ICH eCTD v4.0

DRAFT Japan Regional Implementation Guide

(Translated version)

> This document is an English translation of "Draft Japan Regional Implementation Guide" made by courtesy of JPMA ICH M8 Expert Working Group to facilitate further understanding thereof. This is for your convenience only and, in the event of any discrepancy between this document and Japanese original document, the original shall prevail. Such Japanese original document is available at MHLW/PMDA web site.

Japan Pharmaceutical Manufacturers Association
ICH M8 Expert Working Group at JPMA

Table of Contents

Notice To Readers

Sections of this document referencing the HL7 Version 3 Standard: Regulatory Product Submission Release 2 is used with the publisher's permission.   These sections are copyrighted by Health Level Seven International ® ALL RIGHTS RESERVED

For Reference Purpose Only

1. Purpose

This implementation guide is a supplemental document of the ICH eCTD v4.0 ICH Implementation Guide (hereafter referred to as "ICH IG"). This implementation guide describes a method for providing Japan specific information (e.g.: administrative information) which is required when creating eCTD v4.0 XML message instance and other components involved in ICH eCTD v4.0 implementation in Japan. If any inconsistencies are found between this implementation guide and ICH IG, concerning the eCTD applications in Japan, the contents in this implementation guide should take precedence.

2. Definitions of Terms, Notation, and Symbols

2.1 Terms

The terms used in this implementation guide are defined in the table below:

Terms	Definitions
UUID	An abbreviation of Universally Unique Identifier. For its definition, refer to ICH IG.
OID	An abbreviation of Object Identifier. For its definition, refer to ICH IG.
JP CV	It refers to Japan specific controlled vocabularies used for eCTD v4.0 implementation.
Initial submission	A submission with a submission sequence number "1".
eCTD application	An application which submits eCTD as an original.
eCTD materials	Reference materials to be submitted on at an eCTD application.
eCTD v4.0 XML message instance	Composes submissionunit.xml, which is submitted to the Regulatory Authority in Japan, complying with ICH IG and this implementation guide.
Payload	Body data excluding a header part.

2.2 Typeface

In this implementation guide, XML components (elements and attributes) are written in an oblique and bold face. Except in cases of the XML writing examples. And the concepts of the XML components are written in a standard face.

2.3 Symbols used in XML writing

Legends in the explanation in Chapter 8 of this implementation guide are shown below:

Symbol	Description
>>	An element indicated on the right of this symbol is a child element of the left one.

2.4   Colors of characters used in XML writing example

Legends of character colors in the XML writing in Chapter 8 of this implementation guide are shown below:

Color of character	Description
Blue	Components for XML notation Example: <, =, ", ", >
Brown	XML elements Example: *id*, *code*
Red	XML attributes Example: *root*, *extension*
Black	Contents of XML elements or a values of attributes Example: *2.16.840.1.113883*

2.5   List of XML Elements and Attributes

A table shown in Chapter 8 of this implementation guide is described below:

Element	Attribute	Multiplicity	Data type *Example of data*	Description
Submission rules of elements and attributes				
Implementation Rules				

Element: Indicates a name of an element. Indentation indicates a parent-child relationship between the elements. The element with colored columns on the right is intended for containing information or storing an attribute and therefore information in the same row in the table, such as attribute or multiplicity, are omitted.

Attribute: Indicates a name of an attribute.

Multiplicity: Under elements, it indicates upper/lower limits of the frequency of occurrence of the element against the parent element. Under attributes, it indicates lower/upper limits of the frequency of occurrence of the attribute against the element. A format of "[n..m]" is used, where n is a lower limit, m is an upper limit and an asterisk ("*") indicates a number of 0 or over. Multiplicity used in this implementation guide is not necessarily consistent with the definition on the schema. For eCTD to be submitted to the Regulatory Authority in Japan, this implementation guide should take precedence.

Value type:	Indicates a type of value allowed as the contents of an element or the value of an attribute. In addition to the types described in ICH IG, the "Japanese Character" type is allowed in some values in this implementation guide. The elements and attributes allowed to contain the Japanese Character type can be specified in Japanese.
Example of value:	Indicates an example of the contents of an element or the value of an attribute.
Description:	Describes the element or the attribute.
Submission rules of elements and attributes:	Regarding submission of elements and attributes, multiplicity and other rules to be followed are described.
Implementation Rules:	When submitting elements or attributes, implementation rules to be followed are described.

3.   Scope

This implementation guide applies when submitting electronic materials required to attach to the application form for manufacturing and marketing approval or for approval of partial modification on the approved information regarding new ethical pharmaceutical drugs. This version applies to ICH Step 2 and will be updated through the subsequent steps.

In addition, eCTDs intended for Two-way Communication, Submission Units with Multiple Submission components, and Forward Compatibility described in ICH IG are not submitted to the Regulatory Authority in Japan.

4.   General Matters

4.1   Components to be accompanied at eCTD application

The eCTD application should be accompanied with the components listed below:

- Folders
- eCTD v4.0 XML Message Instance
- Files*

* There are various types of files as shown below:
1) ICH CTD document files referred from the instance
2) Japan specific document files referred to by the instance (e.g. Module 1 document).
3) Files not referred to by the instance (e.g.: a file of hash values).

4.2   Components not to be accompanied at eCTD applications in Japan

When applying in Japan, the following components should not be accompanied.

1) Files containing specific information defined in the implementation guides for other regions except Japan and not described in this implementation guide.

2) Elements, attributes, and their values defined in the implementation guides for other regions except Japan and not described in this implementation guide.

4.3   Important Points of Submission

Following the approval application procedure, the applicant should submit the eCTD materials to the Regulatory Authority. Detailed procedures will be provided separately.

4.4   Requirements of Operations

When applying by eCTD, the applicant should consider the standard environment for reviewing announced by the Regulatory Authority and guarantee that the functions required through the eCTD Notice (views, links, etc.) operate appropriately. The applicant should report the environment validated for operations to the Regulatory Authority at the submission.

At the Regulatory Authority, when some of the functions above cannot be validated under the standard environment for reviewing or when an invalid view is found, the applicant is asked for correction by using their own time clock independent of the administrative side. When it is found impossible to do eCTD submission due to an error in viewing eCTD materials, the applicant should consult the Regulatory Authority in advance to decide whether to switch to the paper submission, how to handle the submission, corrective actions and so on. For the method for validating the operations before submission, the applicant should check on the Regulatory Authority website and follow the instructions as appropriates.

Using plug-in software for viewing eCTD documents is not allowed as a general rule. Except in cases of plug-in software used for creating documents.

4.5   Requirements of eCTD Submission

On the eCTD application, all of the submission documents must be provided in electronic format. Until the digital signature becomes acceptable, however, the pages with signature, seal, or the like can be scanned and stored as electronic files to be attached to the eCTD. In this case, a statement should be submitted to ensure that the relevant pages were scanned appropriately. This statement in electronic format should be included in Module 1.3. Also, a written statement should be prepared for ready submission on a request from the Regulatory Authority.

4.6   Controlled Vocabularies

In addition to the controlled vocabularies defined in ICH (hereafter referred to as "ICH CV"), the Japan specific controlled vocabularies (hereafter referred to as "JP CV") are used. JP CVs are defined separately.

5.   Requirements of Folder Structure and File Path Included in eCTD Package

5.1   Basic Folder Structure

The basic folder structure should be built according to the ICH IG. The first level folder should be named the eCTD receipt number, and the second level folder should be the submission sequence number. For the configuration of Module 1, please refer to 12.1 in this implementation guide. Creating a jp folder under the m1 folder, all files related to Module 1 along with the Cover Letter (if submitted not through the portal site) should be stored in the m1/jp folder. When creating report folders in Module 4 and 5, as a general rule, one folder per study report should be created and named the studyt number, while being named "ise" for integrated analysis concerning efficacy and "iss" concerning safety. The study number should be same as a value of the study id keyword to be added to Context of Use.

5.2   Naming Conventions

Folders, in principle, should be named in accordance with the folder & file naming conventions defined in ICH IG.

5.3   Maximum Path Length

The maximum path length defined in the ICH IG applies to the implementation in Japan.

6.   Requirements of File Formats Included in eCTD Package

Described below are the requirements of eCTD file formats to be submitted to the Regulatory Authority in Japan. Consult the Regulatory Authority in advance, if the format of the file referenced from the eCTD XML message instance, except study data files, needs to be in the format other than PDF or Microsoft Excel (.xls or .xlsx). The file format for study data will be noticed separately.

- Narrative: Portable Document Format (PDF)
- Tabulation*: Microsoft Excel
- Structured: XML (Extensible Markup Language)
- Graphic: PDF, whenever possible. The following formats can be used when appropriate or when PDF is not available: Joint Photographic Experts Group (JPEG), Portable Network Graphics (PNG), Scalable Vector Graphics (SVG), and Graphics Interchange Format (GIF). Special formats for very high resolutions (DICOM etc.) could be appropriate on a case-by-case basis.

7. Requirements of PDF Files Included in eCTD Package

7.1 PDF Files

PDF files for eCTD submission to the Regulatory Authority in Japan should comply with the ICH eCTD v4.0 Implementation Package Specification for Submission Format and be created based on the specifications in this section.

7.1.1 Font Specifications

1) Recommended Fonts

Unicode-supported MS Gothic, MS Mincho, Chu-Gothic and Sai-Mincho are recommended for Japanese fonts. For English fonts, Times New Roman, Arial, Courier and the fonts supported by a set of Acrobat products itself are recommended.

2) Font Size

For Japanese documents, a font size of 10.5 pt should be used as a general rule. A Japanese font size of 8 pt and larger, as far as legible, can be used in figures and tables.

3) Font Colors

The use of a black font color is recommended. If another font color is to be used, light colors that do not print well on gray-scale printers should be avoided. The use of background shadowing should be avoided. In the text PDF, a blue font color is recommended for the text for hypertext links.

7.1.2 PDF Files Containing Images

When creating PDF files containing images, the images should not be processed by downsampling. Downsampling does not preserve all of the pixels in the original. For the images in PDF, one of the following lossless compression techniques should be used:

- For lossless compression of color and gray-scale images, Zip/Flate (one technique having two different names) should be used. This is specified in Internet RFC 1950 and RFC 1951 (http://www.ietf.org/rfc/rfc1950.txt).
- For lossless compression of black and white images, the CCITT Group 4 Fax compression technique should be used. It is specified as CCITT recommendations T.6 (1988) - Facsimile coding schemes and coding control functions for Group 4 facsimile apparatus.

7.1.3 Resolution of Scanned Document

The paper documents should be scanned at the resolution high enough to ensure the contents are legible considering the readability at the Regulatory Authority.

7.1.4   File Size

PDF files should be no larger than 100 megabytes and be optimized for a view on the web screen. When the size of an electronic file exceeds 100MB, the file should be split into multiple files, which should be referenced from Context of Use containing the same types and values of Code, Code System, and Keyword. In such case, the order of the files should be specified by Priority Number. It is recommended that the document title explicitly describes that the files are for the same purpose.

7.1.5   Hypertext Links and Bookmarks

Hypertext links can be designated by rectangles using fine lines or by blue text (recommended) as appropriate. Hypertext links to lead to annotations, related sections, reference materials, appendixes, tables, or figures across multiple pages throughout the document are useful and contribute the efficiency of navigation. Relative paths should be used when creating hypertext links or bookmarks directing to another file. These relative paths, however, should always include the first-level folder name. When creating bookmarks and hyperlinks, Inherit Zoom for the magnification setting should be used. For the documents with a table of contents, bookmarks for each item listed in the table of contents should be provided including all tables, figures, publications, other references, and appendixes. It is useful to create hypertext links on the major items in the table of contents of the application documents or modules. The bookmark hierarchy should be identical in hierarchical level and order to the table of contents and no bookmark levels should be added beyond those present in the table of contents. Using bookmarks with no more than 4 levels in the hierarchy is recommended. For the contents of whole module, for example, there is no need to set bookmarks referring to another file. When a document is composed of multiple physical files due to a file size restriction (refer to M4 Granularity Annex), however, the bookmarks across this document can be set or the document should be clearly recognized as a composite of multiple files. As excessive bookmarks in PDF files may impair visibility, the second level and lower can be hidden in consideration of readability.

7.1.6   Page Size

The print area for pages should fit on a sheet of A4 size (210 x 297 mm) and Letter size (8.5" x 11") paper. A sufficient margin (at least 2.5 cm) on the both sides of each page should be provided to avoid obscuring information when the reviewer subsequently prints and stores the pages in a binder for temporary use. For pages in landscape orientation (typically tables and publications), smaller margins (at least 2.0 cm at the top and 0.8 cm left and right) can be set to display more information on the page. Header and footer information may appear within these margins but should not be so close to the page edge to risk being lost upon printing.

7.1.7   Limitations and Restrictions

- No security settings or password protection should be included.
- Security fields should be set so as to allow printing, changes to the document, selecting text and graphics, and adding or changing notes and form fields.
- Use of any annotation type defined in ISO 32000-1:2008, except for Links (e.g.: notes, stamps, highlights (markers)), should be avoided whenever possible.
- Use of any of the followings defined in ISO 32000-1:2008 should be avoided.
  - Actions, except for GoTo and GoToR
  - Interactive Forms
  - Multimedia Features

7.1.8   Handling of Documents Created in the Past

It is acceptable to include the reports in Module 3, 4, or 5 as scanned PDF files in the eCTD submission package only if they had already been created in paper format prior to March 2006 and those scanned PDF files are legible. Any document created since then should be the PDF file (text PDF) converted from the electronic file.

7.1.9   Handling of PDF Documents with Excel Files Attached

When files in Microsoft Excel format are requested for submission in addition to PDF files, the PDF files do not absolutely need to be visually identical to the Excel files. However, there should be no inconsistency in the contents between these two files.

8.   Requirements of Instances included in eCTD Package

8.1   Character Encoding

UTF-8 is used.

8.2   Handling Elements/Attributes without Meaningful Values

In the payload of eCTD v4.0 XML Message Instance for Japan, no element can have a value except for the ***integrityCheck*** element. The ***integrityCheck*** element containing a dummy value or no value cannot be provided. Any attribute containing a dummy value, a null value, or no value cannot be provided.

8.3   How to Use Japan Specific Elements/Attributes

The schema of eCTD v4.0 XML Message Instance includes the elements/attributes not used in Japan, used in Japan in the manner different from other regions, and used only in Japan. For details of eCTD v4.0 XML Message Instances for Japan, see the relevant section in this implementation guide.

8.3.1 submissionUnit

The *submissionUnit* element is a group of documents and information provided by a single submitting action to the Regulatory Authority.

8.3.1.1 Programming Positions

There is no difference in the programming positions of *SubmissionUnit* elements from what defined in ICH IG. Refer to ICH IG for details.

8.3.1.2 XML Programming Example

An example of XML programming of the *submissionUnit* element is shown below:

```
<subject typeCode="SUBJ">
    <submissionUnit>
        <id root="12345678.1234.1234.1234.123456789012" extension="240505001"/>
        <code code="jp official" codeSystem="jp-submission-unit"/>
        <component>
            ...[partly omitted]...
        </component>
        <componentOf1>
            ...[partly omitted]...
        </componentOf1>
        <componentOf2>
            ...[partly omitted]...
        </componentOf2>
    </submissionUnit>
</subject>
```

8.3.1.3 XML Elements and Attributes

In the table below, the submissionUnit element, the subordinate elements, and their attributes are listed.

Element	Attribute	Multiplicity	Data type *Example of data*	Description
submissionUnit		[1..1]		Comply with the ICH IG definition.
id		[1..1]		Comply with the ICH IG definition.
	root	[1..1]	Valid UUID *Example: root="36589652-78 94-6589-3256-3218 52697531"*	Comply with the ICH IG definition.

Element	Attribute	Multiplicity	Data type *Example of data*	Description
	extension	[1..1]	Alpha Numeric *Example: extension="2405050 01-1"*	A value composed of the eCTD receipt number and the submission sequence number connected by a hyphen.
code		[1..1]		Comply with the ICH IG definition.
	code	[1..1]	Alpha Numeric *Example: code="jp official"*	A code indicating a type of the Submission Unit. The code value is selected from the "JP Submission Unit" code list of JP CV.
	codeSystem	[1..1]	Valid OID *Example: codeSystem="jp-sub mission-unit"*	OID of the "JP Submission Unit" code list.
title		[0..1]		Comply with the ICH IG definition.
	value	[0..1]	Alpha Numeric+Japanese Character *Example: Presubmission*	Comply with the ICH IG definition.
component		[0..*]		This element is provided to store the *contextOfUse* element. For details of the *contextOfUse* element, see 8.3.4.
componentOf 1		[1..1]		This element is provided to store the *sequenceNumber* element and the *submission* element. For details of the *sequenceNumber* element, see 8.3.2 and 10.3.3.2. For details of the *submission* element, see 8.3.8 and 10.3.3.8.
componentOf 2		[1..1]		This element is provided to store the *categoryEvent* element. See 8.3.18 and 10.3.3.18 for details of the *categoryEvent* element.

Element	Attribute	Multiplicity	Data type *Example of data*	Description
Submission rules of elements and attributes	At the initial submission, the ***component*** element must be included. If there is no ***contextOfUse*** element to be submitted at eCTD update, the ***component*** element is not included.			
Implementation Rules	The ***id@extension*** attribute must be unique to each ***submissionUnit***. The ***submissionUnit.statusCode*** element is not used in Japan. Consult the Regulatory Authority when you need to withdraw a Submission Unit. Although the ***submissionUnit.title*** element can be submitted, you should not assume that the Regulatory Authority refers to the value in ***title@value***.			

8.3.2   sequenceNumber

There is no difference in the use of ***componentOf1.sequenceNumber*** from those defined in ICH IG. Refer to ICH IG for details.

8.3.3   priorityNumber for contextOfUse

There is no difference in the use of ***component.priorityNumber*** from those defined in ICH IG. Refer to ICH IG for details.

8.3.4   contextOfUse

There is no difference in the use of ***contextOfUse*** from those defined in ICH IG. Refer to ICH IG for details.

8.3.5   relatedContextOfUse

There is no difference in the use of ***relatedContextOfUse*** from those defined in ICH IG. Refer to ICH IG for details.

8.3.6   documentReference

There is no difference in the use of ***documentReference*** from those defined in ICH IG. Refer to ICH IG for details.

8.3.7   keyword

There is no difference in the use of ***keyword*** from those defined in ICH IG. Refer to ICH IG for details. The study data of the clinical pharmacology area among the data included in the module 5 should be attached with "jp clinical Pharmacology study" selected from the "JP Study Type" code list of JP CV as a keyword.

8.3.8   submission

The ***submission*** element exists between the elements of ***submissionUnit*** and ***application,*** providing information of one or more items submitted with strings attached to one Submission

Unit. As a general rule, one *submissionUnit* element has one *submission* element, while one *submission* element has one *application* element.

8.3.8.1 Programming Positions

On the eCTD v4.0 XML Message Instance, the *submission* element should be written at the place shown below.

- *controlActProcess >> submissionUnit >> componentOf >> submission*

8.3.8.2 XML Programming Example

An example of XML programming of the *submission* element is shown below:

```
<submission>
    <id>
        <item root="36589652-7894-6589-3256-321852697531" extension="240505001"/>
    </id>
    <code code="jp original" codeSystem=" jp-submission "/>
    <subject2>
        ...[partly omitted]...
    </subject2>
    <componentOf>
        ...[partly omitted]...
    </componentOf>
</submission>
```

8.3.8.3 XML Elements and Attributes

In the table below, the *submission* element, the subordinate elements, and their attributes are listed.

Element	Attribute	Multiplicity	Data type *Example of data*	Description
submission		[1..1]		This element stores information of the items submitted with strings attached to the Submission Unit.
id		[1..1]		This element stores an identifier of the eCTD application.
item		[1..1]		This element stores an identifier of the eCTD application.

Element	Attribute	Multiplicity	Data type *Example of data*	Description
	root	[1..1]	Valid UUID *Example: root=" 36589652-7894-658 9-3256-3218526975 31"*	UUID of this Submission. According to the algorithm defined in ICH IG, the applicant issues the number.
	extension	[1..1]	Alpha Numeric *Example: extension= "240505001"*	eCTD receipt number
code		[1..1]		This element stores a condition of the eCTD application (original submitted, submitted as reference, etc.).
	code	[1..1]	Alpha Numeric *Example: code="jp original"*	This is a code value indicating a condition of the eCTD application. The code value is selected from the "JP Submission" code list of JP CV.
	codeSystem	[1..1]	Valid OID *Example: codeSystem="jp-sub mission"*	OID of the "JP Submission" code list.
subject2		[0..*]		This element is provided to store the *review* element. For details of the *review* element, see 8.3.9 and 10.3.3.9.
Submission rules of elements and attributes	The *submission* element must be always submitted. When submitting a new *review* element or changing information of the existing *review* subordinate elements, the *subject2* element should be submitted. For details of submitting the *review* element, see 8.3.9 and 10.3.3.9.			
Implementation Rules	As a general rule, the following attributes, regardless of whether information of any subordinates of the *submission* element are changed, should provide the same values through the entire life cycle of one application. • *id.item@root* • *id.item@extension* • *code@code* • *code@codeSystem* When these values need to be changed, consult the Regulatory Authority in advance.			

8.3.9 review

The *review* elements should be submitted for each application to provide application information.

8.3.9.1 Programming Positions

On the eCTD v4.0 XML Message Instance, the *review* element should be written at the place shown below.

- *controlActProcess >> submissionUnit >> componentOf >> submission >> subject2 >>review*

8.3.9.2 XML Programming Example

An example of XML programming of the *review* element is shown below:

```
<subject2>
    <review>
        <id root="36589652-7894-6589-3256-321852697531"/>
        <statusCode code="active"/>
        <subject1>
            ...[partly omitted]...
        </subject1>
        <holder>
            ...[partly omitted]...
        </holder>
        <subject2>
            ...[partly omitted]...
        </subject2>
    </review>
</subject2>
```

8.3.9.3 XML Elements and Attributes

In the table below, the *review* element, the subordinate elements, and their attributes are listed.

Element	Attribute	Multiplicity	Data type *Example of data*	Description
review		[1..1]		This element stores information of the application form.
id		[1..1]		This element stores an identifier of the *review* element.

Element	Attribute	Multiplicity	Data type *Example of data*	Description
	root	[1..1]	Valid UUID *Example: root=" 36589652-7894-658 9-3256-3218526975 31"*	UUID of the application information. According to the algorithm defined in ICH IG, the applicant issues the number.
statusCode		[1..1]		This element stores information indicating a status of the *review* element.
	code	[1..1]	"active" or "suspended" *Example: code="active"*	A code indicating a status of this review. For details, see 10.3.3.9 in this implementation guide.
subject1		[0..1]		This element is provided to store the *manufacturedProduct* element. For details of the *manufacturedProduct* element, see 8.3.10 and 10.3.3.10 in this implementation guide.
holder		[0..1]		This element is provided to store the *applicant* element. For details of the *applicant* element, see 8.3.12 and 10.3.3.12 in this implementation guide.
subject2		[0..*]		This element is provided to store the *productCategory* element. For details of the *productCategory* element, see 8.3.13 and 10.3.3.13 in this implementation guide.
Submission rules of elements and attributes	At the initial submission, all of the elements and attributes described above should be provided. For details of submission at eCTD update, see 10.3.3.9. The *subject2* element should be submitted for each application category.			
Implementation Rules	Through the entire life cycle including the initial submission, a value in *statusCode@code* of the *review* element must be "active". Through the entire life cycle, *review.statusCode@code* should not provide any value other than "active" or "suspended". For details of submission at eCTD update, see 10.3.3.9.			

8.3.10   manufacturedProduct

The *manufacturedProduct* element containing product information should be provided for

every *review* element one-on-one. One *manufacturedProduct* element has one subordinate

which name includes the same string of **manufacturedProduct**; in this implementation guide, the former is called as the **manufacturedProduct** element and the latter the **manufacturedProduct.manufacturedProduct** element.

8.3.10.1   Programming Positions

On the eCTD v4.0 XML Message Instance, the **manufacturedProduct** element should be written at the place shown below.

- *controlActProcess >> submissionUnit >> componentOf >> submission >> subject2 >> review >> subject1 >>manufacturedProduct*

8.3.10.2   XML Programming Example

The XML programming example of the **manufacturedProduct** element is shown below:

```
<subject1>
    <manufacturedProduct>
        <manufacturedProduct>
            <name>
                <part value="Feel Good 10mg 錠"/>
            </name>
            <ingredient>
                ...[partly omitted]...
            </ingredient>
        </manufacturedProduct>
    </manufacturedProduct>
</subject1>
```

8.3.10.3   XML Elements and Attributes

In the table below, the **manufacturedProduct** element, the subordinate elements, and their attributes are listed.

Element	Attribute	Multiplicity	Data type *Example of data*	Description
manufacturedProduct		[1..1]		This element stores product information.
manufacturedProduct		[1..1]		This element stores product information.
name		[1..1]		This element stores a product name.
part		[1..1]		This element stores a product name.

Element	Attribute	Multiplicity	Data type *Example of data*	Description
	value	[1..1]	Alpha Numeric+Japanese Character *Example: value="セイヤクキョール 錠 10mg"*	A product name of the drug formulation tied to this application.
ingredient		[1..*]		This element is provided to store the ***ingredientSubstance*** element. For details of the ***ingredientSubstance*** element, see 8.3.11 and 10.3.3.11 in this implementation guide.
Submission rules of elements and attributes	Submitting the ***review.subject1*** element involves all of the elements and attributes described above. For the necessity of submission of the ***review.subject1*** element, see 10.3.3.9. The ***ingredient*** element should be submitted for each active ingredient contained in the product.			
Implementation Rules	A value of ***part@value*** should be specified by a string identical to the product name described in the application form and then submitted.			

8.3.11   ingredientSubstance

The ***ingredientSubstance*** element should be submitted for each active ingredient in each drug formulation along with the ***ingredient*** element and has a name of the active ingredient as an attribute value of its subordinate element.

8.3.11.1   Programming Positions

On the eCTD v4.0 XML Message Instance, the ***ingredientSubstance*** element should be written at the place shown below.

- *controlActProcess >> submissionUnit >> componentOf >> submission >> subject2 >> review >> subject1 >> manufacturedProduct >>manufacturedProduct >>ingredient >>ingredientSubstance*

8.3.11.2   XML Programming Example

An example of XML programming of the ***ingredientSubstance*** element is shown below:

```
<ingredient classCode="INGR">
    <ingredientSubstance>
      <name>
          <part value="Drug123" code="jp jan" codeSystem="jp-substance-name-type"/>
```

           </name>

    </ingredientSubstance>

</ingredient>

8.3.11.3 XML Elements and Attributes

In the table below, the ***ingredientSubstance*** element, the subordinate elements, and their attributes are listed.

Element	Attribute	Multiplicity	Data type *Example of data*	Description
ingredientSubstance		[1..1]		This element stores a name of the active ingredient.
name		[1..1]		This element stores a name of the active ingredient.
part		[1..1]		This element stores a name of the active ingredient.
	value	[1..1]	Alpha Numeric+Japanese Character *Example*: value= "イーアイ塩酸塩"	General name of the active ingredient.
	code	[1..1]	Alpha Numeric *Example: code="jp jan"*	A code indicating a type of the general name of the active ingredient. It is selected from the "JP Substance Name Type" code list of JP CV.
	codeSystem	[1..1]	Alpha Numeric *Example: code="jp-substance-name-type"*	OID of the "JP Substance Name Type" code list.
Submission rules of elements and attributes	Submitting the ***ingredient*** element involves all of the elements and attributes described above.			
Implementation Rules	A value of ***part@value*** should be specified by a string identical to the general name described in the application form and then submitted.			

8.3.12 applicant

The ***applicant*** element provides information of the applicant. For eCTD application in Japan, the applicant information is associated only with the ***review*** element. One ***review*** element can contain one ***applicant*** element.

8.3.12.1 Programming Positions

On the eCTD v4.0 XML Message Instance, the ***applicant*** element should be written at the place shown below.

- *controlActProcess >> submissionUnit >> componentOf >> submission >> subject2 >> review >> holder >> applicant*

8.3.12.2   XML Programming Example

An example of XML programming of the ***applicant*** element is shown below:

```
<holder>
    <applicant>
        <sponsorOrganization>
            <name>
                <part value="New Wave Pharmaceutical"/>
            </name>
        </sponsorOrganization>
    </applicant>
</holder>
```

8.3.12.3   XML Elements and Attributes

In the table below, the ***applicant*** element, the subordinate elements, and their attributes are listed.

Element	Attribute	Multiplicity	Data type *Example of data*	Description
applicant		[1..1]		This element stores a name of the applicant.
sponsorOrganization		[1..1]		This element stores a name of the applicant.
name		[1..1]		This element stores a name of the applicant.
part		[1..1]		This element stores a name of the applicant.
	value	[1..1]	Alpha Numeric + Japanese characters *Example: extension="JPMA 製薬株式会社"*	Applicant name of this application.
Submission rules of elements and attributes	Submitting the ***review.holder*** element involves all of the elements and attributes described above. For the necessity of submission of the ***review.holder*** element, see 10.3.3.9.			
Implementation Rules	A value of the ***part@value*** attribute should be specified by a string identical to the applicant name described in the application form.			

8.3.13　productCategory

The *productCategory* element provides a category of application. One *review* element can have one or more *subject2.productCategory* elements that are stated for each product category described in the application form.

8.3.13.1　Programming Positions

On the eCTD v4.0 XML Message Instance, the *productCategory* element should be written at the place shown below.

- *controlActProcess >> submissionUnit >> componentOf >> submission >> subject2 >> review >> subject2 >> productCategory*

8.3.13.2　XML Programming Example

An example of XML programming of the *productCategory* element is shown below:

```
<subject2>
    <productCategory>
        <code code="jp 1-1" codeSystem="jp-product-category"/>
    </productCategory>
</subject2>
```

8.3.13.3　XML Elements and Attributes

In the table below, the *productCategory* element, the subordinate elements, and their attributes are listed.

Element	Attribute	Multiplicity	Data type *Example of data*	Description
productCategory		[1..1]		This element stores a category of application.
code		[1..1]		This element stores a category of application.
	code	[1..1]	Alpha Numeric *Example: code=" jp 1-1"*	A code indicating a category of application. It is selected from the "JP Product Category" code list of JP CV.
	codeSystem	[1..1]	Valid OID *Example: codeSystem="jp-product-category"*	OID of the "JP Product Category" code list.
Submission rules of elements and attributes	Submitting the *review.subject2* element involves all of the elements and attributes described above. For the necessity of submission of the *review.subject2* element, see 10.3.3.9.			
Implementation Rules	A value of the *code@code* attribute should be specified by a value identical to the applicant category described in the application form.			

8.3.14 application

The *application* element provides both of document information and additional information submitted with strings attached to both of this application and another application related to one Submission Unit. One *submission* element always contains one *application* element.

8.3.14.1 Programming Positions

On the eCTD v4.0 XML Message Instance, the *application* element should be written at the place shown below.

- *controlActProcess >> submissionUnit >> componentOf >> submission >> componentOf >> application*

8.3.14.2 XML Programming Example

An example of XML programming of the *application* element is shown below:

```
<componentOf>
    <application>
        <id>
            <item root="69165720-5006-0001-0000-100100000001" extension="250205001"/>
        </id>
        <code code="jp maa" codeSystem="jp-application"/>
        <reference>
        ...[partly omitted]...
        </reference>
        <component>
        ...[partly omitted]...
        </component>
        <referencedBy>
        ...[partly omitted]...
        </referencedBy>
    </application>
</componentOf>
```

8.3.14.3 XML Elements and Attributes

In the table below, the *application* element, the subordinate elements, and their attributes are listed.

Element	Attribute	Multiplicity	Data type *Example of data*	Description
application		[1..1]		This element stores information of the application submitted with strings attached to the Submission Unit.
id		[1..1]		This element stores an identifier of the eCTD application.
item		[1..1]		This element stores an identifier of the eCTD application.
	root	[1..1]	Valid UUID *Example: root=" 36589652-7894-658 9-3256-3218526975 31"*	UUID of this Application. According to the algorithm defined in ICH IG, the applicant issues the number.
	extension	[1..1]	Alpha Numeric *Example: extension="2405050 01"*	eCTD receipt number
code		[1..1]		This element stores a type of the eCTD application (e.g. manufacturing and marketing approval application).
	code	[1..1]	Alpha Numeric *Example: code="jp maa"*	A code indicating a type of the eCTD application. The code value is selected from the "JP Application" code list of JP CV.
	codeSystem	[1..1]	Valid OID *Example: codeSystem="jp-app lication"*	OID of the "JP Application" code list.
reference		[0..*]		This element is provided to store the *applicationReference* element. For details of the *applicationReference* element, see 8.3.15 and 10.3.3.15 in this implementation guide.

Element	Attribute	Multiplicity	Data type *Example of data*	Description
component		[0..*]		This element is provided to store the *document* element. For details of the *document* element, see 8.3.16 and 10.3.3.16 in this implementation guide.
referencedBy		[0..*]		This element is provided to store the *keywordDefinition* element. For details of the *keywordDefinition* element, see 8.3.17 and 10.3.3.17 in this implementation guide.
Submission rules of elements and attributes	The *application* element must be always submitted. When there are other applications related to this one (hereafter referred to as "related applications"), the *reference* element must be submitted for every related application. The related applications should be submitted for each Submission Unit. For details of related applications, see 8.3.16 and 10.3.3.16. When there is a new Document to be submitted by the Submission Unit, the *component* element should be submitted for every Document. For details of Document, see 8.3.16 and 10.3.3.16. When submitting a new Keyword Definition to be used in this application, the *referencedBy* element should be submitted for every Keyword Definition. For details of Keyword Definition, see 8.3.17 and 10.3.3.17.			
Implementation Rules	As a general rule, the following attributes, regardless of whether information of the subordinate elements of *application* are changed, should provide the same values through the entire life cycle of one application. • *id.item@root* • *id.item@extension* • *code@code* • *code@codeSystem* When these values need to be changed, consult the Regulatory Authority in advance.			

8.3.15　applicationReference

　　　The *applicationReference* element provides information about related applications. For example, it can be used to refer to the application of already-approved items at the application for partial change approval. In this case, the related application must be submitted by eCTD as an original. One *application* element can have one or more *applicationReference* elements in the submission; however, when there is no related eCTD application, no *applicationReference* element is required. When there are multiple related eCTD applications, the *applicationReference* element should be described for every related eCTD application.

8.3.15.1　Programming Positions

　　　On the eCTD v4.0 XML Message Instance, the *applicationReference* element should be written at the place shown below.

- *controlActProcess >> submissionUnit >> componentOf >> submission >> componentOf >> application >>reference >> applicationReference*

8.3.15.2   XML Programming Example

An example of XML programming of the *applicationReference* element is shown below:

```xml
<reference>
    <applicationReference>
        <id root="36589652-7894-6589-3256-321852697531"/>
        <reasonCode>
            <item>
                <code code="jp ichihen" codeSystem="jp-application-reference-reason"/>
            </item>
        </reasonCode>
    </applicationReference>
<reference>
```

8.3.15.3   XML Elements and Attributes

In the table below, the *applicationReference* element, the subordinate elements, and their attributes are listed.

Element	Attribute	Multiplicity	Data type *Example of data*	Description
applicationReference		[1..1]		This element stores information of the related application.
id		[1..1]		This element stores an identifier of the related application.
	root	[1..1]	Alpha Numeric *Example: root="1234.1234.12 34.12345.0002.0003 .0001"*	A value of ***application.id.item@root*** of the related application. An eCTD receipt number for the related application of eCTD v3.2.2.
reasonCode		[1..1]		This element stores a type of relationship.
item		[1..*]		This element stores a type of relationship.

Element			Attribute	Multiplicity	Data type *Example of data*	Description
			code	[1..1]	Alpha Numeric *Example: code=" jp ichihen"*	A code indicating a type of relationship with the related application defined by ***applicationReference.id@root***. The code value is selected from the "JP Application Reference Reason" code list of JP CV.
			codeSystem	[1..1]	Valid OID *Example: codeSystem="jp-app lication-reference-re ason"*	OID of the "JP Application Reference Reason" code list.
Submission rules of elements and attributes			Submitting the ***applicationReference*** element involves all of the elements and attributes described above. The ***reasonCode.item*** element should be submitted for every type of relationship.			
Implementation Rules			At the submission of each Submission Unit, all of the existing related applications should be submitted. For example, when the initial submission involving two related applications was made without the submission sequence number "2" specified, it is assumed that these related applications are not associated with the submission sequence number "2".			

8.3.16 document

Basically there is no difference in the use of ***document*** from those defined in ICH IG. Refer to ICH IG for details. It is recommended not to submit the attributes shown below:

- ***document.text@language***
- ***document.text@mediaType***

And the ***document*** element must be referred to by the Context of Use of the Submission Unit where this document element has been submitted.

8.3.17 keywordDefinition

There is no difference in the use of ***keywordDefinition*** from those defined in ICH IG. Refer to ICH IG for details.

8.3.18 categoryEvent

The ***categoryEvent*** element indicates the time at which the Submission Unit was submitted during the review. One ***submissionUnit*** element contains one ***categoryEvent*** element.

8.3.18.1 Programming Positions

On the eCTD v4.0 XML Message Instance, the ***categoryEvent*** element should be written at the place shown below.

- *controlActProcess >> submissionUnit >> componentOf2 >> categoryEvent*

8.3.18.2   XML Programming Example

An example of XML programming of the *categoryEvent* element is shown below:

```
<componentOf2>
    <categoryEvent>
        <code code="jp first" codeSystem=" jp-category-event "/>
    </categoryEvent>
</componentOf2>
```

8.3.18.3   XML Elements and Attributes

In the table below, the *categoryEvent* element, the subordinate elements, and their attributes are listed.

Element	Attribute	Multiplicity	Data type *Example of data*	Description
categoryEvent		[1..1]		This element stores the time at which the Submission Unit was submitted.
code		[1..1]		This element stores the time at which the Submission Unit was submitted.
	code	[1..1]	Alpha Numeric *Example: code= " jp first"*	A code indicating when the Submission Unit was submitted during the review. The code value is selected from the "JP Category Event" code list of JP CV.
	codeSystem	[1..1]	Valid OID *Example: codeSystem= "jp-category-event"*	OID of the "JP Category Event" code list.
Submission rules of elements and attributes	The *categoryEvent* element should be always submitted.			
Implementation Rules	As a general rule, the Submission Unit intended for the initial submission, expert consultation, or working party should be submitted only once throughout the life cycle. When these *code@code* values need to be submitted several times in one eCTD application, consult the Regulatory Authority in advance.			

9.   Security

9.1   Checksum

- The eCTD application should contain checksums for individual files including a checksum file for the eCTD v4.0 XML message instance.

- Checksum of each file should be described as the contents of the ***integrityCheck*** element under the ***document*** element in the eCTD v4.0 XML message instance (submissionunit.xml).
- Checksum of the XML v4.0 eCTD message instance should be described in a text file named as sha256.txt to store in the folder containing submissionunit.xml. This checksum value should be also written on the eCTD cover letter for submission. When submitting via the portal site provided by the Regulatory Authority, however, the cover letter PDF file is not required to be separately submitted because the similar information is entered on the portal site to send.

9.2 Encryption, Transportation:

- When creating individual files for eCTD, the applicant should not include security settings and password protection at the file level in those files.
- When sending information by mail or other means, the applicant should assume all liability for the eCTD until it is delivered to the Regulatory Authority.

10. Life Cycle Management

10.1 Overview

The eCTD life cycle management in Japan is managing individual applications for additions and/or changes made on the application materials, instead of collectively managing applications of one product for a new marketing approval, a partial change approval, etc. For individual eCTD submissions, the application materials are stored in the folders (m1, m2, m3, m4, and m5) numbered according to the submission sequence number (1, 2...) under the eCTD receipt number. The scope of the eCTD life cycle management in Japan is, when any addition, change, or deletion have been made to an application, to identify which file in the application materials is relevant for the review of the submission and manage such files individually by its attribute information.

The eCTD v4.0 life cycle management in Japan, in principle, takes the difference submission approach to the XML message instances and files. For the eCTD submission with the sequence number "2" or higher, the applicant should submit only new or modified information. Note that, by the nature or technical definition of information or specifications, there may be cases where some unchanged information also needs to be provided. For details, see 10.3 in this implementation guide.

10.2   Requirements for eCTD Initial Submission

10.2.1   Folder Structure at Initial Submission

To create a folder structure, refer to Section 5 in this implementation guide. Note that an empty folder (i.e. containing no files) should not be created.

10.2.2   Files at Initial Submission

The components of the initial eCTD submission should be prepared in reference to Section 4.1, 4.2, and Section 6 through 8 in this implementation guide.

10.2.3   eCTD v4.0 XML Message Instance at Initial Submission

The fundamental structures should comply with ICH IG. This section describes Japan specific issues. For details, see 12.2 Sample of eCTD v4.0 XML Message Instance in this implementation guide.

1)   XML snippet from *submissionUnit* to *categoryEvent*

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

-------(For details of contextOfUse and submission, refer to 2) and 3) in this section.)-------

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

A: UUID of this submissionUnit based on ICH IG
B: eCTD Receipt Number-Submission Sequence Number (e.g.: "240505001-1")
C: A code indicating a type of the submissionUnit (See "JP Submission Unit" in JP CV.)
D: OID of the code list defining a code of the Submission Unit (C: shown above)
E: A code indicating the time at which the Submission Unit was submitted during the review (See "JP Category Event" in JP CV.)
F: OID of the code list defining a code of this Category Event (E: shown above)

2)   XML snippet for the *contextOfUse* element

```
<component>
    <priorityNumber value="G"/>
    <contextOfUse>
        <id root="H"/>
        <code code="I" codeSystem="J"/>
        <statusCode code="K"/>
        <derivedFrom>
            <documentReference>
                <id root="L"/>
            </documentReference>
        </derivedFrom>
    </contextOfUse>
</component>
```

G: A value for defining the display order of CoUs in case where multiple CoUs with the same combination of code and keyword exist (required even when only one CoU of the same combination exists).

H: UUID of this CoU defined in ICH IG

I: A code indicating the CTD number where the document referred by the CoU is assigned (See "ICH CoU" in ICH CV or "JP Context of Use" in JP CV.)

J: OID of the code list defining a code of this CoU (I: shown above)

K: Status of this CoU defined in ICH IG

L: id@root of the reference document

3)   XML snippet for the ***submission*** element

```
<componentOf1>
    <sequenceNumber value="M"/>
    <submission>
        <id>
            <item root="N" extension="O"/>
        </id>
        <code code="P" codeSystem="Q"/>
        <subject2>
            <review>
                <id root="R"/>
                <statusCode code="S"/>
                <subject1>
                    <manufacturedProduct>
                        <manufacturedProduct>
                            <name>
                                <part value="T"/>
                            </name>
                            <ingredient classCode="INGR">
                                <ingredientSubstance>
                                    <name>
                                        <part value="U"/>
                                    </name>
                                </ingredientSubstance>
                            </ingredient>
                        </manufacturedProduct>
                    </manufacturedProduct>
                </subject1>
                <holder>
                    <applicant>
                        <sponsorOrganization>
                            <name>
                                <part value="V"/>
                            </name>
                        </sponsorOrganization>
                    </applicant>
                </holder>
                <subject2>
                    <productCategory>
                        <code code="W" codeSystem="X"/>
                    </productCategory>
                </subject2>
```

```
-------(For details of application, see 4) described below.)-------

            </review>
        </subject2>
    </submission>
</componentOf1>
```

M: A submission sequence number of this submissionUnit ("1" for the initial submission)
N: UUID of this submission
O: eCTD receipt number
P: A code indicating a condition of this submission (original submitted, submitted as reference, etc.) (See "JP Submission" in JP CV.)
Q: OID of the code list defining a code of this submission (P: shown above)
R: UUID of this review
S: Status of the application form ("active" or "suspended")
T: Product name
U: Name of active ingredient
V: Name of applicant
W: A code indicating the application category (See JP CV "JP Product Category".)
X: OID of the code list defining a code of the Product Category (W: shown above)

4) XML snippet from application to applicationReference

```
<componentOf>
    <application>
        <id>
            <item root="Y" extension="Z"/>
        </id>
        <code code="AA" codeSystem="AB"/>
        <reference>
            <applicationReference>
                <id root="AC"/>
                <reasonCode>
                    <item code="AD" codeSystem="AE"/>
                </reasonCode>
            </applicationReference>
        </reference>
```

Y: UUID of this Application.
Z: eCTD receipt number
AA: A code indicating a type of this Application (e.g. manufacturing and marketing approval application) (See JP CV "JP Application".)
AB: OID of the code list defining a code of this Application (AA: shown above)
AC: id@root of the Application related to this Application (a partial change approval application etc.) or an eCTD receipt number when the related application is eCTD v3.2.2.
AD: A code indicating a type of relationship as described above by AC (See JP CV "JP Application Reference Reason".)
AE: OID of the code list defining a code of the type of relationship (AD: shown above)

10.3   Requirements for eCTD Update

10.3.1   Folder Structure at Update

When updating eCTD (with the submission sequence number "2" or higher), only the

following folders should be submitted in accordance with the folder structure defined in ICH IG.

In the cases where there is no file to be included in the submission unit because of reusing the documents or files, a folder for the relevant CTD number should not be created.

- Top level folders
- Second-level folders (which name consists of the submission sequence number)
- Folders containing files to be submitted at this update and their parent folders

10.3.2   Document Files at Update

The following files should be included in the submission.

- Cover Letter
- eCTD v4.0 XML Message Instance (submissionunit.xml)
- sha256.txt
- Files added in the relevant submission unit

When submitting via the portal site provided by the Regulatory Authority, however, the cover letter is not necessarily.

10.3.3   eCTD v4.0 XML Message Instance at Update

The basic structure of eCTD v4.0 XML message instance should be built according to ICH IG. This section describes how to describe the Japan specific instances. For details, see 12.2 Sample of eCTD v4.0 XML Message Instance in this implementation guide.

10.3.3.1   submissionUnit

There is no difference in the use of this element from those defined in ICH IG as far as it goes. Refer to ICH IG for details. How to use the Japan specific elements and attributes is same as the way at the initial submission. See 8.3.1 and 10.2.3 in this implementation guide.

10.3.3.2   sequenceNumber

There is no difference in the use of this element from those defined in ICH IG as far as it goes. Refer to ICH IG for details. Note that a value in *sequenceNumber@value* must be increased by one.

10.3.3.3   priorityNumber for contextOfUse

There is no difference in the use of this element at update from those defined in ICH IG. Refer to ICH IG for details.

10.3.3.4   contextOfUse

There is no difference in the basic use of this element from those defined in ICH IG as far as it goes. Refer to ICH IG for details. The followings are some rules for changes made through life cycle.

- The value of *contextOfUse.code@code* is not allowed to be changed. When the CTD number of the previously submitted file needs to be changed to another (including

upper/lower level of granularity), the relevant Context of Use should be removed and then a new Context of Use should be submitted with the proper Code and Code System assigned.

- The value of ***contextOfUse.code@codeSystem*** is not allowed to be changed. When the CTD number of the previously submitted file needs to be changed to another on the different code list, the Context of Use should be removed and a new Context of Use should be submitted with the proper Code and Code System assigned.

- Replacement of Context of Use can be conducted only when there is a clear relationship between the replaced-from file (original) and the replaced-to file (replacing one). For example, if the replaced-to file is a succeeding version with the original conditions kept, yet includes a partial change, replacement is a proper action. However, when an irrelevant file had been mistakenly submitted at the past submission and replacing to a new correct file is required, as there is no relationship between these two files, replacement is not a proper action. In this case, the irrelevant file should be deleted and a new correct file should be submitted.

10.3.3.5 relatedContextOfUse

There is no difference in the use of this element at update from those defined in ICH IG. Refer to ICH IG for details.

10.3.3.6 documentReference

There is no difference in the use of this element at update from those defined in ICH IG. Refer to ICH IG for details.

10.3.3.7 keyword

There is no difference in the use of this element at update from those defined in ICH IG. Refer to ICH IG for details.

10.3.3.8 submission

This element is provided in all of the Submission Units. The following attributes should provide the same values through the entire life cycle of the submission.

- ***submission.id.item@root***
- ***submission.id.item@extension***
- ***submission.code@code***
- ***submission.code@codeSystem***

How to submit these attributes is same as the way at the initial submission. See 8.3.8 and 10.2.3 in this implementation guide. When changing or withdrawing the previously submitted application form information, or adding a new application form, the ***subject2*** element should be provided. For details, see 10.3.3.9.

10.3.3.9   review

One ***submission.subject2.review*** element should be submitted per application form; for multiple application forms, the ***subject2*** element should be repeated. When any changes occur in the contents of the application form through the life cycle of the review, such changes should be detailed in submissionunit.xml and submitted as described below:

- General Matters
  - ➢ The value of ***id@root*** in the ***review*** element once submitted should never be changed through the entire life cycle.
  - ➢ The ***review*** element once submitted should never be submitted again, unless any changes occur in the information of its subordinates.
- Additions
  - ➢ When adding a new application form at the submission with a submission sequence number "2" or higher, a new ***subject2*** element should be submitted along with all elements and attributes defined in 8.3.9 in this implementation guide.
- Withdrawing
  - ➢ eCTD submission is not required only for the purpose of withdrawing.
  - ➢ When an eCTD submission involves multiple application forms and some of those are to be withdrawn at the submission with a submission sequence number "2" or higher, at the eCTD update right after the submission of withdrawing application, the ***review*** element to be withdrawn should be provided along with ***id@root*** and ***statusCode@code***. In this case, a value of ***statusCode@code*** should be "suspended". No need to provide ***review.subject1***, ***review.holder***, nor ***review.subject2***.
- Modification
  - ➢ When changing the contents of application form at the submission with a submission sequence number "2" or higher, the ***review*** element to be modified should be submitted along with all elements and attributes defined in 8.3.9 in this implementation guide. In this case, the value of ***id@root*** should not be changed.

10.3.3.10   manufacturedProduct

When the contents in this element need to be changed midway through life cycle, all of the subordinate elements and attributes under the ***review*** element containing this ***manufacturedProduct*** element should be submitted. How to use these elements and attributes is same as the way at the initial submission. See 8.3.10 and 10.2.3 in this implementation guide.

10.3.3.11 ingredientSubstance

When the contents in this element need to be changed midway through life cycle, all of the subordinate elements and attributes under the *review* element containing this *ingredient* element should be submitted. How to use these elements and attributes is same as the way at the initial submission. See 8.3.11 and 10.2.3 in this implementation guide.

10.3.3.12 applicant

When the contents in this element need to be changed midway through life cycle, all of the subordinate elements and attributes under the *review* element containing this *applicant* element should be submitted. How to use these elements and attributes is same as the way at the initial submission. See 8.3.12 and 10.2.3 in this implementation guide.

10.3.3.13 productCategory

When the contents in this element need to be changed midway through life cycle, all of the subordinate elements and attributes under the *review* element containing this *productCategory* element should be submitted. How to use these elements and attributes is same as the way at the initial submission. See 8.3.13 and 10.2.3 in this implementation guide.

10.3.3.14 application

This element is provided in all of the Submission Units. The following attributes, in principle, should provide the same values through the entire life cycle of the submission.

- *application.id.item@root*
- *application.id.item@extension*
- *application.code@code*
- *application.code@codeSystem*

When these values need to be changed, consult the Regulatory Authority in advance. How to submit these attributes is same as the way at the initial submission. See 8.3.14 and 10.2.3 in this implementation guide.

10.3.3.15 applicationReference

Regardless of whether the initial or revision submission, the related applications, if any, should be provided using this element at the submission of the Submission Unit. How to submit the element is same as the way at the initial submission. See 8.3.15 and 10.2.3 in this implementation guide.

10.3.3.16 document

There is no difference in the use of this element at update from those defined in ICH IG. Refer to ICH IG for details.

10.3.3.17   keywordDefinition

There is no difference in the use of this element at update from those defined in ICH IG. Refer to ICH IG for details.

10.3.3.18   categoryEvent

This element is provided in all of the Submission Units. Regardless of whether the initial or revision submission, this element indicates the time at which the Submission Unit was submitted during the review. How to submit the element is same as the way at the initial submission. See 8.3.18 and 10.2.3 in this implementation guide.

10.4   Other Requirements

10.4.1   Reuse of Documents

There is no difference in techniques for reusing documents from those defined in ICH IG. Refer to ICH IG for details. For eCTD applications in Japan, documents can be reused when the application where the documents to be reused are defined and another application containing the *documentReference* element which refers to the documents to be reused have been submitted according to the eCTD v4.0 specifications, as well as the conditions of 1) and 2) described below are met.

1)   All conditions below must be met:

   1.   The application materials where the documents to be reused are defined should fall within the scope of document management by the Regulatory Authority and are submitted within the prescribed retention period.

2)   At least either one of the conditions below must be met.

   1.   The application where the documents to be reused are defined should have been approved.

   1.   A Submission Unit where the documents to be reused are defined and another Submission Unit containing the *documentReference* element for reference should reside under the same Application.

10.4.2   Reuse of Files

There is no difference in techniques for reusing files from those defined in ICH IG. Refer to ICH IG for details. Files can be reused when a Submission Unit providing the files to be reused and another Submission Unit containing the *document* element referring to the files to be reused comply with the eCTD v4.0 specifications and reside under the same Application. For the files having the same Document Title, the Document should be reused instead of the Files.

10.4.3 Document Title Update

There is no difference in techniques for Document Title update from those defined in ICH IG. Refer to ICH IG for details. It is assumed that Document Title update is intended to apply to all Submission Units (including those under another Application) referring to the same *document.id@root* value. When applying the update only to the specific Submission Unit, a new document with another value of *document.id@root* should be defined. And when at least either one of the following conditions is true, updating the Document Title is not permitted.

1) To update the title of the approved Document.
2) Under the Application where the Submission Unit involving Document Title update resides, the objective Document is not referred nor defined.
3) To update the title of the document submitted in other format than eCTD v4.0.

10.4.4 Update of Display Name in Keyword Definition

There is no difference in techniques for updating Display Name in Keyword Definition from those defined in ICH IG. Refer to ICH IG for details. It is assumed that Display Name update is intended to apply to all other Submission Units (including those submitted in the past) reside under the same Application. When changing Display Name only of the specific Submission Unit, a new Keyword Definition should be defined. Note that updating the Display Name does not affect the Submission Units under another Application.

10.4.5 Compatibility with eCTD v3.2.2

For eCTD application in Japan, the eCTD of the same version must be used from the initial submission through the end of life cycle. Therefore, for example, the leaf ID of the document submitted by v3.2.2 or earlier cannot be referred to by the application created by v4.0 or later. For the associations via the *applicationReference* element, however, the existing approval documents can be referred to using *applicationReference.id@root* containing the eCTD receipt number of the application created by v3.2.2 or earlier.

11. Contact Information

Contact information for eCTD v4.0 implementation in Japan is as follows: In principle, we consider that general questions should be addressed in public to be widespread in the entire industry, instead of responding to individual companies, and therefore any questions should be submitted through the pharmaceutical industry groups, such as JPMA. Except in cases where the specific items are concerned.

ectd@pmda.go.jp

12.   Appendixes

12.1   Specification of Module 1

12.1.1   Purpose

This section provides specifications when creating Module 1 by the electronic method.

12.1.2   Folder Structures and Naming Conventions

Folders in Module 1, in principle, should be structured and named as described below. The applicant may create folders under the jp folder, as required.

m1/jp

12.1.3   File Naming in Module 1

To name a file in Module 1, refer to the following list. Note that the cover letter file must be named as cover.pdf.

Listed below are the file names used in Module 1:

Title	File Name
Cover Letter	cover.pdf
1.1-1 Table of contents of the application materials containing Part 1 (Module 1)	m1-01-01.pdf
1.1-2 Summary table	m1-01-02.pdf
1.2 Approval application form (copy)	m1-02-XX.pdf
1.3-1 Statement of personnel responsible for collection and compilation of data for approval application materials	m1-03-01.pdf
1.3-2 Statement about scanning of paper document	m1-03-02.pdf
1.4 Information on patent matters	m1-04-01.pdf
1.5 Details of origin, discovery, and development	m1-05-01.pdf
1.6 Information of foreign countries concerning drug usage, etc.	m1-06-01.pdf
1.7 List of similar products with the same therapeutic category and the same efficacy	m1-07-01.pdf
1.8 Package insert (draft)	m1-08-01.pdf
1.9 Documents pertaining to general (non-proprietary) name of the drug	m1-09-01.pdf
1.10 Summary of review data for the designation of poisonous/powerful drugs, etc.	m1-10-01.pdf
1.11 Master plan for risk management of pharmaceutical drugs (daft)	m1-11-01.pdf
1.12-1 List of appendixes (PDF)	m1-12-01.pdf
1.12-2 List of appendixes (MS Excel)	m1-12-02.xls(x)
1.13-1-1 Approval certificate (copy)	m1-13-01-01.pdf
1.13-1-2 Review report	m1-13-01-02.pdf
1.13-1-3 Summary of reference materials	m1-13-01-03.pdf
1.13-1-4 List of appendixes	m1-13-01-04.pdf
1.13-2 Records of clinical trial consultation (copy)	m1-13-02-XX.pdf
1.13-3 Inquiries (copy) and responses (copy)	m1-13-03-XX.pdf
1.13-4-1-1-1 List of appendixes concerning new additives	m1-13-04-01-01-01.pdf
1.13-4-1-1-2 Summary of individual review items	m1-13-04-01-01-02.pdf

Title	File Name
1.13-4-1-1-3 Approval application form (copy)	m1-13-04-01-01-03.pdf
1.13-4-1-1-4 Summary of new additives	m1-13-04-01-01-04.pdf
1.13-4-1-1-XX Reference materials concerning new additives: Appendix XX	m1-13-04-01-01-XX.pdf
1.13-4-1-2 List of main manufacturing process parameters not mentioned in approval application form	m1-13-04-01-02.pdf

12.2 Sample of eCTD v4.0 XML Message Instance

12.2.1 At Initial Submission

```
<?xml version="1.0" encoding="UTF-8"?>
<PORP_IN000001UV ITSVersion="XML_1.0" xmlns="urn:hl7-org:v3" xmlns:xsi="http://
www.w3.org/2001/XMLSchema-instance" xsi:schemaLocation="urn:hl7-org:v3 ../../schema/P
ORP_IN000001UV.xsd">
  <id/>
  <creationTime/>
  <interactionId/>
  <processingCode/>
  <processingModeCode/>
  <acceptAckCode/>
  <receiver typeCode="RCV">
      <device classCode="DEV" determinerCode="INSTANCE">
          <id/>
      </device>
  </receiver>
  <sender typeCode="SND">
      <device classCode="DEV" determinerCode="INSTANCE">
          <id/>
      </device>
  </sender>
  <controlActProcess classCode="ACTN" moodCode="EVN">
      <subject typeCode="SUBJ">
          <submissionUnit>
              <id root="1234.1234.1234.12345.0000" extension="230525001-1"/>
              <code code="jp official" codeSystem="jp-submission-unit"/>
              <component>
                  <priorityNumber value="1000"/>
                  <contextOfUse>
                      <id root="0.123.456.230525001.0812.0000001"/>
                      <code code="jp 1.1" codeSystem="jp-context-of-use"/>
                      <statusCode code="active"/>
                      <derivedFrom>
                          <documentReference>
                              <id root="0.321.456.230525001.0812.0000001"/>
                          </documentReference>
                      </derivedFrom>
                  </contextOfUse>
              </component>
              <component>
                  <priorityNumber value="2000"/>
                  <contextOfUse>
                      <id root="0.123.456.230525001.0812.0000002"/>
```

```
                <code code="jp 1.1" codeSystem="jp-context-of-use"/>
                <statusCode code="active"/>
                <derivedFrom>
                    <documentReference>
                        <id root="0.321.456.230525001.0812.0000002"/>
                    </documentReference>
                </derivedFrom>
            </contextOfUse>
        </component>
        <component>
            <priorityNumber value="1000"/>
            <contextOfUse>
                <id root="0.123.456.230525001.0812.0000003"/>
                <code code="jp 1.2" codeSystem="jp-context-of-use"/>
                <statusCode code="active"/>
                <derivedFrom>
                    <documentReference>
                        <id root="0.321.456.230525001.0812.0000003"/>
                    </documentReference>
                </derivedFrom>
            </contextOfUse>
        </component>
        <component>
            <priorityNumber value="2000"/>
            <contextOfUse>
                <id root="0.123.456.230525001.0812.0000004"/>
                <code code="jp 1.2" codeSystem="jp-context-of-use"/>
                <statusCode code="active"/>
                <derivedFrom>
                    <documentReference>
                        <id root="0.321.456.230525001.0812.0000004"/>
                    </documentReference>
                </derivedFrom>
            </contextOfUse>
        </component>
        <component>
            <priorityNumber value="1000"/>
            <contextOfUse>
                <id root="0.123.456.230525001.0812.0000005"/>
                <code code="jp 1.3" codeSystem="jp-context-of-use"/>
                <statusCode code="active"/>
                <derivedFrom>
                    <documentReference>
                        <id root="0.321.456.230525001.0812.0000005"/>
                    </documentReference>
                </derivedFrom>
            </contextOfUse>
        </component>
        <component>
            <priorityNumber value="2000"/>
            <contextOfUse>
                <id root="0.123.456.230525001.0812.0000006"/>
                <code code="jp 1.3" codeSystem="jp-context-of-use"/>
                <statusCode code="active"/>
```

```
            <derivedFrom>
               <documentReference>
                  <id root="0.321.456.230525001.0812.0000006"/>
               </documentReference>
            </derivedFrom>
         </contextOfUse>
      </component>
      <component>
         <priorityNumber value="1000"/>
         <contextOfUse>
            <id root="0.123.456.230525001.0812.0000007"/>
            <code code="jp 1.4" codeSystem="jp-context-of-use"/>
            <statusCode code="active"/>
            <derivedFrom>
               <documentReference>
                  <id root="0.321.456.230525001.0812.0000007"/>
               </documentReference>
            </derivedFrom>
         </contextOfUse>
      </component>
      <component>
         <priorityNumber value="1000"/>
         <contextOfUse>
            <id root="0.123.456.230525001.0812.0000008"/>
            <code code="jp 1.5" codeSystem="jp-context-of-use"/>
            <statusCode code="active"/>
            <derivedFrom>
               <documentReference>
                  <id root="0.321.456.230525001.0812.0000008"/>
               </documentReference>
            </derivedFrom>
         </contextOfUse>
      </component>
      <component>
         <priorityNumber value="1000"/>
         <contextOfUse>
            <id root="0.123.456.230525001.0812.0000009"/>
            <code code="jp 1.6" codeSystem="jp-context-of-use"/>
            <statusCode code="active"/>
            <derivedFrom>
               <documentReference>
                  <id root="0.321.456.230525001.0812.0000009"/>
               </documentReference>
            </derivedFrom>
         </contextOfUse>
      </component>
      <component>
         <priorityNumber value="1000"/>
         <contextOfUse>
            <id root="0.123.456.230525001.0812.0000010"/>
            <code code="jp 1.7" codeSystem="jp-context-of-use"/>
            <statusCode code="active"/>
            <derivedFrom>
               <documentReference>
```

```
                    <id root="0.321.456.230525001.0812.0000010"/>
                </documentReference>
            </derivedFrom>
        </contextOfUse>
    </component>
    <component>
        <priorityNumber value="1000"/>
        <contextOfUse>
            <id root="0.123.456.230525001.0812.0000011"/>
            <code code="jp 1.8" codeSystem="jp-context-of-use"/>
            <statusCode code="active"/>
            <derivedFrom>
                <documentReference>
                    <id root="0.321.456.230525001.0812.0000011"/>
                </documentReference>
            </derivedFrom>
        </contextOfUse>
    </component>
    <component>
        <priorityNumber value="1000"/>
        <contextOfUse>
            <id root="0.123.456.230525001.0812.0000012"/>
            <code code="jp 1.9" codeSystem="jp-context-of-use"/>
            <statusCode code="active"/>
            <derivedFrom>
                <documentReference>
                    <id root="0.321.456.230525001.0812.0000012"/>
                </documentReference>
            </derivedFrom>
        </contextOfUse>
    </component>
    <component>
        <priorityNumber value="1000"/>
        <contextOfUse>
            <id root="0.123.456.230525001.0812.0000013"/>
            <code code="jp 1.10" codeSystem="jp-context-of-use"/>
            <statusCode code="active"/>
            <derivedFrom>
                <documentReference>
                    <id root="0.321.456.230525001.0812.0000013"/>
                </documentReference>
            </derivedFrom>
        </contextOfUse>
    </component>
    <component>
        <priorityNumber value="1000"/>
        <contextOfUse>
            <id root="0.123.456.230525001.0812.0000014"/>
            <code code="jp 1.11" codeSystem="jp-context-of-use"/>
            <statusCode code="active"/>
            <derivedFrom>
                <documentReference>
                    <id root="0.321.456.230525001.0812.0000014"/>
                </documentReference>
```

```
            </derivedFrom>
          </contextOfUse>
      </component>
      <component>
          <priorityNumber value="1000"/>
          <contextOfUse>
            <id root="0.123.456.230525001.0812.0000015"/>
            <code code="jp 1.12" codeSystem="jp-context-of-use"/>
            <statusCode code="active"/>
            <derivedFrom>
                <documentReference>
                  <id root="0.321.456.230525001.0812.0000015"/>
                </documentReference>
            </derivedFrom>
          </contextOfUse>
      </component>
      <component>
          <priorityNumber value="2000"/>
          <contextOfUse>
            <id root="0.123.456.230525001.0812.0000016"/>
            <code code="jp 1.12" codeSystem="jp-context-of-use"/>
            <statusCode code="active"/>
            <derivedFrom>
                <documentReference>
                  <id root="0.321.456.230525001.0812.0000016"/>
                </documentReference>
            </derivedFrom>
          </contextOfUse>
      </component>
      <component>
          <priorityNumber value="1000"/>
          <contextOfUse>
            <id root="0.123.456.230525001.0812.0000017"/>
            <code code="jp 1.13.2" codeSystem="jp-context-of-use"/>
            <statusCode code="active"/>
            <derivedFrom>
                <documentReference>
                  <id root="0.321.456.230525001.0812.0000017"/>
                </documentReference>
            </derivedFrom>
          </contextOfUse>
      </component>
      <component>
          <priorityNumber value="1000"/>
          <contextOfUse>
            <id root="0.123.456.230525001.0812.0000018"/>
            <code code="jp 1.13.4.1.1" codeSystem="jp-context-of-use"/>
            <statusCode code="active"/>
            <derivedFrom>
                <documentReference>
                  <id root="0.321.456.230525001.0812.0000018"/>
                </documentReference>
            </derivedFrom>
          </contextOfUse>
```

```
        </component>
        <component>
           <priorityNumber value="2000"/>
           <contextOfUse>
              <id root="0.123.456.230525001.0812.0000019"/>
              <code code="jp 1.13.4.1.1" codeSystem="jp-context-of-use"/>
              <statusCode code="active"/>
              <derivedFrom>
                 <documentReference>
                    <id root="0.321.456.230525001.0812.0000019"/>
                 </documentReference>
              </derivedFrom>
           </contextOfUse>
        </component>
        <component>
           <priorityNumber value="3000"/>
           <contextOfUse>
              <id root="0.123.456.230525001.0812.0000020"/>
              <code code="jp 1.13.4.1.1" codeSystem="jp-context-of-use"/>
              <statusCode code="active"/>
              <derivedFrom>
                 <documentReference>
                    <id root="0.321.456.230525001.0812.0000020"/>
                 </documentReference>
              </derivedFrom>
           </contextOfUse>
        </component>
        <component>
           <priorityNumber value="4000"/>
           <contextOfUse>
              <id root="0.123.456.230525001.0812.0000021"/>
              <code code="jp 1.13.4.1.1" codeSystem="jp-context-of-use"/>
              <statusCode code="active"/>
              <derivedFrom>
                 <documentReference>
                    <id root="0.321.456.230525001.0812.0000021"/>
                 </documentReference>
              </derivedFrom>
           </contextOfUse>
        </component>
        <component>
           <priorityNumber value="5000"/>
           <contextOfUse>
              <id root="0.123.456.230525001.0812.0000022"/>
              <code code="jp 1.13.4.1.1" codeSystem="jp-context-of-use"/>
              <statusCode code="active"/>
              <derivedFrom>
                 <documentReference>
                    <id root="0.321.456.230525001.0812.0000022"/>
                 </documentReference>
              </derivedFrom>
           </contextOfUse>
        </component>
        <component>
```

```
          <priorityNumber  value="6000"/>
          <contextOfUse>
            <id  root="0.123.456.230525001.0812.0000023"/>
            <code code="jp 1.13.4.1.1" codeSystem="jp-context-of-use"/>
            <statusCode  code="active"/>
            <derivedFrom>
              <documentReference>
                <id  root="0.321.456.230525001.0812.0000023"/>
              </documentReference>
            </derivedFrom>
          </contextOfUse>
      </component>
      <component>
          <priorityNumber  value="1000"/>
          <contextOfUse>
            <id  root="0.123.456.230525001.0812.0000024"/>
            <code code="jp 1.13.4.1" codeSystem="jp-context-of-use"/>
            <statusCode  code="active"/>
            <derivedFrom>
              <documentReference>
                <id  root="0.321.456.230525001.0812.0000024"/>
              </documentReference>
            </derivedFrom>
          </contextOfUse>
      </component>
      <component>
          <priorityNumber  value="1000"/>
          <contextOfUse>
            <id  root="0.123.456.230525001.0812.0000025"/>
            <code code="ich 2.2" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/>
            <statusCode  code="active"/>
            <derivedFrom>
              <documentReference>
                <id  root="0.321.456.230525001.0812.0000025"/>
              </documentReference>
            </derivedFrom>
          </contextOfUse>
      </component>
      <component>
          <priorityNumber  value="1000"/>
          <contextOfUse>
            <id  root="0.123.456.230525001.0812.0000026"/>
            <code code="ich 2.3" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/>
            <statusCode  code="active"/>
            <derivedFrom>
              <documentReference>
                <id  root="0.321.456.230525001.0812.0000026"/>
              </documentReference>
            </derivedFrom>
          </contextOfUse>
      </component>
      <component>
          <priorityNumber  value="1000"/>
          <contextOfUse>
```

```
            <id root="0.123.456.230525001.0812.0000027"/>
            <code code="ich 2.3.s" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/
>
            <statusCode code="active"/>
            <derivedFrom>
               <documentReference>
                  <id root="0.321.456.230525001.0812.0000027"/>
               </documentReference>
            </derivedFrom>
            <referencedBy typeCode="REFR">
               <keyword>
                  <code code="MANU001" codeSystem="0.123.456.230525001.1209.
10003"/>
               </keyword>
            </referencedBy>
            <referencedBy typeCode="REFR">
               <keyword>
                  <code code="SUBS001" codeSystem="0.123.456.230525001.1209.1
0002"/>
               </keyword>
            </referencedBy>
         </contextOfUse>
      </component>
      <component>
         <priorityNumber value="1000"/>
         <contextOfUse>
            <id root="0.123.456.230525001.0812.0000028"/>
            <code code="ich 2.3.p" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/
>
            <statusCode code="active"/>
            <derivedFrom>
               <documentReference>
                  <id root="0.321.456.230525001.0812.0000028"/>
               </documentReference>
            </derivedFrom>
            <referencedBy typeCode="REFR">
               <keyword>
                  <code code="MANU001" codeSystem="0.123.456.230525001.1209.
10003"/>
               </keyword>
            </referencedBy>
            <referencedBy typeCode="REFR">
               <keyword>
                  <code code="PROD001" codeSystem="0.123.456.230525001.1209.
10004"/>
               </keyword>
            </referencedBy>
            <referencedBy typeCode="REFR">
               <keyword>
                  <code code="DOSA001" codeSystem="0.123.456.230525001.1209.
10005"/>
               </keyword>
            </referencedBy>
         </contextOfUse>
```

```
        </component>
        <component>
            <priorityNumber value="1000"/>
            <contextOfUse>
                <id root="0.123.456.230525001.0812.0000029"/>
                <code code="ich 2.3.p" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/>
                <statusCode code="active"/>
                <derivedFrom>
                    <documentReference>
                        <id root="0.321.456.230525001.0812.0000029"/>
                    </documentReference>
                </derivedFrom>
                <referencedBy typeCode="REFR">
                    <keyword>
                        <code code="MANU001" codeSystem="0.123.456.230525001.1209.10003"/>
                    </keyword>
                </referencedBy>
                <referencedBy typeCode="REFR">
                    <keyword>
                        <code code="PROD002" codeSystem="0.123.456.230525001.1209.10004"/>
                    </keyword>
                </referencedBy>
                <referencedBy typeCode="REFR">
                    <keyword>
                        <code code="DOSA002" codeSystem="0.123.456.230525001.1209.10005"/>
                    </keyword>
                </referencedBy>
            </contextOfUse>
        </component>
        <component>
            <priorityNumber value="1000"/>
            <contextOfUse>
                <id root="0.123.456.230525001.0812.0000030"/>
                <code code="ich 2.3.a" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/>
                <statusCode code="active"/>
                <derivedFrom>
                    <documentReference>
                        <id root="0.321.456.230525001.0812.0000030"/>
                    </documentReference>
                </derivedFrom>
            </contextOfUse>
        </component>
        <component>
            <priorityNumber value="1000"/>
            <contextOfUse>
                <id root="0.123.456.230525001.0812.0000031"/>
                <code code="ich 2.4" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/>
                <statusCode code="active"/>
                <derivedFrom>
```

```
                <documentReference>
                    <id root="0.321.456.230525001.0812.0000031"/>
                </documentReference>
            </derivedFrom>
        </contextOfUse>
    </component>
    <component>
        <priorityNumber value="1000"/>
        <contextOfUse>
            <id root="0.123.456.230525001.0812.0000032"/>
            <code code="ich 2.5" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/>
            <statusCode code="active"/>
            <derivedFrom>
                <documentReference>
                    <id root="0.321.456.230525001.0812.0000032"/>
                </documentReference>
            </derivedFrom>
        </contextOfUse>
    </component>
    <component>
        <priorityNumber value="1000"/>
        <contextOfUse>
            <id root="0.123.456.230525001.0812.0000033"/>
            <code code="ich 2.6.1" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/
>
            <statusCode code="active"/>
            <derivedFrom>
                <documentReference>
                    <id root="0.321.456.230525001.0812.0000033"/>
                </documentReference>
            </derivedFrom>
        </contextOfUse>
    </component>
    <component>
        <priorityNumber value="1000"/>
        <contextOfUse>
            <id root="0.123.456.230525001.0812.0000034"/>
            <code code="ich 2.6.2" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/
>
            <statusCode code="active"/>
            <derivedFrom>
                <documentReference>
                    <id root="0.321.456.230525001.0812.0000034"/>
                </documentReference>
            </derivedFrom>
        </contextOfUse>
    </component>
    <component>
        <priorityNumber value="1000"/>
        <contextOfUse>
            <id root="0.123.456.230525001.0812.0000035"/>
            <code code="ich 2.6.3" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/
>
            <statusCode code="active"/>
```

```
                    <derivedFrom>
                      <documentReference>
                        <id  root="0.321.456.230525001.0812.0000035"/>
                      </documentReference>
                    </derivedFrom>
                  </contextOfUse>
              </component>
              <component>
                  <priorityNumber  value="1000"/>
                  <contextOfUse>
                    <id  root="0.123.456.230525001.0812.0000036"/>
                    <code  code="ich 2.6.4"  codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/
>
                    <statusCode  code="active"/>
                    <derivedFrom>
                      <documentReference>
                        <id  root="0.321.456.230525001.0812.0000036"/>
                      </documentReference>
                    </derivedFrom>
                  </contextOfUse>
              </component>
              <component>
                  <priorityNumber  value="1000"/>
                  <contextOfUse>
                    <id  root="0.123.456.230525001.0812.0000037"/>
                    <code  code="ich 2.6.5"  codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/
>
                    <statusCode  code="active"/>
                    <derivedFrom>
                      <documentReference>
                        <id  root="0.321.456.230525001.0812.0000037"/>
                      </documentReference>
                    </derivedFrom>
                  </contextOfUse>
              </component>
              <component>
                  <priorityNumber  value="1000"/>
                  <contextOfUse>
                    <id  root="0.123.456.230525001.0812.0000038"/>
                    <code  code="ich 2.6.6"  codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/
>
                    <statusCode  code="active"/>
                    <derivedFrom>
                      <documentReference>
                        <id  root="0.321.456.230525001.0812.0000038"/>
                      </documentReference>
                    </derivedFrom>
                  </contextOfUse>
              </component>
              <component>
                  <priorityNumber  value="1000"/>
                  <contextOfUse>
                    <id  root="0.123.456.230525001.0812.0000039"/>
```

```
                        <code code="ich 2.6.7" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/
>
                    <statusCode code="active"/>
                    <derivedFrom>
                        <documentReference>
                            <id root="0.321.456.230525001.0812.0000039"/>
                        </documentReference>
                    </derivedFrom>
                </contextOfUse>
            </component>
            <component>
                <priorityNumber value="1000"/>
                <contextOfUse>
                    <id root="0.123.456.230525001.0812.0000040"/>
                    <code code="ich 2.7.1" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/
>
                    <statusCode code="active"/>
                    <derivedFrom>
                        <documentReference>
                            <id root="0.321.456.230525001.0812.0000040"/>
                        </documentReference>
                    </derivedFrom>
                </contextOfUse>
            </component>
            <component>
                <priorityNumber value="1000"/>
                <contextOfUse>
                    <id root="0.123.456.230525001.0812.0000041"/>
                    <code code="ich 2.7.2" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/
>
                    <statusCode code="active"/>
                    <derivedFrom>
                        <documentReference>
                            <id root="0.321.456.230525001.0812.0000041"/>
                        </documentReference>
                    </derivedFrom>
                </contextOfUse>
            </component>
            <component>
                <priorityNumber value="1000"/>
                <contextOfUse>
                    <id root="0.123.456.230525001.0812.0000042"/>
                    <code code="ich 2.7.3" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/
>
                    <statusCode code="active"/>
                    <derivedFrom>
                        <documentReference>
                            <id root="0.321.456.230525001.0812.0000042"/>
                        </documentReference>
                    </derivedFrom>
                    <referencedBy typeCode="REFR">
                        <keyword>
                            <code code="INDI001" codeSystem="0.123.456.230525001.1209.1
0001"/>
```

```
                </keyword>
              </referencedBy>
            </contextOfUse>
        </component>
        <component>
          <priorityNumber value="1000"/>
          <contextOfUse>
            <id root="0.123.456.230525001.0812.0000043"/>
            <code code="ich 2.7.4" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/
>
            <statusCode code="active"/>
            <derivedFrom>
              <documentReference>
                <id root="0.321.456.230525001.0812.0000043"/>
              </documentReference>
            </derivedFrom>
          </contextOfUse>
        </component>
        <component>
          <priorityNumber value="1000"/>
          <contextOfUse>
            <id root="0.123.456.230525001.0812.0000044"/>
            <code code="ich 2.7.5" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/
>
            <statusCode code="active"/>
            <derivedFrom>
              <documentReference>
                <id root="0.321.456.230525001.0812.0000044"/>
              </documentReference>
            </derivedFrom>
          </contextOfUse>
        </component>
        <component>
          <priorityNumber value="1000"/>
          <contextOfUse>
            <id root="0.123.456.230525001.0812.0000045"/>
            <code code="ich 2.7.6" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/
>
            <statusCode code="active"/>
            <derivedFrom>
              <documentReference>
                <id root="0.321.456.230525001.0812.0000045"/>
              </documentReference>
            </derivedFrom>
          </contextOfUse>
        </component>
        <component>
          <priorityNumber value="1000"/>
          <contextOfUse>
            <id root="0.123.456.230525001.0812.0000046"/>
            <code code="ich 3.2.p.4.1" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.
1"/>
            <statusCode code="active"/>
            <derivedFrom>
```

```
                    <documentReference>
                       <id root="0.321.456.230525001.0812.0000046"/>
                    </documentReference>
                </derivedFrom>
                <referencedBy typeCode="REFR">
                   <keyword>
                       <code code="MANU001" codeSystem="0.123.456.230525001.1209.
10003"/>
                   </keyword>
                </referencedBy>
                <referencedBy typeCode="REFR">
                   <keyword>
                       <code code="PROD001" codeSystem="0.123.456.230525001.1209.
10004"/>
                   </keyword>
                </referencedBy>
                <referencedBy typeCode="REFR">
                   <keyword>
                       <code code="DOSA001" codeSystem="0.123.456.230525001.1209.
10005"/>
                   </keyword>
                </referencedBy>
                <referencedBy typeCode="REFR">
                   <keyword>
                       <code code="EXCI001" codeSystem="0.123.456.230525001.1209.1
0006"/>
                   </keyword>
                </referencedBy>
            </contextOfUse>
         </component>
         <component>
            <priorityNumber value="1000"/>
            <contextOfUse>
                <id root="0.123.456.230525001.0812.0000047"/>
                <code code="ich 3.2.p.4.1" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.
1"/>
                <statusCode code="active"/>
                <derivedFrom>
                   <documentReference>
                       <id root="0.321.456.230525001.0812.0000047"/>
                   </documentReference>
                </derivedFrom>
                <referencedBy typeCode="REFR">
                   <keyword>
                       <code code="MANU001" codeSystem="0.123.456.230525001.1209.
10003"/>
                   </keyword>
                </referencedBy>
                <referencedBy typeCode="REFR">
                   <keyword>
                       <code code="PROD001" codeSystem="0.123.456.230525001.1209.
10004"/>
                   </keyword>
                </referencedBy>
```

```
                    <referencedBy typeCode="REFR">
                       <keyword>
                          <code code="DOSA001" codeSystem="0.123.456.230525001.1209.
10005"/>
                       </keyword>
                    </referencedBy>
                    <referencedBy typeCode="REFR">
                       <keyword>
                          <code code="EXCI002" codeSystem="0.123.456.230525001.1209.1
0006"/>
                       </keyword>
                    </referencedBy>
                </contextOfUse>
             </component>
             <component>
                <priorityNumber value="1000"/>
                <contextOfUse>
                    <id root="0.123.456.230525001.0812.0000048"/>
                    <code code="ich 3.2.p.4.6" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.
1"/>
                    <statusCode code="active"/>
                    <derivedFrom>
                       <documentReference>
                          <id root="0.321.456.230525001.0812.0000048"/>
                       </documentReference>
                    </derivedFrom>
                    <referencedBy typeCode="REFR">
                       <keyword>
                          <code code="MANU001" codeSystem="0.123.456.230525001.1209.
10003"/>
                       </keyword>
                    </referencedBy>
                    <referencedBy typeCode="REFR">
                       <keyword>
                          <code code="PROD001" codeSystem="0.123.456.230525001.1209.
10004"/>
                       </keyword>
                    </referencedBy>
                    <referencedBy typeCode="REFR">
                       <keyword>
                          <code code="DOSA001" codeSystem="0.123.456.230525001.1209.
10005"/>
                       </keyword>
                    </referencedBy>
                    <referencedBy typeCode="REFR">
                       <keyword>
                          <code code="EXCI003" codeSystem="0.123.456.230525001.1209.1
0006"/>
                       </keyword>
                    </referencedBy>
                </contextOfUse>
             </component>
             <component>
                <priorityNumber value="1000"/>
```

```
                    <contextOfUse>
                        <id root="0.123.456.230525001.0812.0000049"/>
                        <code code="ich 3.2.p.8.1" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.
1"/>
                        <statusCode code="active"/>
                        <derivedFrom>
                            <documentReference>
                                <id root="0.321.456.230525001.0812.0000049"/>
                            </documentReference>
                        </derivedFrom>
                        <referencedBy typeCode="REFR">
                            <keyword>
                                <code code="MANU001" codeSystem="0.123.456.230525001.1209.
10003"/>
                            </keyword>
                        </referencedBy>
                        <referencedBy typeCode="REFR">
                            <keyword>
                                <code code="PROD001" codeSystem="0.123.456.230525001.1209.
10004"/>
                            </keyword>
                        </referencedBy>
                        <referencedBy typeCode="REFR">
                            <keyword>
                                <code code="DOSA001" codeSystem="0.123.456.230525001.1209.
10005"/>
                            </keyword>
                        </referencedBy>
                    </contextOfUse>
                </component>
                <component>
                    <priorityNumber value="1000"/>
                    <contextOfUse>
                        <id root="0.123.456.230525001.0812.0000050"/>
                        <code code="ich 3.2.p.8.2" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.
1"/>
                        <statusCode code="active"/>
                        <derivedFrom>
                            <documentReference>
                                <id root="0.321.456.230525001.0812.0000050"/>
                            </documentReference>
                        </derivedFrom>
                        <referencedBy typeCode="REFR">
                            <keyword>
                                <code code="MANU001" codeSystem="0.123.456.230525001.1209.
10003"/>
                            </keyword>
                        </referencedBy>
                        <referencedBy typeCode="REFR">
                            <keyword>
                                <code code="PROD001" codeSystem="0.123.456.230525001.1209.
10004"/>
                            </keyword>
                        </referencedBy>
```

```
                          <referencedBy typeCode="REFR">
                              <keyword>
                                  <code code="DOSA001" codeSystem="0.123.456.230525001.1209.
10005"/>
                              </keyword>
                          </referencedBy>
                       </contextOfUse>
                  </component>
                  <component>
                     <priorityNumber value="1000"/>
                     <contextOfUse>
                         <id root="0.123.456.230525001.0812.0000051"/>
                         <code code="ich 3.2.p.8.3" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.
1"/>
                          <statusCode code="active"/>
                          <derivedFrom>
                             <documentReference>
                                 <id root="0.321.456.230525001.0812.0000051"/>
                             </documentReference>
                          </derivedFrom>
                          <referencedBy typeCode="REFR">
                              <keyword>
                                  <code code="MANU001" codeSystem="0.123.456.230525001.1209.
10003"/>
                              </keyword>
                          </referencedBy>
                          <referencedBy typeCode="REFR">
                              <keyword>
                                  <code code="PROD001" codeSystem="0.123.456.230525001.1209.
10004"/>
                              </keyword>
                          </referencedBy>
                          <referencedBy typeCode="REFR">
                              <keyword>
                                  <code code="DOSA001" codeSystem="0.123.456.230525001.1209.
10005"/>
                              </keyword>
                          </referencedBy>
                       </contextOfUse>
                  </component>
                  <component>
                     <priorityNumber value="1000"/>
                     <contextOfUse>
                         <id root="0.123.456.230525001.0812.0000052"/>
                         <code code="ich 3.2.p.4.1" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.
1"/>
                          <statusCode code="active"/>
                          <derivedFrom>
                             <documentReference>
                                 <id root="0.321.456.230525001.0812.0000052"/>
                             </documentReference>
                          </derivedFrom>
                          <referencedBy typeCode="REFR">
                              <keyword>
```

```
                            <code code="MANU001" codeSystem="0.123.456.230525001.1209.
10003"/>
                        </keyword>
                    </referencedBy>
                    <referencedBy typeCode="REFR">
                        <keyword>
                            <code code="PROD002" codeSystem="0.123.456.230525001.1209.
10004"/>
                        </keyword>
                    </referencedBy>
                    <referencedBy typeCode="REFR">
                        <keyword>
                            <code code="DOSA002" codeSystem="0.123.456.230525001.1209.
10005"/>
                        </keyword>
                    </referencedBy>
                    <referencedBy typeCode="REFR">
                        <keyword>
                            <code code="EXCI001" codeSystem="0.123.456.230525001.1209.1
0006"/>
                        </keyword>
                    </referencedBy>
                </contextOfUse>
            </component>
            <component>
                <priorityNumber value="1000"/>
                <contextOfUse>
                    <id root="0.123.456.230525001.0812.0000053"/>
                    <code code="ich 3.2.p.4.1" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.
1"/>
                    <statusCode code="active"/>
                    <derivedFrom>
                        <documentReference>
                            <id root="0.321.456.230525001.0812.0000053"/>
                        </documentReference>
                    </derivedFrom>
                    <referencedBy typeCode="REFR">
                        <keyword>
                            <code code="MANU001" codeSystem="0.123.456.230525001.1209.
10003"/>
                        </keyword>
                    </referencedBy>
                    <referencedBy typeCode="REFR">
                        <keyword>
                            <code code="PROD002" codeSystem="0.123.456.230525001.1209.
10004"/>
                        </keyword>
                    </referencedBy>
                    <referencedBy typeCode="REFR">
                        <keyword>
                            <code code="DOSA002" codeSystem="0.123.456.230525001.1209.
10005"/>
                        </keyword>
                    </referencedBy>
```

```
                    <referencedBy typeCode="REFR">
                       <keyword>
                          <code code="EXCI002" codeSystem="0.123.456.230525001.1209.1
0006"/>
                       </keyword>
                    </referencedBy>
                 </contextOfUse>
            </component>
            <component>
                <priorityNumber value="1000"/>
                <contextOfUse>
                   <id root="0.123.456.230525001.0812.0000054"/>
                   <code code="ich 3.2.p.4.6" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.
1"/>
                   <statusCode code="active"/>
                   <derivedFrom>
                      <documentReference>
                         <id root="0.321.456.230525001.0812.0000054"/>
                      </documentReference>
                   </derivedFrom>
                   <referencedBy typeCode="REFR">
                      <keyword>
                         <code code="MANU001" codeSystem="0.123.456.230525001.1209.
10003"/>
                      </keyword>
                   </referencedBy>
                   <referencedBy typeCode="REFR">
                      <keyword>
                         <code code="PROD002" codeSystem="0.123.456.230525001.1209.
10004"/>
                      </keyword>
                   </referencedBy>
                   <referencedBy typeCode="REFR">
                      <keyword>
                         <code code="DOSA002" codeSystem="0.123.456.230525001.1209.
10005"/>
                      </keyword>
                   </referencedBy>
                   <referencedBy typeCode="REFR">
                      <keyword>
                         <code code="EXCI001" codeSystem="0.123.456.230525001.1209.1
0006"/>
                      </keyword>
                   </referencedBy>
                </contextOfUse>
            </component>
            <component>
                <priorityNumber value="1000"/>
                <contextOfUse>
                   <id root="0.123.456.230525001.0812.0000055"/>
                   <code code="ich 3.2.p.8.1" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.
1"/>
                   <statusCode code="active"/>
                   <derivedFrom>
```

```
                <documentReference>
                    <id root="0.321.456.230525001.0812.0000055"/>
                </documentReference>
            </derivedFrom>
            <referencedBy typeCode="REFR">
                <keyword>
                    <code code="MANU001" codeSystem="0.123.456.230525001.1209.
10003"/>
                </keyword>
            </referencedBy>
            <referencedBy typeCode="REFR">
                <keyword>
                    <code code="PROD002" codeSystem="0.123.456.230525001.1209.
10004"/>
                </keyword>
            </referencedBy>
            <referencedBy typeCode="REFR">
                <keyword>
                    <code code="DOSA002" codeSystem="0.123.456.230525001.1209.
10005"/>
                </keyword>
            </referencedBy>
        </contextOfUse>
    </component>
    <component>
        <priorityNumber value="1000"/>
        <contextOfUse>
            <id root="0.123.456.230525001.0812.0000056"/>
            <code code="ich 3.2.p.8.2" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.
1"/>
            <statusCode code="active"/>
            <derivedFrom>
                <documentReference>
                    <id root="0.321.456.230525001.0812.0000056"/>
                </documentReference>
            </derivedFrom>
            <referencedBy typeCode="REFR">
                <keyword>
                    <code code="MANU001" codeSystem="0.123.456.230525001.1209.
10003"/>
                </keyword>
            </referencedBy>
            <referencedBy typeCode="REFR">
                <keyword>
                    <code code="PROD002" codeSystem="0.123.456.230525001.1209.
10004"/>
                </keyword>
            </referencedBy>
            <referencedBy typeCode="REFR">
                <keyword>
                    <code code="DOSA002" codeSystem="0.123.456.230525001.1209.
10005"/>
                </keyword>
            </referencedBy>
```

```
                </contextOfUse>
            </component>
            <component>
                <priorityNumber value="1000"/>
                <contextOfUse>
                    <id root="0.123.456.230525001.0812.0000057"/>
                    <code code="ich 3.2.p.8.3" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.
1"/>
                    <statusCode code="active"/>
                    <derivedFrom>
                        <documentReference>
                            <id root="0.321.456.230525001.0812.0000057"/>
                        </documentReference>
                    </derivedFrom>
                    <referencedBy typeCode="REFR">
                        <keyword>
                            <code code="MANU001" codeSystem="0.123.456.230525001.1209.
10003"/>
                        </keyword>
                    </referencedBy>
                    <referencedBy typeCode="REFR">
                        <keyword>
                            <code code="PROD002" codeSystem="0.123.456.230525001.1209.
10004"/>
                        </keyword>
                    </referencedBy>
                    <referencedBy typeCode="REFR">
                        <keyword>
                            <code code="DOSA002" codeSystem="0.123.456.230525001.1209.
10005"/>
                        </keyword>
                    </referencedBy>
                </contextOfUse>
            </component>
            <component>
                <priorityNumber value="1000"/>
                <contextOfUse>
                    <id root="0.123.456.230525001.0812.0000058"/>
                    <code code="ich 4.2.1.1" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1
"/>
                    <statusCode code="active"/>
                    <derivedFrom>
                        <documentReference>
                            <id root="0.321.456.230525001.0812.0000058"/>
                        </documentReference>
                    </derivedFrom>
                    <referencedBy typeCode="REFR">
                        <keyword>
                            <code code="id0000001" codeSystem="0.123.456.230525001.1209.
10007"/>
                        </keyword>
                    </referencedBy>
                </contextOfUse>
            </component>
```

```
            <component>
                <priorityNumber value="1000"/>
                <contextOfUse>
                    <id root="0.123.456.230525001.0812.0000059"/>
                    <code code="ich 5.2" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/>
                    <statusCode code="active"/>
                    <derivedFrom>
                        <documentReference>
                            <id root="0.321.456.230525001.0812.0000059"/>
                        </documentReference>
                    </derivedFrom>
                </contextOfUse>
            </component>
            <component>
                <priorityNumber value="1000"/>
                <contextOfUse>
                    <id root="0.123.456.230525001.0812.0000060"/>
                    <code code="ich 5.3.1.1" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1
"/>
                    <statusCode code="active"/>
                    <derivedFrom>
                        <documentReference>
                            <id root="0.321.456.230525001.0812.0000060"/>
                        </documentReference>
                    </derivedFrom>
                    <referencedBy typeCode="REFR">
                        <keyword>
                            <code code="id0000002" codeSystem="0.123.456.230525001.1209.
10008"/>
                        </keyword>
                    </referencedBy>
                </contextOfUse>
            </component>
            <component>
                <priorityNumber value="1000"/>
                <contextOfUse>
                    <id root="0.123.456.230525001.0812.0000061"/>
                    <code code="ich 5.3.5.1" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1
"/>
                    <statusCode code="active"/>
                    <derivedFrom>
                        <documentReference>
                            <id root="0.321.456.230525001.0812.0000061"/>
                        </documentReference>
                    </derivedFrom>
                    <referencedBy typeCode="REFR">
                        <keyword>
                            <code code="INDI001" codeSystem="0.123.456.230525001.1209.1
0001"/>
                        </keyword>
                    </referencedBy>
                    <referencedBy typeCode="REFR">
                        <keyword>
```

```xml
                    <code code="id0000003" codeSystem="0.123.456.230525001.1209.
10008"/>
                </keyword>
            </referencedBy>
        </contextOfUse>
    </component>
    <component>
        <priorityNumber value="2000"/>
        <contextOfUse>
            <id root="0.123.456.230525001.0812.0000062"/>
            <code code="ich 5.3.5.1" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1
"/>
            <statusCode code="active"/>
            <derivedFrom>
                <documentReference>
                    <id root="0.321.456.230525001.0812.0000062"/>
                </documentReference>
            </derivedFrom>
            <referencedBy typeCode="REFR">
                <keyword>
                    <code code="INDI001" codeSystem="0.123.456.230525001.1209.1
0001"/>
                </keyword>
            </referencedBy>
            <referencedBy typeCode="REFR">
                <keyword>
                    <code code="id0000003" codeSystem="0.123.456.230525001.1209.
10008"/>
                </keyword>
            </referencedBy>
        </contextOfUse>
    </component>
    <component>
        <priorityNumber value="1000"/>
        <contextOfUse>
            <id root="0.123.456.230525001.0812.0000063"/>
            <code code="ich 5.3.5.2" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1
"/>
            <statusCode code="active"/>
            <derivedFrom>
                <documentReference>
                    <id root="0.321.456.230525001.0812.0000063"/>
                </documentReference>
            </derivedFrom>
            <referencedBy typeCode="REFR">
                <keyword>
                    <code code="INDI001" codeSystem="0.123.456.230525001.1209.1
0001"/>
                </keyword>
            </referencedBy>
            <referencedBy typeCode="REFR">
                <keyword>
                    <code code="id0000004" codeSystem="0.123.456.230525001.1209.
10008"/>
```

```
                    </keyword>
                  </referencedBy>
                </contextOfUse>
              </component>
              <component>
                <priorityNumber value="2000"/>
                <contextOfUse>
                  <id root="0.123.456.230525001.0812.0000064"/>
                  <code code="ich 5.3.5.2" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1
"/>
                  <statusCode code="active"/>
                  <derivedFrom>
                    <documentReference>
                      <id root="0.321.456.230525001.0812.0000064"/>
                    </documentReference>
                  </derivedFrom>
                  <referencedBy typeCode="REFR">
                    <keyword>
                      <code code="INDI001" codeSystem="0.123.456.230525001.1209.1
0001"/>
                    </keyword>
                  </referencedBy>
                  <referencedBy typeCode="REFR">
                    <keyword>
                      <code code="id0000004" codeSystem="0.123.456.230525001.1209.
10008"/>
                    </keyword>
                  </referencedBy>
                </contextOfUse>
              </component>
              <component>
                <priorityNumber value="3000"/>
                <contextOfUse>
                  <id root="0.123.456.230525001.0812.0000065"/>
                  <code code="ich 5.3.5.2" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1
"/>
                  <statusCode code="active"/>
                  <derivedFrom>
                    <documentReference>
                      <id root="0.321.456.230525001.0812.0000065"/>
                    </documentReference>
                  </derivedFrom>
                  <referencedBy typeCode="REFR">
                    <keyword>
                      <code code="INDI001" codeSystem="0.123.456.230525001.1209.1
0001"/>
                    </keyword>
                  </referencedBy>
                  <referencedBy typeCode="REFR">
                    <keyword>
                      <code code="id0000004" codeSystem="0.123.456.230525001.1209.
10008"/>
                    </keyword>
                  </referencedBy>
```

```
                        </contextOfUse>
                  </component>
                  <component>
                      <priorityNumber value="4000"/>
                      <contextOfUse>
                          <id root="0.123.456.230525001.0812.0000066"/>
                          <code code="ich 5.3.5.2" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1
"/>
                          <statusCode code="active"/>
                          <derivedFrom>
                              <documentReference>
                                  <id root="0.321.456.230525001.0812.0000066"/>
                              </documentReference>
                          </derivedFrom>
                          <referencedBy typeCode="REFR">
                              <keyword>
                                  <code code="INDI001" codeSystem="0.123.456.230525001.1209.1
0001"/>
                              </keyword>
                          </referencedBy>
                          <referencedBy typeCode="REFR">
                              <keyword>
                                  <code code="id0000004" codeSystem="0.123.456.230525001.1209.
10008"/>
                              </keyword>
                          </referencedBy>
                      </contextOfUse>
                  </component>
                  <component>
                      <priorityNumber value="5000"/>
                      <contextOfUse>
                          <id root="0.123.456.230525001.0812.0000067"/>
                          <code code="ich 5.3.5.2" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1
"/>
                          <statusCode code="active"/>
                          <derivedFrom>
                              <documentReference>
                                  <id root="0.321.456.230525001.0812.0000067"/>
                              </documentReference>
                          </derivedFrom>
                          <referencedBy typeCode="REFR">
                              <keyword>
                                  <code code="INDI001" codeSystem="0.123.456.230525001.1209.1
0001"/>
                              </keyword>
                          </referencedBy>
                          <referencedBy typeCode="REFR">
                              <keyword>
                                  <code code="id0000004" codeSystem="0.123.456.230525001.1209.
10008"/>
                              </keyword>
                          </referencedBy>
                      </contextOfUse>
                  </component>
```

```
        <component>
            <priorityNumber value="1000"/>
            <contextOfUse>
                <id root="0.123.456.230525001.0812.0000068"/>
                <code code="ich 5.3.7" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/
>
                <statusCode code="active"/>
                <derivedFrom>
                    <documentReference>
                        <id root="0.321.456.230525001.0812.0000068"/>
                    </documentReference>
                </derivedFrom>
                <referencedBy typeCode="REFR">
                    <keyword>
                        <code code="id0000005" codeSystem="0.123.456.230525001.1209.
10008"/>
                    </keyword>
                </referencedBy>
            </contextOfUse>
        </component>
        <component>
            <priorityNumber value="2000"/>
            <contextOfUse>
                <id root="0.123.456.230525001.0812.0000069"/>
                <code code="ich 5.3.7" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/
>
                <statusCode code="active"/>
                <derivedFrom>
                    <documentReference>
                        <id root="0.321.456.230525001.0812.0000069"/>
                    </documentReference>
                </derivedFrom>
                <referencedBy typeCode="REFR">
                    <keyword>
                        <code code="id0000005" codeSystem="0.123.456.230525001.1209.
10008"/>
                    </keyword>
                </referencedBy>
            </contextOfUse>
        </component>
        <component>
            <priorityNumber value="3000"/>
            <contextOfUse>
                <id root="0.123.456.230525001.0812.0000070"/>
                <code code="ich 5.3.7" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/
>
                <statusCode code="active"/>
                <derivedFrom>
                    <documentReference>
                        <id root="0.321.456.230525001.0812.0000070"/>
                    </documentReference>
                </derivedFrom>
                <referencedBy typeCode="REFR">
                    <keyword>
```

```
                                    <code code="id0000005" codeSystem="0.123.456.230525001.1209.
10008"/>
                            </keyword>
                        </referencedBy>
                    </contextOfUse>
            </component>
            <component>
                <priorityNumber value="4000"/>
                <contextOfUse>
                    <id root="0.123.456.230525001.0812.0000071"/>
                    <code code="ich 5.3.7" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/
>
                        <statusCode code="active"/>
                        <derivedFrom>
                            <documentReference>
                                <id root="0.321.456.230525001.0812.0000071"/>
                            </documentReference>
                        </derivedFrom>
                        <referencedBy typeCode="REFR">
                            <keyword>
                                <code code="id0000005" codeSystem="0.123.456.230525001.1209.
10008"/>
                            </keyword>
                        </referencedBy>
                    </contextOfUse>
            </component>
            <component>
                <priorityNumber value="5000"/>
                <contextOfUse>
                    <id root="0.123.456.230525001.0812.0000072"/>
                    <code code="ich 5.3.7" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/
>
                        <statusCode code="active"/>
                        <derivedFrom>
                            <documentReference>
                                <id root="0.321.456.230525001.0812.0000072"/>
                            </documentReference>
                        </derivedFrom>
                        <referencedBy typeCode="REFR">
                            <keyword>
                                <code code="id0000005" codeSystem="0.123.456.230525001.1209.
10008"/>
                            </keyword>
                        </referencedBy>
                    </contextOfUse>
            </component>
            <component>
                <priorityNumber value="1000"/>
                <contextOfUse>
                    <id root="0.123.456.230525001.0812.0000073"/>
                    <code code="ich 5.3.7" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/
>
                        <statusCode code="active"/>
                        <derivedFrom>
```

```
                    <documentReference>
                       <id root="0.321.456.230525001.0812.0000073"/>
                    </documentReference>
                 </derivedFrom>
                 <referencedBy typeCode="REFR">
                    <keyword>
                       <code code="id0000006" codeSystem="0.123.456.230525001.12
09.10008"/>
                    </keyword>
                 </referencedBy>
              </contextOfUse>
           </component>
           <component>
              <priorityNumber value="1000"/>
              <contextOfUse>
                 <id root="0.123.456.230525001.0812.0000074"/>
                 <code code="ich 5.4" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/>
                 <statusCode code="active"/>
                 <derivedFrom>
                    <documentReference>
                       <id root="0.321.456.230525001.0812.0000074"/>
                    </documentReference>
                 </derivedFrom>
              </contextOfUse>
           </component>
           <component>
              <priorityNumber value="2000"/>
              <contextOfUse>
                 <id root="0.123.456.230525001.0812.0000075"/>
                 <code code="ich 5.4" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/>
                 <statusCode code="active"/>
                 <derivedFrom>
                    <documentReference>
                       <id root="0.321.456.230525001.0812.0000075"/>
                    </documentReference>
                 </derivedFrom>
              </contextOfUse>
           </component>
           <component>
              <priorityNumber value="3000"/>
              <contextOfUse>
                 <id root="0.123.456.230525001.0812.0000076"/>
                 <code code="ich 5.4" codeSystem="2.16.840.1.113883.3.989.2.2.4.1.1"/>
                 <statusCode code="active"/>
                 <derivedFrom>
                    <documentReference>
                       <id root="0.321.456.230525001.0812.0000076"/>
                    </documentReference>
                 </derivedFrom>
              </contextOfUse>
           </component>
           <componentOf1>
              <sequenceNumber value="1"/>
              <submission>
```

```xml
            <id>
               <item root="1234.1234.1234.12345.0002.0003.0001" extension="23052
5001"/>
            </id>
            <code code="jp original" codeSystem="jp-submission"/>
            <subject2>
               <review>
                  <id root="1234.1234.1234.12345.0002.0003.0001"/>
                  <statusCode code="active"/>
                  <subject1>
                     <manufacturedProduct>
                        <manufacturedProduct>
                           <name>
                              <part value="セイヤクキョール 10mg 錠"/>
                           </name>
                           <ingredient classCode="INGR">
                              <ingredientSubstance>
                                 <name>
                                    <part value="イーアイ塩酸塩" code="jp jan"
codeSystem="jp-substance-name-type"/>
                                 </name>
                              </ingredientSubstance>
                           </ingredient>
                        </manufacturedProduct>
                     </manufacturedProduct>
                  </subject1>
                  <holder>
                     <applicant>
                        <sponsorOrganization>
                           <name>
                              <part value="日本製薬工業株式会社"/>
                           </name>
                        </sponsorOrganization>
                     </applicant>
                  </holder>
                  <subject2>
                     <productCategory>
                        <code code="jp 1-1" codeSystem="jp-product-category"/>
                     </productCategory>
                  </subject2>
               </review>
            </subject2>
            <subject2>
               <review>
                  <id root="5678.1234.1234.12345.0002.0003.0001"/>
                  <statusCode code="active"/>
                  <subject1>
                     <manufacturedProduct>
                        <manufacturedProduct>
                           <name>
                              <part value="セイヤクキョール 20mg 錠"/>
                           </name>
                           <ingredient classCode="INGR">
```

```
                              <ingredientSubstance>
                                 <name>
                                    <part value="イーアイ塩酸塩" code="jp jan"
codeSystem="jp-substance-name-type"/>
                                 </name>
                              </ingredientSubstance>
                           </ingredient>
                        </manufacturedProduct>
                     </manufacturedProduct>
                  </subject1>
                  <holder>
                     <applicant>
                        <sponsorOrganization>
                           <name>
                              <part value="日本製薬工業株式会社"/>
                           </name>
                        </sponsorOrganization>
                     </applicant>
                  </holder>
                  <subject2>
                     <productCategory>
                        <code code="jp 1-1" codeSystem="jp-product-category"/>
                     </productCategory>
                  </subject2>
               </review>
            </subject2>
            <componentOf>
               <application>
                  <id>
                     <item root="12345678.1234.1234.1234.123456789012" extensio
n="230525001"/>
                  </id>
                  <code code="jp maa" codeSystem="jp-application"/>
                  <reference>
                     <applicationReference>
                        <id root="1234.1234.1234.12345.0002.0003.0001"/>
                        <reasonCode>
                           <item code="jp related" codeSystem="jp-application-refer
ence-reason"/>
                        </reasonCode>
                     </applicationReference>
                  </reference>
                  <component>
                     <document>
                        <id root="0.321.456.230525001.0812.0000001"/>
                        <title value="1.1-1 第 1 部(モジュール 1)を含む申請資料の
目次"/>
                        <text integrityCheckAlgorithm="SHA256">
                           <reference value="m1/jp/m1-01-01.pdf"/>
                           <integrityCheck>dca5863207b07f7ef6feb623019d69a1</int
egrityCheck>
                        </text>
                     </document>
```

```
                    </component>
                    <component>
                      <document>
                        <id root="0.321.456.230525001.0812.0000002"/>
                        <title value="1.1-2 概説表"/>
                        <text integrityCheckAlgorithm="SHA256">
                          <reference value="m1/jp/m1-01-02.pdf"/>
                          <integrityCheck>b71511dae6e7794f6aa3b3138d91a9f8</in
tegrityCheck>
                        </text>
                      </document>
                    </component>
                    <component>
                      <document>
                        <id root="0.321.456.230525001.0812.0000003"/>
                        <title value="1.2-1 セイヤクキョール錠 10mg 承認申請
書(写)"/>
                        <text integrityCheckAlgorithm="SHA256">
                          <reference value="m1/jp/m1-02-01.pdf"/>
                          <integrityCheck>149d8a97d8e3183884a1ebcd40f0d087</in
tegrityCheck>
                        </text>
                      </document>
                    </component>
                    <component>
                      <document>
                        <id root="0.321.456.230525001.0812.0000004"/>
                        <title value="1.2-2 セイヤクキョール錠 20mg 承認申請
書(写)"/>
                        <text integrityCheckAlgorithm="SHA256">
                          <reference value="m1/jp/m1-02-02.pdf"/>
                          <integrityCheck>9cf7e989b5cb8f6d6c1940e5534012d8</in
tegrityCheck>
                        </text>
                      </document>
                    </component>
                    <component>
                      <document>
                        <id root="0.321.456.230525001.0812.0000005"/>
                        <title value="1.3-1 申請資料の信頼性基準遵守に関する陳
述書(業務統括責任者)"/>
                        <text integrityCheckAlgorithm="SHA256">
                          <reference value="m1/jp/m1-03-01.pdf"/>
                          <integrityCheck>3d3c38496c662d9072d4ba7bc7b181f1</i
ntegrityCheck>
                        </text>
                      </document>
                    </component>
                    <component>
                      <document>
                        <id root="0.321.456.230525001.0812.0000006"/>
                        <title value="1.3-2 スキャニングに関する陳述書"/>
                        <text integrityCheckAlgorithm="SHA256">
```

```
                                          <reference value="m1/jp/m1-03-02.pdf"/>
                                          <integrityCheck>ea1259188feae55242f692b6980c0d09</in
tegrityCheck>
                                     </text>
                                 </document>
                             </component>
                             <component>
                                 <document>
                                     <id root="0.321.456.230525001.0812.0000007"/>
                                     <title value="1.4 特許状況"/>
                                     <text integrityCheckAlgorithm="SHA256">
                                          <reference value="m1/jp/m1-04-01.pdf"/>
                                          <integrityCheck>5e0b43e41ed94641e843ca8e1abebde5</in
tegrityCheck>
                                     </text>
                                 </document>
                             </component>
                             <component>
                                 <document>
                                     <id root="0.321.456.230525001.0812.0000008"/>
                                     <title value="1.5 起原又は発見の経緯及び開発の経緯"/>
                                     <text integrityCheckAlgorithm="SHA256">
                                          <reference value="m1/jp/m1-05-01.pdf"/>
                                          <integrityCheck>194861213a08f6346493cdef80edcf87</int
egrityCheck>
                                     </text>
                                 </document>
                             </component>
                             <component>
                                 <document>
                                     <id root="0.321.456.230525001.0812.0000009"/>
                                     <title value="1.6 外国における使用状況等に関する資料"/
>
                                     <text integrityCheckAlgorithm="SHA256">
                                          <reference value="m1/jp/m1-06-01.pdf"/>
                                          <integrityCheck>33579db29cb3774d4d8aa79b8e17cef9</in
tegrityCheck>
                                     </text>
                                 </document>
                             </component>
                             <component>
                                 <document>
                                     <id root="0.321.456.230525001.0812.0000010"/>
                                     <title value="1.7 同種同効品一覧表"/>
                                     <text integrityCheckAlgorithm="SHA256">
                                          <reference value="m1/jp/m1-07-01.pdf"/>
                                          <integrityCheck>56e41bdece298d1f1a23659e76bb6477</in
tegrityCheck>
                                     </text>
                                 </document>
                             </component>
                             <component>
                                 <document>
```

```
                                    <id root="0.321.456.230525001.0812.0000011"/>
                                    <title value="1.8 添付文書(案)"/>
                                    <text integrityCheckAlgorithm="SHA256">
                                        <reference value="m1/jp/m1-08-01.pdf"/>
                                        <integrityCheck>e81f637df72d9bb3a181d20d19a54b09</in
tegrityCheck>
                                    </text>
                                </document>
                            </component>
                            <component>
                                <document>
                                    <id root="0.321.456.230525001.0812.0000012"/>
                                    <title value="1.9 一般的名称に係る文書"/>
                                    <text integrityCheckAlgorithm="SHA256">
                                        <reference value="m1/jp/m1-09-01.pdf"/>
                                        <integrityCheck>03e15f7d5f49e9277120a4cb19219204</in
tegrityCheck>
                                    </text>
                                </document>
                            </component>
                            <component>
                                <document>
                                    <id root="0.321.456.230525001.0812.0000013"/>
                                    <title value="1.10 毒薬・劇薬等の指定審査資料のまとめ"/
>
                                    <text integrityCheckAlgorithm="SHA256">
                                        <reference value="m1/jp/m1-10-01.pdf"/>
                                        <integrityCheck>d289f6733279aef8f337657ca871fef8</int
egrityCheck>
                                    </text>
                                </document>
                            </component>
                            <component>
                                <document>
                                    <id root="0.321.456.230525001.0812.0000014"/>
                                    <title value="1.11 製造販売後調査等基本計画書(案)"/>
                                    <text integrityCheckAlgorithm="SHA256">
                                        <reference value="m1/jp/m1-11-01.pdf"/>
                                        <integrityCheck>e3fd66cd6b6d1a72372dfc237cf9a2ec</int
egrityCheck>
                                    </text>
                                </document>
                            </component>
                            <component>
                                <document>
                                    <id root="0.321.456.230525001.0812.0000015"/>
                                    <title value="1.12-1 添付資料一覧(PDF 形式)"/>
                                    <text integrityCheckAlgorithm="SHA256">
                                        <reference value="m1/jp/m1-12-01.pdf"/>
                                        <integrityCheck>ac853cb994b568e544ecaaa52d9ef2ab</int
egrityCheck>
                                    </text>
                                </document>
```

```
                                </component>
                                <component>
                                    <document>
                                        <id root="0.321.456.230525001.0812.0000016"/>
                                        <title value="1.12-2 添付資料一覧(Excel 形式)"/>
                                        <text integrityCheckAlgorithm="SHA256">
                                            <reference value="m1/jp/m1-12-02.xlsx"/>
                                            <integrityCheck>0b454bb39f93959397fe9dc5c86c428e</in
tegrityCheck>
                                        </text>
                                    </document>
                                </component>
                                <component>
                                    <document>
                                        <id root="0.321.456.230525001.0812.0000017"/>
                                        <title value="既承認医薬品に係る資料"/>
                                        <text integrityCheckAlgorithm="SHA256">
                                            <reference value="m1/jp/m1-13-02-01.pdf"/>
                                            <integrityCheck>c5e7cd1334cf312f6d24183a745aeb6d</int
egrityCheck>
                                        </text>
                                    </document>
                                </component>
                                <component>
                                    <document>
                                        <id root="0.321.456.230525001.0812.0000018"/>
                                        <title value="新添加物に関する提出資料一覧"/>
                                        <text integrityCheckAlgorithm="SHA256">
                                            <reference value="m1/jp/m1-13-04-01-01-01.pdf"/>
                                            <integrityCheck>634c9b8aba26bf15186a90b7ecb37e53</in
tegrityCheck>
                                        </text>
                                    </document>
                                </component>
                                <component>
                                    <document>
                                        <id root="0.321.456.230525001.0812.0000019"/>
                                        <title value="個別審議品目概要表"/>
                                        <text integrityCheckAlgorithm="SHA256">
                                            <reference value="m1/jp/m1-13-04-01-01-02.pdf"/>
                                            <integrityCheck>6b916b9689b49683b135f3a561cdf076</in
tegrityCheck>
                                        </text>
                                    </document>
                                </component>
                                <component>
                                    <document>
                                        <id root="0.321.456.230525001.0812.0000020"/>
                                        <title value="承認申請書(写)"/>
                                        <text integrityCheckAlgorithm="SHA256">
                                            <reference value="m1/jp/m1-13-04-01-01-03.pdf"/>
                                            <integrityCheck>b9587d4bf3ecf8bc6073543364a949b7</in
tegrityCheck>
```

```
                                    </text>
                                </document>
                            </component>
                            <component>
                                <document>
                                    <id root="0.321.456.230525001.0812.0000021"/>
                                    <title value="新添加物に関する概要"/>
                                    <text integrityCheckAlgorithm="SHA256">
                                        <reference value="m1/jp/m1-13-04-01-01-04.pdf"/>
                                        <integrityCheck>492ae2a08163d60f0606b7513696100e</i
ntegrityCheck>
                                    </text>
                                </document>
                            </component>
                            <component>
                                <document>
                                    <id root="0.321.456.230525001.0812.0000022"/>
                                    <title value="新添加物に関する資料:添付資料 1"/>
                                    <text integrityCheckAlgorithm="SHA256">
                                        <reference value="m1/jp/m1-13-04-01-01-05.pdf"/>
                                        <integrityCheck>1350321c1bdc990a71ce0359811a6cb8</i
ntegrityCheck>
                                    </text>
                                </document>
                            </component>
                            <component>
                                <document>
                                    <id root="0.321.456.230525001.0812.0000023"/>
                                    <title value="新添加物に関する資料:添付資料 2"/>
                                    <text integrityCheckAlgorithm="SHA256">
                                        <reference value="m1/jp/m1-13-04-01-01-06.pdf"/>
                                        <integrityCheck>13060a84ca2c571c57fda9125632caab</in
tegrityCheck>
                                    </text>
                                </document>
                            </component>
                            <component>
                                <document>
                                    <id root="0.321.456.230525001.0812.0000024"/>
                                    <title value="承認申請書に記載しなかった主な製造工程
パラメータ"/>
                                    <text integrityCheckAlgorithm="SHA256">
                                        <reference value="m1/jp/m1-13-04-01-02.pdf"/>
                                        <integrityCheck>4e837da596b645f1e0a010f151107d1b</in
tegrityCheck>
                                    </text>
                                </document>
                            </component>
                            <component>
                                <document>
                                    <id root="0.321.456.230525001.0812.0000025"/>
                                    <title value="2.2 緒言"/>
                                    <text integrityCheckAlgorithm="SHA256">
```

```
                                          <reference value="m2/m2-2-introduction.pdf"/>
                                          <integrityCheck>717716c542a642a0ef698a4318c8e788</in
tegrityCheck>
                                      </text>
                                  </document>
                              </component>
                              <component>
                                  <document>
                                      <id root="0.321.456.230525001.0812.0000026"/>
                                      <title value="2.3 緒言"/>
                                      <text integrityCheckAlgorithm="SHA256">
                                          <reference value="m2/m2-3-introduction.pdf"/>
                                          <integrityCheck>d22d778571e184fab7ba88b7ff7f64ad</int
egrityCheck>
                                      </text>
                                  </document>
                              </component>
                              <component>
                                  <document>
                                      <id root="0.321.456.230525001.0812.0000027"/>
                                      <title value="2.3.S 原薬(イーアイ塩酸塩、日本製薬工業東
京工場)"/>
                                      <text integrityCheckAlgorithm="SHA256">
                                          <reference value="m2/drug-substance-tokyo.pdf"/>
                                          <integrityCheck>cac5ce586364f595623ee2d87252d591</in
tegrityCheck>
                                      </text>
                                  </document>
                              </component>
                              <component>
                                  <document>
                                      <id root="0.321.456.230525001.0812.0000028"/>
                                      <title value="2.3.P 製剤(セイヤクキョール錠 10mg、錠剤)
"/>
                                      <text integrityCheckAlgorithm="SHA256">
                                          <reference value="m2/drug-product-tablet-10mg.pdf"/>
                                          <integrityCheck>4c6a9c77eb74344c23abc1071335d6d1</i
ntegrityCheck>
                                      </text>
                                  </document>
                              </component>
                              <component>
                                  <document>
                                      <id root="0.321.456.230525001.0812.0000029"/>
                                      <title value="2.3.P 製剤(セイヤクキョール錠 20mg、錠剤)
"/>
                                      <text integrityCheckAlgorithm="SHA256">
                                          <reference value="m2/drug-product-tablet-20mg.pdf"/>
                                          <integrityCheck>99bde2bf23bfb6894d15758888f61080</in
tegrityCheck>
                                      </text>
                                  </document>
                              </component>
```

```
                        <component>
                           <document>
                              <id root="0.321.456.230525001.0812.0000030"/>
                              <title value="2.3.A その他"/>
                              <text integrityCheckAlgorithm="SHA256">
                                 <reference value="m2/appendices.pdf"/>
                                 <integrityCheck>81779480b0a32bcf148ad6e8628f426e</in
tegrityCheck>
                              </text>
                           </document>
                        </component>
                        <component>
                           <document>
                              <id root="0.321.456.230525001.0812.0000031"/>
                              <title value="2.4 非臨床試験の概括評価"/>
                              <text integrityCheckAlgorithm="SHA256">
                                 <reference value="m2/nonclinical-overview.pdf"/>
                                 <integrityCheck>2ef99e2bce57c27d058b8c7d83d1d77a</in
tegrityCheck>
                              </text>
                           </document>
                        </component>
                        <component>
                           <document>
                              <id root="0.321.456.230525001.0812.0000032"/>
                              <title value="2.5 臨床に関する概括評価"/>
                              <text integrityCheckAlgorithm="SHA256">
                                 <reference value="m2/clinical-overview.pdf"/>
                                 <integrityCheck>778e35ef1673c24ca92071fa3bc22107</int
egrityCheck>
                              </text>
                           </document>
                        </component>
                        <component>
                           <document>
                              <id root="0.321.456.230525001.0812.0000033"/>
                              <title value="2.6.1 緒言"/>
                              <text integrityCheckAlgorithm="SHA256">
                                 <reference value="m2/m2-6-1-introduction.pdf"/>
                                 <integrityCheck>bfa45658c5a4a9b281334e9895ea8538</in
tegrityCheck>
                              </text>
                           </document>
                        </component>
                        <component>
                           <document>
                              <id root="0.321.456.230525001.0812.0000034"/>
                              <title value="2.6.2 薬理試験の概要文"/>
                              <text integrityCheckAlgorithm="SHA256">
                                 <reference value="m2/pharmacol-written-summary.pdf"/>
                                 <integrityCheck>a9283bf95cfd3c021637ddadefec1101</int
egrityCheck>
                              </text>
```

```
                                </document>
                            </component>
                            <component>
                                <document>
                                    <id root="0.321.456.230525001.0812.0000035"/>
                                    <title value="2.6.3 薬理試験の概要表"/>
                                    <text integrityCheckAlgorithm="SHA256">
                                        <reference value="m2/pharmacol-tabulated-summary.pdf"/
>
                                        <integrityCheck>bebb1740e4a6202d007c39b75a10acb1</i
ntegrityCheck>
                                    </text>
                                </document>
                            </component>
                            <component>
                                <document>
                                    <id root="0.321.456.230525001.0812.0000036"/>
                                    <title value="2.6.4 薬物動態試験の概要文"/>
                                    <text integrityCheckAlgorithm="SHA256">
                                        <reference value="m2/pharmkin-written-summary.pdf"/>
                                        <integrityCheck>4b3822a275494be5c127d59e517d2645</i
ntegrityCheck>
                                    </text>
                                </document>
                            </component>
                            <component>
                                <document>
                                    <id root="0.321.456.230525001.0812.0000037"/>
                                    <title value="2.6.5 薬物動態試験の概要表"/>
                                    <text integrityCheckAlgorithm="SHA256">
                                        <reference value="m2/pharmkin-tabulated-summary.pdf"/>
                                        <integrityCheck>750731a99635113ed4ade7dbd80c4120</i
ntegrityCheck>
                                    </text>
                                </document>
                            </component>
                            <component>
                                <document>
                                    <id root="0.321.456.230525001.0812.0000038"/>
                                    <title value="2.6.6 毒性試験の概要文"/>
                                    <text integrityCheckAlgorithm="SHA256">
                                        <reference value="m2/toxicology-written-summary.pdf"/>
                                        <integrityCheck>f1fd806b177d80ef5ebaffb878c4953c</int
egrityCheck>
                                    </text>
                                </document>
                            </component>
                            <component>
                                <document>
                                    <id root="0.321.456.230525001.0812.0000039"/>
                                    <title value="2.6.7 毒性試験の概要表"/>
                                    <text integrityCheckAlgorithm="SHA256">
```

```
                                    <reference value="m2/toxicology-tabulated-summary.pdf"/
>
                                    <integrityCheck>7970c3296793b29f1fcd899da8ba3465</in
tegrityCheck>
                                </text>
                            </document>
                        </component>
                        <component>
                            <document>
                                <id root="0.321.456.230525001.0812.0000040"/>
                                <title value="2.7.1 生物薬剤学試験及び関連する分析法"/>
                                <text integrityCheckAlgorithm="SHA256">
                                    <reference value="m2/summary-biopharm.pdf"/>
                                    <integrityCheck>dd9b7c891175b6a34f1b71c6b5bd6be7</i
ntegrityCheck>
                                </text>
                            </document>
                        </component>
                        <component>
                            <document>
                                <id root="0.321.456.230525001.0812.0000041"/>
                                <title value="2.7.2 臨床薬理試験"/>
                                <text integrityCheckAlgorithm="SHA256">
                                    <reference value="m2/summary-clin-pharm.pdf"/>
                                    <integrityCheck>979f654c6309c568678449d466c2d2a5</i
ntegrityCheck>
                                </text>
                            </document>
                        </component>
                        <component>
                            <document>
                                <id root="0.321.456.230525001.0812.0000042"/>
                                <title value="2.7.3 臨床的有効性 - 高血圧"/>
                                <text integrityCheckAlgorithm="SHA256">
                                    <reference value="m2/summary-clin-efficacy-hypertensio
n.pdf"/>
                                    <integrityCheck>a346782620790ac3e49ab289492511d9</i
ntegrityCheck>
                                </text>
                            </document>
                        </component>
                        <component>
                            <document>
                                <id root="0.321.456.230525001.0812.0000043"/>
                                <title value="2.7.4 臨床的安全性"/>
                                <text integrityCheckAlgorithm="SHA256">
                                    <reference value="m2/summary-clin-safety.pdf"/>
                                    <integrityCheck>5b57bcc2a8810e82e266337207930ec0</i
ntegrityCheck>
                                </text>
                            </document>
                        </component>
                        <component>
```

```
                              <document>
                                 <id root="0.321.456.230525001.0812.0000044"/>
                                 <title value="2.7.5 参考文献"/>
                                 <text integrityCheckAlgorithm="SHA256">
                                    <reference value="m2/literature-references.pdf"/>
                                    <integrityCheck>f239b1eeec8d74f1570a20dd96b013fb</int
egrityCheck>
                                 </text>
                              </document>
                           </component>
                           <component>
                              <document>
                                 <id root="0.321.456.230525001.0812.0000045"/>
                                 <title value="2.7.6 個々の試験のまとめ"/>
                                 <text integrityCheckAlgorithm="SHA256">
                                    <reference value="m2/synopses-indiv-studies.pdf"/>
                                    <integrityCheck>70e660be9e16818ca00b97a410f40bb7</in
tegrityCheck>
                                 </text>
                              </document>
                           </component>
                           <component>
                              <document>
                                 <id root="0.321.456.230525001.0812.0000046"/>
                                 <title value="3.2.P.4.1 規格及び試験方法(セイヤクキョー
ル錠 10mg、錠剤)"/>
                                 <text integrityCheckAlgorithm="SHA256">
                                    <reference value="m3/32-prod/1/c-specifications.pdf"/>
                                    <integrityCheck>07ccbf7835bd18e764767ebe87de1d27</in
tegrityCheck>
                                 </text>
                              </document>
                           </component>
                           <component>
                              <document>
                                 <id root="0.321.456.230525001.0812.0000047"/>
                                 <title value="3.2.P.4.1 規格及び試験方法(セイヤクキョー
ル錠 10mg、錠剤)"/>
                                 <text integrityCheckAlgorithm="SHA256">
                                    <reference value="m3/32-prod/1/h-specifications.pdf"/>
                                    <integrityCheck>61beb804ab960ca4931bb2756309cc29</i
ntegrityCheck>
                                 </text>
                              </document>
                           </component>
                           <component>
                              <document>
                                 <id root="0.321.456.230525001.0812.0000048"/>
                                 <title value="3.2.P.4.6 新規添加剤(セイヤクキョール錠 1
0mg、錠剤)"/>
                                 <text integrityCheckAlgorithm="SHA256">
                                    <reference value="m3/32-prod/1/novel-excipients.pdf"/>
```

```
                                    <integrityCheck>841a140fa9d1029f1acc365432d9ce8d</int
egrityCheck>
                                </text>
                            </document>
                        </component>
                        <component>
                            <document>
                                <id root="0.321.456.230525001.0812.0000049"/>
                                <title value="3.2.P.8.1 安定性のまとめ及び結論(セイヤク
キョール錠 10mg、錠剤)"/>
                                <text integrityCheckAlgorithm="SHA256">
                                    <reference value="m3/32-prod/1/stability-summary.pdf"/>
                                    <integrityCheck>466e2d59f79f71c93bf65d675ac9b9d6</int
egrityCheck>
                                </text>
                            </document>
                        </component>
                        <component>
                            <document>
                                <id root="0.321.456.230525001.0812.0000050"/>
                                <title value="3.2.P.8.2 承認後の安定性試験計画の作成及
び実施(セイヤクキョール錠 10mg、錠剤)"/>
                                <text integrityCheckAlgorithm="SHA256">
                                    <reference value="m3/32-prod/1/postapproval-stability.pdf
"/>
                                    <integrityCheck>e000ab89ef2c2d777af401ea2a37585a</int
egrityCheck>
                                </text>
                            </document>
                        </component>
                        <component>
                            <document>
                                <id root="0.321.456.230525001.0812.0000051"/>
                                <title value="3.2.P.8.3 安定性データ(セイヤクキョール錠
 10mg、錠剤)"/>
                                <text integrityCheckAlgorithm="SHA256">
                                    <reference value="m3/32-prod/1/stability-data.pdf"/>
                                    <integrityCheck>334648f1ef675d8c6168f29423ac93a4 </i
ntegrityCheck>
                                </text>
                            </document>
                        </component>
                        <component>
                            <document>
                                <id root="0.321.456.230525001.0812.0000052"/>
                                <title value="3.2.P.4.1 規格及び試験方法(セイヤクキョー
ル錠 20mg、錠剤)"/>
                                <text integrityCheckAlgorithm="SHA256">
                                    <reference value="m3/32-prod/2/c-specifications.pdf"/>
                                    <integrityCheck>4bd9ba5afcf5f01f8a13cffe21ec7fde</integ
rityCheck>
                                </text>
                            </document>
```

```
                              </component>
                              <component>
                                 <document>
                                    <id root="0.321.456.230525001.0812.0000053"/>
                                    <title value="3.2.P.4.1 規格及び試験方法(セイヤクキョー
ル錠 20mg、錠剤)"/>
                                    <text integrityCheckAlgorithm="SHA256">
                                       <reference value="m3/32-prod/2/h-specifications.pdf"/>
                                       <integrityCheck>7715ef3b9e907ffb44ff40fda3f32990</inte
grityCheck>
                                    </text>
                                 </document>
                              </component>
                              <component>
                                 <document>
                                    <id root="0.321.456.230525001.0812.0000054"/>
                                    <title value="3.2.P.4.6 新規添加剤(セイヤクキョール錠 2
0mg、錠剤)"/>
                                    <text integrityCheckAlgorithm="SHA256">
                                       <reference value="m3/32-prod/2/novel-excipients.pdf"/>
                                       <integrityCheck>778636949b7582290a1acb2fa683e618</in
tegrityCheck>
                                    </text>
                                 </document>
                              </component>
                              <component>
                                 <document>
                                    <id root="0.321.456.230525001.0812.0000055"/>
                                    <title value="3.2.P.8.1 安定性のまとめ及び結論(セイヤク
キョール錠 20mg、錠剤)"/>
                                    <text integrityCheckAlgorithm="SHA256">
                                       <reference value="m3/32-prod/2/stability-summary.pdf"/>
                                       <integrityCheck>c827ed7a22ae5595c393d3409f8416f2</in
tegrityCheck>
                                    </text>
                                 </document>
                              </component>
                              <component>
                                 <document>
                                    <id root="0.321.456.230525001.0812.0000056"/>
                                    <title value="3.2.P.8.2 承認後の安定性試験計画の作成及
び実施(セイヤクキョール錠 20mg、錠剤)"/>
                                    <text integrityCheckAlgorithm="SHA256">
                                       <reference value="m3/32-prod/2/postapproval-stability.pdf
"/>
                                       <integrityCheck>851d42de465fc27cff1a40d3e48785aa</int
egrityCheck>
                                    </text>
                                 </document>
                              </component>
                              <component>
                                 <document>
                                    <id root="0.321.456.230525001.0812.0000057"/>
```

```
                                    <title value="3.2.P.8.3 安定性データ(セイヤクキョール錠
  20mg、錠剤)"/>
                                    <text integrityCheckAlgorithm="SHA256">
                                       <reference value="m3/32-prod/2/stability-data.pdf"/>
                                       <integrityCheck>3824be61af173f7c2050945262628d96</in
tegrityCheck>
                                    </text>
                                 </document>
                              </component>
                              <component>
                                 <document>
                                    <id root="0.321.456.230525001.0812.0000058"/>
                                    <title value="4.2.1.1-1 試験番号 NSK-N-001 : XXX に関
する試験報告書"/>
                                    <text integrityCheckAlgorithm="SHA256">
                                       <reference value="m4/421-phm/nsk-n-001/4211-1-nsk-n-0
01.pdf"/>
                                       <integrityCheck>28682e4600fd560502ee081eeba9b8fe</int
egrityCheck>
                                    </text>
                                 </document>
                              </component>
                              <component>
                                 <document>
                                    <id root="0.321.456.230525001.0812.0000059"/>
                                    <title value="5.2 全臨床試験一覧表"/>
                                    <text integrityCheckAlgorithm="SHA256">
                                       <reference value="m5/tabular-listing.pdf"/>
                                       <integrityCheck>f5350e169661c066dbf34836929f2bf0</int
egrityCheck>
                                    </text>
                                 </document>
                              </component>
                              <component>
                                 <document>
                                    <id root="0.321.456.230525001.0812.0000060"/>
                                    <title value="5.3.1.1-1 試験番号 NSK-C-001 : XXX 試験
総括報告書"/>
                                    <text integrityCheckAlgorithm="SHA256">
                                       <reference value="m5/531-biopharm/nsk-c-001/5311-1-nsk
-c-001.pdf"/>
                                       <integrityCheck>a35fe990b13482b49eacf6b93d39778b</in
tegrityCheck>
                                    </text>
                                 </document>
                              </component>
                              <component>
                                 <document>
                                    <id root="0.321.456.230525001.0812.0000061"/>
                                    <title value="5.3.5.1-3 試験番号 NSK-C-017 : XXX 試験
総括報告書(1/2)"/>
                                    <text integrityCheckAlgorithm="SHA256">
```

```
                                                    <reference value="m5/535-eff-safe/nsk-c-017/5351-3-nsk-c
-017-1.pdf"/>
                                                    <integrityCheck>02d10ef30f3fa666e7574e004f41e363</int
egrityCheck>
                                                 </text>
                                              </document>
                                           </component>
                                           <component>
                                              <document>
                                                 <id root="0.321.456.230525001.0812.0000062"/>
                                                 <title value="5.3.5.1-3 試験番号 NSK-C-017 ： XXX 試験
総括報告書(続)(2/2)"/>
                                                 <text integrityCheckAlgorithm="SHA256">
                                                    <reference value="m5/535-eff-safe/nsk-c-017/5351-3-nsk-c
-017-2.pdf"/>
                                                    <integrityCheck>f3c1da0410cc0b192e0b35f46e01b6ab</int
egrityCheck>
                                                 </text>
                                              </document>
                                           </component>
                                           <component>
                                              <document>
                                                 <id root="0.321.456.230525001.0812.0000063"/>
                                                 <title value="5.3.5.2-1 試験番号 NSK-C-018 ： XXX 試験
総括報告書 シノプシス"/>
                                                 <text integrityCheckAlgorithm="SHA256">
                                                    <reference value="m5/535-eff-safe/nsk-c-018/5352-1-nsk-c
-018-1.pdf"/>
                                                    <integrityCheck>0f87bfeb82c4a9993fbcf0f362316c27</int
egrityCheck>
                                                 </text>
                                              </document>
                                           </component>
                                           <component>
                                              <document>
                                                 <id root="0.321.456.230525001.0812.0000064"/>
                                                 <title value="5.3.5.2-1 試験番号 NSK-C-018 ： XXX 試験
総括報告書 本文"/>
                                                 <text integrityCheckAlgorithm="SHA256">
                                                    <reference value="m5/535-eff-safe/nsk-c-018/5352-1-nsk-c
-018-2.pdf"/>
                                                    <integrityCheck>0f87bfeb82c4a9993fbcf0f362316c28</int
egrityCheck>
                                                 </text>
                                              </document>
                                           </component>
                                           <component>
                                              <document>
                                                 <id root="0.321.456.230525001.0812.0000065"/>
                                                 <title value="5.3.5.2-1 試験番号 NSK-C-018 ： XXX 試験
総括報告書 治験実施計画書及びその改訂"/>
                                                 <text integrityCheckAlgorithm="SHA256">
```

```
                                    <reference value="m5/535-eff-safe/nsk-c-018/5352-1-nsk-c
-018-3.pdf"/>
                                        <integrityCheck>0f87bfeb82c4a9993fbcf0f362316c29</int
egrityCheck>
                                    </text>
                                </document>
                            </component>
                            <component>
                                <document>
                                    <id root="0.321.456.230525001.0812.0000066"/>
                                    <title value="5.3.5.2-1 試験番号 NSK-C-018：XXX 試験
総括報告書 症例記録用紙の見本"/>
                                    <text integrityCheckAlgorithm="SHA256">
                                        <reference value="m5/535-eff-safe/nsk-c-018/5352-1-nsk-c
-018-4.pdf"/>
                                        <integrityCheck>0f87bfeb82c4a9993fbcf0f362316c30</int
egrityCheck>
                                    </text>
                                </document>
                            </component>
                            <component>
                                <document>
                                    <id root="0.321.456.230525001.0812.0000067"/>
                                    <title value="5.3.5.2-1 試験番号 NSK-C-018：XXX 試験
総括報告書 患者への説明文書及び同意書"/>
                                    <text integrityCheckAlgorithm="SHA256">
                                        <reference value="m5/535-eff-safe/nsk-c-018/5352-1-nsk-c
-018-5.pdf"/>
                                        <integrityCheck>0f87bfeb82c4a9993fbcf0f362316c31</int
egrityCheck>
                                    </text>
                                </document>
                            </component>
                            <component>
                                <document>
                                    <id root="0.321.456.230525001.0812.0000068"/>
                                    <title value="5.3.7.1-1 症例一覧表 XXX 試験(試験番号 N
SK-C-015)"/>
                                    <text integrityCheckAlgorithm="SHA256">
                                        <reference value="m5/537-listing/nsk-c-015/5371-1-nsk-c-
015-patients-lists.pdf"/>
                                        <integrityCheck>e73c98406787e9f04496ae80c27f95de</int
egrityCheck>
                                    </text>
                                </document>
                            </component>
                            <component>
                                <document>
                                    <id root="0.321.456.230525001.0812.0000069"/>
                                    <title value=" 5.3.7.2-1 患者ごとの副作用一覧表 XXX 試
験(試験番号 NSK-C-015)"/>
                                    <text integrityCheckAlgorithm="SHA256">
```

```
                                    <reference value="m5/537-listing/nsk-c-
015-ae-lists.pdf"/>
                                    <integrityCheck>510c0b25a4a0cf80550a3fef1b4be8a7</int
egrityCheck>
                                </text>
                            </document>
                        </component>
                        <component>
                            <document>
                                <id root="0.321.456.230525001.0812.0000070"/>
                                <title value="5.3.7.3-1 重篤な有害事象一覧表 XXX 試験
(試験番号 NSK-C-015)"/>
                                <text integrityCheckAlgorithm="SHA256">
                                    <reference value="m5/537-listing/nsk-c-015/5373-1-nsk-c-
015-sae-lists.pdf"/>
                                    <integrityCheck>45d430500f68b8e7cce21c6d8afdc37b</int
egrityCheck>
                                </text>
                            </document>
                        </component>
                        <component>
                            <document>
                                <id root="0.321.456.230525001.0812.0000071"/>
                                <title value="5.3.7.4-1 臨床検査値異常変動一覧表 XXX 試
験(試験番号 NSK-C-015)"/>
                                <text integrityCheckAlgorithm="SHA256">
                                    <reference value="m5/537-listing/nsk-c-015/5374-1-nsk-c-
015-lab-lists.pdf"/>
                                    <integrityCheck>f49c465f07c7984dcf64049791b83ca0</int
egrityCheck>
                                </text>
                            </document>
                        </component>
                        <component>
                            <document>
                                <id root="0.321.456.230525001.0812.0000072"/>
                                <title value="5.3.7.5-1 臨床検査値変動図 XXX 試験(試験
番号 NSK-C-015)"/>
                                <text integrityCheckAlgorithm="SHA256">
                                    <reference value="m5/537-listing/nsk-c-015/5375-1-nsk-c-
015-lab-figs.pdf"/>
                                    <integrityCheck>d2f44cda8543dd8c6de33bd7044241ba</in
tegrityCheck>
                                </text>
                            </document>
                        </component>
                        <component>
                            <document>
                                <id root="0.321.456.230525001.0812.0000073"/>
                                <title value="5.3.7.1-2 症例一覧表 XXX 試験(試験番号 N
SK-C-016)"/>
                                <text integrityCheckAlgorithm="SHA256">
```

```
                                    <reference value="m5/537-listing/nsk-c-016/5371-2-nsk-c-
016-patients-lists.pdf"/>
                                    <integrityCheck>0402836d28bd9fd84b1ddaf1a7d5173f</in
tegrityCheck>
                                </text>
                            </document>
                        </component>
                        <component>
                            <document>
                                <id root="0.321.456.230525001.0812.0000074"/>
                                <title value="5.4-1 参考文献 1"/>
                                <text integrityCheckAlgorithm="SHA256">
                                    <reference value="m5/54-lit/reference-1.pdf"/>
                                    <integrityCheck>337506ec672fb0b9e3ae1ae24680aad6</in
tegrityCheck>
                                </text>
                            </document>
                        </component>
                        <component>
                            <document>
                                <id root="0.321.456.230525001.0812.0000075"/>
                                <title value="5.4-2 参考文献 2"/>
                                <text integrityCheckAlgorithm="SHA256">
                                    <reference value="m5/54-lit/reference-2.pdf"/>
                                    <integrityCheck>208ebb8c78ca587db427cfc706c42be7</in
tegrityCheck>
                                </text>
                            </document>
                        </component>
                        <component>
                            <document>
                                <id root="0.321.456.230525001.0812.0000076"/>
                                <title value="5.4-3 参考文献 3"/>
                                <text integrityCheckAlgorithm="SHA256">
                                    <reference value="m5/54-lit/reference-3.pdf"/>
                                    <integrityCheck>8fc1350b66e45b0209b8e9522a9facdc</int
egrityCheck>
                                </text>
                            </document>
                        </component>
                        <referencedBy typeCode="REFR">
                            <keywordDefinition>
                                <code code="ich keyword type 1" codeSystem="2.16.840.1.
113883.3.989.2.2.4.1.2"/>
                                <statusCode code="active"/>
                                <value>
                                    <item code="INDI001" codeSystem="0.123.456.23052500
1.1209.10001">
                                        <displayName value="hypertension"/>
                                    </item>
                                </value>
                            </keywordDefinition>
                        </referencedBy>
```

```
                              <referencedBy typeCode="REFR">
                                 <keywordDefinition>
                                    <code code="ich keyword type 2" codeSystem="2.16.840.1.
113883.3.989.2.2.4.1.2"/>
                                    <statusCode code="active"/>
                                    <value>
                                       <item code="SUBS001" codeSystem="0.123.456.2305250
01.1209.10002">
                                          <displayName value="EI Hydrochloride"/>
                                       </item>
                                    </value>
                                 </keywordDefinition>
                              </referencedBy>
                              <referencedBy typeCode="REFR">
                                 <keywordDefinition>
                                    <code code="ich keyword type 3" codeSystem="2.16.840.1.
113883.3.989.2.2.4.1.2"/>
                                    <statusCode code="active"/>
                                    <value>
                                       <item code="MANU001" codeSystem="0.123.456.230525
001.1209.10003">
                                          <displayName value="JPMA Pharmaceuticals Tokyo"/
>
                                       </item>
                                    </value>
                                 </keywordDefinition>
                              </referencedBy>
                              <referencedBy typeCode="REFR">
                                 <keywordDefinition>
                                    <code code="ich keyword type 4" codeSystem="2.16.840.1.
113883.3.989.2.2.4.1.2"/>
                                    <statusCode code="active"/>
                                    <value>
                                       <item code="PROD001" codeSystem="0.123.456.230525
001.1209.10004">
                                          <displayName value="Seiyakukyol Tablet 10mg"/>
                                       </item>
                                    </value>
                                 </keywordDefinition>
                              </referencedBy>
                              <referencedBy typeCode="REFR">
                                 <keywordDefinition>
                                    <code code="ich keyword type 4" codeSystem="2.16.840.1.
113883.3.989.2.2.4.1.2"/>
                                    <statusCode code="active"/>
                                    <value>
                                       <item code="PROD002" codeSystem="0.123.456.230525
001.1209.10004">
                                          <displayName value="Seiyakukyol Tablet 20mg"/>
                                       </item>
                                    </value>
                                 </keywordDefinition>
                              </referencedBy>
                              <referencedBy typeCode="REFR">
```

```
                                <keywordDefinition>
                                  <code code="ich keyword type 5" codeSystem="2.16.840.1.
113883.3.989.2.2.4.1.2"/>
                                  <statusCode code="active"/>
                                  <value>
                                     <item code="DOSA001" codeSystem="0.123.456.230525
001.1209.10005">
                                        <displayName value="Tablet 10mg"/>
                                     </item>
                                  </value>
                                </keywordDefinition>
                             </referencedBy>
                             <referencedBy typeCode="REFR">
                                <keywordDefinition>
                                  <code code="ich keyword type 5" codeSystem="2.16.840.1.
113883.3.989.2.2.4.1.2"/>
                                  <statusCode code="active"/>
                                  <value>
                                     <item code="DOSA002" codeSystem="0.123.456.230525
001.1209.10005">
                                        <displayName value="Tablet 20mg"/>
                                     </item>
                                  </value>
                                </keywordDefinition>
                             </referencedBy>
                             <referencedBy typeCode="REFR">
                                <keywordDefinition>
                                  <code code="ich keyword type 6" codeSystem="2.16.840.1.
113883.3.989.2.2.4.1.2"/>
                                  <statusCode code="active"/>
                                  <value>
                                     <item code="EXCI001" codeSystem="0.123.456.2305250
01.1209.10006">
                                        <displayName value="compendial-excipient"/>
                                     </item>
                                  </value>
                                </keywordDefinition>
                             </referencedBy>
                             <referencedBy typeCode="REFR">
                                <keywordDefinition>
                                  <code code="ich keyword type 6" codeSystem="2.16.840.1.
113883.3.989.2.2.4.1.2"/>
                                  <statusCode code="active"/>
                                  <value>
                                     <item code="EXCI002" codeSystem="0.123.456.2305250
01.1209.10006">
                                        <displayName value="hydroxyethylmethylcellulose"/>
                                     </item>
                                  </value>
                                </keywordDefinition>
                             </referencedBy>
                             <referencedBy typeCode="REFR">
                                <keywordDefinition>
```

```
                                    <code code="ich keyword type 6" codeSystem="2.16.840.1.
113883.3.989.2.2.4.1.2"/>
                                    <statusCode code="active"/>
                                    <value>
                                        <item code="EXCI003" codeSystem="0.123.456.2305250
01.1209.10006">
                                            <displayName value="amylopectin"/>
                                        </item>
                                    </value>
                                </keywordDefinition>
                            </referencedBy>
                            <referencedBy typeCode="REFR">
                                <keywordDefinition>
                                    <code code="ich keyword type 9" codeSystem="2.16.840.1.
113883.3.989.2.2.4.1.2"/>
                                    <statusCode code="active"/>
                                    <value>
                                        <item code="id0000001" codeSystem="0.123.456.230525
001.1209.10007">
                                            <displayName value="NSK-N-001"/>
                                        </item>
                                    </value>
                                </keywordDefinition>
                            </referencedBy>
                            <referencedBy typeCode="REFR">
                                <keywordDefinition>
                                    <code code="ich keyword type 9" codeSystem="2.16.840.1.
113883.3.989.2.2.4.1.2"/>
                                    <statusCode code="active"/>
                                    <value>
                                        <item code="id0000002" codeSystem="0.123.456.230525
001.1209.10008">
                                            <displayName value="NSK-C-001"/>
                                        </item>
                                    </value>
                                </keywordDefinition>
                            </referencedBy>
                            <referencedBy typeCode="REFR">
                                <keywordDefinition>
                                    <code code="ich keyword type 9" codeSystem="2.16.840.1.
113883.3.989.2.2.4.1.2"/>
                                    <statusCode code="active"/>
                                    <value>
                                        <item code="id0000003" codeSystem="0.123.456.230525
001.1209.10008">
                                            <displayName value="NSK-C-017"/>
                                        </item>
                                    </value>
                                </keywordDefinition>
                            </referencedBy>
                            <referencedBy typeCode="REFR">
                                <keywordDefinition>
                                    <code code="ich keyword type 9" codeSystem="2.16.840.1.
113883.3.989.2.2.4.1.2"/>
```

```
                                <statusCode code="active"/>
                                <value>
                                    <item code="id0000004" codeSystem="0.123.456.230525
001.1209.10008">
                                        <displayName value="NSK-C-018"/>
                                    </item>
                                </value>
                            </keywordDefinition>
                        </referencedBy>
                        <referencedBy typeCode="REFR">
                            <keywordDefinition>
                                <code code="ich keyword type 9" codeSystem="2.16.840.1.
113883.3.989.2.2.4.1.2"/>
                                <statusCode code="active"/>
                                <value>
                                    <item code="id0000005" codeSystem="0.123.456.230525
001.1209.10008">
                                        <displayName value="NSK-C-015"/>
                                    </item>
                                </value>
                            </keywordDefinition>
                        </referencedBy>
                        <referencedBy typeCode="REFR">
                            <keywordDefinition>
                                <code code="ich keyword type 9" codeSystem="2.16.840.1.
113883.3.989.2.2.4.1.2"/>
                                <statusCode code="active"/>
                                <value>
                                    <item code="id0000006" codeSystem="0.123.456.230525
001.1209.10008">
                                        <displayName value="NSK-C-016"/>
                                    </item>
                                </value>
                            </keywordDefinition>
                        </referencedBy>
                    </application>
                </componentOf>
            </submission>
        </componentOf1>
        <componentOf2>
            <categoryEvent>
                <code code="jp first" codeSystem="jp-category-event"/>
            </categoryEvent>
        </componentOf2>
    </submissionUnit>
  </subject>
 </controlActProcess>
</PORP_IN000001UV>
```

12.3 Cover Letter Format

To be defined separately.

12.4   Validation Rules

Validation rules of eCTD application in Japan are to be defined separately, in addition to those defined in ICH IG.