PSB/PED Notification No. 0115-1
PSB/PSD Notification No. 0115-1
January 15, 2024

To: Directors of Prefectural Health Departments (Bureaus)

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

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

Partial Revision of "Post-marketing Reports of Adverse Reactions, etc. and Reports of Adverse Reactions, etc. in Clinical Trials According To the E2B (R3) Implementation Guide"

The handling, etc. of post-marketing reports of adverse reactions, etc. in accordance with the "Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs)" compiled based on the agreement at the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (referring to reports of adverse drug reactions, etc., specified in Article 68-10, Paragraph 1 of the Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices [Act No. 145 of 1960; hereinafter referred to as the "Act"]; however, the periodic reports of unknown/non-serious adverse drug reactions specified in Article 228-20, Paragraph 1, Item 3 of the Regulation for Enforcement of the Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices [Ministry of Health and Welfare Ordinance No. 1 of 1961] are excluded) and reports of adverse reactions, etc. in clinical trials (referring to reports of adverse reactions, etc. associated with clinical trials specified in Article 80-2, Paragraph 6 of the Act) has been shown in "Post-marketing Reports of Adverse Reactions, etc. and Reports of Adverse Reactions, etc. in Clinical Trials According To the E2B (R3) Implementation Guide" (PSEHB/PED Notification No. 0831-12, PSEHB/PSD Notification No. 0831-3 issued jointly by the Director of Pharmaceutical Evaluation Division and the Director of Pharmaceutical Safety Division, Pharmaceutical Safety and Environmental Health Bureau, Ministry of Health, Labour and Welfare, dated August 31, 2020; hereinafter referred to as "E2B Two Director Notification").

We have recently decided to change their handling as follows. Please be aware of these changes and inform related businesses under your jurisdiction of them.

The revised E2B Two Director Notification is shown in the attachment.

Note

<table>
<tr><th>Corresponding part</th><th>New</th><th>Old</th></tr>
<tr><td>Attachment 8. (3) A.</td><td>A. In cases where a clinical trial for application related to the test drug is being conducted or all clinical trials related to the test drug concerned have been completed and the application for the test drug is being prepared or has been filed, if any measures, etc. for study drugs that may affect the content of the clinical trials or application are taken for drugs with the same ingredient marketed in Japan, a foreign corrective action report related to the study drug should immediately be made by the reporting deadline. The mandatory reporting period for study drugs other than the test drug is specified in 8. (3) C. (a) [2] in the attachment of this notification.</td><td>A. In cases where a clinical trial for application for a partial change, etc. of approved product information of a drug already approved in Japan is being conducted or all clinical trials related to the drug concerned have been completed and the application for the partial change, etc. of approved product information is being prepared or has been filed, if any measures, etc. that may affect the content of the clinical trials or application are taken for drugs with the same ingredient marketed in Japan, a foreign corrective action report should immediately be made by the reporting deadline.</td></tr>
<tr><td>Attachment 8. (3) C. (a)</td><td>(a)
[1] Omitted
[2]The mandatory reporting period for study drugs other than the test drug shall be from the date of submission of the notification for the clinical trial conducted using the study drug concerned, to between the submission of a clinical trial completion notification or clinical trial discontinuation notification for the clinical trial concerned, the approval of the test drug in the clinical trial concerned, or the submission of a development discontinuation notification for the test drug concerned.</td><td>(a)
[1] Omitted
[2]The mandatory reporting period for study drugs other than the test drug shall be from the date of submission of the notification for the clinical trial conducted using the study drug concerned, to between the submission of a clinical trial completion notification for the clinical trial concerned, the approval of the test drug in the clinical trial concerned, or the submission of a development discontinuation notification for the test drug concerned.</td></tr>
<tr><td>Appendix 1</td><td>
<table>
<tr><th rowspan="2">Data element (R3)</th><th rowspan="2">Title (R3)</th><th rowspan="2">...</th><th colspan="4">Value allowed-related</th></tr>
<tr><th>Type of input</th><th>Value allowed</th><th>NullFlavor</th><th>Supplement</th></tr>
<tr><td>J2.13.r.1</td><td>Number of notifications</td><td>...</td><td>NUM</td><td>3</td><td></td><td></td></tr>
</table>
</td><td>
<table>
<tr><th rowspan="2">Data element (R3)</th><th rowspan="2">Title (R3)</th><th rowspan="2">...</th><th colspan="4">Value allowed-related</th></tr>
<tr><th>Type of input</th><th>Value allowed</th><th>NullFlavor</th><th>Supplement</th></tr>
<tr><td>J2.13.r.1</td><td>Number of notifications</td><td>...</td><td>NUM</td><td>2</td><td></td><td></td></tr>
</table>
</td></tr>
<tr><td>Appendix 4</td><td>
<table>
<tr><th colspan="2">J2.13.r.1 Number of notifications</th></tr>
<tr><td>Description of element</td><td>Enter the number of clinical trial notifications of the main test drug for each clinical trial.</td></tr>
<tr><td>Description method</td><td>If no clinical trial notification has been submitted, leave the column blank.</td></tr>
<tr><td>Data type</td><td>3N</td></tr>
</table>
</td><td>
<table>
<tr><th colspan="2">J2.13.r.1 Number of notifications</th></tr>
<tr><td>Description of element</td><td>Enter the number of clinical trial notifications of the main test drug for each clinical trial.</td></tr>
<tr><td>Description method</td><td>If no clinical trial notification has been submitted, leave the column blank.</td></tr>
<tr><td>Data type</td><td>2N</td></tr>
</table>
</td></tr>
</table>

Appendix 5

Code value	J2.13.r.3 Development phase	Post-marketing/ clinical trial
0	Microdose study, etc.	Clinical trial
1	Phase I	Clinical trial
2	Phase II	Clinical trial
3	Phase III	Clinical trial
4	Phase I/II	Clinical trial
5	Phase II/III	Clinical trial
6	Phase I/III	Clinical trial
7	Under application	Clinical trial
8	Other	Clinical trial

Code value	J2.13.r.3 Development phase	Post-marketing/ clinical trial
0	Microdose study, etc.	Clinical trial
1	Phase I	Clinical trial
2	Phase II	Clinical trial
3	Phase III	Clinical trial
4	Phase I/II	Clinical trial
5	Phase II/III	Clinical trial
7	Under application	Clinical trial
8	Other	Clinical trial

End of Document

Attachment

PSEHB/PED Notification No. 0831-12
PSEHB/SD Notification No. 0831-3
August 31, 2020
[Partially revised] July 30, 2021
[Partially revised] February 7, 2022
[Partially revised] June 24, 2022
[Partially revised] January 15, 2024

To: Directors of Prefectural Health Departments (Bureaus)

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

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

Post-marketing Reports of Adverse Reactions, etc. and Reports of Adverse Reactions, etc. in Clinical Trials According To the E2B (R3) Implementation Guide

The handling, etc. of post-marketing reports of adverse reactions, etc. (referring to reports of adverse drug reactions, etc. specified in Article 68-10, Paragraph 1 of the Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices [Act No. 145 of 1960; hereinafter referred to as the "Act"]; however, the periodic reports of unknown/non-serious adverse drug reactions specified in Article 228-20, Paragraph 1, Item 3 of the Regulation for Enforcement of the Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices [Ministry of Health and Welfare Ordinance No. 1 of 1961, hereinafter referred to as the "Regulation"] are excluded) based on the E2B (R3) implementation guide shown in the "Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs)" (PFSB/ELD Notification No. 0708-5, PFSB/SD Notification No. 0708-1 issued jointly by the Director of Evaluation and Licensing Division and the Director of Safety Division, Pharmaceutical and Food Safety

Bureau, Ministry of Health, Labour and Welfare, dated July 8, 2013; hereinafter referred to as the "E2B (R3) Implementation Guide Notification") and reports of adverse reactions, etc. in clinical trials (referring to reports of adverse drug reactions, etc. associated with clinical trials specified in Article 80-2, Paragraph 6 of the Act) have been shown in "Post-marketing Reports of Adverse Reactions, etc. and Reports of Adverse Reactions, etc. in Clinical Trials According To the E2B (R3) Implementation Guide" (PSEHB/PED Notification No. 0331-6, PSEHB/SD Notification No. 0331-1 issued jointly by the Director of Pharmaceutical Evaluation Division and the Director of Safety Division, Pharmaceutical Safety and Environmental Health Bureau, Ministry of Health, Labour and Welfare, dated March 31, 2017; hereinafter referred to as "2017 E2B (R3) Two Director Notification").

With the enforcement of the Act Partially Amending the Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices (Act No. 63 of 2019) and the Ministerial Ordinance on the Development of Related Ministerial Ordinances in Accordance with Enforcement of the Act Partially Amending the Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices (Ordinance No. 155 of Ministry of Health, Labour and Welfare in 2020), we have recently decided to change the handling of the above reports as follows. Please be aware of these changes and inform related businesses under your jurisdiction of them.

The 2017 E2B (R3) Two Director Notification will be abolished on August 31, 2022.

Note

1. Reporting method

(1) Post-marketing reports of adverse reactions, etc. for drugs and research reports or reports of adverse reactions, etc. in clinical trials for drugs, quasi-drugs, and cosmetics (reports specified in Article 228-20, Paragraph 1, Items 1 and 2 and Paragraph 5, Item 2 B or Article 273, Paragraphs 1 and 2 of the Regulation)

Receipt of reports via electronic data processing systems has been promoted based on the Act on Use of Information and Communications Technology in Administrative Procedure (Act No. 151 of 2002), in order to promote electronic government toward the realization of efficient government, and digitization of adverse reaction reports, etc. and their management in databases contribute to prompt safety measures. Therefore, the method in [1] shall be used, in principle. If reporting via electronic data processing systems is difficult because of unavoidable circumstances, [2] or [3] may be used, but your cooperation by switching to the use of electronic data processing systems for reporting as much as possible would be appreciated.

[1] Reporting via electronic data processing systems

The items listed in Appendices 1 and 2 of the attachment shall be recorded in XML format corresponding to the E2B (R3) Implementation Guide Notification and Appendix 3 of the attachment, and reported to PMDA via electronic data processing

systems.

[2] Reporting by CD, etc.

CD-R (ROM) or DVD-R (ROM) (hereinafter referred to as "CD, etc.") in which the items listed in Appendices 1 and 2 of the attachment are recorded in XML format corresponding to the E2B (R3) Implementation Guide Notification and Appendix 3 of the attachment and a document (one original and, if return of a copy is desired, one copy) including the name and address of the reporter, reporting date, and other necessary items shall be submitted to PMDA.

[3] Paper-based reporting

The report (one original and, if return of a copy is desired, one copy) including the necessary items specified in the attached form of "Reporting of Adverse Reactions, etc. to Drugs, etc." (PFSB Notification No. 1002-20 of the Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare, dated October 2, 2014; hereinafter referred to as "Post-marketing Director-General Notification") or the attached form of "Reports of Adverse Reactions, etc. in Clinical Trials to Pharmaceuticals and Medical Devices Agency" (PSEHB Notification No. 0831-8 of the Pharmaceutical Safety and Environmental Health Bureau, Ministry of Health, Labour and Welfare, dated August 31, 2020), after revision to "Partial Revision of 'Reporting of Adverse Reactions, etc. to Drugs, etc.' and 'Reports of Adverse Reactions, etc. in Clinical Trials to Pharmaceuticals and Medical Devices Agency'" (PSEHB Notification No. 0331-4 of the Pharmaceutical Safety and Environmental Health Bureau, Ministry of Health, Labour and Welfare, dated March 31, 2016), and the CD, etc. in which the items listed in Appendices 1 and 2 of the attachment are recorded in XML format corresponding to the E2B (R3) Implementation Guide Notification and Appendix 3 of the attachment, shall be submitted to PMDA.

However, if it is difficult to submit the report and CD, etc. at the same time because of unavoidable circumstances, it is acceptable to separately submit the CD, etc. later, but it should be submitted as soon as possible.

(2) Reports of adverse reactions to quasi-drugs and cosmetics (reports specified in Article 228-20, Paragraph 5, Items 1 and 2, A of the Regulation)

The method specified in [1] or [2] shall be used, in principle. If it is difficult to report by [1] or [2] because of unavoidable circumstances, [3] can be used for reporting.

[1] Reporting via electronic data processing systems

The items listed in Appendices 1 and 2 of the attachment shall be recorded in XML format corresponding to the E2B (R3) Implementation Guide Notification and Appendix 3 of the attachment, and reported to Pharmaceuticals and Medical Devices Agency (hereinafter referred to as "PMDA") via electronic data processing systems.

[2] Reporting by e-mail

The items listed in Appendices 1 and 2 of the attachment shall be recorded in XML

format corresponding to the E2B (R3) Implementation Guide Notification and Appendix 3 of the attachment and submitted as an e-mail attachment to the e-mail address separately specified by PMDA, and the report (one original and, if return of a copy is desired, one copy) including the necessary items specified in the attached form of "Reporting of Adverse Reactions, etc. to Quasi-drugs and Cosmetics" (PSEHB Notification No. 0331-7 of the Pharmaceutical Safety and Environmental Health Bureau, Ministry of Health, Labour and Welfare, dated March 31, 2017; hereinafter referred to as the "2017 Quasi-drug/Cosmetic Director-General Notification") shall be submitted to PMDA.

[3] Paper-based reporting

The report (one original and, if return of a copy is desired, one copy) in which the necessary items specified in the attached form of the 2017 Quasi-drug/Cosmetic Director-General Notification are entered and the CD, etc. in which the items listed in Appendices 1 and 2 of the attachment are recorded in XML format corresponding to the E2B (R3) Implementation Guide Notification and Appendix 3 of the attachment shall be submitted to PMDA.

However, if it is difficult to submit the report and CD, etc. at the same time because of unavoidable circumstances, it is acceptable to separately submit the CD, etc. later, but it should be submitted as soon as possible.

2. Handling of reports in 2 (1) [2] in the attachment of the Post-marketing Director-General Notification

Regarding the initial report by fax, etc. based on the provisions in 2 (1) [2] in the attachment of the Post-marketing Director-General Notification (hereinafter referred to as "immediate report"), the usual initial report via electronic data processing systems in 1 (1) [1] can be submitted as an immediate report when the reported content meets the definition of "items required to be entered" shown in Appendices 1 and 2 of the attachment.

3. Attention should be paid to the attachment as points to consider in reporting.

4. Application timing

This notification shall apply from September 1, 2020. However, based on "Handling of Notifications, etc. of Clinical Trial Plans Related To Drugs by Persons Who Intend to Sponsor Clinical Trials (PSEHB/PED Notification No. 0831-10 of the Pharmaceutical Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, Ministry of Health, Labour and Welfare, dated August 31, 2020)," in cases where a clinical trial notification was submitted in accordance with previous rules, reports of adverse reactions, etc. in clinical trials should be made according to the previous rules.

Attachment

Points to Consider in Reporting

1. Report categories

Each reporting category is as follows.

AA = Reports of infection cases in Japan (post-marketing) (related to Article 228-20, Paragraph 1, Item 1, F and G of the Regulation)

AB = Reports of adverse reaction cases in Japan (post-marketing) (related to Article 228-20, Paragraph 1, Item 1, A, B, C, D, and E, and the same paragraph, Item 2, A of the Regulation)

AC = Reports of overseas infection cases (post-marketing) (related to Article 228-20, Paragraph 1, Item 1, G of the Regulation)

AD = Reports of overseas adverse reaction cases (post-marketing) (related to Article 228-20, Paragraph 1, Item 1, B and C of the Regulation)

AE = Infection research reports (post-marketing) (related to Article 228-20, Paragraph 1, Item 2, B of the Regulation)

AF = Adverse reaction research reports (post-marketing) (related to Article 228-20, Paragraph 1, Item 2, B of the Regulation)

AG = Foreign corrective action reports (including discontinuation of manufacturing, etc., recalls, and disposal) (post-marketing) (related to Article 228-20, Paragraph 1, Item 1, H of the Regulation)

BA = Quasi-drug adverse reaction reports (post-marketing) (related to Article 228-20, Paragraph 5, Items 1 and 2, A of the Regulation)

BB = Cosmetic adverse reaction reports (post-marketing) (related to Article 228-20, Paragraph 5, Items 1 and 2, A of the Regulation)

BC = Quasi-drug research reports (post-marketing) (related to Article 228-20, Paragraph 5, Item 2, B of the Regulation)

BD = Cosmetic research reports (post-marketing) (related to Article 228-20, Paragraph 5, Item 2, B of the Regulation)

DA = Reports of infection cases in Japan (clinical trials) (related to Article 273, Paragraph 1, Items 1 and 2 of the Regulation)

DB = Reports of adverse reaction cases in Japan (clinical trials) (related to Article 273, Paragraph 1, Items 1 and 2 of the Regulation)

DC = Reports of overseas infection cases (clinical trials) (related to Article 273, Paragraph 1, Items 1 and 2, Paragraph 2, Item 1 and the same paragraph, Item 2, A and B of the Regulation)

DD = Reports of overseas adverse reaction cases (clinical trials) (related to Article 273, Paragraph 1, Items 1 and 2, Paragraph 2, Item 1 and the same paragraph, Item 2, A and B of the Regulation)

DE = Infection research reports (clinical trials) (related to Article 273, Paragraph 2, Item 2, D of the Regulation)

DF = Adverse reaction research reports (clinical trials) (related to Article 273, Paragraph 2, Item 2, D of the Regulation)

DG = Foreign corrective action reports (including discontinuation of manufacturing, etc., recalls, and disposal) (clinical trials) (related to Article 273, Paragraph 2, Item 2, C of the Regulation)

Withdrawal = Withdrawal report

2. Definition of terms

(1) Post-marketing reports of adverse reactions, etc.

It is a collective term for reporting categories AA, AB, AC, AD, AE, AF, AG, BA, BB, BC, and BD.

(2) Reports of adverse reactions, etc. in clinical trials

It is a collective term for reporting categories DA, DB, DC, DD, DE, DF, and DG.

(3) J data elements

J data elements refer to elements listed in Appendix 4 among those included in reports.

(4) E2B data elements

E2B data elements refer to elements listed in Chapter 3.4 of "Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs)" in Attachment 1 of the E2B (R3) Implementation Guide Notification, among those included in reports.

(5) Elements for acknowledgement message

The term, "acknowledgement message," refers to a message that PMDA sends to the sender of the report in response to the report, and its elements are those listed in Appendix 6 and Chapter 4.2 of "Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs)" in Attachment 1 of the E2B (R3) Implementation Guide Notification.

(6) Identification numbers

Identification numbers refer to unique numbers assigned by PMDA to post-marketing reports of adverse reactions, etc. and reports of adverse reactions, etc. in clinical trials. They are included in the acknowledgement message element, "ACK.B.r.2 Local report number."

(7) Withdrawal reports

This term refers to withdrawal of a report in the case where wrong "C.1.1 Sender's (case) Safety Report Unique Identifier," etc. are reported, by entering the identification number of the report concerned in "J2.1b Identification Number (Number)" and entering necessary items such as "C.1.11.1 Report Nullification / Amendment" and "C.1.11.2 Reason for Nullification / Amendment."

(8) Reporters

This term refers to primary source of information. The primary source of information is a person who has reported the information on adverse reactions, etc., and includes healthcare professionals, authors of literature, users, and lawyers. If there are multiple sources of information, the person who initially reported the fact to the sender concerned should be the "primary source for regulatory purposes." The primary source of information should be distinguished from the sender.

(9) Senders

The term refers to organizations or individuals that send (report) information on adverse reactions, etc. to PMDA. Marketing authorization holders, foreign exceptional approval holders, and sponsors are included.

3. J data elements and E2B data elements

For input types and allowable values and J data elements, E2B data elements, etc. to be entered in reports, refer to the following (1) to (4), Appendices 1 and 2.

(1) Character code and input type/allowable value

The character code to be used shall be UTF-8.

The input type is any of "NUM," "TXT," "Date (minimum precision)," "list," "code list," "Boolean," and "UUID" below, and the allowable value differs depending on the input type. The input type and allowable value for the description of each element shall be as shown in the input type/allowable value columns in Appendices 1 and 2.

If “<,” “>,” and “&” are used, they can be displayed by replacing them with “<,” “>,” and “&” in XML, respectively.

A. NUM

Used for integers or floating point numbers. Only the characters of “0 to 9, ., E, +, and –” can be used.

The numbers in the allowable value columns in Appendices 1 and 2 are not the data size in XML, but the number of characters that can be entered.

B. TXT

Use Chinese characters, hiragana, katakana, alphanumeric characters, Greek characters, special symbols, and spaces. However, for a Chinese character that is not currently used and has a new form among the Chinese characters in common use, change it to the new form in description.

The numbers in the allowable value columns in Appendices 1 and 2 are not the data size in XML, but the number of characters that can be entered.

C. Date (minimum precision)

To be used in date/time format (CCYYMMDDhhmmss.UUUU[+|-ZZzz]). CCYY indicates the Western calendar year, MM month, DD day, hh hour, mm minute, ss second, UUUU millisecond, [+|-ZZzz] the time difference from the Coordinate Universal Time (UTC), with + for the time earlier than UTC and with - for the time later than UTC.

The numbers in the allowable value columns in Appendices 1 and 2 indicate the minimum precision of the date required to be entered.

D. List

Select from specific values for use.

The numbers in the allowable value columns or null flavor columns in Appendices 1 and 2 can be selected.

E. Code list

The codes defined by Health Level Seven (hereinafter referred to as “HL7”), an international organization that develops standards for health information exchange, shall be used.

The codes used for J data elements are shown in Appendix 5.

F. Boolean

Used for binary values of present and absent. When describing in XML, present = true and absent = false.

The values in the allowable value columns in Appendices 1 and 2 can be actually used. However, only true or false can be used for some data elements.

G. UUID

Enter the ID in UUID format.

The numbers in the allowable value columns in Appendices 1 and 2 are not the data size in XML, but the number of characters that can be entered.

H. Null flavor

Code defined by HL7 that allows null values to have some meaning. When using it for J data elements, select from null flavors shown in Appendix 5. Null flavor indicates the reason for the blank column, and it is not considered that any value has been entered, in principle. However, there are exceptions. For details, see Appendices 1 and 2.

(2) Object Identifier (OID)

OIDs used for J data elements are shown in XPath in Appendix 4.

(3) Essential elements, elements that need to be entered in conjunction with other elements, compliance elements, and elements that cannot be reported

As shown in the report category column in Appendices 1 and 2, each element corresponds to any of the following elements from A to D or elements (■) that can be briefly described.

A. Elements required to be entered (essential elements [◎])

"D.1 Patient (name or initials)" is an essential element in the reporting categories, AA, AB, AC, AD, BA, BB, DA, DB, DC, and DD. In addition, in the reporting categories, AA, AB, AC, AD, DA, DB, DC, and DD, at least one of the elements that identify patients ("D.1 Patient (name or initials)," "D.1.1.1 to D.1.1.4 Patient Medical Record Number(s) and Source(s) of the Patient Medical Record Number," "D.2.1 Date of Birth," "D.2.2 Age at Time of Onset of Reaction / Event," "D.2.2.1a and D.2.2.1b Gestation Period When Reaction / Event Was Observed in the Foetus," "D.2.3 Patient Age Group (as per reporter)," and "D.5 Sex" among E2B data elements) should be entered. See Appendix 2 for entering these elements.

B. Elements that become necessary to be entered depending on entry of other elements (elements that need to be entered in conjunction with other elements [□])

These are elements that need to be entered depending on entry or no entry of other elements, the values entered in other elements, or the conditions of the entry guideline.

C. Elements to be entered as much as possible (compliance elements [▲])

Reports will be received even if compliance elements are not entered. However, the elements without entries are regarded as unknown. Therefore, efforts should be made to collect information and report them as much as possible.

When reports are withdrawn based on additional information, the compliance elements shall be read as "elements that are unnecessary but do not become errors even if they are entered (however, if the data type is incorrect, the element shall be handled as an error)."

D. Elements that must not be entered (elements that cannot be reported [x])

Reports cannot be received if the elements that cannot be reported are entered. Even if null flavor is entered, the entry will be regarded as entered data, and the report cannot be received.

(4) XPath

For J data elements, XML shall be described according to XPath shown in Appendix 4. For E2B data elements, XML shall be described according to XPath shown in Appendix I (G) of Attachment 1, "Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs)," of the E2B (R3) Implementation Guide Notification.

4. Contents and methods of description for individual case safety reports

In case reports of infection (reporting categories of AA, AC, DA, and DC, and their withdrawal) and case reports of adverse reactions (reporting categories of AB, AD, BA, BB, DB, and DD, and their withdrawal), enter the elements specified in Appendices 1 and 2. When entering elements, refer to Appendix 4 for J data elements and the E2B (R3) Implementation Guide Notification for E2B data elements, and pay attention to the following points.

(1) Setting of reporting deadline

In setting the deadline for reporting, specify the deadline with the date of obtaining information as Day 0. If the deadline for reporting is not a business day for PMDA, the next business day should be the deadline for reporting. In the case of information from foreign countries, set the reporting deadline by using the date on which the information concerned was obtained in Japan as the date of obtaining information, not the local time (date) in the country (local) of the primary information source.

(2) Case report of infection and case report of adverse reactions as a single case

Select "AA" or "DA" for cases in Japan and "AC" or "DC" for overseas cases for "J2.la Identification Number (reporting category)," and describe the details of both infection and adverse reactions.

(3) When reporting additional information on reports of adverse reactions, etc. in overseas clinical trials on or after approval date

The information shall be reported as a "post-marketing report of adverse reactions, etc. (initial report)."

(4) Senders

If the sender is a corporation, the name of its representative should be entered in "Sender's Given Name (C.3.3.3)" and "Sender's Family Name (C.3.3.5)," and the address of its main facility should be entered in "Sender's Address (from C.3.4.1 to C.3.4.5)."

(5) Post-marketing (excluding quasi-drug adverse reaction reports and cosmetic adverse reaction reports)

A. Does This Case Fulfil the Local Criteria for an Expedited Report? (C.1.7)

Enter "Yes" for 15-day reports and "No" for 30-day reports.

As the reporting deadline is determined at the time of obtaining the information, it is acceptable to switch from 15-day reports to 30-day reports in an additional report.

B. Adverse reactions/adverse events (E data elements)

(a) Reaction / Event (E.i.2.1b)

Enter the MedDRA code corresponding to the name of the adverse reaction.

(b) Term Highlighted by the Reporter (E.i.3.1) and Seriousness Criteria at Event Level (E.i.3.2)

The sender is responsible for judging the seriousness based on the contents of seriousness evaluation (provided information) described in the adverse reaction report from the reporter. All events evaluated as serious by the reporter shall be regarded as "serious." However, even when the reporter has evaluated an event as non-serious, the event shall be reported as "serious" if the sender evaluated it as serious.

C. Drug(s) information (G data elements)

Describe the drugs in the order of suspected company drugs, other suspected drugs, and other drugs. If there are multiple drugs, enter them in the order of Day 1 of administration (the drug with the earliest Day 1 first). In reports of overseas infection cases (post-marketing) and reports of overseas adverse reaction cases (post-marketing), when reporting by attaching the materials including case information to the ICSR file, it is acceptable to enter only suspected drugs including other companies' products.

(a) Investigational Product Blinded (G.k.2.5)

In the reports of adverse reactions, etc. in clinical studies, etc. conducted on the company's own drugs after marketing, adverse reactions should be reported before unblinding even

when the suspected drug is blinded. In this case, this element should be reported as “true.”

(b) Pharmaceutical Dose Form (free text) (G.k.4.r.9.1)

This element should be entered in half-width alphabet characters according to Appendix 7, “List of Dosage Forms.”

(c) Route of Administration TermID (G.k.4.r.10.2b)/Parent Route of Administration TermID (G.k.4.r.11.2b)

These elements shall be described in half-width numeric characters according to Appendix I (F) of Attachment 1, “Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs),” of the E2B (R3) Implementation Guide Notification.

(d) Additional Information on Drug (G.k.11)

In reports of overseas infection cases and reports of overseas adverse reaction cases, if a clinical trial is being conducted for the purpose of partial changes in approved product information for addition, change, or removal of dosage and administration or indications of the drug that has already been approved for marketing in Japan, “TIKEN” should be entered in half-width alphabet characters.

(6) Clinical trial

A. Does This Case Fulfil the Local Criteria for an Expedited Report? (C.1.7)

Enter “Yes” for 7-day reports and “No” for 15-day reports.

B. Adverse reactions/adverse events (E data elements)

(a) Reaction / Event (E.i.2.1b)

Enter the MedDRA code corresponding to the name of the adverse reaction.

(b) Term Highlighted by the Reporter (E.i.3.1) and Seriousness Criteria at Event Level (E.i.3.2)

The sender is responsible for judging the seriousness based on the contents of seriousness evaluation (provided information) described in the adverse reaction report from the reporter. All events evaluated as serious by the reporter shall be regarded as “serious.” However, even when the reporter has evaluated an event as non-serious, the event shall be reported as “serious” if the sender evaluated it as serious.

C. Drug(s) information (G data elements)

The study drugs and other drugs (including anesthetics, blood transfusion, etc.) considered to be suspected drugs by the attending physician, etc. and other study drugs and other drugs used during the use of the suspected drugs should be described.

Describe suspected drugs first, followed by drugs other than the suspected drugs for reporting categories of DA and DB. If there are multiple suspected drugs, enter them in the order of the test drug, study drugs other than the test drug, and other drugs, and if there are multiple drugs with the same positioning, enter them in the order of Day 1 of administration (the drug with the earliest Day 1 first). For reporting categories of DC and DD, describe the drugs in the above order, in principle.

For drugs other than suspected drugs, the test drug, study drugs other than the test drug, and other drugs can be entered in any order. However, they should be entered in the order of Day 1 of administration (the drug with the earliest Day 1 first), in principle.

(a) Medicinal Product Name as Reported by the Primary Source (G.k.2.2)

If the report is from a double-blind study and it cannot be determined whether the suspected drug is the test drug or comparator because the study has not been unblinded, enter the information of the test drug. An additional report should be submitted based on the

information obtained after unblinding.

If the suspected drug turns out to be placebo based on the information obtained after unblinding and there is no longer any suspected drug subject to reporting, the report should be withdrawn.

(b) Pharmaceutical dose form (free text) (G.k.4.r.9.1)

This element should be entered in half-width alphabet characters according to Appendix 7, "List of Dosage Forms."

(c) Route of Administration TermID (G.k.4.r.10.2b)/Parent Route of Administration TermID (G.k.4.r.11.2b)

These elements shall be described in half-width numeric characters according to Appendix I (F) of Attachment 1, "Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs)," of the E2B (R3) Implementation Guide Notification.

(7) Quasi-drug adverse reaction reports and cosmetic adverse reaction reports

A. Seriousness, etc. (J2.26.i)

The sender is responsible for judging the seriousness based on the contents of seriousness evaluation (provided information) described in the adverse reaction report from the reporter. All events evaluated as serious by the reporter shall be regarded as "serious." However, even when the reporter has evaluated an event as non-serious, the event shall be reported as "serious" if the sender evaluated it as serious.

B. Does This Case Fulfil the Local Criteria for an Expedited Report? (C.1.7)

Enter "Yes" for 15-day reports and "No" for 30-day reports.

As the reporting deadline is determined at the time of obtaining the information, it is acceptable to switch from 15-day reports to 30-day reports in an additional report.

C. Reaction / Event (E.i.2.1b)

Select a MedDRA code corresponding to the name of the adverse reaction or an appropriate term from Appendix 8, "Quasi-drug, etc. adverse reaction codes," and enter the code.

D. Product information (G data elements)

For suspected products, describe the company's own suspected product that is most strongly suspected to be related to the adverse reaction first as the primary suspected product, followed by the products in the descending order of the level of suspicion concerning the relationship with the onset of the adverse reaction, whether they are the company's products or not.

5. Use of ISO/HL7 standards

As indicated in the attachment of the E2B (R3) Implementation Guide Notification, the E2B data elements and message specifications for reporting via electronic data processing systems are set referring to the standard developed by International Organization for Standardization (ISO) and HL7, "ISO/HL7 27953-2: 2011 Health informatics--Individual case safety reports (ICSRs) in pharmacovigilance--Part 2: Human pharmaceutical reporting requirements for ICSR" (hereinafter referred to as "ISO/HL7 27953-2 Standard"). Similarly, J data elements set with reference to this standard are used with permission of the issuer. The copyright of the ISO/HL7 27953-2 standard is jointly owned by ISO and HL7, and unauthorized copying, duplication, and reproduction are prohibited.

6. Use of MedDRA

MedDRA is provided and the listed terms are maintained and managed by JMO of Pharmaceutical and Medical Device Regulatory Science Society of Japan based on the agreement

with the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (hereinafter referred to as "ICH"). When selecting MedDRA terms, refer to "MedDRA TERM SELECTION: POINTS TO CONSIDER" (PTC), which is compiled as a part of ICH activities.

(1) Elements for which MedDRA terms are used and levels used

For the elements for which MedDRA terms are used and the level to be used for selection of MedDRA terms, see the E2B (R3) Implementation Guide Notification.

(2) Selection of MedDRA terms

Among MedDRA terms, the most appropriate term should be selected based on medical judgment.

A. Name of adverse reaction

(a) Cases in Japan

Select the term for which the English currency flag is Y.

(b) Overseas cases

For cases transmitted from foreign countries, if they are included in "Reaction / Event as Reported by the Primary Source in Native Language (E.i.1.1a)," it is acceptable to report the contents as they are.

Select the term for which the English currency flag is Y.

7. Contents and methods of descriptions for research reports and foreign corrective action reports

In research reports (reporting categories of AE, AF, BC, BD, DE, and DF, and their withdrawal) and foreign corrective action reports (reporting categories of AG and DG and their withdrawal), enter the elements specified in Appendices 1 and 2. For the method for entering each data element, refer to Appendix 4 for J data elements and the E2B (R3) Implementation Guide Notification for E2B data elements, and pay attention to the following points.

(1) Setting of reporting deadline

In setting the reporting deadline, specify the deadline with the date of obtaining information as Day 0. If the reporting deadline is not a business day for PMDA, the next business day should be the reporting deadline. In the case of information from foreign countries, set the reporting deadline by using the date on which the information concerned was obtained in Japan as the date of obtaining information, not the local time (date) in the country (local) of the primary information source.

(2) Senders

If the sender is a corporation, the name of its representative should be entered in "Sender's Given Name (C.3.3.3)" and "Sender's Family Name (C.3.3.5)," and the address of its main facility should be entered in "Sender's Address (from C.3.4.1 to C.3.4.5)."

(3) Post-marketing

A. Identification of the case safety report (C.1 data elements)

(a) Type of report (C.1.3)

When reporting pharmacoepidemiological investigations in research reports, enter "Report from study." When reporting literature search papers, etc., enter "Other."

B. Literature Reference(s) (C.4 data elements)

(a) Literature Reference(s) (C.4.r.1)

"Literature Reference(s) (C.4.r.1)" should be read as "Publication status of research reports or actions taken overseas (C.4.r.1)."

1) Research reports

Citations should be provided according to the Vancouver Convention (known as "Vancouver style") proposed by the International Committee of Medical Journal Editors. The conventional styles, including styles for special situations, can be found in the following reference.

If information on "Recommendation for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals" by International Committee of Medical Journal Editors has not been published in the company's own materials, etc., report to that effect ("unpublished," etc.) and enter the title, reporter, affiliation of the reporter or study site, implementation year, etc.

If the information is derived from a website, enter the URL, etc. If the information is derived from other sources, specify the source.

2) Foreign corrective action reports

If the same action is taken by regulatory authorities of multiple countries, it may be reported in one report. In such cases, the publication status in the representative country should be described first, and the publication status in other countries should be described after that using repetition. If the same action is taken in other countries at later dates, the publication status in these countries should be additionally reported. In such cases, the publication status in the representative country in the above additional report should be described after the previous report. If there are multiple countries in the additional report, the publication status in other countries should be described using repetition.

Refer to 1) above when describing literature references.

C. Drug(s) information (G data elements)

Describe drugs, etc. that are subject to reporting. If multiple in-house products are subject to reporting, all of them shall be described.

(a) Authorisation / Application Number (G.k.3.1)

Enter approval numbers of drugs, etc. subject to reporting.

For cosmetic research reports, enter the prefecture code (JIS standard) of the prefecture that has jurisdiction over the product and the date on which the cosmetic manufacturing and marketing notification was submitted. If there is an approval number, enter the approval date.

D. Narrative case summary and further information (H data elements)

(a) Case Narrative Including Clinical Course, Therapeutic Measures, Outcome and Additional Relevant Information (H.1)

"Case Narrative Including Clinical Course, Therapeutic Measures, Outcome and Additional Relevant Information (H.1)" shall be read as "Summary of research reports or actions taken overseas (H.1)."

1) Research reports

The outline of the study/research results, etc. and the authors' opinions, etc. should be briefly summarized. For reports on marked changes in occurrence tendency, describe the period related to the incidence, analytical method, interpretation of results, etc.

2) Foreign corrective action reports

Describe briefly the contents of the action, opinions of regulatory authorities, etc.

(b) Sender's Comments (H.4)

Describe the sender's comments.

(4) Clinical trial

A. Identification of the case safety report (C.1 data elements)

(a) Type of report (C.1.3)

When reporting pharmacoepidemiological investigations in research reports, enter "Report from study." When reporting literature search papers, etc., enter "Other."

B. Literature reference(s) (C.4 data elements)

(a) Literature Reference(s) (C.4.r.1)

"Literature Reference(s) (C.4.r.1)" should be read as "Publication status of research reports or actions taken overseas (C.4.r.1)."

1) Research reports

Citations should be provided according to the Vancouver Convention (known as "Vancouver style") proposed by the International Committee of Medical Journal Editors. The conventional styles, including styles for special situations, can be found in the following reference:

If information on "Recommendation for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals" by International Committee of Medical Journal Editors has not been published in the company's own materials, etc., report to that effect ("unpublished," etc.) and enter the title, reporter, affiliation of the reporter or study site, implementation year, etc.

If the information is derived from a website, enter the URL, etc. If the information is derived from other sources, specify the source.

2) Foreign corrective action reports

If the same action is taken by regulatory authorities of multiple countries, it may be reported in one report. In such cases, the publication status in the representative country should be described first, and the publication status in other countries should be described after that using repetition. If the same action is taken in other countries at later dates, the publication status in these countries should be additionally reported. In such cases, the publication status in the representative country in the above additional report should be described after the previous report. If there are multiple countries in the additional report, the publication status in other countries should be described using repetition.

Refer to 1) above when describing literature references.

C. Drug(s) information (G data elements)

Describe the study drugs, etc. that are subject to reporting.

(a) Medicinal Product Name as Reported by the Primary Source (G.k.2.2)

Apply 4. (6) C. with modifications.

(b) Authorisation number (G.k.3.1)

Describe at least in-house products among study drugs with approval numbers in Japan.

D. Narrative case summary and further information (H data elements)

(a) Case Narrative Including Clinical Course, Therapeutic Measures, Outcome and Additional Relevant Information (H.1)

"Case Narrative Including Clinical Course, Therapeutic Measures, Outcome and Additional Relevant Information (H.1)" shall be read as "Summary of research reports or actions taken overseas (H.1)."

1) Research reports

The outline of the study/research results, etc. and the authors' opinions, etc. should be briefly summarized. For reports on marked changes in occurrence tendency, describe the period related to the incidence (phase of development), analytical method, interpretation of results, etc.

2) Foreign corrective action reports

Describe briefly the contents of the action, opinions of regulatory authorities, etc.

(b) Sender's Comments (H.4)

Describe the sender's comments.

8. Other precautions for reports of adverse reactions, etc. in clinical trials

When submitting reports of adverse reactions, etc. in clinical trials, pay attention to the following points.

(1) Criteria for determination of expectedness, etc.

In reports of adverse reactions, etc. in clinical trials, expectedness shall be judged based on the following.

A. In terms of the test drug, expectedness shall be judged based on the adverse events described in the latest Investigator's Brochure. However, in cases where a person who intends to sponsor a clinical trial is going to conduct a clinical trial using more than one test drug and cannot prepare the Investigator's Brochures of the test drugs to be concomitantly used with a test drug the person is planning to market, because the former test drugs are marketed by other companies or for other reasons, it is acceptable to judge the expectedness based on the documents describing the latest scientific findings regarding the test drugs concerned (package inserts, interview forms, academic papers, etc.) instead of the Investigator's Brochures of the test drugs concerned, only if the active ingredient has already been approved in Japan and the person who intends to sponsor the clinical trial considers that the subject safety can be ensured when the test drugs concerned are used in the clinical trial. In terms of study drugs other than test drugs, expectedness shall be judged based on the documents describing the latest scientific findings.

B. An adverse reaction shall be judged as being "expected" on the day of preparation or revision of the latest Investigator's Brochure or the documents describing the latest scientific findings.

However, if the written procedures of the sponsor stipulated that documents notifying cases of adverse reactions, etc. to medical institutions should be retained as a separate volume of the Investigator's Brochure or the documents describing the latest scientific findings, the date of preparation of the notification documents can be regarded as the day of revision of the Investigator's Brochure or the documents describing the latest scientific findings.

The sponsor should fully understand the occurrence tendency such as the number of cases and frequency of the adverse reaction, etc. and appropriately judge whether the occurrence trend can be predicted from the latest Investigator's Brochure or the documents describing the latest scientific findings or not, without error.

C. Even if the adverse reaction is described in the latest Investigator's Brochure or documents describing the latest scientific findings, it shall be judged "unexpected" if the occurrence tendency such as the number of cases and frequency is not consistent with the description.

D. For the test drug for which approval application has been filed and no clinical trial for the application for partial changes in approved product information such as addition of indications has been conducted separately, expectedness shall be judged based on the adverse events listed in the summary of the product application.

E. For the test drug, when any clinical trial has been conducted on the same ingredient as that of a product for which approval application has been filed, the expectedness shall be judged based on the adverse events listed in the Investigator's Brochure among the summary of the product application and the Investigator's Brochure.

F. If any long-term study, etc. has continued even after approval application for the test drug and the long-term study, etc. has been completed before approval, the rationale for judgment of expectedness shall be switched from the Investigator's Brochure to the summary of product application as of the date of submission of the clinical trial completion notification for the long-term study, etc.

(2) Causal relationship

In reports of adverse reactions, etc. in clinical trials, a causal relationship shall be handled as follows.

A. All cases shall be reported unless both the investigator, etc. and sponsor rule out a causal relationship.

B. Overseas cases based on the information from sources other than healthcare professionals, such as patients or their families are not subject to reporting if the sponsor judges that the causal relationship can be ruled out.

(3) Other matters related to reports of adverse reactions, etc. in clinical trials

A. In cases where a clinical trial for application related to the test drug is being conducted or all clinical trials related to the test drug concerned have been completed and the application for the test drug is being prepared or has been filed, if any measures, etc. for study drugs that may affect the content of the clinical trials or application are taken for drugs with the same ingredient as the test drug marketed in Japan, a foreign corrective action report related to the study drug should immediately be made by the reporting deadline. The mandatory reporting period for study drugs other than the test drug is specified in 8. (3) C. (a) [2] in the attachment of this notification.

B.Handling of special events subject to reporting

(a) Handling of worsening, etc. of target disease

[1] In clinical trials using fatal or certain other serious outcome as an efficacy evaluation index, serious adverse events that are medically difficult to be differentiated from worsening, etc. of the target disease will be handled as events related to the disease and will be excluded from expedited reporting as events not subject to routine expedited reporting, only if the data monitoring committee has been established. However, if the data monitoring committee determines that the study drug may increase the risk leading to such serious outcome based on accumulated data, these events should be reported promptly.

[2] When submitting a clinical trial notification, a document describing the following should be submitted. If these matters are described in the protocol, etc., it is not necessary to prepare a new document.

1) Outline of the test drug concerned (proposed indication, mechanism of action, development status in Japan and overseas, etc.)
2) Outline of the clinical trial plan concerned (for clinical trials to be conducted in Japan, also enter the number of notifications, date of notification, or scheduled date of notification)
3) Scope of events handled as events related to the disease and rationale for the scope
4) If any similar agreement has been reached with overseas regulatory authorities, the

details of the agreement

5) Roles, etc. of the data monitoring committee

(b) Handling of adverse reactions to narcotics, etc. used for non-medical purposes

[1] Adverse reactions that occurred in the use of narcotics, etc. for non-medical purposes, such as drug abuse, shall not be subject to expedited reporting, only if such events are determined in advance between the sponsor and the Review Planning Division, Office of Review Management, PMDA as events not subject to usual expedited reporting. However, this does not apply to ingredients not approved in Japan or when an unexpected event occurs.

[2] Prepare a document describing the following as a document to be submitted regarding the agreement and contact the Review Planning Division, Office of Review Management, PMDA.

1) Outline of the test drug concerned (proposed indication, mechanism of action, development status in Japan and overseas, etc.)
2) Outline of the clinical trial plan concerned (for clinical trials to be conducted in Japan, also enter the number of notifications, date of notification, or scheduled date of notification)
3) Materials on the status of use for non-medical purposes such as drug abuse and the status of occurrence of adverse reactions
4) Scope of events handled as those not subject to expedited reporting and rationale for the scope
5) If any similar agreement has been reached with overseas regulatory authorities, the details of the agreement

C. Handling of mandatory reporting period

(a) Mandatory reporting period

[1] The mandatory reporting period for a test drug shall be from the date of first submission of notification on the test drug concerned to its approval or the submission of a development discontinuation notification. If the submission of the clinical trial notification is not required, the mandatory reporting period shall be from the start date of the implementation period specified in the protocol for the test drug concerned to its approval or the notification of planned discontinuation of development to the Review Planning Division, Office of Review Management, PMDA in writing (in any format).

[2] The mandatory reporting period for study drugs other than the test drug shall be from the date of submission of the notification for the clinical trial conducted using the study drug concerned to the submission of a clinical trial completion notification or clinical trial discontinuation notification for the clinical trial concerned, or the approval of the test drug in the clinical trial concerned, or the submission of a development discontinuation notification for the test drug concerned. If the submission of the clinical trial notification is not required, the mandatory reporting period shall be from the start date of the implementation period specified in the protocol for the clinical trial using the study drug concerned to the completion date, or the approval of the test drug in the clinical trial concerned, or the notification of planned discontinuation of development of the test drug concerned to the Review Planning Division, Office of Review Management, PMDA in writing (in any format).

(b) Long-term suspension of development, etc.

[1] If development is expected to be suspended for a long time, or if it is expected to take a

long time to prepare responses to inquiries after expert discussion while the application is reviewed, reporting can be withheld until the development is resumed or the responses to the inquiries are submitted, by notifying the Review Planning Division, Office of Review Management, PMDA of the situation in writing. Efforts shall be made to collect safety information even while reports of adverse reactions, etc. in clinical trials (excluding research reports and foreign corrective action reports) are withheld, and the information concerned shall be reflected in the Investigator's Brochure, etc. and the protocol or summary of product application when the development is resumed. When resuming the reporting of adverse reactions, etc., along with the resumption of development, submit necessary documents to the Review Planning Division, Office of Review Management, PMDA.

[2] Document notifying withholding

Prepare a document describing the following and submit it to the Review Planning Division, Office of Review Management, PMDA.

1) The title should be "Notification of withholding of adverse reaction/infection cases reports associated with the investigational product."
2) Enter the investigational ingredient code and the generic name in parentheses.
3) Enter the number of clinical trial notifications and the date of the first clinical trial notification.
4) Enter the proposed indication.
5) Enter the development phase in which clinical trials are to be suspended.
6) Specify the "reason for withholding reporting."
7) State that the party withholding reporting "will continue to make efforts to collect information on adverse reactions, etc.," "will report the adverse reactions, etc. collected while the development is suspended, when the development is resumed," and "will contact the Review Planning Division, Office of Review Management, PMDA in advance when the development is resumed."
8) Enter the name of the person in charge and the contact information.
9) Address the document to "Chief Executive, Pharmaceuticals and Medical Devices Agency."

(c) Document to be submitted at the time of resumption of development

When the development is resumed, stop withholding and resume the reporting of adverse reactions, etc. In such cases, prepare a document describing the following and submit it to the Review Planning Division, Office of Review Management, PMDA.

[1] The title should be "Notification of termination of withholding of adverse reaction/infection cases reports associated with the investigational product" and enter the reason for withholding, withholding period, and reason for termination of withholding.

[2] Submit Attached Forms 1 and 2 of "Points to Consider for Periodic Reporting of Cases of Clinical Trial Adverse Reactions, etc." (PSEHB/PED Notification No. 0831-14 of the Pharmaceutical Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, Ministry of Health, Labour and Welfare, dated August 31, 2020) and the Development Safety Update Report (DSUR).

[3] Revised or corresponding parts of the Investigator's Brochure, etc. or protocol and summary of product application prepared based on the information collected during the withholding period

D. For the reporting categories of DA, DB, DC, and DD, if multiple study drugs are used and

each of them is a suspected drug, all suspected drugs should be reported in one report.

For the reporting categories of DE, DF, and DG, reports should be made for each investigational ingredient code of the main test drug.

E. For a drug that has already been approved in Japan, if a clinical trial is conducted for a partial change application for indications, and dosage and administration with a person other than the party that has obtained the approval of the drug concerned as the clinical trial in-country representative and the information is appropriately shared between the parties, it is acceptable for the party that has obtained approval to submit the reports of overseas cases of adverse reactions, etc. However, the sponsor and the party that obtained approval should prepare a document describing the agreement between them on matters related to reporting of overseas cases of adverse reactions, etc. and information sharing in advance, and submit it to the Review Planning Division, Office of Review Management, PMDA.

The party that obtained approval shall enter "TIKEN" in half-width alphabet characters in the column for "G.k.11 Additional Information on Drug" when making post-marketing reports of adverse reactions, etc. for the drug concerned.

F. If multiple clinical trials of the test drug concerned are being conducted in Japan by different sponsors or sponsor-investigators, it is acceptable to submit the report of cases of adverse reactions, etc. in Japan related to each clinical trial to regulatory authorities. However, even in such cases, information shall be appropriately shared between the two parties.