the disease being studied") should be reported in the Infectious Disease Research Report or the Adverse Drug Reaction Research Report?

A140: Post-marketing and Clinical trials

It should be reported as an adverse reaction study report.

Q141: (Post-marketing) and (Clinical trials)

When reporting the results of animal experiments as a research report, what should the "C.1.3 Types of Reports" choose?

A141: Post-marketing and Clinical trials

Select 2 = Report from study.

Q142: (Post-marketing) and (Clinical trials)

Among the published literature, case reports are those reporting adverse reactions or infections. Which to report as?

A142: Post-marketing and Clinical trials

Case reports that contain the information listed in "3.3.1 Minimum Required Information" in Appendix 1 of the E2B (R3) Implementation Guide should be case reports of adverse drug reactions or infections.

However, published literature containing information indicating significant changes in the incidence of adverse reactions or infections or that the drug does not have the approved indication or effect should also be reported as a research report.

Q143: Post-marketing

In research reports on quasi-drugs/cosmetics, where there are multiple products containing specific ingredients, how should "G.k.2.2 Drug names reported by primary sources" be described?

A143: Post marketing

When reporting information about specific ingredients, as a general rule, list all applicable in-house products. However, if there are a large number of products in question, "G.k.2.2" may also include statements such as "representative product name, etc." In this case, obtain a code for reporting adverse reactions to "G.k.2.3.r.1 Ingredient/Specific Ingredient Name," enter the code in the ICSR file, and enter the name of the ingredient in the ICSR file.

(3) Report on Foreign Measures

Q144: Post-marketing

With regard to measures taken in foreign countries, which of the following measures fall under the category of "Suspension of manufacture, import or sale, collection, disposal or other measures to prevent the occurrence or spread of hazards to public health and hygiene" can be considered?

(1) Changes in Indications, Dosage and Administration
(2) Production, importation and discontinuance of sales
(3) Collection and disposal of products
(4) Revision of Precautions (WARNINGS AND PRECAUTIONS, etc.)
(5) interruption of the trial

A144: Post marketing

The following cases fall under measures taken in foreign countries.

(1) A change in indication or dosage and administration that is restricted because of an efficacy or safety issue. Expanding the indication or dosage and administration does not apply when reporting.
(2) Manufacture, importation, discontinuation of marketing, or change in manufacturing method, etc., if done because of efficacy or safety issues (For example, when inactivation process is introduced to prevent virus contamination in blood products, etc.). Production, import, discontinuation of sales and change of manufacturing method, etc.
Of these, those solely for business reasons are not applicable when reporting.
(3) Collection and disposal of products, including those voluntarily collected for reasons such as efficacy or safety. Collection or disposal of products solely for business reasons does not apply to reporting.
(4) In the case of significant changes, etc. in the revision of the Precautions.
(5) Discontinuation of the entire trial due to safety issues.

Q145: Clinical trial

As for measures taken in foreign countries, what are the examples of those falling under "Suspension of manufacture, import or sale, collection, disposal or other measures to prevent the occurrence or spread of hazards to public health personnel"?

A145: Clinical trial

The following cases fall under measures taken in foreign countries.

(1) Changes or restrictions to the indication, dosage and administration made on the grounds of efficacy or safety issues

(2) Discontinuation of manufacture, import or sale, and changes in manufacturing methods, etc., due to lack of efficacy or safety issues (e.g., prevention of virus contamination in blood products (e.g., when the inactivation process has been introduced for a long time)

(3) Collection or disposal of products for reasons of efficacy, safety, etc. (including voluntary collection)

(4) Significant changes, etc. in revisions to PRECAUTIONS (WARNINGS AND PRECAUTIONS, etc.)

(5) Suspension or discontinuation of an entire trial due to quality, efficacy or safety issues

(6) Enhancement of safety measures by rooster cloth such as doctor's letters during clinical trials

Q146: (Post-marketing) and (Clinical trials)

When a foreign regulatory authority provides information on efficacy, safety, and proper use, for example, information necessary to prevent or mitigate a serious adverse reaction, serious adverse event, or serious medical accident, whether or not it can be predicted from necessary precautions for use or the Investigator's Brochure, is it reported as a foreign action report?

Also, what specific cases should be considered?

A146: Post-marketing and Clinical trials

Happy reporting.

Information provided by a foreign regulatory authority can be considered to be information such as a revision of Precautions (WARNINGS AND PRECAUTIONS, etc.) or recall information.

Foreign action reports include, for example, the addition of a note on serious adverse drug reactions to the section on BOXED WARNINGJ in the U.S. Drug Labeling, and if information is obtained about the revision of the Precautions, it should be determined whether the report falls under the category of foreign action reports after an appropriate assessment of whether it is a "Information necessary to prevent or reduce serious adverse reactions, serious adverse events, serious medical accidents, etc."

It should be noted that foreign regulators are not limited to the United States, the European Union and the United Kingdom, as shown above. In addition, information on measures taken in foreign countries obtained from foreign partner companies should be handled in the same manner as described above.

Q147: Clinical trial

What are foreign action reports on investigational new drugs other than the Suspect Drug? subject to?

A147: Clinical trial

It covers measures based on quality, efficacy, and safety issues that could cause or spread health hazards in the use in clinical trials.

4. Unknown (Un-labelled) "Non-serious adverse reaction periodic report

(1) Method of reporting

Q 14 8: Post-marketing

For "other drugs" that are not covered by periodic safety reports, can the same active ingredients in different routes of administration be reported together as a single periodic report on unknown and non-serious adverse drug reactions?

A148: Post marketing

A separate report should be submitted if the same active ingredient is used in a different route of administration. However, if the Package insert (Include electronic Package insert.) are identical, they may be submitted together as a single report.

Q149: Post-marketing

Can products with multiple approval dates due to additional indications, content differences, etc., be reported together as a single periodic report of unknown and non-serious adverse drug reactions?

A149: Post marketing

(Acceptable): The sender may report in the manner presented in the question. In such cases, the initial reporting date should be the approval date, among the approval dates for additional indications and for different strengths, the earliest date for submission after April 1, 2005.

Q150: (Post-marketing)

In the case of OTC drugs, can products with the same ingredients but different amounts of ingredients be reported together as a single periodic report of unknown and non-serious adverse drug reactions?

A150: Post-marketing

Products with identical ingredients may be submitted together as a single report.

Q151: Post-marketing

In the case of OTC cold remedies, antipyretic analgesics, etc., in which only some of the active ingredients are different, one unknown and non-serious adverse drug reaction is reported collectively as a periodic report. May I report as?

A151: Post marketing

If a pharmaceutical, etc. for which manufacturing (import) approval standards for cold medicine, antipyretic and analgesic drugs, etc. have been established and the types of the main active ingredients, etc. that must be combined are the same, and the manufacturer of the pharmaceutical determines that it is appropriate to simultaneously take safety assurance measures, such as revising the Precautions section of the Precautions section of the Package insert, it may be acceptable to submit a single report for multiple drugs.

In such cases, the reasons why the reports were compiled into one report should be stated in the "Remarks" column in Form 7 attached to the Post-marketing Director's Notice.

Q152: Post-marketing

If drugs with different strengths, dosage forms, etc. are to be submitted together as a single report, should the names of drugs with no unknown or non-serious adverse reactions be included in the "brand names" column of the Appendix Form 7?

A152: Post marketing

The names of all drugs investigated in the report, including those with no unknown or non-serious adverse reactions during the period under review, should be listed.

Q153: Post-marketing

In the case of co-developed products, can they be prepared jointly even after the end of the reexamination period and submitted in joint names?

A153: Post marketing

No problem (Acceptable).

(2) Date of Initial Reporting, etc.

Q154: Post-marketing

For drugs subject to the periodic safety report, may the expiration date of the investigation unit period be changed to an arbitrary investigation unit period after the completion of the periodic safety report, if deemed necessary from the viewpoint of safety measures?

A154: Post marketing

(Acceptable): The sender may report in the manner presented in the question. However, the first report after the change should be for a period in which the relevant investigation unit period is one year or less, and the reason for the change should be stated in the preliminary column. Subsequent reports should be made annually.

For example, for items whose investigation unit period is from June 1 to May 31 of the following year, if the investigation unit period is changed from April 1 to March 31 of the following year, it should be reported once for the investigation unit period from June 1 to March 31 of the following year, and then annually for the investigation unit period from April 1 to March 31 of the following year.

If there was no information on adverse reactions to be reported during the first investigation unit period after the change and no periodic reports on unknown/non-serious adverse reactions were submitted, the statement that there was no information on adverse reactions to be reported during the previous investigation unit period and the reason for the change in the investigation unit period should be included in the remarks column at the time of the next report.

Q155: Post-marketing

The unit period for investigation of unknown/non-serious adverse drug reaction periodic reports for product B, which is the same active ingredient as a specific safety periodic reportable drug A and for which concurrent safety measures are appropriate, may be adjusted to the unit period for investigation of safety periodic reportable drug A?

A155: Post marketing

No problem. However, if any product is under the re-examination period and within two years after approval, the investigation unit period should not exceed six months.

Q156: Post-marketing

What exactly does the term "International Birthday, the approval date, etc., of the drug," which can be the initial reporting date, refer to "other drugs" that are not subject to periodic safety reporting?

A156: Post marketing

- International Birthday
- Approval Date

•Start date for reporting periodic safety reports (When a drug subject to periodic safety reports still uses the initial reporting date after the end of the reexamination period)

- Date specified by the MAH when reporting CDs, etc.

refers to.

Q157: Post-marketing

For "other drugs" that are not subject to periodic safety reporting, the initial reporting date is supposed to be the international birth date, the approval date of the drug, etc., but is it acceptable to change the expiry date of the investigation unit period to an arbitrary investigation unit period when deemed necessary from the viewpoint of safety measures?

A157: Post marketing

(Acceptable): The sender may report in the manner presented in the question. However, the first report after the change should be for a period in which the relevant investigation unit period is one year or less, and the reason for the change should be stated in the preliminary column. Subsequent reports should be made annually.

For example, for items whose investigation unit period is from June 1 to May 31 of the following year, if the investigation unit period is changed from April 1 to March 31 of the following year, the investigation unit period should be reported once for the investigation unit period from June 1 to March 31 of the following year, and then annually for the investigation unit period from April 1 to March 31 of the following year.

If there was no information on adverse reactions to be reported during the first investigation unit period after the change and no periodic reports on unknown/non-serious adverse reactions were submitted, the statement that there was no information on adverse reactions to be reported during the previous investigation unit period and the reason for the change in the investigation unit period should be included in the remarks column at the time of the next report.

Q158: Post-marketing

If the International Birth Date, the approval date, etc. of the drug were reported as the starting date as "other drugs" that are not subject to periodic safety reporting, but the starting date for periodic safety reporting is new due to the addition of an indication, etc., what should be done?

A158: Post marketing

The investigation unit period for unknown/non-serious adverse drug reaction periodic reports should be changed in accordance with the investigation unit period for safety periodic reports, but the investigation unit period for unknown/non-serious adverse drug reaction periodic reports before the change should not exceed one year. In this case, it is not necessary to change the "reporting start date" column in the periodic reports of unknown and non-serious adverse drug reactions and to consult the PMDA in advance. However, the reason for the change should be stated in the preliminary column of the report when the initial report after the change is made.

If there is no information on adverse reactions to be reported during the first investigation unit period after the change and no periodic reports on unknown/non-serious adverse drug reactions were submitted, the statement that there was no information on adverse reactions to be reported during the previous investigation unit period and the reason for the change in the investigation unit period above should be included in the remarks column of the report at the time of the next report.

Q159: Post-marketing

When an application for approval of a new substitute product is submitted through medical accident prevention measures, a new approval date and approval number are granted. When should the reporting start date be in such cases?

A159: Post marketing

When the approval date is used as the starting date, neither the previous approval date nor the new approval date can be used as the starting date.

If the previous approval date is reported as the initial reporting date, the remarks column should indicate the new approval date and approval number, and the fact that alternative new approval was received during the investigation unit period.

If the new approval date is to be reported as the starting date, the report based on the previous approval should be conducted for the period up to the day before the new alternative approval was received, and the remarks column should state that the report will be made for a period of less than one year because a new alternative application was filed. After that, reports should be made counting again from the new approval date. If there is no adverse reaction information to be reported during the first reporting period after the change in the initial reporting date, and the unknown/non-serious periodic report was not submitted, a statement that there was no adverse reaction information to be reported during the previous investigation unit period should be included in the next report. If information on adverse reactions associated with previously approved products is obtained after the new approval date, it should be regarded as newly approved and reported.

Q160: (Post-marketing)

The deadline for submission of unknown/non-serious periodic reports to the PMDA for drugs subject to periodic safety reports is 70 days after the expiration date of the investigation period. How many days should the expiration date of the investigation period be used?

A160: (Post marketing)

The deadline for submission of the report shall be set with the expiration date of the investigation unit period as 0 days.

If the deadline for submission of the report falls on a non-business day of the PMDA, the next business day shall be the deadline for submission of the report.

(3) Subject of report

Q161: Post-marketing

How do you respond to the following?

(1) When an adverse drug reaction for which an individual case safety report was submitted is subject to periodic reports of unknown and non-serious adverse drug reactions due to additional information.
(2) Adverse drug reactions that were subject to periodic reports of unknown or non-serious adverse drug reactions are no longer subject to reporting due to additional information.
(3) Adverse drug reactions that were subject to periodic reports of unknown or non-serious adverse drug reactions are subject to individual case safety reports with additional information.
(4) Unknown or non-serious adverse drug reactions: An adverse drug reaction for which periodic reporting has been made is not subject to reporting due to additional information.
(5) Unknown or non-serious adverse drug reactions for which periodic reports were made are subject to individual case safety reports due to additional information.

A161: (Post marketing)

(1) Unknown and non-serious adverse drug reactions should be reported as periodic reports. Individual case safety reports should be reported as non-reportable, not withdrawn. See Attachment 2 of E2B (R3) 5 Director's Notice for details.

(3) Reports should be made as individual case safety reports within the reporting deadline, starting from the date on which information that can be judged to be the subject of the individual case safety report was obtained. In doing so, the details should be clearly described in the "J2.2.2 Comments on the Initial Reporting Date."

(4) Withdrawal (Nullification) or replacement of periodic reports of unknown and non-serious adverse drug reactions is unnecessary.

(5) Reports should be made as individual case safety reports within the reporting deadline, starting from the date on which information that can be judged to be the subject of the individual case safety report was obtained. In doing so, the details should be clearly described in the "J2.2.2 Comments on the Initial Reporting Date."

Q162: Post-marketing

How should we handle the following cases?

(1) If a case for which a periodic report of unknown/non-serious adverse drug reactions was made during the relevant investigation unit period is denied as a relevant case during the next investigation unit period, is it necessary to state this in the next report?

(2) There is no change in the fact that the cases for which periodic reports of unknown/non-serious adverse drug reactions were made during the relevant investigation unit period are still unknown/non-serious cases during the next investigation unit period. However, if additional information is obtained, is it necessary to report them again as periodic reports of unknown/non-serious adverse drug reactions?

(3) If a new unknown or non-serious adverse drug reaction is found to have occurred in a case for which a periodic report of unknown or non-serious adverse drug reactions was made during the investigation unit period, does it need to be reported as a periodic report of unknown or non-serious adverse drug reactions?

A162: Post marketing

It should be treated as follows.

(1) No entry is necessary.

(2) If there is no change in the judgment of seriousness, no report is required.

(3) New unknown and non-serious adverse reactions should be reported.

Q163: Post-marketing

When unknown/serious and unknown/non-serious adverse reactions occur and are reported including the name of unknown/non-serious adverse reaction in the unknown/serious individual case safety report, is a separate periodic report of unknown/non-serious adverse reactions required?

A163: Post marketing

Necessary.

Q164: Post-marketing

How should we handle the following cases?

(1) A generic name could be identified, but the product name was not.

(2) The manufacturer or name of the product is identified, but the specification, dosage form or route of administration is not.

A164: Post marketing

Reports should be made as follows:

(1) It should be handled as an in-house product and reported as a periodic report on unknown and non-serious adverse drug reactions.

(2) Based on the information obtained, the product should be reported as the most likely specification, dosage form or route of administration.

Q165: Post-marketing

For minor adverse reactions that are not subject to reporting under the old reporting standards and are not foreseeable based on precautions required for use, see Heisei 1? If additional information is obtained after April 1, but there is no particular change in the evaluation, is it necessary to report the adverse reaction as an unknown/non-serious adverse drug reaction periodic report?

A165: (Post marketing)

No reporting is necessary.

4. **Handling of cases reported directly to the authorities**

Q166: Post-marketing

Is it necessary for the MAH to resubmit the case information on adverse reactions, etc. provided by the PMDA?

A166: Post marketing

As a general rule, the MAH is not required to report adverse reactions to the case information provided by the PMDA. However, adverse reactions must be reported in the following cases:

① The case provided by the PMDA is a case for which detailed investigation is not conducted by the PMDA and the case falls under the provisions of Article 228, 20 of the Enforcement Regulations.

② The same case information (regardless of the amount of information) is obtained from other medical institutions, literature, etc., for a case that falls under the provisions of Article 228, 20 of the Enforcement Regulations, even if the case is to be investigated in detail by the PMDA.

③ Relief for Sufferers from Adverse Drug Reactions/Biological Products Infections Relief cases provided by the PMDA fall under the provisions of Article 228, 20 of the Enforcement Regulations, and additional information is obtained from medical institutions, literature, etc. other than the PMDA.

Q167: Post-marketing

The PMDA states that the cases that were investigated in detail can be used for safety measures, but what should be done if we want to list the cases as the basis for the notification documents for the revision of precautions and other information?

A167: Post marketing

If you wish to publish such information, contact the Information Management Division of the Planning and Management Department in advance.

Q168: Post-marketing

Is it necessary for MAHs to update the case information obtained from the information about adverse drug reaction reports from patients published by "PMDA" to "PMDA" as adverse drug reaction reports?

A168: Post marketing

The MAH is required to report adverse reactions, etc., in a case that falls under the provisions of Article 228, 20 of the Enforcement Regulations, whether or not the information is published by the PMDA, if the same case information (regardless of the amount of information) is obtained from medical institutions, literature, etc., other than the information on adverse reaction reports from patients published by the PMDA.

However, if the information available to the MAH does not include more information than the published information, there is no need to report additional adverse reactions.

6. Case of long-term suspension of development, etc.

Q169: Clinical trial

When releasing the reservation and resuming the reporting of adverse drug reactions, etc., the applicant is required to submit the "Application for Releasing Reservation to Report Adverse Drug Reactions and Infectious Diseases Cases for Investigational Products" as well as the "Notes on Periodic Reporting of Adverse Drug Reactions in Investigational Products" (Notification No. 14 0831 of the Evaluation and Licensing Division, Pharmaceutical and Pharmacological Evaluation and Licensing Division, the Ministry of Health, Labour and Welfare, dated August 31, 2020) in Exhibit Form 1, Exhibit Form 2, and the Clinical Trial Safety Update Report (DSUR).

A169: Clinical trial

The number of reports should be left blank, and the investigation unit period should be from the day following the investigation unit period of the last periodic report to the day before the latest starting date. The Clinical Trial Safety Update Report (DSUR) may be accompanied by a one-year report up to the day before the most recent start date.

When submitting a request to release a reservation, contact the Review Planning Division of the Review Management Department of the PMDA in advance.