Appendix 1

ICH Electronic Common Technical Document (eCTD) v4.0 Implementation Guide in Japan v1.6.0

Provisional Translation (as of March 2025) *

DOCUMENT CHANGE HISTORY

Version No.	Date	Overview
1.2.0	July 5, 2017	First version
1.3.0	Feb 19, 2020	• Editorial corrections • Revisions due to consistency with ICH IG v1.3

1.4.0	Feb 18, 2022	• Revisions to remove and change of description related to the response life cycle abolition
		• Adds to the single-byte ampersand (&) to character types (Section 2.5) that can be used as text type
		• Corrections to the description when submitting the eCTD to the PMDA reception desk to be more accurate
		• Changes to the number of characters limit for the following attribute values:
		   ➢ *submissionUnit.title@value*
		   ➢ *document.title@value*
		   ➢ *document.text.thumbnail@value*
		   ➢ *keywordDefinition.value.item.displayName@value*
		• Adds to the business rule regarding the file path description for the *document.text.reference@value* attribute value due to the addition of the file path description when reusing files in ICH IG v1.4
		• Add the description that the study id of attribute " study id_study title Keyword" in the Context of Use refering to the electronic study data and the folder name of study ID does not always need to mach the alphabet letter
		• Revisions to the cover letter for eCTD (Format 1)
		• Revisions to make clearer expressions and correction of clerical errors

1.5.0	Feb 6, 2023	• Revisions due to consistency with ICH IG v1.5 • Expanded the available scope of escape characters in the character types that can be used as text type (Section 2.5) • Changes in the notation of the notification name, etc., due to the revision of the electronic study data-related notification • Added "Submission type of eCTD application" as information to be described in electronic media when submitting to the PMDA reception (Section 3.3.2) • Moved the description about Security settings for each file to JP SSF and remove it. • Revisions of business rules (Section 7.4.17.3 and 8.2) regarding file path description method in *document.text.reference@value* attribute value • Added a supplement to how to express the attachment numbers (Section 12.3) • Clerical corrections

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Version No.	Date	Overview
1.6.0	Mar 10, 2025	・ Revisions due to consistency with ICH IG v1.6 ・ Added "SSF" to Terminology (Section 2.1) ・ Changes to Controlled vocabulary Business Rules (Section 3.7) ・ Revisions to the business rules for using the OID of the implementation guide specified in the message header (Section 7.2) due to the change in the format of the JP OID Listing ・ Corrections to the supplementary information on the use of Application Reference in How to submit the data related to the already approved pharmaceutical products (Section 15.4) ・ Clerical corrections

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1. Purpose

This document describes the handling of Appendix 3 "ICH electronic common technical document (eCTD) v4.0 Implementation guide v1.6" (hereinafter referred to as "ICH IG") in Japan upon implementing eCTD. As the requirement for creating eCTD v4.0 XML messages and other components, it describes how the applicant should electronically submit the information related to the approval application for pharmaceutical products to the regulatory authority. This document shall be used together with ICH IG. If there is any different onthe descriptions between this document and the description of ICH IG, the description of this document shall take precedence.

2. Definitions of terminology, notations, symbols, etc.

2.1 Terminology

The terminology used in this document is defined in the table below.

Terminology	Definition
UUID	Abbreviation of Universally Unique Identifier. For the definition, refer to ICH IG
OID	Abbreviation of Object Identifier. For the definition, refer to ICH IG
JP CV	Japan-specific controlled vocabulary used for operation of eCTD v4.0
SSF	Abbreviation of Specification for Submission Formats for eCTD. Refers to the electronic file specifications to be included in eCTD. ICH SSF refers to the SSF harmonized by ICH (Appendix 4), and JP SSF refers to the SSF specific to Japan (Appendix 2).
CTD	Acronym of Common Technical Document Format of the data that should be attached to the marketing application when making a marketing application for manufacturing or import of new drugs, which was agreed upon in The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH).
eCTD	Acronym of Electronic Common Technical Document Technical specifications that enable CTD to be electronically submitted by the applicant to the regulatory authority.
eCTD application	Pharmaceutical product marketing approval application with eCTD submitted as the original of an attachment to the approval application
eCTD data	Data to be submitted for eCTD application
eCTD v4.0 XML message	Submissionunit.xml to be submitted to the regulatory authority according to ICH IG and this document
PMDA	Pharmaceuticals and Medical Devices Agency
Payload	The body of the data excluding the header section
Application dossier	Documents that should be attached to the approval application form for the approval application of a prescription drug
Electronic study data (Study dataset files)	Electronic clinical study results and associated documents In this document, it refers to the electronic study data indicated by "Notification on Handling of Submission of Electronic Study Data for New Drug Applications" (PSEHB/PED

	Notification No. 0401-10 as of April 1, 2022, Notification by the Director, Pharmaceutical Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, Ministry of Health, Labour and Welfare) (hereinafter referred to as "electronic study data notification").
Electronic study data system	The system to provide the function for the applicant to submit electronic study data via the Internet, the advance notice function for application, the function to response inquiries, the function to confirm the review status, etc. It is sometimes referred to as the "gateway system".

2.2   Character notation

In this document, components of XML (elements and attributes) are notated in bold italic characters. However, this does not apply to XML snippets. Also, the concepts indicated by components of XML are expressed in the standard characters.

2.3   Symbol used in this document

Legends of Symbol used in 7 of this document is provided below.

Symbol	Description
>>	The element described on the right to this symbol is a child element of the element described on the left.

2.4   Color of the characters in XML snippets

Legends of the color of characters in XML snippets in 7 of this document are provided below.

Character color	Description
Blue	Components in terms of XML notation Example: <, =, ", ", >
Brown	XML element Example: *id*, *code*
Red	XML attribute Example: *root*, *extension*
Black	Contents of the XML element or attribute value Example: *2.16.840.1.113883*

2.5   XML element and attribute table

The section below describes how to view the table provided in 7 of this document.

Element	Attribute	Cardinality	Value(s) Allowed *Example of value*	Description
Submission rules for elements and attributes				
Business Rules	General			
	a)			
	b)			
	c)			

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Element:	It indicates the name of the element. Indentation indicates the parent-child relationship between elements. The element expressed in the colored right column is an element holding information or an element to store attributes; therefore, the information on the attribute, Cardinality, etc. in the same line in the table is omitted.
Attribute:	It indicates the name of the attribute.
Cardinality:	If the object is an element, then it indicates the lower limit and the upper limit of the number of occurrences of the relevant element for the parent element. If the object is an attribute, then it indicates the lower limit and the upper limit of the number of occurrences of the relevant attribute for the element. Expressed the "[n..m]" format. n denotes the lower limit. m denotes the upper limit. An asterisk ("*") denotes 0 times or more. The Cardinality described in this document does not necessarily agree with the definition on the schema. Give priority to this document in eCTD submitted to the regulatory authority.
Value Type	It indicates the contents of the relevant element or the type which the value of the attribute can take. The kinds of values allowed are as follows.

- Text: UTF-8 characters (including Japanese characters)* can be used.

- Fixed: Only the values provided as examples can be used.

- Single-byte alphabets: Only single-byte alphabetic characters (from a to z and from A to Z) can be used.

- Single-byte numbers: Single-byte Arabic numerals (from 0 to 9) can only be used.

- Single-byte alphanumeric characters: Only single-byte alphabets and single-byte numbers can be used.

*In principle, the character types that can be used as text types are as follows.

[The character types that can be used as a text type]
- Single-byte alphabets upper and lower case
- Single-byte numbers
- Single-byte symbols ($'(),+-./;:!?[]_#@) and white space
  Note: The following symbols are prohibited characters in XML, so do not use them in principle. If applicants have to use it, they can use the escape character instead as an exception.

  - & (ampersand) [Escape character: &]
  - " (double-quote) [Escape character: "]
  - < (less-than) [Escape character: <]
  - > (greater-than) [Escape character: >]

- Double-byte characters in the JISX0208 range (Kanji (JIS 1st level, JIS 2nd level), alphabets upper and lower case, numbers, hiragana, katakana, symbols, white space, etc.)
- Model-dependent characters (limited to 30 characters from ① to ⑳ and I to X)

Theabove rules are applied only about the required or used text type elements/attributes by the Regulatory Authority – i.e., the character types that

	can be used for text type elements/attributes such as ***application.id.item@extension*** are not limited to the above character types.
Example of value:	It shows an example of the contents of the relevant element or the value of the attribute.
Description:	The relevant element or attribute is described.
Submission rules for elements and attributes:	The rules for providing the relevant element or attribute are shown in addition to the contents of "Cardinality", "Value type" and "Description" above.
Business Rules - General:	Of the business rules that should be followed upon providing the relevant element or attribute, the rules to be applied to all of a), b) and c) indicated in 3.3.1 of this document are shown.
Business Rules -a):	Of the business rules that should be followed upon providing the relevant element or attribute, the rules to be applied to a) indicated in 3.3.1 of this document in addition to "Business Rules - General" above are shown.
Business Rules -b):	Of the business rules that should be followed upon providing the relevant element or attribute, the rules to be applied to b) indicated in 3.3.1 of this document in addition to "Business Rules - General" above are shown.
Business Rules -c):	Of the business rules that should be followed upon providing the relevant element or attribute, the rules to be applied to c) indicated in 3.3.1 of this document in addition to "business rules - General" above are shown.

3. General matters

3.1 Components that should be included for eCTD application

Components that should be included for eCTD application are shown below.
- Folder
- eCTD v4.0 XML message
- File*

* The following types of files are available.
1) ICH CTD document file referred to from the eCTD v4.0 XML message
2) Japan-specific document file referred to from the eCTD v4.0 XML message (Example: Module 1 document)
3) Electronic study data referred to from the eCTD v4.0 XML message
4) The file to be submitted to the regulatory authority but not referred to from the eCTD v4.0 XML message (Example: A file containing the checksum for the eCTD v4.0 XML message (sha256.txt))

3.2 Components not to be included in eCTD to be submitted to the regulatory authority

The following component shall not be included in the eCTD to be submitted to the regulatory authority.
1) Folders or files not described in this document
2) XML elements and attributes not described in this document

3.3 Matters related to submission

There are 2 methods for the applicant to submit eCTD to the regulatory authority in association with the approval application procedures: The method to submit it via the electronic study data system, and the method to deliver it to the reception (including mail) of the Pharmaceuticals and Medical Devices Agency (hereinafter referred to as "PMDA").

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For the approval application supposed to be submitted in the method to use the gateway system according to the "Notification on New Drug Applications Using the Gateway System" (PSEHB/PED Notification 0401 No.7 as of April 1, 2022 Notification by the Director of the Pharmaceutical Evaluation Division,Pharmaceutical Safety and Environmental Health Bureau, Ministry of Health, Labour and Welfare) (hereinafter referred to as "Notification on gateway application"), follow this.

3.3.1   Submission method via the electronic study data system

For the specific submission method and procedures via the electronic study data system, refer to the Notification on gateway application and "Technical Conformance Guide on Electronic Study Data Submissions" (PMDA/CPE Notification No. 0401003 and PMDA/CRS Notification No.0401001 as of April 1, 2022 Notification by the Director Center for Product Evaluation, Director of Center for Regulatory Science, Pharmaceuticals and Medical Devices Agency) (hereinafter referred to as "Technical Conformance Guide"), etc.
Of the following 3 eCTD types, either submit a) or submit b) and c).

a) eCTD to be submitted referring to the material specified by "About guidelines for creating the data that should be attached for new drug marketing approval application" as of June 21, 2001 Pharmaceutical Affairs Bureau Notification No 899 Notification by the Director of the Evaluation and Licensing Division, Pharmaceutical (and Food Safety) Bureau, Ministry of Health, Labour and Welfare) (hereinafter referred to as "CTD notification") as well as the electronic study data from one eCTD v4.0 XML message.

b) eCTD to be submitted by referring to only the electronic study data from 1 eCTD v4.0 XML message among a) above.

c) eCTD to be submitted by referring to the data specified by the CTD notification from 1 eCTD v4.0 XML message among a) above.

In this document, the method to submit a) is called "Method 1", and the method to submit b) and c) is called "Method 2". When submitting the first version of the data attached to the marketing application, submit it through either Method 1 or Method 2. In any other situation than the first version submission, it is only allowed through submission by Method 1.
In Method 1, only the electronic study data or the data specified by the CTD notification may be included depending on the situation of submission and the type of the data. Also, in Method 2, be sure to submit b) prior to c). For details of the eCTD type and the submission method, refer to 10 of this document.

3.3.2   Method to deliver to the reception of PMDA

To deliver the eCTD to the reception of PMDA, create a cover letter for eCTD (format 1) to submit it in writing, and include it in eCTD, too. In this case, an electronic file of the cover letter (cover.pdf) shall be included in "m1/jp" and does not need to be referred to from the eCTD v4.0 XML message. If there are multiple applicants, the cover letter may be created for each applicant.
If applicants also submit a copy of the cover letter, PMDA will return the copy with a seal of receipt when the submitted electronic files are deemed acceptable. Applicants can use it as proof that the eCTD has been received by PMDA. In the case of mail, PMDA send back a copy of the cover letter, so the applicant shall enclose with a return envelope. The return envelope can also be used in combination with the envelope used to copy the approval application.
In principle, the medium to be submitted shall be DVD-R/RW or BD-R/RE (each of which includes a multi-layer disk). If you wish to submit it in any other medium, consult PMDA in advance.
Attach a label describing the following contents for identification to the electronic medium to be submitted or directly describe them on it. When multiple applications are made in the one eCTD, then representative application information will do.

1. eCTD reception number
2. Application category

3. Application date
4. Data submission date
5. Brand name
6. Applicant name
7. The number to identify the sequence of the media if multiple media are submitted (The number of the relevant medium / total number of media)
8. Submission sequence number
9. Submission type of eCTD application (submission for original or reference, etc.)
10. Remarks

3.4 Operation requirements

When making an eCTD application, you must guarantee that the functions (display, link, etc.) required by the Appendix 2 will work considering the standard environment for review to be announced by the Regulatory Authority. Applicants should notify the Regulatory Authority of the environment in which they have confirmed the operation of the eCTD. When submitting to the reception counter, include it in the cover letter, or when submitting via the electronic study data system, transmit it via the electronic study data system. If the file referenced by hypertext links in other files is replaced among the eCTD revision, the link destination may not be displayed correctly. In this case, submit the revised version of all files affected by the change. If the Regulatory Authority cannot confirm the above-mentioned operation in the announced standard environment for review or judges that there will be a problem in review such as misrepresentations recognized, then the applicant will be requested to replace it. If there is a display problem in the eCTD data in the applicant's environment making it impossible to electronically submit it, then consult the regulatory authority about handling and procedures for taking action, etc. in advance to take action appropriately. For how to confirm the operation before submission, confirm the information posted on the PMDA web site (https://www.pmda.go.jp/) to carry it out appropriately.
Also, the use of any plug-in software required for perusal is not permitted in principle. However, this does not apply to plug-in software used for creation.

3.5 Requirements for using eCTD

When making an eCTD application, you must submit all the documents to be submitted, which should be included in eCTD, in electronic files. Scan the relevant page signed or signed and sealed, etc. on a paper medium, replace it with the corresponding page on the electronic medium and save it and include it in eCTD. In that case, submit a statement indicating that the corresponding page has been correctly scanned. Although it is not necessary to submit any written statement at the time of application, prepare it so that you can submit it upon request from the regulatory authority. Include an electronic file of the statement in Section 3 of Module 1.
Only if you confirm with the regulatory authority in advance and it is permitted, then you may submit eCTD which deviates from the handling according to this document and Appendix 2. In this case, submit a document containing the reason for the deviation and points of attention. Include an electronic file of this document in the submission to the Ministry of Health, Labour and Welfare in Section 13 of Module 1.
Note that you must not submit an eCTD intended for bidirectional communication described in ICH IG, and an application associated with more than one submission and forward compatibility from v3.2.2 to v4.0 to the regulatory authority.

3.6 Handling of electronic signatures

When electronically signing the data to be submitted to the regulatory authority, if the target of indication of your intention by the relevant act of the signature is not the regulatory authority (for example, internal document approval, a contract with an outsourcing company, etc.), then you may submit eCTD containing the electronically signed file. However, any electronic signature, for which signer verification is required by the regulatory authority upon perusing the relevant data, is not permitted. If the electronic signature

hinders the regulatory authority perusing the data, then you may be requested to remove the relevant electronic signature.

3.7 Controlled vocabulary

In addition to the controlled vocabulary specified by ICH (hereinafter referred to as "ICH CV"), the controlled vocabulary specific to Japan (hereinafter referred to as "JP CV") specified separately shall be used. JP CV is provided by the eCTD v4.0 domestic implementation package.

3.7.1 Code List Versioning

Each code list included in ICH CV and JP CV is version-controlled. The valid version of each code list in Japan is specified in the "JP OID Listing" separately from the "ICH Support Period" described in ICH CV. Therefore, when using the ICH CV and JP CV code lists in Japan, use the version that meets the conditions of "Available Application" described in the "JP OID Listing". The "JP OID Listing" is provided in the eCTD v4.0 domestic implementation package.

名前	Ver.	OID	利用可能な申請	説明
ICH M8 OID List				
ICH Context of Use	1	2.16.840.1.113883.3.989.2.2.1.1.1	–	「ICH Cont
	2	2.16.840.1.113883.3.989.2.2.1.1.2	–	
	3	2.16.840.1.113883.3.989.2.2.1.1.3	申請日が2022年4月1日～2023年1月27日の間	
	4	2.16.840.1.113883.3.989.2.2.1.1.4	申請日が2022年4月1日以降	

For example, if the application date of the approval application provided by the eCTD is "January 30, 2023" and the "JP OID Listing" is specified as shown in the image above, the version that can be used with the eCTD will be "4". In addition, if one eCTD provides multiple approval applications, the approval application with the earliest application date provided by the eCTD is used as the basis.

3.7.2 Code Value Status

A status is set for each code in a code list, and the status of codes that can no longer be used becomes "Retired." Therefore, in the code list of the specific version, the codes with "Active" in the "Status" column of the CV are available, but "Retired" codes must not be used.

However, in the case of a code list that does not have a "Status" column, the status of all codes listed is considered to be "Active."

4. Security
4.1 Checksums

In eCTD application, submit a file containing the checksum for the eCTD v4.0 XML message (sha256.txt) (hereinafter referred to as the "checksum file"), and include the checksums of the individual submitted files except for the checksum file in the eCTD v4.0 XML message. For how to submit the checksum file and how to include the checksum in the eCTD v4.0 XML message, refer to "5.1 Contents of Submission Unit" and "5.6 Checksums", etc., in the ICH IG.

5. Requirements for the folder structure and file path contained in eCTD
5.1 Basic folder structure

The basic folder structure shall be as follows.
- To be created based on the folder structure described in ICH IG.

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- If there is no file to be stored due to reuse of the document or file, then do not create any folder for the corresponding CTD number.
- The first level folder name shall be the eCTD reception number, and the second level folder name shall be the submission sequence number.
- The folder of each section of CTD ("m1", "m2", "m3", "m4" and "m5") shall be placed at the third level. However, do not create any lower folder or folder not having any file to be stored in the folder at the third level or lower.
- For the structure of Module 1, refer to 15 of this document.
- Create a folder for each individual report that makes up Module 4 and Module 5.
- Place the electronic study data indicated under the "m5" folder in the folder structure described in ICH IG. In this case, place it as follows by regarding the relevant "m5" folder and the "m5" folder of the folder structure indicated in the technical conformance guide as the same folder.

```
📁 m5
    📁 531-biopharm
    📁 532-pkbiomat
    📁 533-humanpk
    📁 534-pd
    📁 535-eff-safe
    📁 536-pms
    📁 537-listing
    📁 54-lit
    📁 datasets
        📁 [study id/iss/ise]
                ⋮
```
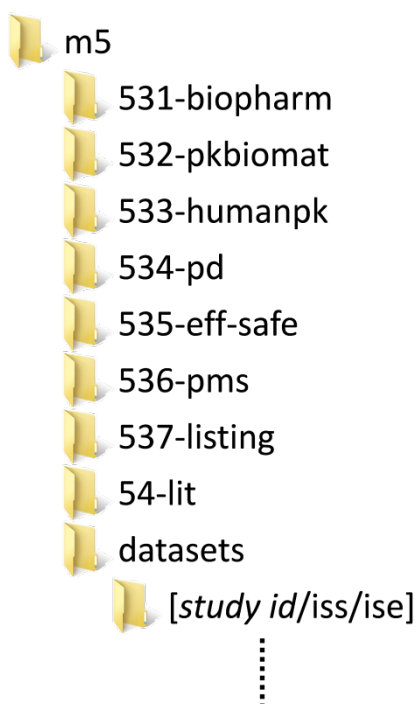
(For the following, refer to the technical conformance guide.)

5.2 Naming Conventions

For the folders and files to be included in Module 1 through Module 5, follow the folder and file naming conventions provided in ICH IG. For the naming conventions for the electronic study data referred to from the eCTD v4.0 XML message, follow the technical conformance guide.

5.3 The maximum path length

For the maximum path length, follow the description of ICH IG.

6. Requirements for the format of the file included in eCTD

Of the files referred to from the eCTD v4.0 XML message, for the format of the file for electronic study data, refer to the technical conformance guide. If it is necessary to submit any other document than the electronic study data in any other file format than the PDF format or the Microsoft Excel format (.xlsx), then consult the regulatory authority in advance.

7. Requirements for the eCTD v4.0 XML message

7.1 Character encode

Use UTF-8.

7.2 Message header

In addition to ICH IG, the following business rules apply to the message header description rules.

- The OID of the implementation guide specified in the *receiver.device.id.item@root* attribute value must be a version that meets the conditions of "Available Applications" stipulated in the "JP OID Listing." If one eCTD provides multiple approval applications, the earliest application date of the approval applications provided by the eCTD is used as the basis.
- The *receiver.device.id.item@identifierName* attribute value shall be 128 characters or less. The Regulatory Authority does not use this attribute value.

7.3 Handling of the elements and attributes not having any value

In the payload of the eCTD v4.0 XML message, do not let any elements except for the *integrityCheck* element have any other contents than the child element. Also, do not submit any *integrityCheck* element having no contents or *integrityCheck* element having dummy value as the content.
As for the attribute, do not submit any attribute having a dummy value or empty value.

7.4 How to use the XML elements and attributes included in the payload

The schema of the eCTD v4.0 XML message contains the elements and attributes not used by the regulatory authority, the elements and attributes whose usage is different from other poles as well as the elements and attributes used only in Japan. For how to use the elements and attributes contained in the eCTD v4.0 XML message to be submitted to the regulatory authority, follow the description of this document, and do not submit any elements or attributes not described in this document. The complete RPS R2 schema includes the Common Product Model schemas, but for the time being, the Regulatory Authorities does not use the Common Product Model schemas. For details on the Common Product Model, refer to the HL7 website.

7.4.1 Required elements (controlActProcess)

For the *controlActProcess* element and attribute required to start the payload of the eCTD v4.0 XML message as well as its child element and attribute, refer to the description of ICH IG. To be provided according to ICH IG

7.4.2 submissionUnit

The Submission Unit refers to a collection of documents and pieces of information to be provided for the regulatory authority through a single act of submission. The Submission Unit will be provided through the *submissionUnit* element.

7.4.2.1 Place of description on XML

For the place to describe the *submissionUnit* element, follow ICH IG.

7.4.2.2 XML snippet

An XML snippet of the *submissionUnit* element is shown below.

```
<subject typeCode="SUBJ">
    <submissionUnit>
        <id root="c64abdbd-c052-439a-bbcc-e00198139790"/>
```

```
<code code="jp_ctd" codeSystem=" 2.16.840.1.113883.3.989.5.1.3.3.1.1.1"/>
<component>
     …[Partially omitted]…
</component>
<componentOf1>
     …[Partially omitted]…
</componentOf1>
<componentOf2>
     …[Partially omitted]…
</componentOf2>
</submissionUnit>
</subject>
```

7.4.2.3 XML elements and attributes

The *submissionUnit* element and the elements under it as well as their attributes are as follows.

Element	Attribute	Cardinality	Value(s) Allowed / *Example of value*	Description
submissionUnit		[1..1]		This element stores the documents and pieces of information to be provided for the regulatory authority.
id		[1..1]		Follow the description of ICH IG.
	root	[1..1]	Valid UUID *Example:* *root="c64abdbd-c052-439a-bbcc-e00198139790"*	Follow the description of ICH IG.
code		[1..1]		Follow the description of ICH IG.
	code	[1..1]	Text *Example:* *code="jp_ctd"*	The code indicating the type of this Submission Unit Select the code value from the "JP Submission Unit" code list of JP CV.
	codeSystem	[1..1]	Valid OID *Example:* *codeSystem="2.16.840.1.113883.3.989.5.1.3.3.1.1.1"*	OID of the "JP Submission Unit" code list of JP CV
title		[0..1]		Follow the description of ICH IG.
	value	[1..1]	Text *Example:* *value="First version"*	Follow the description of ICH IG.

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Element	Attribute	Cardinality	Value(s) Allowed *Example of value*	Description
component		[0..*]		This element stores the *contextOfUse* element. For details of the *contextOfUse* element, refer to 7.4.4 of this document.
componentOf1		[1..1]		This element stores the *sequenceNumber* element and the *submission* element. For details of the *sequenceNumber* element, refer to 7.4.8 of this document. For details of the *submission* element, refer to 7.4.9.
componentOf2		[1..1]		This element stores the *categoryEvent* element. For details of the *categoryEvent* element, refer to 7.4.19 of this document.
Submission rules for elements and attributes		➢ When providing a new Context of Use, or when replacing, deleting or updating an existing Context of Use, provide the *component* element for each Context of Use. For details on the Context of Use, refer to 7.4.4 of this document. ➢ The applicant shall determine whether to provide the *submissionUnit.title* element arbitrarily.		
Business Rules	**General**	➢ In addition to the business rules provided in ICH IG, the following will be applied. • The Submission Unit, which falls under any of the following, will be rejected. ◇ Multiple *submissionUnit* elements are provided. ◇ The *submissionUnit* element is not provided. ◇ The *title@value* attribute value has 1001 characters or more. ◇ When submitting the first version, the *component* element is not provided. • The *submissionUnit.statusCode* element is not used. To withdraw the Submission Unit, consult the regulatory authority. • The regulatory authority does not use the *submissionUnit.title@value* attribute in principle. In addition, the character types that can be used for this attribute is not limited to the character types specified in 2.5 [The character types that can be used as a text type] in this document.		
	a)	There are no business rules that should be followed in addition to General above in particular.		
	b)	There are no business rules that should be followed in addition to General above in particular.		
	c)	There are no business rules that should be followed in addition to General above in particular.		

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7.4.3 priorityNumber for contextOfUse

Priority Number defines the display order of the Context of Use within the context group and is provided by the *priorityNumber* element. The Context of Use will be displayed in ascending order of the Priority Number for each context group. In plinciple, the electronic study data will be displayed in ascending order of the folder name or the file name atthe Regulatory Authority's viewing tool.

7.4.3.1 Place of description on XML

For the place to describe the *priorityNumber* element, refer to "9.2.5 Priority Number for Context of Use", etc., in the ICH IG.

7.4.3.2 XML snippet

An XML snippet of the *priorityNumber* element is shown below.

```
<component>
    <priorityNumber value="1000" updateMode="R"/>
    <contextOfUse>
    …[Partially omitted]…
    </contextOfUse>
</component>
```

7.4.3.3 XML elements and attributes

The *priorityNumber* element and the elements under it as well as their attributes are as follows.

Element	Attribute	Cardinality	Value(s) Allowed *Example of value*	Description
priorityNumber		[1..1]		This element stores the information indicating the display order of the Contexts of Use in the context group.
	value	[1..1]	Single-byte numbers Example: *value="1000"*	Specify the integer to be used for display ordering of the Context of Use element.
	updateMode	[0..1]	Fixed *updateMode="R"*	When updating the Priority Number, specify "R".
Submission rules for elements and attributes	➢ If the *contextOfUse* element is provided, the following is required. • *priorityNumber@value* ➢ When updating the *priorityNumber@value* attribute value of the already submitted Context of Use, the following is required. • *priorityNumber@updateMode*			

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Element	Attribute	Cardinality	Value(s) Allowed *Example of value*	Description
Business Rules	General	➢ In addition to the business rules provided in ICH IG, the following will be applied. • The Submission Unit, which falls under any of the following, will be rejected. ✧ Multiple valid Contexts of Use within the same context group have the same (value of the) Priority Number in the application. ✧ The *priorityNumber@updateMode* is included in the Context of Use submitted for the first time throughout the life cycle. ✧ At the time of revision, the *priorityNumber@updateMode* attribute value is provided, but the *priorityNumber@value* attribute value is not updated. • The Priority Number assigned to the Context of Use, which refers to the electronic study data, does not affect the display order of the electronic study data at the regulatory authority. • It is desirable that the *priorityNumber@value* attribute value provided when deleting the submitted Context of Use is the same as the Priority Number of the Context of Use to be deleted. If other values are provided, it is not recognized that the values have been provided to the regulatory authority. The Priority Number of the Context of Use to be deleted will be available in the same Submission Unit and later. • When replacing a submitted Context of Use with a new Context of Use, the Priority Numbers before and after the replacement does not have to match, unless they overlap with the Context of Use in the same context group. Also, do not provide the *priorityNumber@updateMode* attribute even if the Priority Numbers before and after replacement do not match.		
	a)	There are no business rules that should be followed in addition to General above in particular.		
	b)	There are no business rules that should be followed in addition to General above in particular.		
	c)	There are no business rules that should be followed in addition to General above in particular.		

7.4.4 contextOfUse

The Context of Use defines the positioning of the document. The Context of Use is provided by the *contextOfUse* element, designates the positioning (CTD heading) in the application dossier through the *code* element under it, and designates 1 Document through the *documentReference* element. This defines which CTD heading the designated Document belongs to in the relevant application.

7.4.4.1 Place of description on XML

For the place to describe the *contextOfUse* element, refer to "9.2.6 Context of Use", etc., in the ICH IG.

7.4.4.2 XML snippet

An XML snippet of the *contextOfUse* element is shown below.

```
<component>
    <priorityNumber value="1000"/>
    <contextOfUse>
        <id root="7c5c61fd-5b88-4018-8323-b21f1a731880"/>
        <code code="ich_3.2.s.2.3" codeSystem="2.16.840.1.113883.3.989.2.2.1.1.2"/>
```

* This English version of the Japanese Notification is provided for reference purposes only. In the event of any inconsistency between the Japanese original and the English translation, the former shall prevail.

```
        <statusCode code="active"/>
    … [Partially omitted] …
    </contextOfUse>
</component>
```

7.4.4.3   XML elements and attributes

The *contextOfUse* element and the elements under it as well as their attributes are as follows.

Element	Attribute	Cardinality	Value(s) Allowed *Example of value*	Description
contextOfUse		[1..1]		This element stores the information to associate the document submitted to the regulatory authority with the CTD heading.
id		[1..1]		Follow the description of ICH IG.
	root	[1..1]	Valid UUID *Example:* *root="7c5c61fd-5b88-4018-8323-b21f1a731880"*	Follow the description of ICH IG.
code		[0..1]		Follow the description of ICH IG.
	code	[1..1]	Text *Example: code="ich_3.2.s.2.3"*	Follow the description of ICH IG. Select the corresponding code from "ICH Context of Use" of ICH CV or "JP Context of Use" of JP CV to provide it.
	codeSystem	[1..1]	Valid OID *Example:* *codeSystem="2.16.840.1.113883.3.989.2.2.1.1.1"*	Follow the description of ICH IG. Provide OID of "ICH Context of Use" of ICH CV or OID of "JP Context of Use" of JP CV.
originalText		[0..1]		Follow the description of ICH IG.
	Value	[1..1]	Text *Example: code="ich_3.2.P.8.3-1"*	Follow the description of ICH IG.
statusCode		[1..1]		Follow the description of ICH IG.
	code	[1..1]	Single-byte alphabets *Example:* *code="active",* *code="suspended"*	Follow the description of ICH IG. If the relevant Context of Use is valid, then provide "active", and if deleted, then provide "suspended".

Element	Attribute	Cardinality	Value(s) Allowed *Example of value*	Description
replacementOf		[0..*]		This element stores the *relatedContextOfUse* element. For details of the *relatedContextOfUse* element, refer to 7.4.5 of this document.
	typeCode	[1..1]	Fixed *typeCode="RPLC"*	This attribute is a structural attribute required to use the *replacementOf* element.
derivedFrom		[0..1]		This element stores the *documentReference* element. For details of the *documentReference* element, refer to 7.4.6 of this document.
referencedBy		[0..*]		This element stores the *keyword* element. For details of the *keyword* element, refer to 7.4.7 of this document.
	typeCode	[1..1]	Fixed *typeCode="REFR"*	This attribute is a structural attribute required to use the *referencedBy* element.
Submission rules for elements and attributes	➢ If the *contextOfUse.statusCode@code* attribute value is "active" and if the *priorityNumber* element does not contain the *updateMode* attribute, then the following is required. • *code@code* • *code@codeSystem* • *derivedFrom* ➢ When the *contextOfUse.statusCode@code* attribute value is "suspended" or the *priorityNumber@updateMode* attribute value is provided, the Submission Unit containing any of the following information is rejected. • *code@code* • *code@codeSystem* • *replacementOf* • *derivedFrom* • *referencedBy* ➢ When replacing a single Context of Use with multiple Context of Uses, provide a *replacementOf* element for each of the new Context of Uses for replacing. For details on replacing the Context of Use, refer to 7.4.5 of this document. ➢ When multiple Keywords are assigned to one Context of Use, provide a *referencedBy* element for each of the Keywords. For details on the Keyword assigned to the Context of Use, refer to 7.4.7 of this document.			

Element	Attribute	Cardinality	Value(s) Allowed *Example of value*	Description

Business Rules	**General**	➢ In addition to the business rules provided in ICH IG, the following will be applied.
		• The Submission Unit, which falls under any of the following, will be rejected.
		  ✧ The *code.originalText@value* attribute value is 129 characters or more.
		  ✧ The *statusCode@code* attribute value is neither "active" nor "suspended".
		  ✧ The *updateMode* attribute is provided for the Priority Number of the Context of Use, whose *statusCode@code* attribute value is "suspended", at the same time.
		  ✧ The *statusCode@code* attribute value of the *contextOfUse* element provided for the first time throughout the life cycle including the submission of the first version is "suspended".
		  ✧ When submitting the first version, the *replacementOf* element is provided.
		  ✧ When submitting the first version, the *contextOfUse* element not containing the *derivedFrom* element is provided.
		  ✧ At the time of revision, the *replacementOf* element is provided under the Context of Use, whose *statusCode@code* attribute value is "suspended".
		• Do not provide the *contextOfUse* element with the same *id@root* attribute value as the replaced or deleted Context of Use. If applicants want to re-enable the replaced or deleted Context of Use, resubmit it as the new Context of Use.			

	a)	There are no business rules that should be followed in addition to General above in particular.		
	b)	If the CTD heading indicated by the *code@code* attribute value does not belong to Section 3 of Module 5, the Submission Unit will be rejected.		
	c)	There are no business rules that should be followed in addition to General above in particular.		

7.4.5 relatedContextOfUse

The *relatedContextOfUse* element is used when replacing the already submitted Context of Use with a new Context of Use. *relatedContextOfUse* element is submitted as a child element of the new Context of Use and specifies the Context of Use to be replaced by the *id* element.

7.4.5.1 Place of description on XML

For the place to describe the *relatedContextOfUse* element, refer to "9.2.7 Related Context of Use (Context of Use Life Cycle)", etc., in the ICH IG.

7.4.5.2 XML snippet

An XML snippet of the *relatedContextOfUse* element is shown below.

```
<replacementOf typeCode="RPLC">
    <relatedContextOfUse>
        <id root="d981c6a9-d57a-43cc-a71b-a8e35a34a39a"/>
    </relatedContextOfUse>
</replacementOf>
```

7.4.5.3 XML elements and attributes

The *relatedContextOfUse* element and the elements under it as well as their attributes are as follows.

Element	Attribute	Cardinality	Value(s) Allowed *Example of value*	Description
relatedContextOfUse		[1..1]		This element stores the information on the Context of Use to be replaced.
id		[1..1]		Follow the description of ICH IG.
	root	[1..1]	Valid UUID *Example: root="d981c6a9-d57a-43cc-a71b-a8e35a34a39a"*	Follow the description of ICH IG.
Submission rules for elements and attributes		➤ When the *contextOfUse.statusCode@code* attribute value is "suspended" or the *priorityNumber@updateMode* attribute value is provided, the Submission Unit containing the following information will be rejected. • *relatedContextOfUse*		

Business Rules	**General**	➤ In addition to the business rules provided in ICH IG, the following will be applied.
		  • The Submission Unit, which falls under any of the following, will be rejected.
		    ✧ The Context of Use indicated by the *id@root* attribute value belongs to a different context group.
		    ✧ The Context of Use indicated by the *id@root* attribute value is provided in the relevant Submission Unit.
		    ✧ The Context of Use indicated by the *id@root* attribute value is not provided through the past submission of the application with the same eCTD reception number.
		    ✧ The Context of Use indicated by the *id@root* attribute value has been deleted or replaced through the past submission of the application with the same eCTD reception number.		

	a)	There are no business rules that should be followed in addition to General above in particular.		
	b)	There are no business rules that should be followed in addition to General above in particular.		
	c)	There are no business rules that should be followed in addition to General above in particular.		

7.4.6 documentReference

The *documentReference* element designates the document. The *documentReference* element designated by Document Reference is associated with the positioning in the application dossier designated by the *code* element of *contextOfUse* element, which is the parent element.

7.4.6.1 Place of description on XML

For the place to describe the *documentReference* element, refer to "9.2.8 Document Reference", etc., in the ICH IG.

7.4.6.2 XML snippet

```xml
<derivedFrom>
    <documentReference>
        <id root="a17b06a2-a040-431d-8e5b-1f678c83af3c"/>
    </documentReference>
</derivedFrom>
```

7.4.6.3 XML elements and attributes

The *documentReference* element and the elements under it as well as their attributes are as follows.

Element	Attribute	Cardinality	Value(s) Allowed *Example of value*	Description
documentReference		[1..1]		This element stores the identifier of the Document to be associated with the Context of Use.
id		[1..1]		Follow the description of ICH IG.
	root	[1..1]	Valid UUID *Example: root="a17b06a2-a040-431d-8e5b-1f678c83af3c"*	Follow the description of ICH IG.
Submission rules for elements and attributes	➢ If the *contextOfUse.statusCode@code* attribute value is "active" and if the *priorityNumber* element does not contain the *updateMode* attribute, then the following is required. • *documentReference* ➢ If the attribute of *contextOfUse.statusCode@code* is "suspended" or the attribute of *priorityNumber@updateMode* is provided, the submission unit including the information below will be rejected. • *documentReference*			
Business Rules	**General**	➢ In addition to the business rules provided in ICH IG, the following will be applied. • The Submission Unit, which falls under any of the following, will be rejected. ✧ The Document indicated by the *id@root* attribute value does not exist in either the relevant Submission Unit or the database of the regulatory authority*. ✧ When submitting the first version, the *contextOfUse* element not containing the *documentReference* element is provided. * The regulatory authority stores the Documents submitted using eCTD v4.0 in the database for the period of time specified by the administrative document management rules of the Ministry of Health, Labor and Welfare (hereinafter referred to as the "prescribed retention period") unless the relevant application is withdrawn.		
	a)	There are no business rules that should be followed in addition to General above in particular.		
	b)	There are no business rules that should be followed in addition to General above in particular.		

Element	Attribute	Cardinality	Value(s) Allowed *Example of value*	Description
		c)	There are no business rules that should be followed in addition to General above in particular.	

7.4.7 Context of Use keyword

The keyword assigned to the Context of Use (hereinafter referred to as "CoU Keyword") provides the additional information for the CTD heading indicated by the Context of Use. The CoU Keyword is provided by the **keyword** element under the **contextOfUse** element, and has the following 2 major types.
1) The one whose keyword type and value are determined by ICH or the regulatory authority.
   Example: ICH Document Type, JP Analysis Type, etc.
2) The one whose keyword type is determined by ICH or the regulatory authority, and whose value is determined by the applicant arbitrarily.
   Example: indication, substance, group title, etc.

When assigning the keyword of 2) above, define its value using the Keyword Definition in the relevant application. For details of the Keyword Definition, refer to 7.4.18 of this document.

7.4.7.1 Place of description on XML

For the place to describe the **keyword** element to be assigned to the Context of Use, refer to "9.2.9 Context of Use Keyword", etc., in the ICH IG.

7.4.7.2 XML snippet

An XML snippet of the **keyword** element to be assigned to the Context of Use is shown below.
Example of 1) above
```
<referencedBy typeCode="REFR">
    <keyword>
        <code code="ich_document_type_65" codeSystem="2.16.840.1.113883.3.989.2.2.1.3.2"/>
    </keyword>
</ referencedBy>

<referencedBy typeCode="REFR">
    <keyword>
        <code code="jp_cdisc_single" codeSystem="2.16.840.1.113883.3.989.5.1.3.3.1.10.1"/>
    </keyword>
</ referencedBy>
```

Example of 2) above
```
<referencedBy typeCode="REFR">
    <keyword>
        <code code="MANU001" codeSystem="My list 001"/>
    </keyword>
</ referencedBy>
<referencedBy typeCode="REFR">
    <keyword>
        <code code="SUB001" codeSystem="My list 001 "/>
    </keyword>
</ referencedBy>
<referencedBy typeCode="REFR">
    <keyword>
        <code code="SDTMDATE" codeSystem="SDTMVer001 "/>
```

```
        </keyword>
    </referencedBy>
```

Note: In case of 2) above, submit the definition of the keyword as Keyword Definition. For details, refer to 7.4.18 of this document.

7.4.7.3   XML elements and attributes

The *keyword* element to be assigned to the Context of Use and the elements under it as well as their attributes are as follows.

Element	Attribute	Cardinality	Value(s) Allowed *Example of value*	Description
keyword		[1..1]		This element stores the information to specify additional information of the Context of Use.
code		[1..1]		Follow the description of ICH IG.
	code	[1..1]	Text *Example:* *code="ich_route_1",* *code="MANU001"*	Follow the description of ICH IG.
	codeSystem	[1..1]	Text *Example:* *codeSystem="My list 001"*	Follow the description of ICH IG.
Submission rules for elements and attributes	There are no submission rules that should be followed in addition to the contents of the above-mentioned "Cardinality", "Value(s) Allowed" and "Description".			

Element	Attribute	Cardinality	Value(s) Allowed *Example of value*	Description

Business Rules	General		➢ In addition to the business rules provided in ICH IG, the following will be applied.
			 • In case that there are multiple drug products and indications in the relevant application (multiple values exist in the relevant application for one type of CoU Keyword) and documents are submitted for each, clearly point out the difference using the CoU Keyword of the relevant type. (Example: In the case of an application that includes multiple drug products, the product Keyword should be assigned and multiple 3.2.P should be listed so that the drug products can be distinguished in the CTD heading.)
			 • The Submission Unit, which falls under any of the following, will be rejected.
			  ✧ A keyword is provided that is not permitted by either "ICH Context of Use" of ICH CV or "JP Context of Use" of JP CV (however, in the case of the Context of Use referring to the electronic study data , with the exception of Keywords in 2) of 11 of this document).
			  ✧ The keyword required by "ICH Context of Use" of ICH CV or "JP Context of Use" of JP CV is not assigned.
			  ✧ Multiple CoU Keywords of the same type are assigned to 1 Context of Use.
			  ✧ The ICH Study Group Order Keyword has been assigned, but the study id_study title Keyword has not been assigned.
			  ✧ Any of the following keywords is assigned for the Context of Use, which does not refer to the electronic study data.
			   ✓ JP Study Data Category
			   ✓ JP Analysis Type
			   ✓ JP Terminology(Tabulation)
			   ✓ JP Terminology(Analysis)
			  ✧ The JP Study Data Category Keyword is not assigned for the Context of Use, which refers to the electronic study data.
			  ✧ The *text.description* element is not provided in the Document referenced by the Context of Use assigned with the JP Analysys Type Keyword that indicates data other than "clinical study data that are not electronic study data on clinical pharmacology" (Non-CP).	

	a)		There are no business rules that should be followed in addition to General above in particular.	
	b)		If the JP Study Data Category Keyword is not provided, the Submission Unit will be rejected.	
	c)		If the JP Study Data Category Keyword is provided, the Submission Unit will be rejected.	

7.4.8 sequenceNumber

The Sequence Number is provided by the *sequenceNumber* element and provides the submission sequence number indicating the submission order and time series of the Submission Units in the same application. The information provided through the Submission Unit to be submitted for application will be revised through the Submission Unit additionally submitted in the review process. The Sequence Number is a number assigned for each Submission Unit and increased for each submission.

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7.4.8.1 Place of description on XML

For the place to describe the *sequenceNumber* element, refer to "9.2.12 Sequence Number", etc., in the ICH IG.

7.4.8.2 XML snippet

An XML snippet of the *sequenceNumber* element is shown below.

```
<componentOf1>
    <sequenceNumber value="1"/ >
    <submission>
    …[Partially omitted]…
</componentOf1>
```

7.4.8.3 XML elements and attributes

The *sequenceNumber* element and the elements under it as well as their attributes are as follows.

Element	Attribute	Cardinality	Value(s) Allowed *Example of value*	Description
sequenceNumber		[1..1]		This element stores the information indicating the submission order and time series of the Submission Units in the same application.
	value	[1..1]	Single-byte numbers *Example:* *value="1"*	Follow the description of ICH IG.
Submission rules for elements and attributes	There are no submission rules that should be followed in addition to the contents of the above-mentioned "Cardinality", "Value(s) Allowed" and "Description".			

Business Rules	**General**	➢ To make a revision, of the sequence numbers already submitted in the same application at the time of submission of the revised version, provide the numeric value obtained by adding 1 to the maximum value as the sequence number. In this case, upon identifying the already submitted Submission Unit having the maximum Sequence Number, distinction of the ***submissionUnit.code@code*** value does not matter.
		➢ The Submission Unit, which falls under any of the following, will be rejected.
		  • A value other than an integer of single-byte Arabic numerals "1" through "999999" is provided as the Sequence Number.
		  • The Sequence Number and the second layer folder name do not match.
		  • When submitting the first version, a value not conforming to the business rules a), b) and c) is provided as the Sequence Number.
		  • At the time of revision, the Sequence Number is not incremented by "1".
		  • At the time of revision, an already submitted Sequence Number value is provided.		

	a)	➢ The Sequence Number of a) when submitting the first version shall be "1". ➢ When re-issuing or re-submitting submissionunit.xml submitted once, provide the Sequence Number of the same value as (that of) the submissionunit.xml to be re-issued or re-submitted.		

Element		Attribute	Cardinality	Value(s) Allowed *Example of value*	Description
	b)			➢ The Sequence Number of b) when submitting the first version shall be "1". ➢ To re-issue or re-submit b) once submitted, the Sequence Number shall be always set to "1".	
	c)			➢ The Sequence Number of c) when submitting the first version shall be "2". ➢ To re-issue or re-submit c) once submitted, the Sequence Number shall be always set to "2".	

7.4.9 submission

Submission is provided by the *submission* element and provides the information on the product item contained in the relevant application. Submission is distinguished by the eCTD reception number, and 1 submission can contain information on one or more product items. The Submission Unit related to the product item provided by Submission is associated as a lower concept of the relevant Submission, but on the eCTD v4.0 XML message, the *submission* element exists as a lower element of the *submissionUnit* element. The *submissionUnit* element provides the information on the Submission associated with itself as a *submission* element.

7.4.9.1 Place of description on XML

On the eCTD v4.0 XML message, the *submission* element is placed as follows.
- *controlActProcess* >> subject >> *submissionUnit* >> *componentOf1* >> *submission*

7.4.9.2 XML snippet

An XML snippet of the *submission* element is shown below.

```
<componentOf1>
    <sequenceNumber value="1"/ >
    <submission>
        <id>
            <item root="c4550245-fa32-444e-8433-702fbba7a8d4" extension="20160505001"/>
        </id>
        <code code="jp_original" codeSystem="2.16.840.1.113883.3.989.5.1.3.3.1.5.1"/>
        …[Partially omitted]…
    </submission>
</componentOf1>
```

7.4.9.3 XML elements and attributes

The *submission* element and the elements under it as well as their attributes are as follows.

Element			Attribute	Cardinality	Value(s) Allowed *Example of value*	Description
submission				[1..1]		This element stores the product item information provided in association with the relevant Submission Unit.
	id			[1..1]		This element stores the identifier of the relevant eCTD application.
		item		[1..1]		This element stores the identifier of the relevant eCTD application.

Element	Attribute	Cardinality	Value(s) Allowed *Example of value*	Description
	root	[1..1]	Valid UUID *Example:* *root="c4550245-fa32-444e-8433-702fbba7a8d4"*	UUID of this submission A number is issued by the applicant according to the algorithm based on the standard specifications provided in ICH IG.
	extension	[1..1]	Single-byte alphanumeric characters *Example:* *extension="201605 05001"*	eCTD reception number
code		[1..1]		This element stores the positioning of the relevant eCTD application (submission of the original, submission of references, etc.).
	code	[1..1]	Text *Example:* *code="jp_original"*	The code value indicating the positioning of the relevant eCTD application is held as a value. Select the code value from the "JP Submission" code list of JP CV.
	codeSystem	[1..1]	Valid OID *Example:* *codeSystem="2.16. 840.1.113883.3.989. 5.1.3.3.1.5.1"*	OID of the "JP Submission" code list
subject2		[0..*]		This element stores the *review* element. For details of the *review* element, refer to 7.4.10 of this document.
componentOf		[1..1]		This element stores the *application* element. For details of the *application* element, refer to 7.4.15 of this document.
Submission rules for elements and attributes	➢ If a new Review or changing information in an existing Review, provide a subject2 element for each the marketing application. For details of Review, refer to 7.4.10 of this document.			

Element	Attribute	Cardinality	Value(s) Allowed *Example of value*	Description
Business Rules	General	➤ Provide the same value for the following attribute throughout the application regardless of change of the information under ***submission*** in principle. If it is necessary to change these values, consult the regulatory authority in advance. • ***id.item@root*** • ***id.item@extension*** • ***code@code*** • ***code@codeSystem**** *The version number included at the end of the OID indicated by the ***code@codeSystem*** attribute does not have to match. ➤ The ***id.item@root*** attribute value shall be a UUID that can uniquely identify this Submission. ➤ The Submission Unit, which falls under the following, will be rejected. • The ***id.item@extension*** attribute value is different from the eCTD reception number of the relevant application.		
	a)	➤ If the ***subject2*** element is not provided at the time of initial submission, the Submission Unit will be rejected. •		
	b)	➤ b) must not contain the ***subject2*** element. Also, if the ***subject2*** element is included in b), that Submission Unit will be rejected.		
	c)	➤ If the subject2 element is not provided, the Submission Unit will be rejected. •		

7.4.10 review

The ***review*** element provides the product item information. The one ***subject2*** element is provided for each product, and the one ***review*** element is provided for each ***subject2*** element.

7.4.10.1 Place of description on XML

The ***review*** element is described in the following place on the eCTD v4.0 XML message.
- *controlActProcess* >> subject >> *submissionUnit* >> *componentOf1* >> *submission* >> *subject2* >> *review*

7.4.10.2 XML snippet

An XML snippet of the ***review*** element is shown below.

```
<subject2>
    <review>
        <id root="c2a664fc-4b41-4425-8631-46b7bf1f58a6"/>
        <statusCode code="active"/>
        <subject1>
            …[Partially omitted]…
        </subject1>
        <holder>
            …[Partially omitted]…
        </holder>
        <subject2>
            …[Partially omitted]…
        </subject2>
    </review>
</subject2>
```

* This English version of the Japanese Notification is provided for reference purposes only. In the event of any inconsistency between the Japanese original and the English translation, the former shall prevail.

7.4.10.3　XML elements and attributes

The *review* element and the elements under it as well as their attributes are as follows.

Element	Attribute	Cardinality	Value(s) Allowed *Example of value*	Description
review		[1..1]		This element stores the product item information.
id		[1..1]		This element stores the identifier of the relevant *review* element.
	root	[1..1]	Valid UUID *Example: root="c2a664fc-4b41-4425-8631-46b7bf1f58a6"*	UUID of this Review. A number is issued by the applicant according to the algorithm described in ICH IG.
statusCode		[1..1]		This element stores the information indicating the state of the application for the relevant product item.
	code	[1..1]	Single-byte alphabets *Example: code="active", code="suspended"*	The code indicating the state of the application When withdrawing only part of eCTD containing more than one application, provide "suspended" for the relevant Review to be withdrawn in the revision immediately after that. In any other case, provide "active".
subject1		[0..1]		This element stores the *manufacturedProduct* element. For details of the *manufacturedProduct* element, refer to 7.4.11 of this document.
holder		[0..1]		This element stores the *applicant* element. For details of the *applicant* element, refer to 7.4.13 of this document.
subject2		[0..*]		This element stores the *productCategory* element. For details of the *productCategory* element, refer to 7.4.14 of this document.

Submission rules for elements and attributes		➢ When submitting the first version, all of the above-mentioned elements and attributes are required.
		➢ At the time of revision, if the ***statusCode@code*** attribute value is "active", all of the above-mentioned elements and attributes are required.
		➢ At the time of revision, if the ***stautsCode@code*** attribute value is "suspended", the Submission Unit containing any of the following will be rejected.
		  • ***subject1***
		  • ***holder***
		  • ***subject2***
		➢ The ***subject2*** element must provide for each application category.

Business Rules	**General**	➢ The Submission Unit, which falls under any of the following, will be rejected.
		  • The ***statusCode@code*** attribute value of the ***review*** element provided for the first time throughout the life cycle including submission of the first version is not "active".
		  • The ***review.statusCode@code*** attribute value is neither "active" nor "suspended".
		  • As a result of providing the ***statusCode@code*** attribute value of the review element with "suspended", the ***review*** element with the ***statusCode@code*** attribute value of "active" no longer exists in the application.
		➢ The ***id@root*** attribute value shall be a UUID that can uniquely identify this Review.
		➢ Do not include the ***review*** element in which the approval application has not been withdrawn at the time of revision or the content has not been changed.
		➢ Do not provide the ***review*** element with the same ***id@root*** attribute value as a review that has become invalid due to withdrawal of the application. If you want to reactivate the Review that was once invalidated by withdrawing an application, resubmit it as the new Review.
		➢

	a)	There are no business rules that should be followed in addition to General above in particular.
	b)	➢ b) must not contain the ***review*** element. Also, if the ***review*** element is included in b), the Submission Unit will be rejected.
	c)	➢ There are no business rules that should be followed in addition to General above in particular.

7.4.11 manufacturedProduct

The ***manufacturedProduct*** element provides the product information. 1 ***manufacturedProduct*** element is provided for each ***review*** element. The ***manufacturedProduct*** element has a ***manufacturedProduct*** element of the same name under it. In this document, the former is called the ***manufacturedProduct*** element, and the latter is called the ***manufacturedProduct.manufacturedProduct*** element.

7.4.11.1 Place of description on XML

The ***manufacturedProduct*** element is described in the following place on the eCTD v4.0 XML message.
- *controlActProcess* >> subject >> *submissionUnit* >> *componentOf1* >> *submission* >> *subject2* >> *review* >> *subject1* >>*manufacturedProduct*

7.4.11.2 XML snippet

An XML snippet of the ***manufacturedProduct*** element is shown below.

```
<subject1>
    <manufacturedProduct>
```

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```
        <manufacturedProduct>
            <name>
                <part value="Seiyakukyol tables 10mg"/>
            </name>
            <ingredient classCode="INGR">
…[Partially omitted]…
            </ingredient>
        </manufacturedProduct>
    </manufacturedProduct>
</subject1>
```

7.4.11.3   XML elements and attributes

The *manufacturedProduct* element and the elements under it as well as their attributes are as follows.

Element	Attribute	Cardinality	Value(s) Allowed *Example of value*	Description
manufacturedProduct		[1..1]		This element stores the product information.
manufacturedProduct		[1..1]		This element stores the product information.
name		[1..1]		This element stores the brand name.
part		[1..1]		This element stores the brand name.
	value	[1..1]	Text *Example: value="Seiyakukyol tablets 10mg"*	The brand name of the drug product.
ingredient		[1..*]		This element stores the *ingredientSubstance* element. For details of the *ingredientSubstance* element, refer to 7.4.12 of this document.
	classCode	[1..1]	Fixed *classCode="INGR"*	This attribute is a structural attribute required to use the *ingredient* element.
Submission rules for elements and attributes		➤ An *ingredient* element must be provided for each active ingredient contained in the relevant product.		
Business Rules	**General**	➤ The *part@value* attribute value must match the brand name described in the application form. ➤ The Submission Unit, which falls under the following, will be rejected. • The *part@value* attribute value is 241 characters or more.		
	a)	There are no business rules that should be followed in addition to General above in particular.		
	b)	➤ b) must not contain the *manufacturedProduct* element. Also, if the *manufacturedProduct* element is included in b), the Submission Unit will be rejected.		

* This English version of the Japanese Notification is provided for reference purposes only. In the event of any inconsistency between the Japanese original and the English translation, the former shall prevail.

Element	Attribute	Cardinality	Value(s) Allowed *Example of value*	Description
		c)	There are no business rules that should be followed in addition to General above in particular.	

7.4.12   ingredientSubstance

The *ingredientSubstance* element provides the name of the active ingredient. 1 *ingredientSubstance* element is provided for each *ingredient* element.

7.4.12.1   Place of description on XML

The *ingredientSubstance* element is described in the following place on the eCTD v4.0 XML message.
- *controlActProcess >> subject >> submissionUnit >> componentOf1 >> submission >> subject2 >> review >> subject1 >> manufacturedProduct >>manufacturedProduct >>ingredient >>ingredientSubstance*

7.4.12.2   XML snippet

An XML snippet of the *ingredientSubstance* element is shown below.

```
<ingredient classCode="INGR">
    <ingredientSubstance>
        <name>
            <part value="E I hydrochloride" code="jp_jan" codeSystem= "
2.16.840.1.113883.3.989.5.1.3.3.1.7.1"/>
        </name>
    </ingredientSubstance>
</ingredient>
```

7.4.12.3   XML elements and attributes

The *ingredientSubstance* element and the elements under it as well as their attributes are as follows.

Element	Attribute	Cardinality	Value(s) Allowed *Example of value*	Description
ingredientSubstance		[1..1]		This element stores the name of the active ingredient.
name		[1..1]		This element stores the name of the active ingredient.
part		[1..1]		This element stores the name of the active ingredient.
	value	[1..1]	Text *Example: value="E I hydrochloride"*	The name of the active ingredient.
	code	[1..1]	Text *Example: code="jp_jan"*	The code indicating the type of the name of the active ingredient To be selected from the "JP Substance Name Type" code list of JP CV

			codeSystem	[1..1]	Valid OID *Example: code="2.16.840.1.1 13883.3.989.5.1.3.3 .1.7.1"*	OID of the "JP Substance Name Type" code list
Submission rules for elements and attributes			There are no submission rules that should be followed in addition to the contents of the above-mentioned "Cardinality", "Value(s) Allowed" and "Description".			
Business Rules	**General**		➢ In principle, the *part@value* attribute value must match the non-proprietary name stated in the application. ➢ The Submission Unit, which falls under the following, will be rejected. • The *part@value* attribute valueis 241 characters of more.			
	a)		There are no business rules that should be followed in addition to General above in particular.			
	b)		➢ b) must not contain the *ingredientSubstance* element. Also, if the *ingredientSubstance* element is included in b), the Submission Unit will be rejected.			
	c)		There are no business rules that should be followed in addition to General above in particular.			

7.4.13 applicant

The *applicant* element provides the applicant information. 1 *applicant* element is provided for each *review* element.

7.4.13.1 Place of description on XML

The *applicant* element is described in the following place on the eCTD v4.0 XML message.
  • *controlActProcess* >> subject >> *submissionUnit* >> *componentOf1* >> *submission* >> *subject2* >> *review* >> *holder* >> *applicant*

7.4.13.2 XML snippet

An XML snippet of the *applicant* element is shown below.

```
<holder>
    <applicant>
        <sponsorOrganization>
            <name>
                <part value="PMDA Pharmaceutical Co., Ltd."/>
            </name>
        </sponsorOrganization>
    </applicant>
</holder>
```

7.4.13.3 XML elements and attributes

The *applicant* element and the elements under it as well as their attributes are as follows.

Element	Attribute	Cardinality	Value(s) Allowed *Example of value*	Description
applicant		[1..1]		This element stores the applicant name.

Element	Attribute	Cardinality	Value(s) Allowed *Example of value*	Description
sponsorOrganization		[1..1]		This element stores the applicant name.
name		[1..1]		This element stores the applicant name.
part		[1..1]		This element stores the applicant name.
	value	[1..1]	Text *Example: value="PMDA Pharmaceutical Co., Ltd."*	The name of the applicant of the relevant application.
Submission rules for elements and attributes		There are no submission rules that should be followed in addition to the contents of the above-mentioned "Cardinality", "Value(s) Allowed" and "Description".		
Business Rules	**General**	➢ The *part@value* attribute value must match the applicant name stated in the application. ➢ The Submission Unit, which falls under the following, will be rejected. • The *part@value* attribute valueis 241 characters or more.		
	a)	There are no business rules that should be followed in addition to General above in particular.		
	b)	➢ b) must not contain the *applicant* element. Also, if the *applicant* element is included in b), the Submission Unit will be rejected.		
	c)	There are no business rules that should be followed in addition to General above in particular.		

7.4.14   productCategory

The *productCategory* element provides the application category. 1 or more *subject2* (element)s are provided for each *review* element, and the *productCategory* element is provided for each *subject2* element. As 1 *productCategory* element always has 1 application category, in case of an application with more than one application category, the same number of *subject2* elements as the number of application categories is provided.

7.4.14.1   Place of description on XML

The *productCategory* element is described in the following place on the eCTD v4.0 XML message.
• *controlActProcess >> subject >> submissionUnit >> componentOf1 >> submission >> subject2 >> review >> subject2 >> productCategory*

7.4.14.2   XML snippet

An XML snippet of the *productCategory* element is shown below.
```
<subject2>
    <productCategory>
        <code code="jp_1_1" codeSystem="2.16.840.1.113883.3.989.5.1.3.3.1.6.1"/>
    </productCategory>
</subject2>
```

7.4.14.3 XML elements and attributes

The *productCategory* element and the elements under it as well as their attributes are as follows.

Element	Attribute	Cardinality	Value(s) Allowed *Example of value*	Description
productCategory		[1..1]		This element stores the application category.
code		[1..1]		This element stores the application category.
	code	[1..1]	Text *Example: code="jp_1_1"*	The code indicating the application category. Select the application category described in the marketing application form from the "JP Product Category" code list of JP CV.
	codeSystem	[1..1]	Valid OID *Example: codeSystem="2.16. 840.1.113883.3.989. 5.1.3.3.1.6.1"*	OID of the "JP Product Category" code list.
Submission rules for elements and attributes		There are no submission rules that should be followed in addition to the contents of the above-mentioned "Cardinality", "Value(s) Allowed" and "Description".		
Business Rules	**General**	➤ The application category indicated by the *code@code* attribute value must much the application category described in the application.		
	a)	There are no business rules that should be followed in addition to General above in particular.		
	b)	➤ b) must not contain the *productCategory* element. Also, if the *productCategory* element is included in b), the Submission Unit will be rejected.		
	c)	There are no business rules that should be followed in addition to General above in particular.		

7.4.15 application

The Application is provided by the *application* element and provides the definition of the information provided by the relevant application and the information related to the entity of the document. The one *submission* element always contains the one *application* element.

7.4.15.1 Place of description on XML

The *application* element is described in the following place on the eCTD v4.0 XML message.
- *controlActProcess >> subject >> submissionUnit >> componentOf1 >> submission >> componentOf >> application*

7.4.15.2 XML snippet

An XML snippet of the *application* element is shown below.

```
<componentOf>
   <application>
      <id>
         <item root="492462f7-81bf-46e0-9b59-b677a86c88a4" extension="sender-specified
value"/>
```

```
            </id>
            <code code="jp_ nda" codeSystem="2.16.840.1.113883.3.989.5.1.3.3.1.8.1"/>
            <reference>
            …[Partially omitted]…
            </reference>
            <component>
            …[Partially omitted]…
            </component>
            <referencedBy>
            …[Partially omitted]…
            </referencedBy>
        </application>
    </componentOf>
```

7.4.15.3   XML elements and attributes

The *application* element and the elements under it as well as their attributes are as follows.

Element	Attribute	Cardinality	Value(s) Allowed *Example of value*	Description
application		[1..1]		This element stores the information on the Application provided in association with the relevant SubmissionUnit.
Id		[1..1]		This element stores the identifier of the relevant eCTD application.
item		[1..1]		This element stores the identifier of the relevant eCTD application.
	root	[1..1]	Valid UUID *Example: root="492462f7-81bf-46e0-9b59-b677a86c88a4"*	UUID of this Application A number is issued by the applicant according to the algorithm described in ICH IG.
	extension	[0..1]	Text *Example: extension="sender-specified value"*	Any value assigned for the purpose of the applicant managing the application
code		[1..1]		This element stores the type of the relevant eCTD application.
	code	[1..1]	Text *Example: code="jp_ nda"*	The code indicating the type of the relevant eCTD application Select the code value from the "JP Application" code list of JP CV.

Element	Attribute	Cardinality	Value(s) Allowed *Example of value*	Description
	codeSystem	[1..1]	Valid OID *Example: codeSystem="2.16.840.1.113883.3.989.5.1.3.3.1.8.1"*	OID of the "JP Application" code list
reference		[0..*]		This element stores the *applicationReference* element. For details of the *applicationReference* element, refer to 7.4.16 of this document.
component		[0..*]		This element stores the *document* element. For details of the *document* element, refer to 7.4.17 of this document.
referencedBy		[0..*]		This element stores the *keywordDefinition* element. For details of the *keywordDefinition* element, refer to 7.4.18 of this document.
Submission rules for elements and attributes	➢ If there are other applications related to the relevant application (hereinafter referred to as the "related applications"), provide a *reference* element for each related application. Also, provide all the related applications for each Submission Unit. For details of the related application, refer to 7.4.16 of this document. ➢ If there are new Documents to be provided through the relevant Submission Unit, provide a *component* element for each Document. For details of the Document, refer to 7.4.17 of this document. ➢ If new Keyword Definitions to be used for the relevant application are provided, provide a *referencedBy* element for each Keyword Definition. For details of the Keyword Definition, refer to 7.4.18 of this document.			

* This English version of the Japanese Notification is provided for reference purposes only. In the event of any inconsistency between the Japanese original and the English translation, the former shall prevail.

Element	Attribute	Cardinality	Value(s) Allowed *Example of value*	Description
Business Rules	**General**	➢ Provide the same value for the following attribute throughout the application regardless of change of the information under *application* in principle. If it is necessary to change these values, consult the regulatory authority in advance. • *id.item@root* • *code@code* • *code@codeSystem* * * The version number included at the end of the OID indicated by the *code@codeSystem* attribute does not have to match. ➢ The *id@root* attribute value shall be a UUID that can uniquely identify this Application. ➢ The *id.item@extension* attribute is intended to be used by the applicant. This attribute may be included in the eCTD v4.0 XML message submitted to the regulatory authority, but the regulatory authority does not use this attribute value. In addition, the type of the value of this attribute is not limited to the character types specified in 2.5 [The character types that can be used as a text type] in this document. ➢ The Submission Unit, which falls under the following, will be rejected. • The *id.item@extension* attribute value is 1001 characters or more.		
	a)	• There are no business rules that should be followed in addition to General above in particular.		
	b)	➢ There are no business rules that should be followed in addition to General above in particular.		
	c)	There are no business rules that should be followed in addition to General above in particular.		

7.4.16 applicationReference

The *applicationReference* element provides the information on the related application. For example, it can be used when referring to the application for the already approved product item at the time of partial change approval application. In this case, the related application must have been made with eCTD v3.2.2 or v4.0 as the original. You may refer to the eCTD reception number of the application using eCTD v3.2.2 from the *applicationReference* element using eCTD v4.0. If there is no related eCTD application, it is not necessary to provide the *applicationReference* element, but if provided, 1 *application* element can have 1 or more *applicationReference* elements. If there are multiple related eCTD applications, describe the *applicationReference* element for each related eCTD application.

7.4.16.1 Place of description on XML

The *applicationReference* element is described in the following place on the eCTD v4.0 XML message.
* *controlActProcess >> subject >> submissionUnit >> componentOf1 >> submission >> componentOf >> application >> reference >> applicationReference*

7.4.16.2 XML snippet

An XML snippet of the *applicationReference* element is shown below.
```
<reference>
    <applicationReference>
        <id root="20160103001"/>
        <reasonCode>
            <item code="jp_pca" codeSystem="2.16.840.1.113883.3.989.5.1.3.3.1.9.1"/>
        </reasonCode>
```

Provisional Translation (as of March 2025) *

```xml
          </applicationReference>
    <reference>
```

7.4.16.3   XML elements and attributes

The *applicationReference* element and the elements under it as well as their attributes are as follows.

Element	Attribute	Cardinality	Value(s) Allowed *Example of value*	Description
applicationReference		[1..1]		This element stores the related application information.
id		[1..1]		This element stores the identifier of the related application.
	root	[1..1]	Single-byte alphanumeric characters *Example: root="20160103001"*	eCTD reception number of the related application
reasonCode		[1..1]		This element stores the type of relationship.
item		[1..*]		This element stores the type of relationship.
	code	[1..1]	Text *Example: code="jp_pca"*	The code indicating the type of relationship with the related application indicated by *applicationReference.id@root*. Select the code value from the "JP Application Reference Reason" code list of JP CV.
	codeSystem	[1..1]	Valid OID *Example: codeSystem="2.16. 840.1.113883.3.989. 5.1.3.3.1.9.1"*	OID of the "JP Application Reference Reason" code list
Submission rules for elements and attributes	➢ If 1 related application has more than one type, provide a *reasonCode.item* element for each related type under 1 *applicationReference* element.			

Element	Attribute	Cardinality	Value(s) Allowed *Example of value*	Description
Business Rules	**General**	➢ Provide all the related applications as of the time of submission of each Submission Unit. For example, if 2 related applications were submitted when the first version was submitted and the related applications were not described in the subsequent submission, it is interpreted as having lost the relevance after submitting the first version. ➢ The Submission Unit, which falls under any of the following, will be rejected. • The eCTD reception number indicated by the *id@root* attribute value is provided in the relevant Submission Unit. • The application having the eCTD reception number indicated by the *id@root* attribute does not exist in the database of the regulatory authority. • The application having the eCTD reception number indicated by the *id@root* attribute was withdrawn in the past. • Multiple *applicationReference* elements having the same *id@root* attribute value are contained in 1 Submission Unit and provided. • Multiple *reasonCode.item* elements with the same combination of *reasonCode.item@code* and *reasonCode.item@codeSystem** are provided under 1 *applicationReference* element. * However, even if the version number included at the end of the OID indicated by the *reasonCode.item@codeSystem* attribute does not match, if other information matches, the combination of *reasonCode.item@code* and *reasonCode.item@codeSystem* will regarded as identical. • The eCTD reception number of an unapproved application is provided for the *id@root* attribute value of the *applicationReference* element indicating the already approved application to be submitted at the time of partial change approval application as the related type.			
	a)	There are no business rules that should be followed in addition to General above in particular.		
	b)	There are no business rules that should be followed in addition to General above in particular.		
	c)	There are no business rules that should be followed in addition to General above in particular.		

7.4.17   document

The Document provides the information on the file to be submitted. The Document is provided by the *document* element. The applicant can provide 0 to multiple *document* elements through 1 Submission Unit. 1 *component* element is provided for each file to be submitted, and 1 *document* element is provided for each *component* element.

7.4.17.1   Place of description on XML

For the place to describe the *document* element, refer to "9.2.15 Document", etc., in the ICH IG.

7.4.17.2   XML snippet

An XML snippet of the *document* element is shown below.

```
<component>
    <document>
        <id root="8505a8b2-7035-47cf-81ec-e8176e1d87be"/>
        <title value="General information"/>
        <text integrityCheckAlgorithm="SHA256">
```

```
                <reference value="m3/32-prod/manuf-process-and-controls.pdf"/>
                <integrityCheck>c0d5623550c997a70b62717d95fca1cada201754d1ed9fbbbbfa97bfd64c
    8ea4</integrityCheck>
            </text>
        </document>
    </component>
```

7.4.17.3 XML elements and attributes

The *document* element and the elements under it as well as their attributes are as follows.

Element	Attribute	Cardinality	Value(s) Allowed *Example of value*	Description
document		[1..1]		This element stores the information on the file to be submitted to the regulatory authority.
id		[1..1]		Follow the description of ICH IG.
	root	[1..1]	Valid UUID *Example: root="8505a8b2-7035-47cf-81ec-e8176e1d87be"*	Follow the description of ICH IG.
title		[1..1]		Follow the description of ICH IG.
	value	[1..1]	Text *Example: value="General information"*	Follow the description of ICH IG.
	updateMode	[0..1]	Fixed *updateMode="R"*	When updating the title of the Document, specify "R".
text		[0..1]		Follow the description of ICH IG.
	integrityCheckAlgorithm	[1..1]	Fixed *integrityCheckAlgorithm="SHA256"*	Follow the description of ICH IG.

Element	Attribute	Cardinality	Value(s) Allowed *Example of value*	Description
	charset	[0..1]	Text *Example:* *charset="jp_utf8"*	This indicates the character code of the Japanese data included in the electronic study data in the Document that references the electronic study data. If the electronic study data to be referenced is in SAS XPORT format (.xpt), select the appropriate code from JP CV "JP Japanese Character Code".
reference		[1..1]		Follow the description of ICH IG.
	value	[1..1]	Text *Example:* *value="../1/m3/32-bodydata/32s-drugsub/32s1-geninfo.pdf"*	Specify the location of the file in the relative path format from submissionunit.xml which includes this attribute.
integrityCheck		[1..1]	Single-byte alphanumeric characters *Example:* *<integrityCheck>c0d56235 50c997a70b62717d95fca1c ada201754d1ed9fbbbbfa97 bfd64c 8ea4<integrityCheck/>*	Follow the description of ICH IG.
thumbnail		[0..1]		Follow the description of ICH IG.
		[1..1]	*Text* *Example:* *value="26145c7a-3dc7-404d-91c1-6e0e5c71f8f6"*	Follow the description of ICH IG.
description		[0..1]		Follow the description of ICH IG.
	value	[1..1]	Text *Example: value="* Dataset for PK analysis (ADaM format)*"*	This is an explanation of the contents of the electronic study data to be referenced in the case of the Document that references the electronic study data in the clinical pharmacology area.

Element		Attribute	Cardinality	Value(s) Allowed *Example of value*	Description

Submission rules for elements and attributes		➢ The *text* element is required except when updating the Document title.
		➢ The *title@updateMode* attribute is required when updating the *title@value* attribute value of a submitted Document.
		➢ The Submission Units containing text elements will be rejected when the *title@updateMode* attribute value is provided.
		➢ The following attributes are described in ICH IG, but even though a Submission Unit is submitted with these included, they are not considered to have been provided for the regulatory authority.
		  • *text@language*
		  • *text@mediaType*
		  • *text@updateMode*			

Business Rules	**General**	➢ In addition to the business rules provided in ICH IG, the following will be applied.
		  • The Submission Unit, which falls under any of the following, will be rejected.
		    ✧ The *title@value* attribute value has 1001 characters or more.
		    ✧ The *description@value* attribute value has 101 characters or more.
		    ✧ The *thumbnail@value* attribute value has 1001 characters or more.
		    ✧ The *title@updateMode* attribute value is provided on the docment element that is provided for the first time through its lifecycle, including initial submission.
		    ✧ The *title@updateMode* attribute value is provided, but the *title@value* attribute value is not updated.
		    ✧ Although the *title@updateMode* attribute value is not provided, the *id@root* attribute value is the same as the *id@root* attribute value of the Document submitted in the past.
		    ✧ A *document* element not referred to from the Context of Use of the same Submission Unit is provided.
		    ✧ The file corresponding to the location indicated by the *reference@value* attribute value does not exist.
		    ✧ The file path that includes a first layer folder name that does not match the eCTD reception number of the relevant eCTD is specified in the *reference@value* attribute value.
		    ✧ The checksum indicated by the contents of the *integrityCheck* element is different from the checksum of the actual file.
		    ✧ The *text@charset* attribute is not provided under the document element that references SAS XPORT format (.xpt) files.
		    ✧ The *text.description* element is not provided under the document element referenced from the Context of Use with JP Analysis Type Keyword indicating other than "non clinical pharmacology data" (Non-CP).
		➢ The regulatory authority does not use the *document.text.thumbnail@value* attribute value in principle. In addition, the type of the value of this attribute is not limited to the character types specified in 2.5 [The character types that can be used as a text type] in this document.
		➢ Note that even if there are multiple files with the same checksum, the UUIDs of the Documents referencing each file are different.			

	a)	There are no business rules that should be followed in addition to General above in particular.			

Element		Attribute	Cardinality	Value(s) Allowed *Example of value*	Description
	b)			➤ The Submission Unit, which falls under the following, will be rejected. • The place indicated by the ***reference@value*** attribute value is not the place to store the electronic study data.	
	c)			➤ The Submission Unit, which falls under the following, will be rejected. • The place indicated by the ***reference@value*** attribute value is the place to store the electronic study data.	

7.4.18   keywordDefinition

Keyword Definition provides the definition of the keyword. The ***contextOfUse*** elements can have a keyword under them, but the ***keyword*** element only specifies the code, and it does not indicate the contents indicated by that code. Each code is defined in (one of) the following 2 methods.

 (1)   The code and the contents are defined by ICH or the regulatory authority.
 (2)   The applicant defines the code and the contents.

When assigning the Keyword falling under (1) above to the Context of Use, the corresponding Keyword Definition must not be provided. When assigning the Keyword falling under (2) above to the Context of Use, the corresponding Keyword Definition needs to be provided for the regulatory authority.

7.4.18.1   Place of description on XML

For the place to describe the ***keywordDefinition*** element, refer to "9.2.18 Keyword Definition", etc., in the ICH IG.

7.4.18.2   XML snippet

An XML snippet of the ***keywordDefinition*** element is shown below.

```xml
<referencedBy>
    <keywordDefinition>
        <code code="ich_keyword_type_3" codeSystem="2.16.840.1.113883.3.989.2.2.1.5.2"/>
        <statusCode code="active"/>
        <value>
            <item code="MANU001" codeSystem="My list 001">
                <displayName value="Big Manufacturer"/>
            </item>
        </value>
    </keywordDefinition>
</referencedBy>
```

7.4.18.3   XML elements and attributes

The ***keywordDefinition*** element and the elements under it as well as their attributes are as follows.

Element		Attribute	Cardinality	Value(s) Allowed *Example of value*	Description
keywordDefinition			[1..1]		This element stores the definition of the keyword.
	code		[1..1]		Follow the description of ICH IG.

Element	Attribute	Cardinality	Value(s) Allowed _Example of value_	Description
	code	[1..1]	Text _Example: code="ich_keyword _type_1"_	Follow the description of ICH IG. Select the corresponding code from "ICH Keyword Definition Type" of ICH CV or "JP Keyword Definition Type" of JP CV.
	codeSystem	[1..1]	Valid OID _Example: codeSystem="2.16. 840.1.113883.3.989. 2.2.1.5.2"_	Follow the description of ICH IG. Provide the OID of "ICH Keyword Definition Type" of ICH CV or OID of "JP Keyword Definition Type" of JP CV.
statusCode		[1..1]		Follow the description of ICH IG.
	code	[1..1]	Fixed _code="active"_	Follow the description of ICH IG.
value		[1..1]		Follow the description of ICH IG.
item		[1..1]		Follow the description of ICH IG.
	code	[1..1]	Text _Example: code="MANU001"_	Follow the description of ICH IG. Any code value specified by the applicant
	codeSystem	[1..1]	Text _Example: codeSystem="My list 001"_	Follow the description of ICH IG. The identifier of the code list, which is specified by the applicant arbitrarily.
displayName		[1..1]		Follow the description of ICH IG.
	value	[1..1]	Text _Example: value="Big Manufacturer"_	Follow the description of ICH IG. The display name of the keyword, which is specified by the applicant arbitrarily.
	updateMode	[0..1]	Fixed _updateMode="R"_	Follow the description of ICH IG. When updating the display name of the Keyword, specify "R".
Submission rules for elements and attributes	➢ When updating the **_displayName@value_** attribute value of the Keyword Definition already submitted, the following is required. • **_displayName@updateMode_**			

Element	Attribute	Cardinality	Value(s) Allowed *Example of value*	Description
Business Rules	**General**	• In addition to the business rules provided in ICH IG, the following will be applied. • The Submission Unit, which falls under any of the following, will be rejected. ✧ The ***value.item@code*** attribute value has 129 characters or more. ✧ The ***value.item@codeSystem*** attribute value has 257 characters or more. ✧ The ***displayName@value*** attribute value has 1001 characters or more. ✧ The displayName@updateMode attribute value is provided under the keywordDefinition element that is provided for the first time throughout the life cycle including the first version submission. ✧ At the time of revision, the ***displayName@updateMode*** attribute value is provided, but the ***displayName@value*** attribute value is not updated. ✧ The combination of the ***value.item@code*** and ***value.item@codeSsytem*** attribute values is the same as (that of) the Keyword Definition submitted in the past in the same application, but the ***displayName@updateMode*** attribute is not provided.			
	a)	There are no business rules that should be followed in addition to General above in particular.			
	b)	➢ The Keyword Definition, which defines the Keyword to be used in b), shall be provided in b). ➢ The Submission Unit with the ***displayName@updateMode*** attribute contained will be rejected.			
	c)	➢ The Keyword Definition to define the Keyword to be used in c) may be submitted in b) in advance. ➢ When the Keyword to be used in b) is also to be used in c), provide the Keyword Definition supporting b) only. ➢ The Submission Unit with the ***displayName@updateMode*** attribute contained will be rejected.			

7.4.19 categoryEvent

The ***categoryEvent*** element indicates the timing of submitting the relevant Submission Unit to the regulatory authority and the type for first version submission. The types for first version submission refer to a), b) and c) indicated in 3.3.1 of this document. 1 Submission Unit has 1 ***categoryEvent*** element.

7.4.19.1 Place of description on XML

The ***categoryEvent*** element is described in the following place on the eCTD v4.0 XML message.
• *controlActProcess >> subject >> submissionUnit >> componentOf2 >> categoryEvent*

7.4.19.2 XML snippet

An XML snippet of the ***categoryEvent*** element is shown below.
```
<componentOf2>
    <categoryEvent>
        <code code="jp_initial" codeSystem="2.16.840.1.113883.3.989.5.1.3.3.1.2.1"/>
        <component>
            <categoryEvent>
                <code code="jp_initial_a" codeSystem="2.16.840.1.113883.3.989.5.1.3.3.1.3.1"/>
            </categoryEvent>
```

```
            </component>
          </categoryEvent>
        </componentOf2>
```

7.4.19.3　XML elements and attributes

The *categoryEvent* element and the elements under it as well as their attributes are as follows.

Element	Attribute	Cardinality	Value(s) Allowed *Example of value*	Description
categoryEvent		[1..1]		This element stores the timing of submitting the relevant Submission Unit and the type for first version submission.
code		[1..1]		This element stores the timing of submitting the relevant Submission Unit.
	code	[1..1]	Text *Example:* *code="jp_initial"*	The code indicating at what timing of the review the relevant Submission Unit was submitted Select the code value from the "JP Category Event" code list of JP CV.
	codeSystem	[1..1]	Valid OID *Example:* *codeSystem="2.16.84 0.1.113883.3.989.5.1. 3.3.1.2.1"*	OID of the "JP Category Event" code list
component		[0..1]		This element stores the positioning of the relevant Submission Unit when submitting the first version.
categoryEvent		[1..1]		This element stores the positioning of the relevant Submission Unit when submitting the first version.
code		[1..1]		This element stores the positioning of the relevant Submission Unit when submitting the first version.
	code	[1..1]	Text *Example:* *code="jp_initial_a"*	The code indicating the type of the relevant Submission Unit for first version submission Select the code value from the "JP Initial Submission Type" code list of JP CV.

Element			Attribute	Cardinality	Value(s) Allowed *Example of value*	Description
			codeSystem	[1..1]	Valid OID *Example:* *codeSystem="2.16.84 0.1.113883.3.989.5.1. 3.3.1.3.1"*	OID of the "JP Initial Submission Type" code list
Submission rules for elements and attributes					➤ When submitting the first version, the *component* element is required for any of a), b) and c) indicated in 3.3.1 of this document. ➤ At the time of revision, the *component* element must not be provided.	
Business Rules	General				➤ The *componentOf2.categoryEvent.code@code* attribute value indicating "first version submission", "for expert discussion "or" for the subcommittee" is provided only once throughout the life cycle in principle. If it is necessary to provide any value for multiple times in 1 eCTD application, consult the regulatory authority in advance. However, for submissions by method 2 shown in 3.3.1 of this document, the *componentOf2.categoryEvent.code@code* attribute value indicating "first version submission" is provided twice throughout the lifecycle.	
	a)				➤ If the Submission Unit to be submitted when submitting the first version is a), the *componentOf2.categoryEvent.code@code* attribute value must be the code indicating a).	
	b)				➤ If the Submission Unit to be submitted is b), the *componentOf2.categoryEvent.code@code* attribute value must be the code indicating b).	
	c)				➤ If the Submission Unit to be submitted is c), the *componentOf2.categoryEvent.code@code* attribute value must be the code indicating c).	

8. Reuse

8.1 Document Reuse

In an application using eCTD v4.0, you may reuse the Document submitted in the past. For how to reuse the Document, refer to "9.2.17.1 Document Reuse", etc., in the ICH IG. The Document may be reused at the applicant's discretion in principle. When reusing the Document, either 1) or 2) must be satisfied in addition to the conditions described in ICH IG.

1) Both the Submission Unit defining the Document to be reused and the Submission Unit that contains the *documentReference* element that references the Document to be reused belong to the same application.
2) All of the following conditions shall be satisfied:
   - The application defining the Document to be reused has already been approved.
   - Both the application defining the Document to be reused and the application containing the *documentReference* element referencing the Document to be reused are submitted as original in accordance with the eCTD v4.0 specifications.
   - The application dossier defining the Document to be reused is subject to document retention by the regulatory authority and is within the prescribed retention period.

8.2 File Reuse

In an application using eCTD v4.0, you may reuse the file submitted in the past. For how to reuse the file, refer to "9.2.17.3 File Reuse", etc., in the ICH IG. The file may be reused at the applicant's discretion in principle. To reuse a file, in addition to (satisfying) the conditions provided in ICH IG, the Submission Unit, in which the file to be reused was submitted, and the submission unit containing the *document* element, which refers to the file to be reused, must belong to the same application. Therefore, do not specify a path that includes the first layer folder name (eCTD reception number) in the *reference@value* attribute value of the document element.

9. Handling of the group title Keyword

If the group title Keyword is used for the eCTD v4.0 XML message submitted to the regulatory authority, it will be displayed as the node with the *displayName@value* attribute value of the relevant group title as a label (hereinafter referred to as the "group title node") on the CTD tree display screen in the review environment. The group title node will be displayed at the level between the CTD heading of the Context of Use, to which the relevant group title is assigned, and the title of the Document referred to by the relevant Context of Use.

⊞ CTD heading

⊞ CTD heading

⊟ CTD heading

   ⊟ group Title node

      [Document title](#)

      [Document title](#)

      [Document title](#)

Note that the group title is also one of the keywords that make up the context group. That is, even in case of a Context of Use to which the same group title Keyword is assigned, if another keyword is different, the context group will be different; therefore, multiple group title nodes of the same value will be displayed.

10. Life cycle management

10.1 Overview

Life cycle management for eCTD in Japan manages addition, change, etc. of application dossier in an individual application but does not collectively manage the new approval application, partial change approval application, etc. for one product. In an individual application, the submission sequence number folder ("1", "2"…) is placed under the eCTD reception number folder, and the application dossier are stored in the folders for Module 1 through Module 5 of the CTD to be placed under that ("m1", "m2", "m3", "m4" and"m5"). The purpose of life cycle management is to manage which file is valid as application dossier for each file according to its attribute information when adding, changing or deleting any file that constitutes the application dossier.

In life cycle management of eCTD v4.0, the differential submission method is adopted for the eCTD v4.0 XML messages and files in principle. In an eCTD submission (package) after submitting the first version, the applicant shall submit the information on new submission or change to the existing information only. However, keep in mind that there is a case where unchanged information must also be submitted each time in terms of the nature of the information or the specification of the standards. For details, refer to 10.3 of this document.

10.2 Requirements for submission of the first version of eCTD

10.2.1 Folder structure for submission of the first version

Create folder structure referring to 5 of this document.

10.2.2 File for first version submission

The following files must submit:
- eCTD v4.0 XML Message (submissionunit.xml)
- Checksum file (sha256.txt)
- Files to be submitted with the first version*
    - * In the case of submission by method 2 shown in 3.3.1 of this document, the files to be submitted for the first version should be submitted separately for type b) and c). For type b), only the electronic study data should be submitted, and for type c), only the data specified by the CTD notification should be submitted.

10.2.3 eCTD v4.0 XML message structure for first version submission

When submitting the first version, submit Type a) if submitted in the submission method 1 indicated in 3.3.1 of this document, and Types b) and c) if submitted in the method 2. This section shows the basic structure of the eCTD v4.0 XML message for the first version. For details of each element and attribute, refer to 7 of this document.

10.2.3.1 Submission of the first version using Method 1

This section shows an example of a description for submitting the first version using "Method 1" indicated in 3.3.1 of this document.

1) Example of description from the ***submissionUnit*** element to the ***categoryEvent*** element

```
<submissionUnit>
    <id root="A"/>
    <code code="B" codeSystem="C"/>

------- (For the Context of Use and Submission, refer to 2) and 3) of this section, respectively.)-------

    <componentOf2>
        <categoryEvent>
            <code code="D" codeSystem="E"/>
            <component>
                <categoryEvent>
                    <code code="F" codeSystem="G"/>
                </categoryEvent>
            </component>
        </categoryEvent>
    </componentOf2>
</submissionUnit>
```

A: UUID of this Submission Unit
B: The code indicating the type of this Submission Unit (Refer to "JP Submission Unit" of JP CV)
C: OID of the code list defining the code of this Submission Unit (above B:)
D: The code indicating at what timing in the review this Submission Unit was submitted (Refer to "JP Category Event" of JP CV)
E: OID of the code list defining the code of this Category Event (above D:)

F: The code indicating that this Submission Unit is a) indicated in 3.3.1 of this document (Refer to "JP Initial Submission Type" of JP CV)

G: OID of the code list defining the code of this Category Event (above F:)

2) Example of description of the **contextOfUse** element

```
<component>
    <priorityNumber value="H"/>
    <contextOfUse>
        <id root="I"/>
        <code code="J" codeSystem="K"/>
        <statusCode code="L"/>
        <derivedFrom>
            <documentReference>
                <id root="M"/>
            </documentReference>
        </derivedFrom>
        <referencedBy typeCode="N">
            <keyword>
                <code code="O" codeSystem="P"/>
            </keyword>
        </referencedBy>

------ (To provide more than one keyword, repeat referencedBy)-------

    </contextOfUse>
</component>

------ (To provide more than one Context of Use, repeat component)-------
```

H: The value to specify the display order if there are multiple context groups (Also describe it even if there are not more than one.)

I: UUID of this Context of Use

J: The code indicating the CTD heading to assign the Document specified by this Context of Use (Refer to "ICH Context of Use" of ICH CV or "JP Context of Use" of JP CV)

K: OID of the code list defining the code of this Context of Use (above J:)

L: Status of this Context of Use

M: The **id@root** attribute value of the Document referred to by this Context of Use

N: Structural attribute required to use the referencedBy element. The value must be "REFR".

O: Code of the keyword assigned to this Context of Use

P: OID of the code list defining the keyword assigned to this Context of Use or any value specified in Keyword Definition

3) Example of description of the **submission** element

```
<componentOf1>
    <sequenceNumber value="Q"/>
    <submission>
        <id>
            <item root="R" extension="S"/>
        </id>
        <code code="T" codeSystem="U"/>
        <subject2>
```

```xml
                    <review>
                        <id root="V"/>
                        <statusCode code="W"/>
                        <subject1>
                            <manufacturedProduct>
                                <manufacturedProduct>
                                    <name>
                                        <part value="X"/>
                                    </name>
                                    <ingredient classCode="Y">
                                        <ingredientSubstance>
                                            <name>
                                                <part value="Z" code="AA" codeSystem="AB" />
                                            </name>
                                        </ingredientSubstance>
                                    </ingredient>
```

------- (To provide more than one Ingredient Substance, repeat *ingredient*)-------

```xml
                                </manufacturedProduct>
                            </manufacturedProduct>
                        </subject1>
                        <holder>
                            <applicant>
                                <sponsorOrganization>
                                    <name>
                                        <part value="AC"/>
                                    </name>
                                </sponsorOrganization>
                            </applicant>
                        </holder>
                        <subject2>
                            <productCategory>
                                <code code="AD" codeSystem="AE"/>
                            </productCategory>
                        </subject2>
                    </review>
```

------- (To provide more than one Review, repeat *subject2*)-------

```xml
                    </subject2>
```

------- (For Application, refer to 4) below) -------

```xml
            </submission>
        </componentOf1>
```

Q: Submission sequence number of this Submission Unit ("1" for first version application)
R: UUID of the submission which this Submission Unit is associated with
S: eCTD reception number
T: The code indicating the positioning of this Submission (Example: Submission of the original, submission of references, etc.) (Refer to "JP Submission" of JP CV)

U: OID of the code list defining the code of this Submission (above T:)
V: UUID of this Review.
W: Status of this Review ("active" for first version submission)
X: Brand name
Y: Structural attribute required to use the ingredient element. The value must be "INGR".
Z: Active ingredient name
AA: The code indicating the type of active ingredient name (Refer to JP CV "JP Substance Name Type")
AB: OID of the code list that defines the Substance Name Type code (above AA:)
AC: Applicant name
AD: The code indicating the application category (Refer to JP CV "JP Product Category")
AE: OID of the code list defining the code of this Product Category (aboveAD:)

4)   Example of description of the *application* element

```
<componentOf>
    <application>
        <id>
            <item root="AF" extension="AG"/>
        </id>
        <code code="AH" codeSystem="AI"/>
        <reference>
            <applicationReference>
                <id root="AJ"/>
                <reasonCode>
                    <item code="AK" codeSystem="AL"/>
                </reasonCode>
            </applicationReference>
        </reference>

    ------- (To provide more than one Application Reference, repeat reference. As for the related
applications, include all the related application as of that point of time for each submission, not limited
to the first version or the revised version.)-------

    ------- (For document and keywordDefinition, refer to 5) and 6) of this section, respectively.)-------

    </application>
</componentOf>
```

AF: UUID of this Application
AG: Any value (specified) by the applicant
AH: The code indicating the type of this Application (marketing approval application, etc.) (Refer to JP CV "JP Application")
AI: OID of the code list defining the code of this Application (aboveAH:)
AJ: eCTD reception number of the application related to this Application (partial change approval application, etc.)
AK: The code indicating the type of the relationship of the related application indicated in AJ:above (Refer to JP CV "JP Application Reference Reason")
AL: OID of the code list defining the code of the type of relationship (aboveAK:)

5)   Example of description of the *document* element

```
<component>
    <document>
```

```
            <id root="AM"/>
            <text integrityCheckAlgorithm="AN ">
                <reference value="AO"/>
                <integrityCheck>AP</integrityCheck>
            </text>
        </document>
    </component>

------- (To provide more than one Document, repeat component.) --------
```

AM: UUID of this Document

AN: Calculation algorithm for the checksum of the file referred to by this Document. The value must be "sha256".

AO: The path of the file referred to by this Document. The path must be a relative path based on submissionunit.xml.

AP: The checksum of the file referred to by this Document. The value must be in the sha256 format.

6)　Example of description of the *keywordDefinition* element

```
<referencedBy>
    <keywordDefinition>
        <code code="AQ" codeSystem=AR"/>
        <statusCode cd="AS"/>
        <value>
            <item code="AT" codeSystem="AU">
                <displayName value="AV"/>
            </item>
        </value>
    </keywordDefinition>
</referencedBy>

------- (To provide more than one keywordDefinition, repeat referencedBy.)-------
```

AQ: The code indicating the type of the Keyword defined by this Keyword Definition (Example: indication, product item name, manufacturer, etc.) (Refer to "ICH Keyword Definition Type" of ICH CV or "JP Keyword Definition Type" of JP CV)

AR: OID of the code list defining the code indicating the type of the Keyword defined by this Keyword Definition (aboveAQ:)

AS: Status of this Keyword Definition The value must be "active".

AT: Any code (specified) by the applicant, which indicates the contents of the Keyword defined by this Keyword Definition (name of the indication, name of the drug product, etc.)

AU: The identifier of the code list defining the code arbitrarily specified by the applicant, which indicates the contents of the Keyword defined by this Keyword Definition (aboveAT:) As the relevant code list shall be possessed by the applicant, any format will do as long as the information can be identified (Example: OID, applicant's arbitrary text).

AV: The displayed characters corresponding to the code arbitrarily specified by the applicant, which indicates the contents of the Keyword defined by this Keyword Definition

10.2.3.2　Submission of the first version using Method 2

This section shows an example of description for submitting the first version using Method 2 indicated in 3.3.1 of this document.

10.2.3.2.1. Submission of the first version of the eCTD Type b)

This section shows an example of description of eCTD Type b) when submitting the first version using Method 2 indicated in 3.3.1 of this document.

1) Example of description from the *submissionUnit* element to the *categoryEvent* element

```
<submissionUnit>
    <id root="AW"/>
    <code code="AX" codeSystem="AY"/>

------- (For contextOfUse and submission, refer to 2) and 3) of this section, respectively) -------

    <componentOf2>
        <categoryEvent>
            <code code="AZ" codeSystem=" BA"/>
            <component>
                <categoryEvent>
                    <code code="BB" codeSystem="BC"/>
                </categoryEvent>
            </component>
        </categoryEvent>
    </componentOf2>
</submissionUnit>
```

AW: UUID of this Submission Unit
AX: The code indicating the type of this Submission Unit (Refer to "JP Submission Unit" of JP CV)
AY: OID of the code list defining the code of this Submission Unit (aboveAX:)
AZ: The code indicating at what timing in this review this Submission Unit was submitted (Refer to "JP Category Event" of JP CV)
BA: OID of the code list defining the code of this Category Event (aboveAZ:)
BB: The code indicating that this Submission Unit is b) indicated in 3.3.1 of this document (Refer to "JP Initial Submission Type" of JP CV)
BC: OID of the code list defining the code of this Category Event (aboveBB:)

2) Example of description of the *contextOfUse* element

```
<component>
    <priorityNumber value="BD"/>
    <contextOfUse>
        <id root="BE"/>
        <code code="BF" codeSystem="BG"/>
        <statusCode code="BH"/>
        <derivedFrom>
            <documentReference>
                <id root="BI"/>
            </documentReference>
        </derivedFrom>
        <referencedBy typeCode="BJ">
            <keyword>
                <code code="BK" codeSystem="BL"/>
            </keyword>
        </referencedBy>
```

```
------- (To provide more than one keyword, repeat referencedBy)-------

    </contextOfUse>
</component>

------- (To provide more than one Context of Use, repeat component)-------
```

BD: The value to specify the display order if there are multiple context groups (Also describe it even if there are not more than one.)
BE: UUID of this Context of Use.
BF: The code indicating the CTD heading to assign the Document specified by this Context of Use (Refer to "ICH Context of Use" of ICH CV or "JP Context of Use" of JP CV)
BG: OID of the code list defining the code of this Context of Use (aboveBF:)
BH: Status of this Context of Use
BI: The *id@root* attribute value of the Document referred to by this Context of Use
BJ: Attribute required when using the *referencedBy* element. The value must be "REFR".
BK: Code of the keyword assigned to this Context of Use
BL: OID of the code list defining the keyword assigned to this Context of Use or any value specified in Keyword Definition

3) Example of description of the *submission* element

```
<componentOf1>
    <sequenceNumber value="BM"/>
    <submission>
        <id>
            <item root="BN" extension="BO"/>
        </id>
        <code code="BP" codeSystem="BQ"/>

------- (For application, refer to 4) below) -------

    </submission>
</componentOf1>
```

BM: Submission sequence number of this Submission Unit ("1" for first version application)
BN: UUID of this submission
BO: eCTD reception number
BP: The code indicating the positioning of this Submission (Example: Submission of the original, submission of references, etc.) (Refer to "JP Submission" of JP CV)
BQ: OID of the code list defining the code of this Submission (aboveBP:).

4) Example of description of the *application* element

```
<componentOf>
    <application>
        <id>
            <item root="BR" extension="BS"/>
        </id>
        <code code="BT" codeSystem="BU"/>

------- (For document and keywordDefinition, refer to 5) and 6) of this section, respectively.)-------

    </application>
</componentOf>
```

BR: UUID of this Application
BS: Any value (specified) by the applicant
BT: The code indicating the type of this Application (marketing approval application, etc.) (Refer to JP CV "JP Application")
BU: OID of the code list defining the code of this Application (aboveBT:)

5) Example of description of the ***document*** element

```
<component>
    <document>
        <id root="BV"/>
        <text integrityCheckAlgorithm="BW">
            <reference value="BX"/>
            <integrityCheck>BY</integrityCheck>
        </text>
    </document>
</component>


------- (To provide more than one Document, repeat component.) --------
```

BV: UUID of this Document
BW: Calculation algorithm for the checksum of the file referred to by this Document. The value must be "sha256".
BX: The path of the file referred to by this Document. The path must be a relative path based on submissionunit.xml.
BY: The checksum of the file referred to by this Document. The value must be in the sha256 format.

6) Example of description of the ***keywordDefinition*** element

```
<referencedBy>
    <keywordDefinition>
        <code code="BZ" codeSystem="CA"/>
        <statusCode code="CB"/>
        <value>
            <item code="CC" codeSystem="CD">
                <displayName value="CE"/>
            </item>
        </value>
    </keywordDefinition>
</referencedBy>


------- (To provide more than one keywordDefinition, repeat referencedBy.)-------
```

BZ: The code indicating the type of the Keyword defined by this Keyword Definition (Example: indication, product item name, manufacturer, etc.) (Refer to "ICH Keyword Definition Type" of ICH CV or "JP Keyword Definition Type" of JP CV)
CA: OID of the code list defining the code indicating the type of the Keyword defined by this Keyword Definition (aboveBZ:)
CB: Status of this Keyword Definition The value must be "active".
CC: Any code (specified) by the applicant, which indicates the contents of the Keyword defined by this Keyword Definition (name of the indication, name of the drug product, etc.)
CD: The identifier of the code list defining the code arbitrarily specified by the applicant, which indicates the contents of the Keyword defined by this Keyword Definition (aboveCC:) As the

relevant code list shall be possessed by the applicant, any format will do as long as the information can be identified (Example: OID, applicant's arbitrary text).

CE: The displayed characters corresponding to the code arbitrarily specified by the applicant, which indicates the contents of the Keyword defined by this Keyword Definition

10.2.3.2.2.   Submission of the first version of the eCTD Type c)

The structure of eCTD Type c) for submitting the first version using Method 2 indicated in 3.3.1 of this document is not different from the structure of Type a) indicated in 10.2.3.1 of this document except for the following. Keep the following 2 points in your mind to refer to 10.2.3.1 of this document.

- F: The code indicating that this Submission Unit is c) indicated in 3.3.1 of this document (Refer to "JP Initial Submission Type" of JP CV).
- Q: Submission sequence number of this Submission Unit ("2" for first version application)

10.3   Requirements for eCTD revision

10.3.1   Folder structure for revision

At the time of revision, create the following folders by referring to 5 of this document.

- First layer folder (the folder with the eCTD reception number as the folder name)
- Second layer folder (the folder whose folder name is the submission sequence number of the relevant revision)
- The folder storing the files to be submitted for the relevant revision and its upper folder(s)

10.3.2   Files for revision

The following files must be submitted.

- eCTD v4.0 XML message (submissionunit.xml)
- Checksum file (sha256.txt)
- The files to be submitted for the relevant revision

10.3.3   eCTD v4.0 XML message structure for revision

For eCTD for revision, use Type a) indicated in 3.3.1 of this document regardless of the submission package. At the time of revision, create an eCTD v4.0 XML message according to ICH IG for the basic structure. This section shows the basic structure of the eCTD v4.0 XML message for the revised version. For details of each element and attribute, refer to 7 of this document.

1) Example of description from the **submissionUnit** element to **categoryEvent** element

```
<submissionUnit>
    <id root="CF"/>
    <code code="CG" codeSystem="CH"/>

------- (For contextOfUse and submission, refer to 2) and 3) of this section, respectively) -------

    <componentOf2>
        <categoryEvent>
            <code code="CI" codeSystem="CJ"/>
        </categoryEvent>
    </componentOf2>
</submissionUnit>
```

CF: UUID of this Submission Unit as the UUID of Submission Unit is assigned for each submission, it does not overlap with the Submission Unit submitted in the past.

CG: The code indicating the type of this Submission Unit (Refer to "JP Submission Unit" of JP CV)

CH: OID of the code list defining the code of this Submission Unit (aboveCG:)

CI: The code indicating at what timing in review this Submission Unit was submitted (Refer to "JP Category Event" of JP CV)

CJ: OID of the code list defining the code of this Category Event (aboveCI:)

2) Example of description of the ***contextOfUse*** element

- The method to describe the Context of Use to be newly provided at the time of revision is not different from the method to describe it for the first version. Refer to 2) of 10.2.3.1 of this document.
- You cannot add, replace or delete any CoU Keyword for the already submitted Context of Use. As for an already submitted Document, if you want to associate it with a different context group, delete the existing Context of Use, which refers to the relevant Document, and provide a new Context of Use. For the relevant new Context of Use, either the already submitted Document or file can be reused or the same file can be re-submitted to refer to this as a new Document.
- An example of description for deleting the Context of Use for the purpose of deleting a document submitted in the past is shown below.

```
<component>
    <priorityNumber value="CK"/>
    <contextOfUse>
        <id root="CL"/>
        <statusCode code="CM"/>
    </contextOfUse>
</component>
```

CK: The value to specify the display order if there are multiple context groups (Also describe it even if there are not more than one.). It is desirable to be the same value as the Priority Number of the Context of Use to be deleted. Even though any other value is provided, the relevant value is not considered to have been provided for the regulatory authority. The Priority Number of the Context of Use deleted will be available in the same Submission Unit and later.

CL: UUID of the Context of Use to be deleted

CM: Status of this Context of Use When deleting the Context of Use, provide "suspended" for this attribute value.

- When replacing the Context of Use for the purpose of replacing the document at the time of revision, the following 4 situations are possible.
  (1) Replace 1 file with 1 file.
  (2) Replace 1 file with multiple files.
  (3) Replace multiple files with 1 file.
  (4) Replace multiple files with multiple files.

  (An example of description) for each of the above is shown below.

  (1) Replace 1 file with 1 file.

```
<component>
    <priorityNumber value="CN"/>
    <contextOfUse>
        <id root="CO"/>
        <code code="CP" codeSystem="CQ"/>
        <statusCode code="CR"/>
        <replacementOf typeCode="CS">
            <relatedContextOfUse>
                <id root="CT">
            </relatedContextOfUse>
```

```
            </replacementOf>
            <derivedFrom>
                <documentReference>
                    <id root="CU"/>
                </documentReference>
            </derivedFrom>


    ------- (If a Keyword is assigned to the Context of Use before replacement, describe the said
Keyword here. As the Keyword description method is not different from (the method of) description for
the first version, refer to 10.2.3 of this document. Note that the number of the Keywords and the code
must be the same between the Contexts of Use before and after replacement.)-------


        </contextOfUse>
    </component>
```

CN: The value to specify the display order if there are multiple context groups (Also describe it even if there are not more than one.) Describe the Priority Number to be assigned to the new Context of Use. As long as it does not overlap with any Context of Use in the same context group, it does not matter if the Priority Numbers of the Contexts of Use before and after replacement are the same or different. Also, even though the Priority Numbers are different before and after replacement, do not provide any *priorityNumber@updateMode* attribute.

CO: UUID of the new Context of Use.

CP: The code indicating the CTD heading to assign the Document specified by the new Context of Use (Refer to "ICH Context of Use" of ICH CV or "JP Context of Use" of JP CV). This value must be the same between the Contexts of Use before and after replacement.

CQ: OID of the code list defining the code of this Context of Use (aboveCP:). This value must be the same between the Contexts of Use before and after replacement. (The version number included at the end of the OID indicated by the *code@codeSystem* attribute does not have to match.)

CR: Status of the new Context of Use The value must be "active".

CS: Structural attribute required to use the *replacementOf* element. The value must be "RPLC".

CT: UUID of the old Context of Use

CU: The *id@root* attribute value of the Document referred to by the new CoU

    (2)   Replace 1 file with multiple files.

```
<component>
    <priorityNumber value="CV"/>
    <contextOfUse>
        <id root="CW"/>
        <code code="CX" codeSystem="CY"/>
        <statusCode code="CZ"/>
        <replacementOf typeCode="DA">
            <relatedContextOfUse>
                <id root="DB">
            </relatedContextOfUse>
        </replacementOf>
        <derivedFrom>
            <documentReference>
                <id root="DC"/>
            </documentReference>
        </derivedFrom>


    ------- (If a Keyword is assigned to the Context of Use before replacement, describe the said
Keyword here. As the Keyword description method is not different from (the method of) description for
```

the first version, refer to 10.2.3 of this document. Note that the number of the Keywords and the code must be the same between the Contexts of Use before and after replacement.)-------

```
        </contextOfUse>
    </component>
    <component>
        <priorityNumber value="DD"/>
        <contextOfUse>
            <id root="DE"/>
            <code code="DF" codeSystem="DG"/>
            <statusCode code="DH"/>
            <replacementOf typeCode="DI">
                <relatedContextOfUse>
                    <id root="DJ">
                </relatedContextOfUse>
            </replacementOf>
            <derivedFrom>
                <documentReference>
                    <id root="DK"/>
                </documentReference>
            </derivedFrom>
```

------- (If a Keyword is assigned to the Context of Use before replacement, describe the said Keyword here. As the Keyword description method is not different from (the method of) description for the first version, refer to 10.2.3 of this document. Note that the number of the Keywords and the code must be the same between the Contexts of Use before and after replacement.)-------

```
        </contextOfUse>
    </component>
```

------- (In this example of description, 2 Contexts of Use replace 1 Context of Use. When more Contexts of Use replace 1 Context of Use, repeat the *component* element for the number of the new Contexts of Use.)

CV: The value to specify the display order if there are multiple context groups (Also describe it even if there are not more than one.) Describe the Priority Number to be assigned to the new Context of Use. As long as it does not overlap with any Context of Use in the same context group, it does not matter if the Priority Numbers of the Contexts of Use before and after replacement are the same or different. Also, even though the Priority Numbers are different before and after replacement, do not provide any *priorityNumber@updateMode* attribute. When multiple Contexts of Use replace 1 Context of Use, only one of the new Contexts of Use can have the same Priority Number as that of the old Context of Use.

CW: UUID of the new Context of Use

CX: The code indicating the CTD heading to assign the Document specified by the new Context of Use (Refer to "ICH Context of Use" of ICH CV or "JP Context of Use" of JP CV). This value must be the same between the Contexts of Use before and after replacement.

CY: OID of the code list defining the code of this Context of Use (aboveCP:). This value must be the same between the Contexts of Use before and after replacement. (The version number included at the end of the OID indicated by the *code@codeSystem* attribute does not have to match.)

CZ: Status of the new Context of Use The value must be "active".

DA: Structural attribute required to use the *replacementOf* element. The value must be "RPLC".

DB: UUID of the old Context of Use If multiple Contexts of Use replace 1 Context of Use, this attribute value of multiple new Contexts of Use will be the same. In this example of description, the values of DB:and DJ:are the same.

DC: The *id@root* attribute value of the Document referred to by the new CoU

DD: Same as CV:

DE: Same as CW:

DF: Same as CX:

DG: Same as CY:

DH: Same as CZ:

DI: Same as DA:

DJ: Same as DB:

DK: Same as DC:

(3) Replace multiple files with 1 file.

```
<component>
    <priorityNumber value="DL"/>
    <contextOfUse>
        <id root="DM"/>
        <code code="DN" codeSystem="DO"/>
        <statusCode code="DP"/>
        <replacementOf typeCode="DQ">
            <relatedContextOfUse>
                <id root="DR">
            </relatedContextOfUse>
        </replacementOf>
        <replacementOf typeCode="DS">
            <relatedContextOfUse>
                <id root="DT">
            </relatedContextOfUse>
        </replacementOf>
        <replacementOf typeCode="DU">
            <relatedContextOfUse>
                <id root="DV">
            </relatedContextOfUse>
        </replacementOf>
        <derivedFrom>
            <documentReference>
                <id root="DW"/>
            </documentReference>
        </derivedFrom>
```

------- (If a Keyword is assigned to the Context of Use before replacement, describe the said Keyword here. As the Keyword description method is not different from (the method of) description for the first version, refer to 10.2.3 of this document. Note that the number of the Keywords and the code must be the same between the Contexts of Use before and after replacement.)-------

```
    </contextOfUse>
</component>
```

DL: The value to specify the display order if there are multiple context groups (Also describe it even if there are not more than one.) Describe the Priority Number to be assigned to the new Context of Use. As long as it does not overlap with any Context of Use in the same context group, it

does not matter if the Priority Numbers of the Contexts of Use before and after replacement are the same or different. Also, even though the Priority Numbers are different before and after replacement, do not provide any *priorityNumber@updateMode* attribute.

DM: UUID of the new Context of Use.

DN: The code indicating the CTD heading to assign the Document specified by the new Context of Use (Refer to "ICH Context of Use" of ICH CV or "JP Context of Use" of JP CV). This value must be the same between the Contexts of Use before and after replacement.

DO: OID of the code list defining the code of this Context of Use (aboveDN:). This value must be the same between the Contexts of Use before and after replacement. (The version number included at the end of the OID indicated by the *code@codeSystem* attribute does not have to match.)

DP: Status of the new Context of Use The value must be "active".

DQ: Structural attribute required to use the *replacementOf* element. The value must be "RPLC".

DR: UUID of the old Context of Use If there are multiple old Contexts of Use, all the old Contexts of Use will be enumerated together with the *replacementOf* element.

DS: Same as DQ:

DT: Same as DR:

DU: Same as DQ:

DV: Same as DR:

DW: The *id@root* attribute value of the Document referred to by the new CoU

    (4)   Replace multiple files with multiple files.

```
<component>
    <priorityNumber value="DX"/>
    <contextOfUse>
        <id root="DY"/>
        <code code="DZ" codeSystem="EA"/>
        <statusCode code="EB"/>
        <replacementOf typeCode="EC">
            <relatedContextOfUse>
                <id root="ED">
            </relatedContextOfUse>
        </replacementOf>
        <replacementOf typeCode="EE">
            <relatedContextOfUse>
                <id root="EF">
            </relatedContextOfUse>
        </replacementOf>
        <derivedFrom>
            <documentReference>
                <id root="EG"/>
            </documentReference>
        </derivedFrom>


------- (If a Keyword is assigned to the Context of Use before replacement, describe the said
Keyword here. As the Keyword description method is not different from (the method of) description for
the first version, refer to 10.2.3 of this document. Note that the number of the Keywords and the code
must be the same between the Contexts of Use before and after replacement.)-------


    </contextOfUse>
</component>
<component>
```

```
            <priorityNumber value="EH"/>
            <contextOfUse>
                    <id root="EI"/>
                    <code code="EJ" codeSystem="EK"/>
                    <statusCode code="EL"/>
                    <replacementOf typeCode="EM">
                            <relatedContextOfUse>
                                    <id root="EN">
                            </relatedContextOfUse>
                    </replacementOf>
                    <replacementOf typeCode="EO">
                            <relatedContextOfUse>
                                    <id root="EP">
                            </relatedContextOfUse>
                    </replacementOf>
                    <derivedFrom>
                            <documentReference>
                                    <id root="EQ"/>
                            </documentReference>
                    </derivedFrom>


    ------- (If a Keyword is assigned to the Context of Use before replacement, describe the said
Keyword here. As the Keyword description method is not different from (the method of) description for
the first version, refer to 10.2.3 of this document. Note that the number of the Keywords and the code
must be the same between the Contexts of Use before and after replacement.)-------


            </contextOfUse>
    </component>
```

DX: The value to specify the display order if there are multiple context groups (Also describe it even if there are not more than one.) Describe the Priority Number to be assigned to the new Context of Use. As long as it does not overlap with any Context of Use in the same context group, it does not matter if the Priority Numbers of the Contexts of Use before and after replacement are the same or different. Also, even though the Priority Numbers are different before and after replacement, do not provide any *priorityNumber@updateMode* attribute.

DY: UUID of the new Context of Use

DZ: The code indicating the CTD heading to assign the Document specified by the new Context of Use (Refer to "ICH Context of Use" of ICH CV or "JP Context of Use" of JP CV). This value must be the same between the Contexts of Use before and after replacement.

EA: OID of the code list defining the code of this Context of Use (aboveDZ:). This value must be the same between the Contexts of Use before and after replacement. (The version number included at the end of the OID indicated by the *code@codeSystem* attribute does not have to match.)

EB: Status of the new Context of Use The value must be "active".

EC: Structural attribute required to use the *replacementOf* element. The value must be "RPLC".

ED: UUID of the old Context of Use If there are multiple old Contexts of Use, all the old Contexts of Use will be enumerated together with the *replacementOf* element.

EE: Same as EB:

EF: Same as ED:

EG: The *id@root* attribute value of the Document referred to by the new CoU

EH: Same as DX:

EI: Same as DY:

EJ: Same as EZ:

EK: Same as EA:

Provisional Translation (as of March 2025) *

EL: Same as EB:
EM: Same as EC:
EN: Same as ED:
EO: Same as EC:
EP: Same as ED:
EQ: Same as EG:

- If you intend to replace the document at the time of revision, replace the Context of Use by using any of the above-mentioned methods in principle. It is not appropriate to delete the Context of Use and provide a new Context of Use while you intend to replace the document. As for the Context of Use that should be replaced, note that if it is judged as a result of the action taken through deletion and new submission that there is an impact on the review, you may be requested to re-submit the Submission Unit.

3) Example of description of the *submission* element
- At the time of revision, if no change is made to the product item information, provide only the minimum-required information under the *submission* element as shown below.

```
<componentOf1>
    <sequenceNumber value="ER"/>
    <submission>
        <id>
            <item root="ES" extension="ET"/>
        </id>
        <code code="EU" codeSystem="EV"/>

------- (For Application, refer to 4) of this section) -------

    </submission>
</componentOf1>
```

ER: Submission sequence number of this Submission Unit (The numeric value obtained by adding 1 to the *sequenceNumber@value* attribute value stated in the Submission Unit received just before it)
ES: UUID of the submission which this Submission Unit is associated with. It must be the same value as the *submission.id.item@root* attribute value of the first version.
ET: eCTD reception number It must be the same value as the eCTD reception number stated in the first version.
EU: The code indicating the positioning of this Submission (Example: Submission of the original, submission of references, etc.) (Refer to "JP Submission" of JP CV). It must be the same value as the *code@code* attribute value stated in the first version.
EV: OID of the code list defining the code of this Submission (aboveEU:). It must be the same value as the *code@codeSystem* attribute value stated in the first version.

- At the time of revision, if a new product item is added, provide a description under the *submission* element as follows.

```
<componentOf1>
    <sequenceNumber value="EW"/>
    <submission>
        <id>
            <item root="EX" extension="EY"/>
        </id>
        <code code="EZ" codeSystem="FA/>
        <subject2>
```

```
                    <review>
                        <id root="FB"/>
                        <statusCode code="FC"/>
                    </review>
                </subject2>

    ------ (Describe the Review related to the newly added product item, and provide the statusCode
attribute value as "active".)-------

    ------ (Do not include any Review that is neither withdrawn nor changed.)-------

            </submission>
        </componentOf1>
```

EW: Submission sequence number of this Submission Unit (The numeric value obtained by adding 1 to the *sequenceNumber@value* attribute value stated in the Submission Unit received just before it)

EX: UUID of the submission which this Submission Unit is associated with. It must be the same value as the *submission.id.item@root* attribute value stated in the first version.

EY: eCTD reception number It must be the same value as the eCTD reception number stated in the first version.

EZ: The code indicating the positioning of this Submission (Example: Submission of the original, submission of references, etc.) (Refer to "JP Submission" of JP CV). It must be the same value as the *code@code* attribute value stated in the first version.

FA: OID of the code list defining the code of this Submission (aboveEZ:). It must be the same value as the *code@codeSystem* attribute value stated in the first version.

FB: UUID of the Review related to the newly added product item

FC: Status of this Review. This attribute value of the Review related to the newly added product item must be "active".

- In the eCTD application containing more than one product item, to withdraw only some product items of the marketing application in the review process, provide a description under the *submission* element as follows at the time of the earliest revision after submitting a withdrawal request. You cannot withdraw any product item of the marketing application only by submitting eCTD. Also, to withdraw all the product items of the marketing application contained in eCTD, you do not need to submit eCTD after submitting a withdrawal request.

```
<componentOf1>
    <sequenceNumber value="FD"/>
    <submission>
        <id>
            <item root="FE" extension="FF"/>
        </id>
        <code code="FG" codeSystem="FH"/>
        <subject2>
            <review>
                <id root="FI"/>
                <statusCode code="FJ"/>
            </review>
        </subject2>

    ------ (If multiple product items are withdrawn, provide each review together with the subject2
element, and provide the statusCode attribute value as "suspended" similarly to the above.)-------
```

```
    ------- (Do not include any Review that is neither withdrawn nor changed.)-------

        </submission>
    </componentOf1>
```

FD: Submission sequence number of this Submission Unit (The numeric value obtained by adding 1 to the **sequenceNumber@value** attribute value stated in the Submission Unit received just before it)

FE: UUID of the submission which this Submission Unit is associated with. It must be the same value as the **submission.id.item@root** attribute value stated in the first version.

FF: eCTD reception number It must be the same value as the eCTD reception number stated in the first version.

FG: The code indicating the positioning of this Submission (Example: Submission of the original, submission of references, etc.) (Refer to "JP Submission" of JP CV). It must be the same value as the **code@code** attribute value stated in the first version.

FH: OID of the code list defining the code of this Submission (aboveFG:). It must be the same value as the **code@codeSystem** attribute value stated in the first version.

FI: UUID of the Review related to the withdrawn product item

FJ: Status of this Review. This attribute value of the Review related to the withdrawn product item must be "suspended".

- To change the product item information at the time of revision, provide a description under the submission element as follows.

```
    <componentOf1>
        <sequenceNumber value="FK/>
        <submission>
            <id>
                <item root="FL" extension="FM"/>
            </id>
            <code code="FN" codeSystem="FO"/>
            <subject2>
                <review>
                    <id root="FP"/>
                    <statusCode code="FQ"/>
                    <subject1>

    ------- (Provide all the elements and attributes submitted in the first version under the **subject1**
element and state the value after a change in the change part. If there are multiple change parts in the
same product item, reflect all the changes under the same **subject1** element. Do not include
**updateMode** in the change part.)-------

                    </subject1>
                </review>
            </subject2>

    ------- (If information on more than one product item is changed, describe all the reviews related to
the changed product items.)-------

    ------- (Do not include any Review that is neither withdrawn nor changed.)-------

        </submission>
    </componentOf1>
```

FK: Submission sequence number of this Submission Unit (The numeric value obtained by adding 1 to the *sequenceNumber@value* attribute value stated in the Submission Unit received just before it)

FL: UUID of the submission which this Submission Unit is associated with. It must be the same value as the *submission.id.item@root* attribute value of the first version.

FM: eCTD reception number It must be the same value as the eCTD reception number stated in the first version.

FN: The code indicating the positioning of this Submission (Example: Submission of the original, submission of references, etc.) (Refer to "JP Submission" of JP CV). It must be the same value as the *code@code* attribute value stated in the first version.

FO: OID of the code list defining the code of this Submission (aboveFN:). It must be the same value as the *code@codeSystem* attribute value stated in the first version.

FP: UUID of the Review related to the product item containing changes.

FQ: Status of this Review. This attribute value of the Review related to the product item containing changes must be "active".

4) Example of description of the *application* element

```
<componentOf>
    <application>
        <id>
            <item root="FR" extension="FS"/>
        </id>
        <code code="FT" codeSystem="FU"/>
        <reference>
            <applicationReference>
                <id root="FV"/>
                <reasonCode>
                    <item code="FW" codeSystem="FX"/>
                </reasonCode>
            </applicationReference>
        </reference>


------- (To provide more than one Application Reference, repeat reference. As for the related
applications, include all the related application as of that point of time for each submission, not limited
to the first version or the revised version.)-------


------- (For document and keywordDefinition, refer to 5) and 6) of this section, respectively.)-------


    </application>
</componentOf>
```

FR: UUID of this Application

FS: Any value (specified) by the applicant

FT: The code indicating the type of this Application (marketing approval application, etc.) (Refer to JP CV "JP Application"). It must be the same value as the *code@code* attribute value stated in the first version.

FU: OID of the code list defining the code indicating the type of this Application (aboveFT:). It must be the same value as the *code@codeSystem* attribute value stated in the first version.

FV: eCTD reception number of the related application of this Application

FW: The code indicating the type of the relationship of the related application indicated in FV:above (Refer to JP CV "JP Application Reference Reason")

FX: OID of the code list defining the code of the type of relationship (aboveFW:)

5) Example of description of the ***document*** element
    *   The method to describe the Document to be newly provided at the time of revision is not different from the method to describe it for the first version. Refer to 10.2.3 of this document.
    *   You cannot change or delete the once submitted Document throughout the life cycle of eCTD except to correct the typo in the title. For how to correct the typo in the title, refer to10.3.4.2.

6) Example of description of the ***keywordDefinition*** element
    *   The method to describe the Keyword Definition to be newly provided at the time of revision is not different from the method to describe it for the first version. Refer to 10.2.3 of this document.
    *   You cannot change or delete the once submitted Keyword Definition throughout the life cycle of eCTD except to modify the notation of the displayed character string indicated by the ***displayName@value*** attribute. For how to modify the notation of the displayed character string, refer to10.3.4.3.

10.3.4   Information update

At the time of revision, the following information can be updated.
1) Change the display order of the Context of Use in the context group
2) Correct the typo in the Document title
3) Modify the notation of the Keyword display character string

However, do not revise eCTD for the purpose of updating the information only in principle.

10.3.4.1   Change the display order of the Context of Use in the context group

The Context of Use display order in the context group is determined by the ***priorityNumber@value*** attribute value, but the display order can be changed by changing the relevant attribute value when revising the eCTD. For how to change the display order of the Context of Use, refer to "9.2.5 Priority Number for Context of Use", etc., in the ICH IG.

10.3.4.2   Correct the typo in the Document title.

If there is a typo in the title of the Document indicated by the ***document.title@value*** attribute value, it can be corrected by changing the relevant attribute value when revising the eCTD. For how to correct the typo in the Document title, refer to "9.2.17.2.1 Document Title Updates", etc., in the ICH IG. Update of the Document title is interpreted as having an intention to apply to all the Submission Units (including the Submission Units of another application) which refer to the same ***document.id@root*** value. If you have an intention to apply the update only in a certain Submission Unit, provide a new Document having the ***document.id@root*** value. If it falls under any of the following, you are not allowed to update the Document title.
*   Update the Document title of another application.
*   Updating the title changes the positioning of the document instead of correction of the typo.

10.3.4.3   Modify the notation of the Keyword display character string.

If it is necessary to modify the display character string of the keyword indicated by the ***displayName@value*** attribute value of the Keyword Definition, it can be corrected by changing the relevant attribute value when revising the eCTD. For how to modify the notation of the keyword display character string, refer to "9.2.18.6 Keyword Definition display name change", etc., in the ICH IG. Modification of the notation of the Keyword display character string is interpreted as having an intention to apply to all the Submission Units submitted in the past in the same application as well. To modify the notation of the Keyword display character string of a certain Submission Unit only, define a new Keyword Definition. Note that modification of the notation of the Keyword display character string does not affect another application.
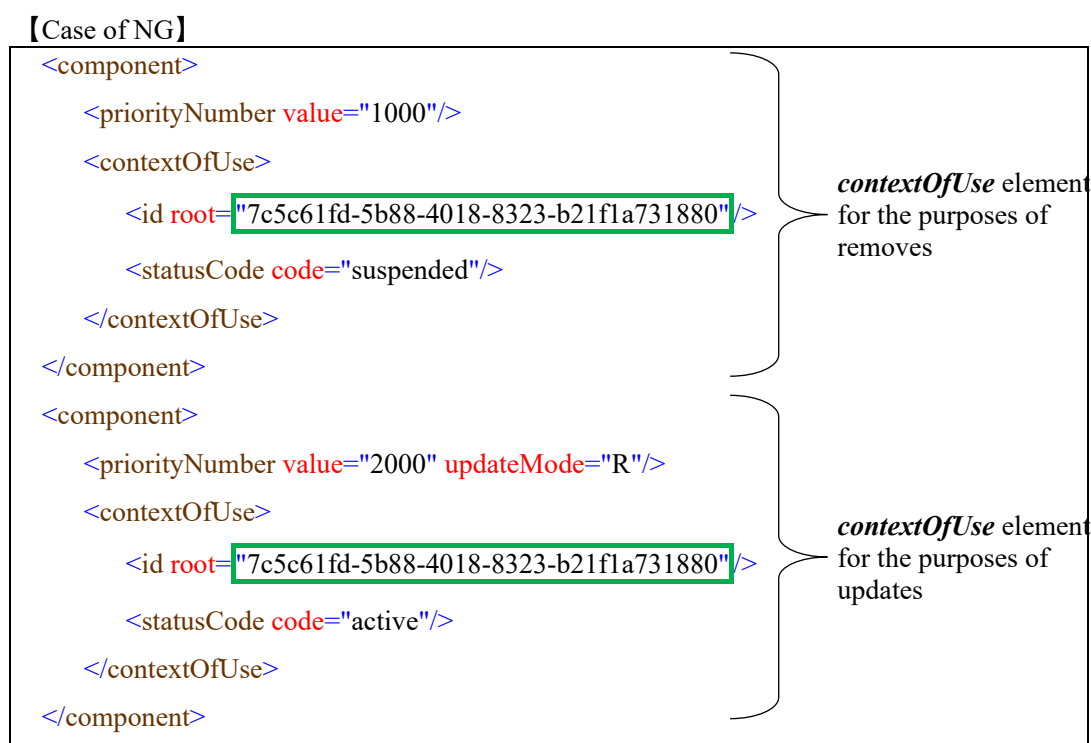
10.3.5　Migration from eCTD v3.2.2

If eCTD v3.2.2 is used when submitting the first version, you cannot make a revision using eCTD v4.0 during the review time period. Use the same version of eCTD from submission of the first version to completion of the life cycle. You are not allowed to inquire the leaf ID, etc. of the document submitted using the version of v3.2.2 or earlier from an application using the version of v4.0 or later.

10.3.6　Important notes for revision

Multiple operations* must not be performed simultaneously within the same Submission Unit for one Context of Use/Review/Document specified by UUID and one Keyword Definition specified by a combination of code and codeSystem attribute values. For example, for one Context of Use, the *contextOfUse* element for remove and the *contextOfUse* element for updating the display order must not be provided in the same Submission Unit at the same time.
* New submissions and replacements, removals and updates, etc.

【Case of NG】

```
<component>
    <priorityNumber value="1000"/>
    <contextOfUse>
        <id root="7c5c61fd-5b88-4018-8323-b21f1a731880"/>
        <statusCode code="suspended"/>
    </contextOfUse>
</component>
<component>
    <priorityNumber value="2000" updateMode="R"/>
    <contextOfUse>
        <id root="7c5c61fd-5b88-4018-8323-b21f1a731880"/>
        <statusCode code="active"/>
    </contextOfUse>
</component>
```

contextOfUse element for the purposes of removes

contextOfUse element for the purposes of updates

11.　Important notes for referring to the electronic study data from the eCTD v4.0 XML message

As the XML description method is not distinguished according to the file to refer to in eCTD v4.0, create an eCTD v4.0 XML message by referring to 7 of this document in principle. However, the electronic study data must conform to the Technical Conformance Guide, even if the electronic study data is referenced from the eCTD v4.0 XML message and submitted. Therefore, note that there are points of difference in the business rules between when referencing the electronic study data from the eCTD v4.0 XML message and referencing other files. Important notes for referring to the electronic study data are provided below.

1) The study id part of the study id_study title Keyword assigned to the Context of Use that refers to the electronic study data shall be the same as the name of the study ID folder in which the relevant electronic study data is stored. However, it is not necessary to match uppercase and lowercase letters.

2) Assign the CoU Keyword to the Context of Use, which refers to the electronic study data, as follows.

Scope	Code list	Code
All the electronic study data	JP Study Data Category	Appropriate code
	JP Analysis Type	Appropriate code
SDTM data set (Files under "sdtm" and "sdtm_j" folders)	JP Terminology (Tabulation)	Appropriate code
ADaM data set (Files under "adam" and "adam_j" folders)	JP Terminology (Analysis)	Appropriate code

3) The following elements/attributes should be provided in the Document that refers to the electronic study data.

Scope	Element/Attribute	Value
Electronic study data in the clinical pharmacology	*document.text.description@value*	Description of the file contents
Electronic study data in SAS XPORT format (.xpt)	*document.text@charset*	Select the appropriate code from JP CV "JP Japanese Character Code"

4) The ICH Document Type Keyword does not need to be assigned to the Context of Use that refers to the electronic study data. Even if it is assigned, the assigned ICH Document Type Keyword does not need to be the same between the Context of Use that refers to the electronic study data and the Context of Use that refers to the corresponding clinical study report.

5) The following conditions must be met for the Context of Use that refers to the electronic study data and the Context of Use that refers to the clinical study report corresponding to the electronic study data.

5)-1 The *code@code* and *code@codeSystem* attribute values of the study id_study title Keyword shall be the same between them.

5)-2 The following information shall match between the Context of Use that references the electronic study data and at least one of the Context of Use that references the clinical study report corresponding to it[1], including the presence or absence of the information:
- The *code@code* and *code@codeSystem* attribute values of Context of Use[2]
- The CoU Keyword *code@code* and *code@codeSystem* attribute values below:
  - ICH Study Group Order[2]
  - indication

   [1]For example, if there are multiple reports corresponding to the electronic study data and each exists under a different CTD heading, only one of the Context of Use that references those reports needs to match the above information with the Context of Use that references the electronic study data.

*²The version numbers included at the end of the OID indicated by the ***code@codeSystem*** attribute of the Context of Use and ICH Study Group Order Keywords does not need to match.

However, the Context of Use that references the corresponding clinical study report is not submitted at the time of submitting eCTD type b) when submitting the first version by "Method 2" shown in 3.3.1 of this document. Therefore, the above conditions 5)-1 and 5)-2 don't need to be met at the time of submitting eCTD type b) but need to be met at the time of submitting the eCTD type c) instead.

6) If the corresponding electronic study data is common among multiple reports with different study ID* within the application, create study ID folders corresponding to each report and submit them by one of the following methods.
- Store the same electronic study data in each study ID folder.
- Store the electronic study data in one study ID folder, and store a document wrriten to refer to the study ID folder in the "misc" folder under the other study ID folder.

*The study ID indicated by the study id part of the study id_study title Keyword assigned to the Context of Use that references the clinical study report.

7) It is necessary that the file path after "m5/datasets" in each electronic study data must be unique because the file to be validated for the electronic study data is uniquely identified. Therefore, keep the following in mind for revision.
- When submitting new electronic study data
  ➢ A valid Context of Use referring to the same file in the same path under m5/datasets folder as a newly submitting Context of Use refers to, must not be happened at the time of this submission sequence of lifecycle. It means that a newly submitting Context of Use can be happened with the same file of same path under m5/datasets folder as the deleted Content of Use referred to from the Submission Unit.
- When replacing previously submitted electronic study data
  ➢ The file path under "m5/datasets" of both the file referenced by Context of Use before replacement and the file referenced by Context of Use after replacement must match.

8) When reusing a Document that references electronic study data, all of the following conditions must be met in addition to 8.1 of this document. The file reuse shown in 8.2 of this document is not permitted in the electronic study data.
- A valid Context of Use referring to a reused Document must not be existed two or more times at the time of this submission sequence of lifecycle.
- A valid Context of Use referring to the same file in the same path under m5/datasets folder as a reused Document referring to, must not be existed at the time of this submission sequence of lifecycle.

If the Document that references the electronic study data is reused, the file name of the file referenced by the reused Document and the folder structure information under the "m5" folder where it is stored will be inherited even after reuse. For example, if a Document that references a file under the "misc" folder is reused, the file referenced by the Document is treated as a file under the "misc" folder even after being reused.

9) As for the Document and Context of Use, which refer to the electronic study data, the following information will not be utilized by the regulatory authority.
   - *priorityNumber@value*
   - *priorityNumber@updateMode*
   - *document.title@value*
   - *document.title@updateMode*

12. Other considerations

12.1 CoU Keyword to be assigned to the clinical study report

For the Context of Use that refers to clinical study reports included in Module 5 of CTD, assign the ICH CV "ICH Document Type" as follows.

When submitting the clinical study report in one file:
Assign "ich_document_type_2" to the Context of Use, which refers to the relevant file.

When submitting the clinical study report consisting of multiple files:
For the Context of Use that refers to each file, assign an appropriate one of the Codes with the item number of the clinical study report provided in the column of "E3-Reference".

12.2 Handling of the Context Group

A Context Group consists of one or more Contexts of Use and Document referenced by those Contexts of Use. One context group is configured for each combination of the values of the code attribute and the codeSystem attribute of both the Context of Use and the Keyword assigned to the Context of Use. If the codeSystem attribute indicates the OID of the ICH CV or JP CV codelist, even if the version number included at the end of the OID is different, if other information matches, combinations of values for the code and codeSystem attributes are considered identical. Therefore, for example, Contexts of Use having the following Context of Use codes are judged to belong to the same context group.

	Context of Use 1	**Context of Use 2**
contextOfUse @code	jp_m1.1	jp_m1.1
contextOfUse @codeSystem	2.16.840.1.113883.3.989.2.2.1.1.**1**	2.16.840.1.113883.3.989.2.2.1.1.**2**

12.3 How to express attachment numbers

In order to facilitate the identification of each document and study, it is possible to assign a finer granularity number (e.g., 3.2.s.2.3-1) to each document and study than the CTD number prescribed in the M4 Granularity Document and JP CV "JP Context of Use". The number can be granted by Document title having it or ether one below.

1) Document Label（*contextOfUse.code.originalText@value* attribute）
   The *code.originalText@value* attribute of the Context of Use provides an arbitrary abbreviation (Document Label) of the Document referenced by the relevant Context of Use. It is possible to assign an attachment number for each document by providing an arbitrary character string as the Document Label. An example of Document Label is shown below.
   ```
   <contextOfUse>
       <id root="7c5c61fd-5b88-4018-8323-b21f1a731880"/>
   ```

```
<code code="ich_3.2.s.2.3" codeSystem="2.16.840.1.113883.3.989.2.2.1.1.2">
    <originalText value="3.2.s.2.3-1"/>
</code>
<statusCode code="active"/>
…[Partially omitted]…
</contextOfUse>
```

2) ICH Study Group Order Keyword

The ICH Study Group Order Keyword is a Keyword for defining the display order between context groups that include the study id_study title Keyword. The ICH Study Group Order Keyword can be used to assign attachment numbers to multiple documents by study ID unit. The ICH Study Group Order Keyword and Document Label can be used together. An example of a Context of Use description with an ICH Study Group Order Keyword is shown below.

```
<contextOfUse>
    <id root="7c5c61fd-5b88-4018-8323-b21f1a731880"/>
    <code code="ich_5.3.1.1" codeSystem="2.16.840.1.113883.3.989.2.2.1.1.2"/>
    <statusCode code="active"/>
        <referencedBy typeCode="REFR"/>
            <keyword>
                <code code="ich_study_group_order_1" codeSystem="2.16.840.1.113883.3.989.2.2.1.12.1"/>
            </keyword>
        </referencedBy>
        <referencedBy typeCode="REFR"/>
            <keyword>
                <code code="STUDYID_TITLE001" codeSystem="StudyID list 001"/>
            </keyword>
        </referencedBy>
…[Partially omitted]…
</contextOfUse>
```

13. Validation rules

In addition to the validation rules provided in ICH IG, the business rules, etc., described in this document apply to the validation rules for eCTD application in Japan. For more specific details of validation for eCTD applications in Japan, refer to the list of check items published on the PMDA website (https://www.pmda.go.jp/) and the operation manual, etc., for the eCTD v4.0 verification tool.

14. Inquiry

If you have any question, etc. about operation of eCTD v4.0, contact us at the below email address. However, submit any (question about a) general matter through an industry organization such as Japan Pharmaceutical Manufacturers Association (JPMA) so that the response to it will spread to the entire industry as it is not desirable to respond to it only for one company. This does not apply to any question about a specific product item. We will receive it at the below email address.

ectd@pmda.go.jp

15. Appendix 1: Module 1 creation guidelines

15.1 Overview

To make an eCTD application using eCTD v4.0, include all of Module 1 through Module 5 of CTD in 1 eCTD v4.0 XML message. The data of Module 1 will be associated with the CTD heading by the code of the Context of Use similarly to the data of other Modules, and included in the same eCTD v4.0 XML message as (that of) the Context of Use, which refers to the data of other Modules, and submitted.

15.2 Folder structure and folder naming rules

The folder structure and folder naming for Module 1 shall be the following folder structure in principle.

The applicant may create folders under the "jp" folder as necessary. However, do not change the hierarchy up to "m1/jp".

15.3 File naming in Module 1

Set up a file in Module 1 referring to the following file name. Note that the following file name is a reference and the applicant may provide any name.

Document type	File name	Remarks
1.1-1 Table of contents of the application dossier containing Module 1	m1-01-01.pdf	In eCTD application, submission shall be optional.
1.1-2 Outline table	m1-01-02.pdf	
1.2 Marketing application form (copy)	m1-02-XX.pdf	
1.3 Certification documents	m1-03-XX.pdf	
1.4 Patent status	m1-04-01.pdf	
1.5 Origin or history of discovery and history of development	m1-05-01.pdf	
1.6 Data on usage conditions in foreign countries	m1-06-01.pdf	
1.7 List of equieffective products of the same kind	m1-07-01.pdf	
1.8 Instructions for use (drafts)	m1-08-01.pdf	
1.9 Document on the generic name	m1-09-01.pdf	
1.10 Summary of designated review data for poisonous drugs, powerful drugs, etc.	m1-10-01.pdf	
1.11 Pharmaceutical product risk management plans (draft)	m1-11-01.pdf	
1.12-1 Attached submission data list (PDF)	m1-12-01.pdf	
1.12-2 Attached submission data list (MS Excel)	m1-12-02.xlsx	
1.13.1-1 Copy of the approval document	m1-13-01-01.pdf	It can be submitted by referring to it as a related application. For details, refer to 15.4 of this document.

Document type	File name	Remarks
1.13.1-2 Review report	m1-13-01-02.pdf	It can be submitted by referring to it as a related application. For details, refer to 15.4 of this document.
1.13.1-3 Overview of the data	m1-13-01-03.pdf	It can be submitted by referring to it as a related application. For details, refer to 15.4 of this document.
1.13.1-4 Attached submission data list	m1-13-01-04.pdf	It can be submitted by referring to it as a related application. For details, refer to 15.4 of this document.
1.13.2 Clinical study consultation records (copy)	m1-13-02-XX.pdf	
1.13.3 Inquiries (copy) and responses to the inquiries (copy)	m1-13-03-XX.pdf	
1.13.4.1.1 List of target values / setting values, etc. in the manufacturing process column on the marketing application	m1-13-04-01-01.pdf	
1.13.4.1.2-1 List of submission data on new additives	m1-13-04-01-02-01.pdf	
1.13.4.1.2-2 Individual review product item outline table	m1-13-04-01-02-02.pdf	
1.13.4.1.2-3 Marketing application (copy)	m1-13-04-01-02-03.pdf	
1.13.4.1.2-4 Overview of new additives	m1-13-04-01-02-04.pdf	
1.13.4.1.2 XX Data on new additives: Attached submission data XX	m1-13-04-01-02-XX.pdf	
1.13.4.1.3 その他	m1-13-04-01-03.pdf	
1.13.4.2 Data submitted to the Ministry of Health, Labour and Welfare	m1-13-4-2.pdf	

15.4 How to submit the data related to the already approved pharmaceutical products

Among the documents related to approved pharmaceutical to be included in Module 1 of the CTD, documents that can be omitted from attachment according to "Simplification of CTD Module 1 for New Drug Approval Application Attachments" (Administrative Notice as of March 24, 2020, by the Pharmaceuticals and Medical Devices Agency, Office of Review Management) can be omitted by using the method 3) below. If submission of the documents don't need to be omitted or cannot be omitted, they must be submitted using method 1) or 2). However, you are not allowed to change the submission method in the middle of the life cycle in principle.

1) Include the relevant files in the "m1/jp" folder, get them referred to from the Document, and associate them with the corresponding CTD headings using the Context of Use.

2) Reuse the Document of the approved application to associate it with the corresponding CTD heading using the Context of Use.
3) Include the eCTD reception number of the relevant already approved application in the id@root attribute of Application Reference.

If the method of 3) above is adopted, any document related to already approved pharmaceutical product that are omitted by method of 3) must not be provided by Module 1 of CTD in duplicate by method of 1) or 2).

eCTD reception number	
Submission sequence number	
Application category	
Application date	
Name　Generic Name	
Brand name	
Modules, etc. to be included in this submission (Check the corresponding module, etc.)	□ Module 1 　□ The response to the inquiry is included. □ Module 2 □ Module 3 □ Module 4 □ Module 5 　□ Electronic study data are included.
Type of the electronic medium	
Number of submitted media	
Size (for each submitted medium)	
Statement regarding virus check	
Checksum of submissionunit.xml	
Operation confirmation environment	OS: PDF Version:
Contact	(Name of the regulatory representative)　Tel: 　　　　　　　　　　　　　　　　　　　　Email:
	(Name of the technical representative)　Tel: 　　　　　　　　　　　　　　　　　　　Email:
Remarks	

We submit electronic application dossier for approval of manufacturing and marketing for a prescription drug according to the above.

(Date)　　　　　　　　　　　　　　　　　　　(Applicant)
　　　　　　　　　　　　　　　　　　　　　　　　Address
　　　　　　　　　　　　　　　　　　　　　　　　Name

To the Minister of Health, Labour and Welfare