HL7 Version 3 Implementation Guide: Drug Stability Reporting (eStability), Release 2

February, 2009

HL7 Informative Document

Sponsored by:
Regulated Clinical Research Information Management

Principal Contributors:

Norbert Bittner

Catherine Hosage-Norman

Norman Gregory

eStabilty Working Group

Questions or comments regarding this document should be directed to Norman Gregory at
norman.gregory@fda.hhs.gov.

Table of contents

Introduction to eStability

Introduction

This Implementation Guide (IG) is for the use of the Health Level 7 (HL7) Stability Standard. The IG describes the basic requirements needed for using the standard and the requirements needed for submitting information to the Food and Drug Administration (FDA) using the standard.

The HL7 Stability Standard is for one way communication between contractor to company, company to company, company to regulatory agency.

HL7 Basics

HL7 is defining data exchange standards with "focus on the electronic interchange of clinical, financial and administrative information among independent healthcare-oriented computer systems".

Besides the definition of data standards, HL7 defines message wrappers that define how to exchange HL7-XML documents between computer systems. These "wrappers" will not be in the scope of this document. Please refer to HL7 "Version 3 Guide, HL7 Messaging Components, V3 message wrappers and Infrastructure" for more details about this.

All Extensible Markup Language (XML) examples given in this Implementation Guide and its appendix are either "fragments" which represent only a small section of the full message and are not valid XML documents or will skip these "control wrappers".

eStability Storyboard

The HL7 storyboard describes three scenarios when using this data standard when sending it from a "Stability Tester" (e.g. a pharmaceutical company) to a "Stability Test Receiver" (e.g. FDA).
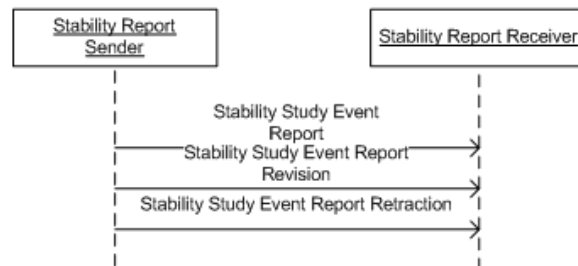
Here are the textual examples given by the HL7 Ballot Site:

Interactions: Stability Report (PORT_IN090001)

ChemCentric Drug Company has been working on a new product, CureAll. Development work on the product has been completed, as have many aspects of the regulatory process. One aspect of the regulatory process is to demonstrate the stability of the CureAll product by testing it against an established Testing Specification using an acceptable protocol. ChemCentric has carried out the necessary testing, and reports the test results to the applicable regulatory authority.

Interactions: Stability Report Revision (PORT_IN090002)

Last month, ChemCentric Drug Company submitted a stability study for its new product, CureAll, to the FDA.

However, Dr. Reggie Review has been going over the results of the test. He has discovered a transcription error that could lead reviewers to get an unfair estimation of CureAll's efficacy even after lengthy storage. In order to correct this state of affairs, ChemCentric submits a revised Stability Study.

Interactions: Stability Report Retraction (PORT_IN090003)

ChemCentric Drug Company recently submitted a stability report on its CureAll product. However, the management of ChemCentric has discovered that Rudy Reliable, a lab technician has submitted false results in order to disguise the fact that he totally neglected to carry out the testing. As a result, ChemCentric has decided to withdraw the Stability Study so that a replacement can be prepared and submitted.

These three types of messages reference one schema definition:

PORT_MT090001UV01

The act of sending, revising and retracting a stability report will be managed within the context of the eCTD or the message wrapper.

Both schema definitions are identical, but to send a correct "retraction" message the second schema has to be referenced.

For this reason, only the implementation of the PORT_MT090001UV01 schema will be in the scope of this document.

For further details on the full message description (Transmission Wrapper and Control Act Wrapper) please refer to the HL7 Ballot site.

The role of the message when using RPS or eCTD

The eStability message may be used stand-alone or in conjunction with an eCTD or an HL7 "Regulated Product Submission" (RPS) message.

When using stand-alone, the participating parties have to decide which part of the HL7 protocol (i.e. which interactions) should be implemented to fulfill the needs of their communication and if the full scope of the message needs to be implemented (e.g. message header). To implement an HL7 compliant system, all interactions need to be implemented.

In conjunction with a regulated, electronic submission the intention is to only use PORT_IN090001 since the status and purpose of the submission and the usage of the submitted file are already documented with the eCTD or RPS. All "protocol" specific lifecycle information is handled using the mechanism implemented within these standards.

The eStability Model (RMIM)

Ctrl Click thumbnail above to open larger graphic in a new window
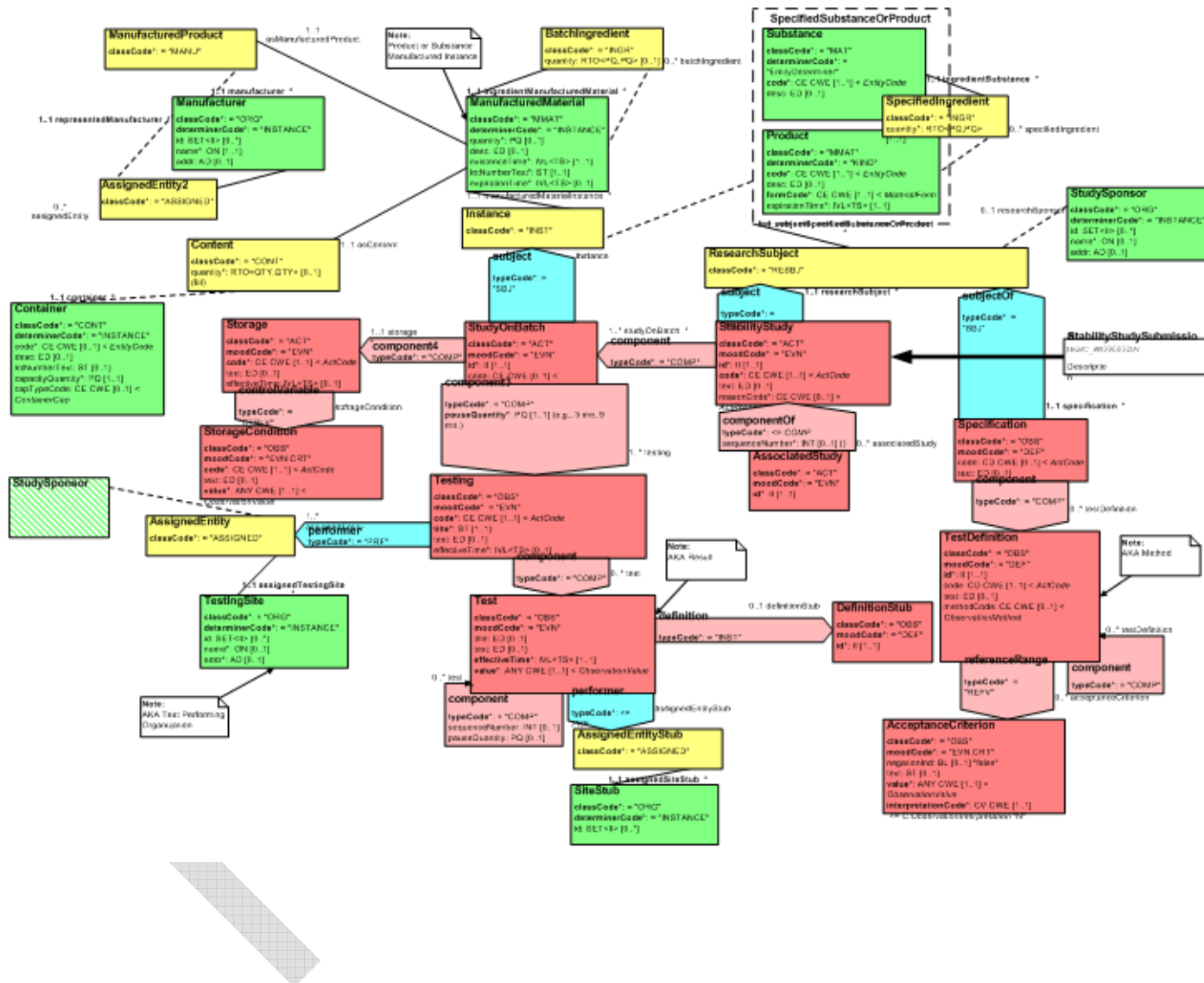
Please refer to the HL7 website for a description on how to interpret this diagram (RMIM picture) .

Elements of an eStability Message

The Drug Stability Report RMIM captures information relevant for the drug stability testing process. This testing is required by regulatory agencies as a component of the drug regulatory process. It verifies the correctness of a manufacturer's claims related to the stability - the ability to be stored over time without losing its therapeutic effectiveness - of a product.

It is important to note that the material that can be reported as part of a Stability Study is not limited to the items explicitly listed as attributes within the RMIM. **This is because the "text' attribute in Acts (shown in red on the diagram), and the "desc" attribute in Entities (shown in green on the diagram) can be valued with a Uniform Resource Locator (URL) which provides a link to additional documentation**. This additional documentation would either be provided along with the stability report, or would be stored at the sender's site at the location indicated by the URL.

This discussion provides some discussion of the data structures within the model. The review of individual classes is ordered by reference to the messaging entry point. (The messaging entry point indicates the starting point for the message. When the model is serialized, the model contents are ordered, starting with the StabilityStudy class, for transmission as a message.)

Stability Study

The Stability Study serves as the high level defining information for the stability study, and as the entry point for messaging. It represents, in essence, the collection of all test results for a single formulation of a product. Note, in some cases such as dissolution studies, multiple stability studies may be carried out to provide the entire picture of a product's stability. This class captures information related to the study as a whole, notably the study type, study id, and the reason for the study.

The associations of this class indicate:

researchSubject

A product or substance that participates as the subject of the study, (Furthermore, the organization associated with the researchSubject indicates the organization sponsoring the study.)

studyOnBatch

A component study which includes the test results related to testing on a single batch.

Note that a stability study is associated with a single research subject, and one to many instances of StudyOnBatch.

AssociatedStudy

This element is a reference to other stability study messages that contain more data e.g. for other storage conditions of the current researchSubject. These messages are defined to be associated to the current message in terms of completeness of information of a submission.

research(SpecifiedSubstanceOrProduct)

The role of research subject is played by either a drug substance or a drug product, about whom the stability study was conducted. It is also possible to use the desc (description) attribute to include a URL link that gives access to additional product information. The organization that scopes the research subject role indicates the submitter of the study.

The associations of the role and playing entity classes indicate:

a)   the Specification that documents the tests that were performed,

b)   the SubstanceBatch or ProductBatch that are the actual batches that provide the samples on which tests are carried out.

Note that a research subject (and hence the stability study) is associated with a single specification.

Specification

Defines the tests that will be performed to demonstrate stability. Information collected directly about the specification includes the specification type, and associated text or other documentation.

The association of the specification indicates:

a)   the research subject on which the tests are to be performed.

b)   the tests that are to be performed.

Note that a specification is associated with one to many tests.

TestDefinition

Defines the tests and test components that are to be performed. Information collected directly about the test definition includes the test type, any relevant description, and the test method. The same can be said regarding the information to be collected for a test component.

The associations of this class indicate that:

a)   an observation may contain component observations,

b)   performed observations (test results) are evaluated by reference to defined acceptance criteria,

c)   a test definition is associated with each of the tests that are performed.

Note that a test definition can have zero to many components, and be associated with zero to many acceptance criteria. It is also true, although the multiplicity is not directly documented; that a test definition can be associated with zero to many tests (performed tests).

AcceptanceCriterion

Defines the limits within which performed observations are interpreted. Information collected directly about the acceptance criterion include the criterion type, the actual criterion value, an indicator showing whether the criterion or its inverse is to be applied, and descriptive text.

StudyOnBatch

Indicates the collection of observations (results) that are performed on samples from a single batch. Information collected directly about the study on batch includes a study type and an identifier.

The associations of this class indicate:

a) the stability study of which this study on batch is a component,

b) the product instance from which samples are drawn,

c) the collection of storage and testing time points that make up the study on batch.

At this point, the primary point of reference is current stability reporting within the United States. The scope of a single transaction or message in this specification has been restricted to only include studies with a single set of storage conditions. However, the stability studies that are filed with regulatory authorities are not simply a study with a single set of storage conditions - the studies include a number of storage conditions plus multiple orientations (upright and inverted). This is especially true for injectable/Parenteral products. These more complex situations, that is to say, studies that require multiple storage conditions and or orientations (e.g. accelerated, room temperature, inverted, upright, etc.), will be handled through the submission of multiple linked reports, with each report covering a single storage condition and orientation (see AssociatedStudy.)

Storage

This class collects the storage conditions that are applicable to the testing done on the samples drawn from a batch. Information collected about storage includes the storage type, descriptive text, and the effective date on which the sample was placed into storage.

The associations of the storage act indicate:

a) the study on batch related to the storage,

b) the storage conditions that define the way the sample is stored.

Note that a storage act is associated with a single study on batch, and with one to many storage conditions.

StorageCondition

A storage condition should be considered as an intervention applied to a collection of samples. Each condition indicates a single parameter of storage, e.g., temperature, humidity, the orientation of the product container. Information collected about the storage condition includes the condition type, the descriptive text, and the condition value.

Instance(Manufactured Material)

The role of instance is played by manufactured material. This is some amount of product or substance drawn from a specific manufactured or formulated batch. As with test definition, the same class is used to define the information captured about the material tested and ingredients of which it is made up. Information collected includes the amount of material provided for testing, descriptive text, the production date, expiration date, and batch lot number.

The associations of the role and playing entity indicate:

a) the product or substance of which the batch is an instance,

b) the study on batch that uses samples from this batch,

c) the ingredients that the product contains (Note that the BatchIngredient role class creates a recursive association. Therefore, it is possible to value the same data and associations for an ingredient of a product as for the product itself.) An ingredient can be part of a product,

d) the manufacturer of the batch,

e) the container used to contain the product.

Note that the manufactured material instance, is an instance of a single product or substance, is used in a single study on batch, is produced by a single manufacturer, is stored in a single type of container, and contains one to many ingredients. A manufactured material in the role of ingredient is used in one and only one product (within the context of this model).

Manufacturer

This role and scoping organization indicates the manufacturer of the product. Information collected includes the manufacturer name, an identifier, and an address.

The association of the organization indicates that the manufacturing site for a product can be carrying out that work as an assignee of another organization - the scoping organization.

Note that the manufacturing site can be carrying out the work as the assignee of zero to many scoping organizations.

Container

This role and scoping entity indicate the container within which the product is to be delivered, and within which samples for study will be contained. Information collected about the container includes the container type, the descriptive text, the container lot number, the capacity of the container, and the cap (closure system) type. The actual quantity in the container is also captured as an attribute of the content role.

(TimePoint)Testing

This class indicates the particular time point at which a sample is drawn from storage so that tests may be performed on it or on portions of the sample. Information collected about the testing act include the testing type, a title that labels the collection of related tests, descriptive text, and the effective date on which samples were drawn. Note, component pause quantity indicates the sampling time point, e.g., three months, associated with the testing.

The associations of the testing act indicate:

a) the study on batch related to the testing,

b) the collection of observations that are performed on the sample or samples drawn at a particular testing time point.

Note that a testing act is associated with a single study on batch, and with one to many tests.

Test

This class indicates the performance of a test on a sample drawn from storage at a particular time point. Information collected about the test includes descriptive text, the specific time at which the test was performed, and the test result (value).

The associations of observation indicate:

a) the observation definition for the observation (test, result) being performed,

b) the testing point in time at which the sample is drawn from storage,

c) whether component test instances are performed at particular points in time - indicated by pause quantity - after being drawn from storage,

d) the organization (location) performing the test.

Note that a test has a single definition, is performed on a sample drawn from storage at a single point in time, and is performed at a single test site. A test may have multiple test components.

AssignedEntity(TestingSite)

The testing site entity makes it possible to indicate the particular site at which the test took place.

Detailed Description of eStability Elements

Required XML Elements

XML Schema and Validation

The eStability file is defined in the PORT_HD090001UV01.xmd schema. However, this file contains only an abstract definition, and thus cannot be used directly for validation of the eStability file. By design, it is the "payload" of an HL7 message of the type PORT_IN090001UV01.

To correctly validate the eStability XML file, it is necessary to wrap it in a message header, though this may be completely empty, i.e. no real data has to be present inside the message header elements.

This is how the message header may look like:

```xml
<?xml version="1.0" encoding="UTF-8"?>
<PORT_IN090001UV01
        xsi:schemaLocation="urn:hl7-org:v3  PORT_IN090001UV01.xsd"
        ITSVersion="XML_1.0" xmlns="urn:hl7-org:v3"
        xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance">
 <id/>
 <creationTime/>
 <interactionId/>
 <processingCode/>
 <processingModeCode/>
 <acceptAckCode/>
 <receiver>
   <device>
     <id/>
   </device>
 </receiver>
 <sender>
   <device>
     <id/>
   </device>
 </sender>
 <controlActProcess moodCode="EVN">
   <subject>
     <!--eStablility data begins here.-->
     <stabilityStudy>
       …
     </stabilityStudy>
     <!--eStablility data ends here.-->
   </subject>
 </controlActProcess>
</PORT_IN090001UV01>
```

The schema location as stated in the example above would require all referenced XML Schemas to reside in the same directory as the eStablility file itself. As these are quite many, this is not very preferable. Instead, a path to the XML Schema can be stated in the xsi:schemaLocation attribute of the PORT_IN090001UV01 element, like:

xsi:schemaLocation="urn:hl7-org:v3
C:\HL7\v3ballot\html\processable\multicacheschemas\PORT_IN090001UV01.xsd"

How to validate an eStability file

To validate an XML file, you need a facility which has the ability to validate an XML file against an XML Schema. This may be a function of the IDE you are using. Described here is a more general approach, which does not rely on any specific IDE.

It makes use of Apache Xerces (Xerces C, to be exact), which is an XML parser. It can be downloaded from http://xml.apache.org/xerces-c/download.cgi . Included in the package (in the "bin" folder) is a small application StdInParse.exe, which is used to validate the file. (On windows, StdInParse.exe relies on xerces-c_x_x.dll, which has to be in the same directory).

On command line level, enter

```
StdInParse.exe -n -s < Path/file.xml
```

If file.xml complies to the referenced SML Schema, you should be presented with a message like

```
stdin: 547 ms (905 elems, 1512 attrs, 14201 spaces,
7022 chars)
```

if file.xml does not comply to the referenced XML Schema, you will be presented with a message like

```
Error at (file stdin, line 229, char 62): Datatype
error: Type:InvalidDatatypeValueException,
Message:Value '' does not match any member types (of
the union)
```

if there is a problem.

Object Identifiers (OID)

Object Identifiers (OID) are used to uniquely identify an object. They are created by self-extending a private enterprise number that is acquired by an institution and are managed hierarchically.

OIDs are intended to be globally unique. They are formed by taking a unique numeric string (e.g. 1.3.5.7.9.24.68) and adding additional digits in a unique fashion (e.g. 1.3.5.7.9.24.68.1, 1.3.5.7.9.24.68.2, 1.3.5.7.9.24.68.1.1, etc.) An institution will acquire an arc (e.g., 1.3.5.7.9.24.68) and then extend the arc (called subarcs) as indicated above to create additional OID's and arcs. There is no limit to the length of an OID, and virtually no computational burden to having a long OID.

OID's are only used for "equality-matching". That is, two objects (e.g. directory attributes or certificate policies) are considered to be the same if they have exactly the same OID. There are no implied navigational or hierarchical capabilities with OID's (unlike IP addresses, for example); given an OID it is not easily possible to deduce who owns the OID, related OID's, etc. OIDs exist to provide a unique identifier, recognizing that in a decentralized world, organizations may pick the same identical names for objects that they manage.

Though acquiring and management of OID's are out of scope in this document, the HL7 Object Identifier Registry may be a good starting point for further investigations: http://www.hl7.org/oid/

Usage of OIDs within eStability (example)

The basis of the OID usage within eStability is a root or arc OID which is identifying the company. This root OID may be used as "id" attribute of the "Organization" element.

This root element is extended by one or more digits to uniquely identify a product – this OID could be used with the "code" attribute of the "Product" or "Substance" element. (e.g. company's OID is 1.3.6.1.4.1.24263, the according product OID might be 1.3.6.1.4.1.24263.1.32 – for some internal reason there is a substructure in the added digits). This OID could be registered with the approving agency and could be used to uniquely identify the product throughout all submissions.

This OID is extended by a "1" to distinguish all subsequent stability related identifiers from identifiers of other HL7 schemas belonging to the same product or substance.

For each product one or many studies are performed, which could be indicated by one or many additional digits. (e.g. the company decides to simply number all studies performed for the product. Thus the 6th study has the OID 1.3.6.1.4.1.24263.1.32.1.6). This OID could be used for the "id" element of "StudyOnBatch".

Each report created for this study could have at least one additional digit within this structure (e.g. the third report is identified by 1.3.6.1.4.1.24263.1.32.1.6.3. A company can decide to map its versioning to this numbering schema).

Since one Stability Data File covers only one storage condition, in some cases many files will be submitted (e.g. when providing additional accelerated data with normal conditions). Each data file is identified by an additional digit (e.g. the first data file for the 3rd report is identified by 1.3.6.1.4.1.24263.1.32.1.6.3.1). This identifier is used as "id" attribute of the "StabilityStudy" element.

All other "id" attributes could be created uniquely within a file, i.e. the OID of the file should be extended in an ambiguous but unique way for each identifier.

Full example of OIDs in one Stability Data File:

Company	1.3.6.1.4.1.24263
Product / Application	1.3.6.1.4.1.24263.1.32
Stability related branch	1.3.6.1.4.1.24263.1.32.1
Study	1.3.6.1.4.1.24263.1.32.1.6
Report	1.3.6.1.4.1.24263.1.32.1.6.3
File of a report	1.3.6.1.4.1.24263.1.32.1.6.3.1
5th Testdefinition of the spec	1.3.6.1.4.1.24263.1.32.1.6.3.1.5
4th parameter of this Testdefinition (i.e. the second level of Testdefinition)	1.3.6.1.4.1.24263.1.32.1.6.3.1.5.4

Usage of GUID within eStability

The usage of GUIDs (Globally Unique Identifier, see http://en.wikipedia.org/wiki/GUID for definition and examples) in the context of the eStability message is an alternative approach for unique identifying objects within this message. The nature of GUIDs does not allow any systematic mapping of a structure as discussed in the last chapter. But as described before in the context of OIDs, the submitting organization has to ensure that the GUIDs used across multiple submissions are consistent and that the same entities can be referenced across multiple messages using the same GUID.

Notation

Each of the following tables describes a structural element of the eStability XML document. They are ordered in the way the HL7 HMD is presenting these elements (i.e. a walk through of the XML model element by element following the "right-hand" rule).

Graphical schema representations are added to give a first impression of the referenced elements XML elements.

For orientation purposes, an XPath is provided to locate the element described in the table. An XPath is comparable to the well known directorypath of PC or UNIX systems:

For example:

"SpecifiedIngredient" is a child element of "Product" which is a child of "ResearchSubject" which is a child of "Subject2" which is a child of the root element "StabilityStudy", written as

/stabilityStudy/subject/researchSubject/subjectProduct/specifiedIngredient

(Note the difference between the Names of the element, and their actual representation in the XPath.)

All element tables have two additional columns to indicate HL7 Optionality (H), and FDA Optionality (F).

Valid values for these columns are:

M – Mandatory (the information has to be provided in any case)

R – Required (the information should be provided if available)

O – Optional (the information can be provided)

N – Not used

Common Elements

ACTCODE

ACTCODE elements describe code values such as:

Element	Attribute	Code List
StabilityStudy	Code	Type of Data File
Product	Code	Product Code
Product	formCode	Product Form Code
Substance	Code	Substance Code
Specification	Code	Internal specification code
Testdefinition	Code	Test Code
StudyOnBatch	Code	Study Type
Container	Code	Container Code
Storage	Code	Storage code
StorageCondition	Code	Storage Condition Code
Testing	Code	Pause Description Code

ACTCODE – Elements

For an ACTCODE in the FDA implementation, only the "displayName" is required.

Attributes:

Name	Description	H	F
code	The code value for the given code system.	R	R
codeSystem	The OID of the code system.	R	R
codeSystemName	The name of the code system.	R	R
codeSystemVersion	The version of the code system used.	R	R
displayName	A displayable name of the code system code.	R	M

Complex Children:

Name	Description	H	F
originalText	Not used.	N	N
translation	Not used.	N	N

Sample Code

Suppose "code" being an ACTCODE:

Full example:

<code code="34391-3" codeSystem="2.16.840.1.113883.6.1" codeSystemName="LOINC" displayName="Human prescription drug"/>

Mandatory example:

<code displayName="Human prescription drug"/>

ACTREASON

ACTREASON elements in eStability describe code values such as:

Element	Attribute	Meaning
StabilityStudy	reasonCode	Reason for Data File
Testdefinition	methodCode	Method Type Code

ACTREASON – Elements

Attributes:

Name	Description	H	F
code	The code value for the given code system.	R	R
codeSystem	The OID of the code system.	R	R
codeSystemName	The name of the code system.	R	R
codeSystemVersion	The version of the code system used.	R	R
displayName	A displayable name of the code system code.	R	M

Complex Children:

Name	Description	H	F
originalText	Not used.	N	N
translation	Not used.	N	N

StabilityStudy – Type

StabilityStudy				
/stabilityStudy				

Description:

The root element of the document.

Simple Children:

Name	Type	Description			H	F
id	II	The global unique identifier for the document.			M	M
		Attributes				
		Root	ID for this document		M	M
		extension			N	N
		assigningAuthorityName			N	N
		displayable			N	N
text	ED	Either a text provided by the submitter or an URI to an external document with further annotations for this submission.			O	O

Complex Children:

Name	Type	Description	H	F
code	CE	An ACTCODE which describes the type of document sent. (see page 55)	M	M
reasonCode	CE	An ACTREASON which describes the reason for this document.	R	M

StabilityStudy

/stabilityStudy

		(see page 56)		
subject	Subject1	A complex structure to describe the researchsubject of the study (exactly one provided).	M	M
component	Component5	A complex structure to describe a batch and the studies performed on this batch and reported in this document (one or many provided).	M	M
componentOf	Component	A complex structure that can occur multiple times containing a reference to a an other eStability message	O	O

Sample Code

```
<stabilityStudy>
    <id root="1.3.6.1.4.1.24263.4711.1.1"/>
    <code displayName=" Stability Study"/>
    <text>JBE1000-7196</text>
    <reasonCode displayName=" New Drug Application "/>
    <subject>
        <researchSubject>
            ...
        </researchSubject>
    </subject>
    <component>
        <studyOnBatch>
            ...
        </studyOnBatch>
    </component>
< componentOf >
        <associatedStudy>
            ...
        </associatedStudy>
</ componentOf >

</stabilityStudy>
```

Subject1 – Type

Subject1

/stabilityStudy/subject

Description:

Intermediate element

Complex Children:

Name	Type	Description	H	F
researchSubject	ResearchSubject	A complex structure to describe the researchsubject (exactly one provided).	M	M

Research Subject – Type

ResearchSubject
/stabilityStudy/subject/researchSubject

Description:

This is the subject of this study. This can either be a "Product" or a "Substance" – only one has to be provided – so the "M" is exclusive on one of the elements.

Information about the included "Substances" of a "Product" can be provided.

Complex Children:

Name	Type	Description	H	F
subjectProduct	Product	Finished dosage form (exactly one).	M	M
subjectSubstance	Substance	Active ingredient (exactly one).	M	M
researchSponsor	StudySponsor	Research Sponsor.	O	R
subjectOf	Subject3	Reference to the specification used in this study.	M	M

Sample Code

```xml
<researchSubject>
  <subjectProduct>
      <code displayName="JBE1000"/>
      <desc>Gummi Bears 100g Bag</desc>
      <formCode displayName="Not provided"/>
      <expirationTime/>
  </subjectProduct>
  <researchSponsor>
      ...
  </researchSponsor>
  <subjectOf>
      <specification>
          ...
      </specification>
  </subjectOf>
</researchSubject>
```
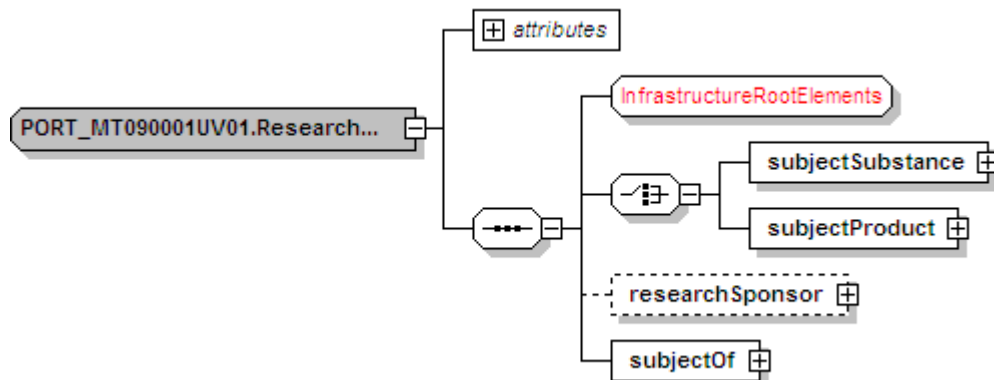
Product – Type

Product
/stabilityStudy/subject/researchSubject/subjectProduct

Description:
Complex structure to describe a finished dosage form.

Simple Children

expirationTime	IVL_TS	The "expected" expiration period (e.g. 24 Months) for NDA, or the existing expiration period for ongoing studies.	R	M
		Either a valid timeperiod using ISO8601 format, e.g. P24M.		
		If a zero-value is provided (e.g. P0M for zero months, P0h for zero hours, …) this means, the expiration period has to be determined.		
		This is an excerpt from ISO 8601 with all allowed "unit" codes:		
		[Y] represents a digit used in the time element "year"; [M] represents a digit used in the time element "month"; [D] represents a digit used in the time element "day"; [w] represents a digit used in the time element "week"; [h] represents a digit used in the time element "hour"; [m] represents a digit used in the time element "minute"; [s] represents a digit used in the time element "second";		
desc	ED	A description of the product provided by the submitter or an URI for additional external documentation.	O	O

Product

/stabilityStudy/subject/researchSubject/subjectProduct

Complex Children:

Name	Type	Description	H	F
code	CE	An ACTCODE: ProductCode (i.e. a unique identifier of the product). (see page 57) For FDA implementation, only the "displayName" (i.e. the product name) is mandatory, the code values might be provided if available. For NDA this is a new identifier. For ongoing studies the identifier must be identical to the already submitted code.	M	M
formCode	CE	An ACTCODE: Form type of this product. (see page 57) For FDA implementation, only the "displayName" (i.e. the product name) is mandatory, the code values might be provided if available.	M	M
specifiedIngredient	SpecifiedIngredient	The formulation of this product (many, if necessary).	O	R

SpecifiedIngredient – Type
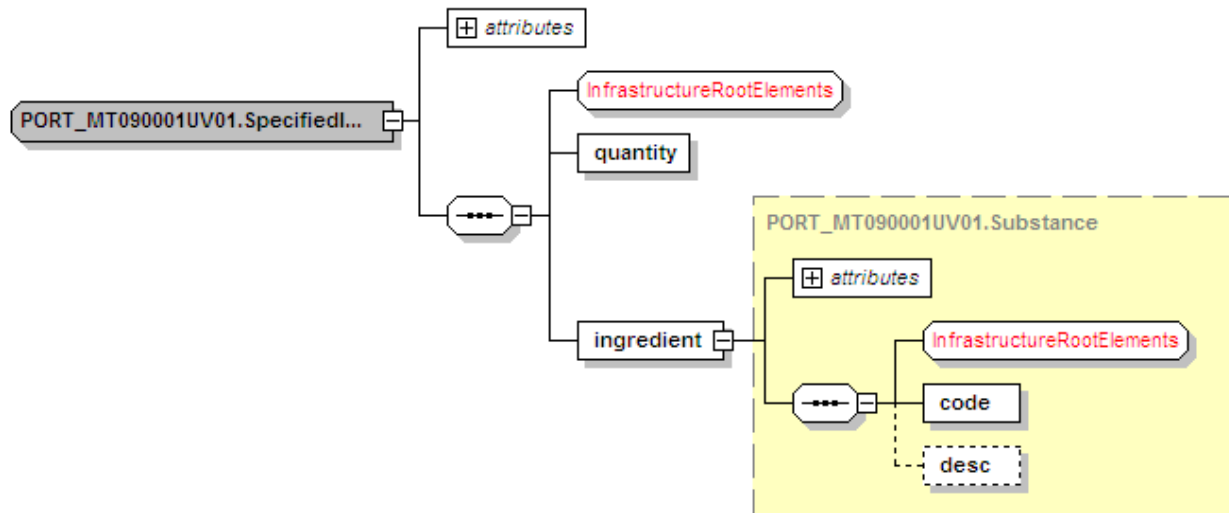
SpecifiedIngredient				
/stabilityStudy/subject/researchSubject/subjectProduct/specifiedIngredient				
Description:				
With this element one can map the formulation of the product by referencing substances and providing information on the quantity of the substance used in the product.				
Complex Children:				
Name	**Type**	**Description**	**H**	**F**
quantity	RTO_PQ_PQ	The quantity of the referenced substance in the product.	R	R
ingredient	Substance	Reference to substance, i.e. active ingredient.	M	M

Substance – Type

Substance				
/stabilityStudy/subject/researchSubject/subjectSubstance **or** /stabilityStudy/subject/researchSubject/subjectProduct/specifiedIngredient				
Description:				
When used as a child of "ResearchSubject" this element describes the substance on which the study is performed. As child of "SpecifiedIngredient" this element describes a substance as part of a formulation.				
Complex Children:				
Name	**Type**	**Description**	**H**	**F**
code	CE	An ACTCODE: code of the substance. (see page 58) For FDA implementation, only the "displayName" (i.e. the substance name)	M	M

		is mandatory, the code values might be provided if available.		
desc	ED	URI for additional documentation.	O	O

StudySponsor – Type

StudySponsor
/stabilityStudy/subject/researchSubject/researchSponsor

Description:

The research sponsor for the study.

Simple Children:

Name		Description	H	F
id	II	A set of identifiers used to uniquely identify the study sponsor. One can be the OID, a global unique identifier for the sponsoring organization assigned by IANA. Other examples can be DUNS number or FEI number. <table><tr><td colspan="3">**Attributes**</td></tr><tr><td>Root</td><td>Identifier</td><td>M</td><td>M</td></tr><tr><td>Extension</td><td></td><td>N</td><td>N</td></tr><tr><td>assigningAuthorityName</td><td></td><td>N</td><td>N</td></tr><tr><td>displayable</td><td></td><td>N</td><td>N</td></tr></table> This identifier should be the same for one organization within all submissions of one company. The provided identifiers should be chosen in a way, that if a company has more than one location (i.e. with different addresses), the identifier is specific for this location (same address – same number).	O	M
name	ON	Name of the organization sponsoring the study.	R	M

Complex Children:

Name	Name	Description	H	F
addr	AD	Address of the organization.	O	M

Sample Code

```
<researchSponsor>
  <id root="1.3.6.1.4.1.24263"/>
  <name>up to data professional service GmbH</name>
  <addr>
      <country>Germany</country>
      <city>Wörrstadt</city>
      <postalCode>55286</postalCode>
      <streetAddressLine>Am Pfädchen 4</streetAddressLine>
  </addr>
</researchSponsor>
```

Subject3 – Type
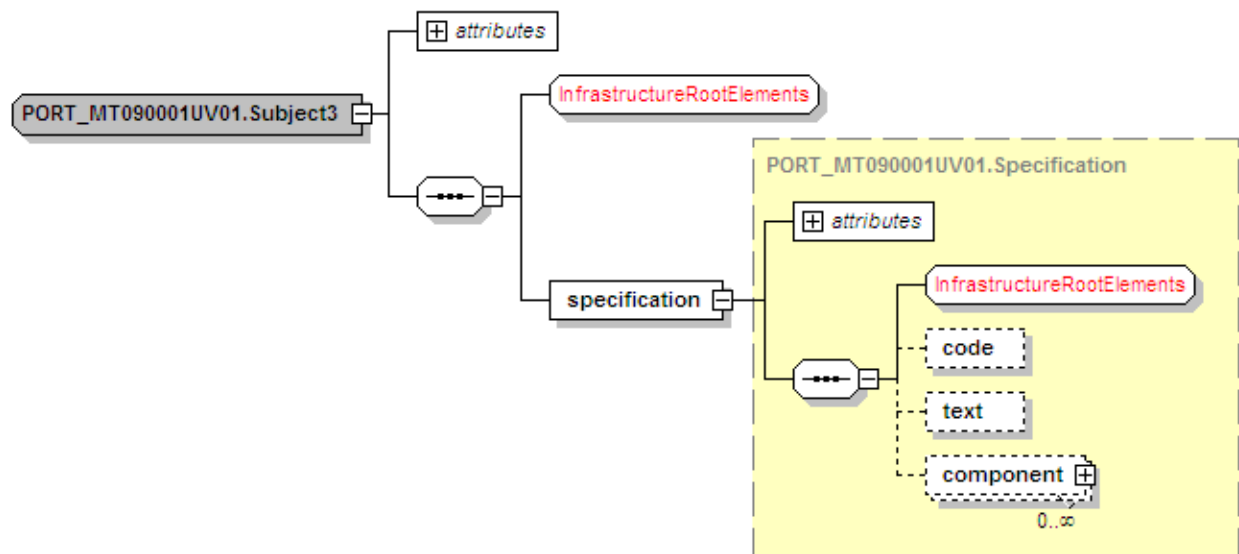
Subject3				
/stabilityStudy/subject/researchSubject/subjectOf				
Description:				
Reference to the specification (intermediate element).				
Complex Children:				
Name	**Type**	**Description**	**H**	**F**
specification	Specification	(Exactly one.)	M	M

Specification - Type

Specification

/stabilityStudy/subject/researchSubject/subjectOf/specification

Description:

For this Element the "full" HL7 structure has to be provided for the specification.

Simple Children:

Name	Type	Description	H	F
text	ED	URI for additional documentation.	O	R

Complex Children:

Name	Type	Description		
code	CD	An ACTCODE: Specification identifier. I.e. the name and version of the specification (as displayName).	O	M
component	Component6	The testdefinition and acceptance criteria for these tests.	O	M

Sample Code

```
<specification>
    <code displayName="JBE1000 Version 3.5 as of 2. Jan 2007"/>
    <text>Spec _JBE1000_3.5.pdf</text>
    <component>
        <testDefinition>
            …
        </testDefinition>
    </component>
</specification>
```

Component6 - Type

Component6

/stabilityStudy/subject/researchSubject/subjectOf/specification/component

Description:

Intermediate element.

Complex Children:

Name	Type	Description	H	F
testDefinition	TestDefinition	Intermediate element	M	M

TestDefinition – Type
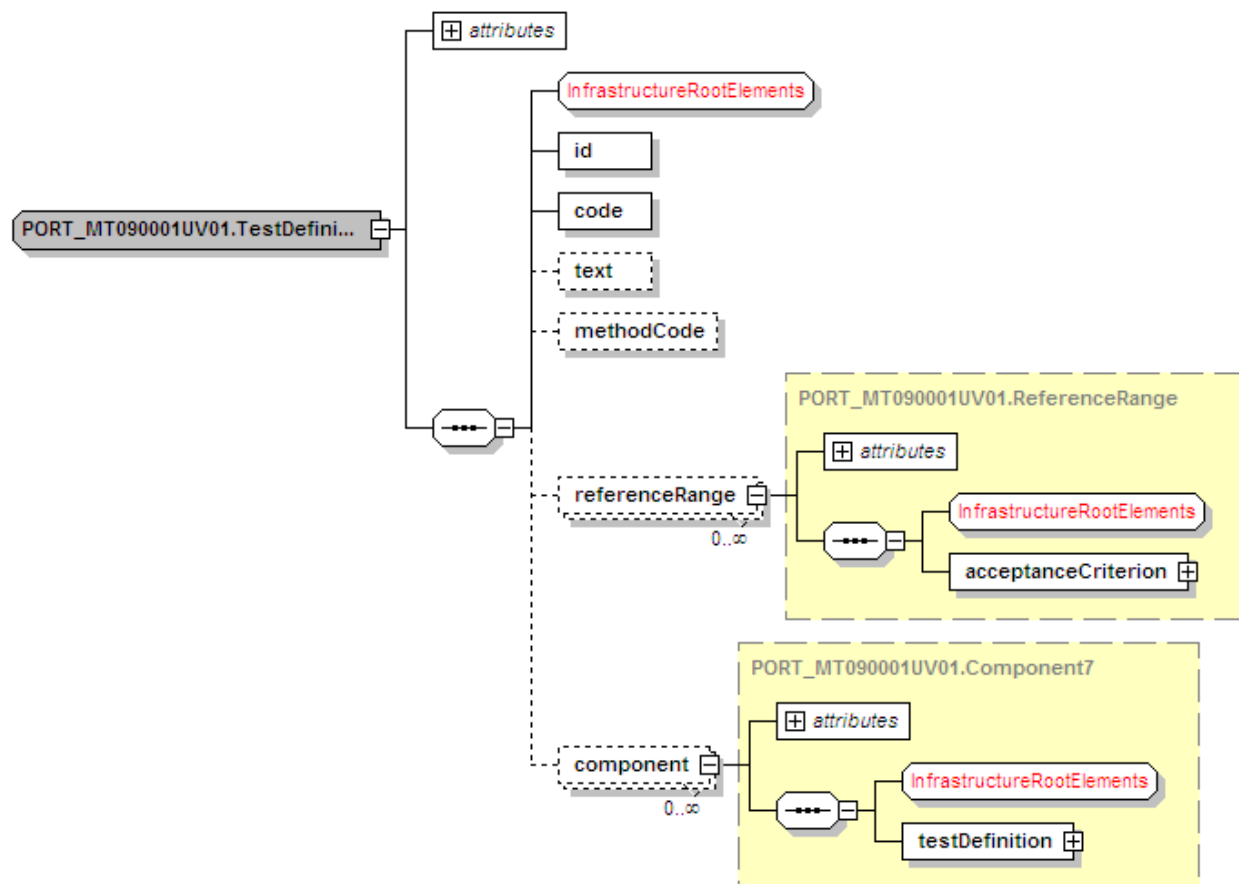
TestDefinition

/stabilityStudy/subject/researchSubject/subjectOf/specification/component/testDefinition

or

/stabilityStudy/subject/researchSubject/subjectOf/specification/component/testDefinition/component/testDefinition

Description:

This is the definition of a method performed during the study or the definition of a parameter of a method. The recursive structure will not be implemented further than one level – methods and method parameters.

Either the external document or the method parameters and the reference range have to be provided.

Simple Children:

Name	Type	Description				H	F
id	II	A global unique identifier for this TestDefinition				M	M
		Attributes					
		Root	OID	M	M		
		Extension		N	N		
		assigningAuthorityName		N	N		
		displayable		N	N		

TestDefinition

/stabilityStudy/subject/researchSubject/subjectOf/specification/component/testDefinition

or

/stabilityStudy/subject/researchSubject/subjectOf/specification/component/testDefinition/component/testDefinition

text	ED	URI for additional documentation for this test, e.g. SOP or Specification document for this method.	O	R

Complex Children:

Name	Type	Description	H	F
code	CD	An ACTCODE: Test code. (see page 58)	O	R
methodCode	CE	An ACTREASON: Method type. (see page 59)	O	M
referenceRange	ReferenceRange	The acceptance criterion for this parameter.	O	M
component	Component7	Recursive reference to TestDefinition to define the method parameter of this method (i.e. a test assay for which the next level can be the ingredients or impurities). Only two additional levels may be provided.	O	M

Sample Code

```xml
<testDefinition>
    <id root="1.3.6.1.4.1.24263.4711.1.1.1"/>
    <code displayName="ASSAY"/>
    <text>Spec_Gummibears_TD1.pdf</text>
    <methodCode displayName="Assay"/>
    <component>
        <testDefinition>
            <id root="1.3.6.1.4.1.24263.4711.1.1.1.1"/>
            <code displayName="Sodium"/>
            <text>Spec_Gummibears_TD2.pdf</text>
            <methodCode displayName="Sodium"/>
            <referenceRange>
                …
            </referenceRange>
            …
        </testDefinition>
    </component>
    ...
</testDefinition>
```

ReferenceRange – Type

ReferenceRange

/stabilityStudy/subject/researchSubject/subjectOf/specification/component/testDefinition/referenceRange

or

/stabilityStudy/subject/researchSubject/subjectOf/specification/component/testDefinition/component/testDefinition/referenceRange

Description:

The container for the set of acceptance criteria for a TestDefinition.

Complex Children:

Name	Type	Description	H	F
acceptanceCriterion	AcceptanceCriterion	One or many acceptance criteria.	O	M

AcceptanceCriterion – Type

AcceptanceCriterion
/stabilityStudy/subject/researchSubject/subjectOf/specification/component/testDefinition/referenceRange/
acceptanceCriterion
or
/stabilityStudy/subject/researchSubject/subjectOf/specification/component/testDefinition/component/testDefinition/referenceRange/
acceptanceCriterion

Description:

Describes one valid specification limit.

Simple Children:

Name	Type	Description	H	F
interpretationCode	CV	E.g. not more than (NMT), not less than (NLT), … (see page 60)	M	M
text	ST	URI for additional documentation.	O	O

Complex Children:

Name	Type	Description	H	F
value	ANY	The value of the criterion.	M	M

Sample Code

For an upper limit:

```
<acceptanceCriterion>
  <value xsi:type="PQ" value="1900" unit="ug"/>
  <interpretationCode displayName="NLT"/>
</acceptanceCriterion>
```

For an upper and lower limit:

```
<acceptanceCriterion>
<text>No determination outside 75-125% of label claim</text>
  <value xsi:type="PQ" value="75" unit="%_LC"/>
  <interpretationCode displayName="NLT"/>
</acceptanceCriterion>

</acceptanceCriterion>
<text>No determination outside 75-125% of label claim</text>
  <value xsi:type="PQ" value="125" unit="%_LC"/>
  <interpretationCode displayName="NMT"/>
</acceptanceCriterion>
```

For a not applicable limit:

```
<acceptanceCriterion>
  <value xsi:type="ST" nullFlavor="NA""/>
  <interpretationCode displayName="NA"/>
</acceptanceCriterion>
```

Component5 – Type
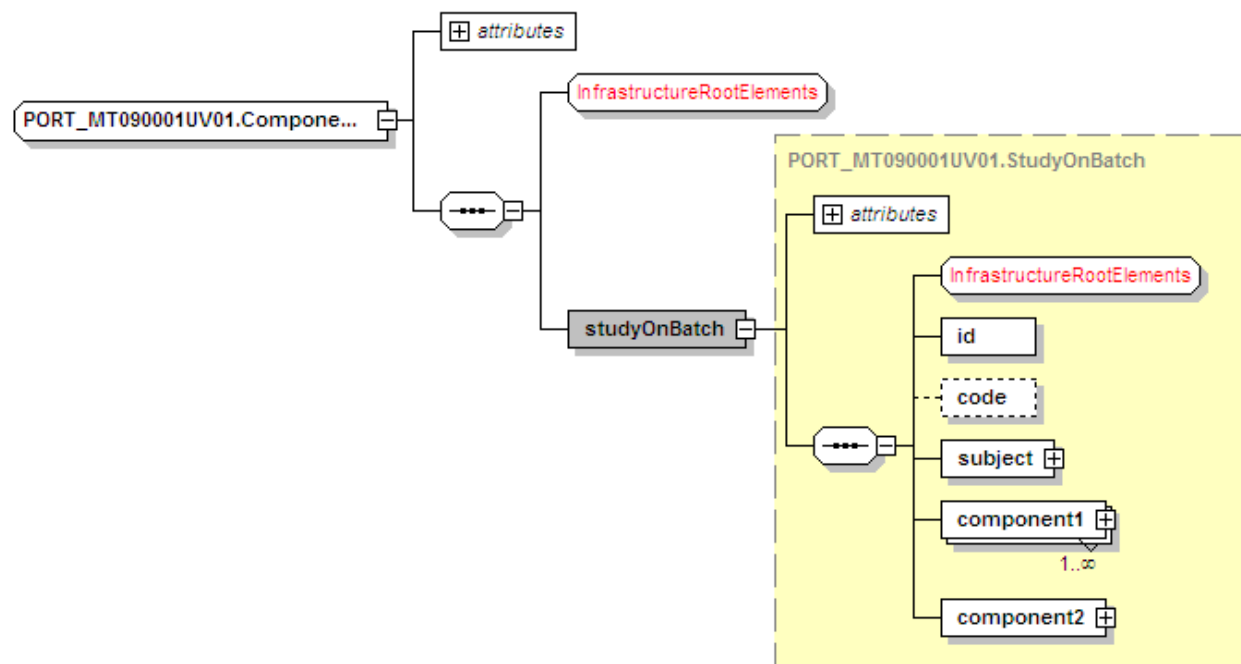
Component5
/stabilityStudy/component

Description:
Reference to the batch and result information for one study on one batch. Many of these elements can be provided.

Complex Children:

Name	Type	Description	H	F
studyOnBatch	StudyOnBatch	Intermediate element	M	M

StudyOnBatch - Type

StudyOnBatch
/stabilityStudy/component/studyOnBatch

Description:

The container for the batch information and results for the study performed on one batch.

Simple Children:

Name	Type	Description	H	F
id	II	A global unique identifier for the study. It should be the same in all submitted files for this study.	R	M

Attributes				
Root	ID		M	M
extension			N	N
assigningAuthorityName			N	N
displayable			N	N

Complex Children:

Name	Type	Description	H	F
code	CE	An ACTCODE: study type (see page 61)	O	R
subject	Subject1	The reference to the information on the material the study is performed on (e.g. a batch).	M	M
component1	Component3	The reference to the storage conditions used	M	M
component2	Component4	The reference to the study design and the results section.	M	M

Sample Code

```xml
<studyOnBatch>
  <id root="1.3.6.1.4.1.24263.4711.1"/>
  <code displayName="Stability"/>
  <subject>
     <instance>
        <manufacturedMaterialInstance>
           ...
        </manufacturedMaterialInstance>
     </instance>
  </subject>
  <component1>
     ...
  </component1>
  <component2>
     ...
  </component2>
</studyOnBatch>
```

Subject2 – Type

Subject2				
/stabilityStudy/component/studyOnBatch/subject				
Description:				
An intermediate element.				
Complex Children:				
Name	**Type**	**Description**	**H**	**F**
instance	Instance	The Instance of the material.	M	M

Instance – Type

Instance				
/stabilityStudy/component/studyOnBatch/subject/instance				
Description:				
An intermediate element.				
Complex Children:				
Name	**Type**	**Description**	**H**	**F**
manufacturedMaterialInstance	ManufacturedMaterial	Intermediate element	M	M

ManufacturedMaterial – Element

ManufacturedMaterial			
/stabilityStudy/component/studyOnBatch/subject/instance/manufacturedMaterialInstance			

Description:

Describes the produced material used in the stability study.

Simple Children:

Name	Description	H	F
Quantity	Total amount of material in the batch.	R	R
Desc	A textual description or/and external reference to a PDF document describing details of this production.	O	O
LotNumberText	Company internal lot number.	R	M

Complex Children:

Name	Type	Description	H	F
ExistenceTime	IVL_TS	Date of production (use ISO 8601 format)	R	M
ExpirationTime	IVL_TS	Date of expiration (based on the provided expirationCode of the "Product" element) or the proposed expiration date of the material. Interpretation for a product: if an interval value is provided this means that this is a *proposed* Expiration date, if a date value is provided this is the already *approved* expiration date Interpretation for "substances" (i.e. intermediates or APIs): if an interval value is provided this means that this is a *proposed* retest period, if a date value is provided this is the already *approved* retest date.	R	M
asManufacturedProduct	ManufacturedProduct	A reference to the manufacturer of this material. If this document is part of an application of a new active ingredient, this information has to be provided.	M	M
AsContent	Content	A reference to the container/closure system.	M	M
BatchIngredient	BatchIngredient	A list of ingredients of type "ManufacturedMaterial", so that a kind of "BatchRecord" can be provided. Using this element leads to a recursive structure.	O	O

Sample Code

<manufacturedMaterialInstance>

```
                <quantity value="0" unit=""/>
                <desc>Production from 2003-01-01</desc>
                <existenceTime>
                    <high value="20030101"/>
                </existenceTime>
                <lotNumberText>JBE1000_001@BAG_PL</lotNumberText>
                <expirationTime>
                    <high value="20050101"/>
                </expirationTime>
                <asManufacturedProduct>
                    <manufacturer>
                        ...
                    </manufacturer>
                </asManufacturedProduct>
                <asContent>
                    ...
                </asContent>
            </manufacturedMaterialInstance>
```

ManufacturedProduct– Element
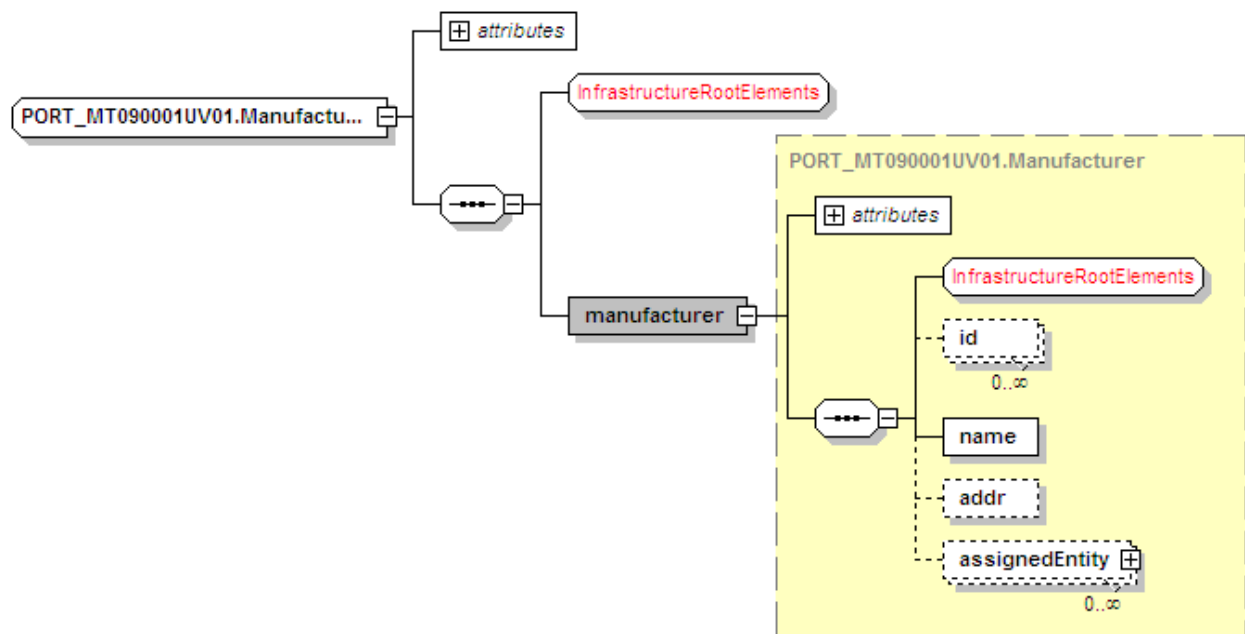
ManufacturedProduct

/stabilityStudy/component/studyOnBatch/subject/instance/manufacturedMaterialInstance/asManufacturedProduct

Description:

Intermediate element, containing the manufacturer of the Manufactured Material.

Complex Children:

Name	Type	Description	H	F
manufacturer	Manufacturer	**Intermediate element**	M	M

Manufacturer – Element

Manufacturer
/stabilityStudy/component/studyOnBatch/subject/instance/manufacturedMaterialInstance/asManufacturedProduct/manufacturer

Description:
The details about a manufacturer or a manufacturing site that produced the "ManufacturedMaterial".

Simple Children:

Name	Type	Description	H	F
id	II	A set of identifiers that is used to uniquely identify the manufacturer or a manufacturing site. One can be the OID, which is a global unique identifier for the manufacturer or manufacturing site assigned by IANA. Other examples are the DUNS number and the FEI number.<table><tr><td colspan="4">Attributes</td></tr><tr><td>Root</td><td>ID</td><td>M</td><td>M</td></tr><tr><td>Extension</td><td></td><td>N</td><td>N</td></tr><tr><td>assigningAuthorityName</td><td></td><td>N</td><td>N</td></tr><tr><td>Displayable</td><td></td><td>N</td><td>N</td></tr></table>	O	M
name	ON	Name of the manufacturer (or manufacturing site).	R	M

Complex Children:

Name	Type	Description	H	F
addr	AD	Address.	O	M
assignedEntity	AssignedEntity2	One or many sub elements of "Manufacturer" type called "representedManufacturer" who produced this product on behalf of the "Manufacturer" given here or who partially produced the product.	O	O

Sample Code

```xml
<manufacturer>
  <id root="1.3.6.1.4.1.24263"/>
  <name>up to data professional service GmbH</name>
  <addr>
      <country>Germany</country>
      <city>Wörrstadt</city>
      <postalCode>55286</postalCode>
      <streetAddressLine>Am Pfädchen 4</streetAddressLine>
  </addr>
</manufacturer>
```

Content - Element
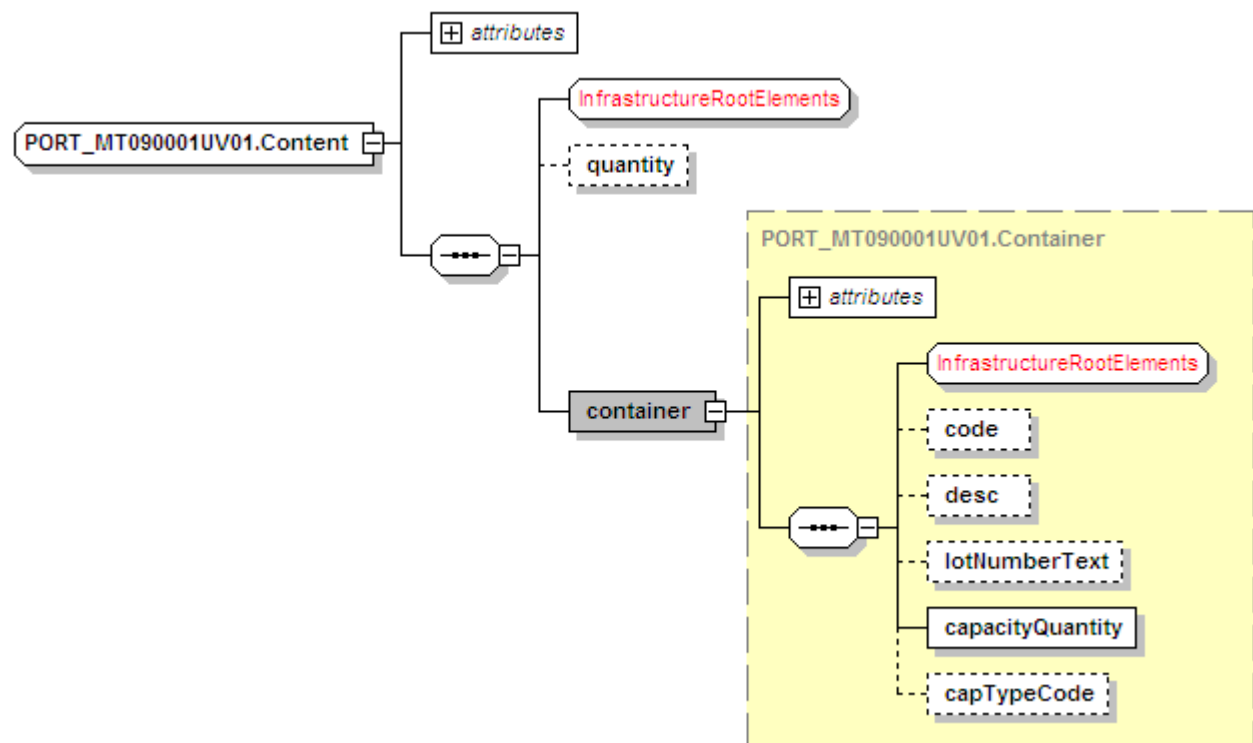
Content

/stabilityStudy/component/studyOnBatch/subject/instance/manufacturedMaterialInstance/asContent

Description:

The container closure system

Simple Children:

Name	Description	H	F
Quantity	The actual quantity of "manufacturedMaterialInstance" in the container (e.g. 50 tablets).	R	R

Complex Children:

Name	Type	Description	H	F
container	Container	A reference to the structure for the container closure system.	M	M

Sample Code

```xml
<asContent>
 <quantity>
     <numerator xsi:type="PQ" value="50" unit="tablets"/>
     <denominator xsi:type="PQ" value="1" unit=""/>
 </quantity>
 <container>
     <code displayName="BAG_PL"/>
     <desc>Plastic Bag</desc>
     <lotNumberText>LOT BAG_PL 23445</lotNumberText>
```

```
                              <capacityQuantity xsi:type="PQ" value="100" unit="ml"/>
                         </container>
                    </asContent>
```

Container - Element

Container
/stabilityStudy/component/studyOnBatch/subject/instance/manufacturedMaterialInstance/asContent/container

Description:

A simple structure to store the makeup of the container closure system.

Simple Children:

Name	Type	Description	H	F
Desc	ED	A verbal description of the container closure system or a reference to an external document which holds this description.	O	O
lotNumberText	ST	The lot number of the production lot for this container.	O	O
capacityQuantity	PQ	The capacity of the container, not necessarily identical to "quantity of the "Content" element (e.g. 100 ml bottle, even if the quantity of tablets in the bottle is 50).	R	R
capTypeCode	CE	The code for the used closure system (e.g. plastic cap). (see page 62)	O	O
Code	CE	Type of Container (e.g. bottle). (see page 64)	R	M

BatchIngredient – Element
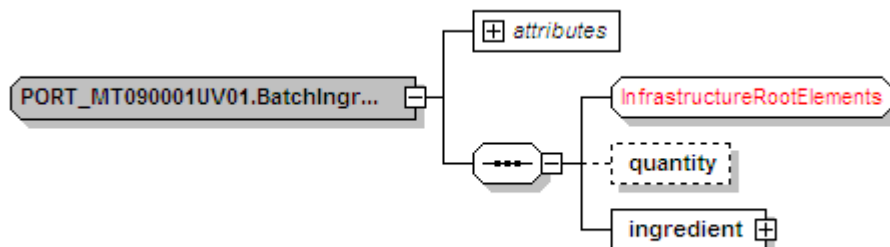
BatchIngredient					
/stabilityStudy/component/studyOnBatch/subject/instance/manufacturedMaterialInstance/batchIngredient					

Description:

An intermediate element to store a recursive reference to a "ManufacturedMaterial" to provide a kind of batch record for the product.

Simple Children:

Name	Type	Description	H	F
quantity	RTO_PQ_PQ	The actual quantity of referenced material used to produce the product (e.g. the referenced material might be used in parts for this product).	O	R

Complex Children:

Name	Type	Description	H	F
ingredient	ManufacturedMaterial	This is a link to ManufacturedMaterial, so that more ingredients of each BatchIngredient can be given – which leads to a recursive structure of a batch record.	M	M

Component4 – Element
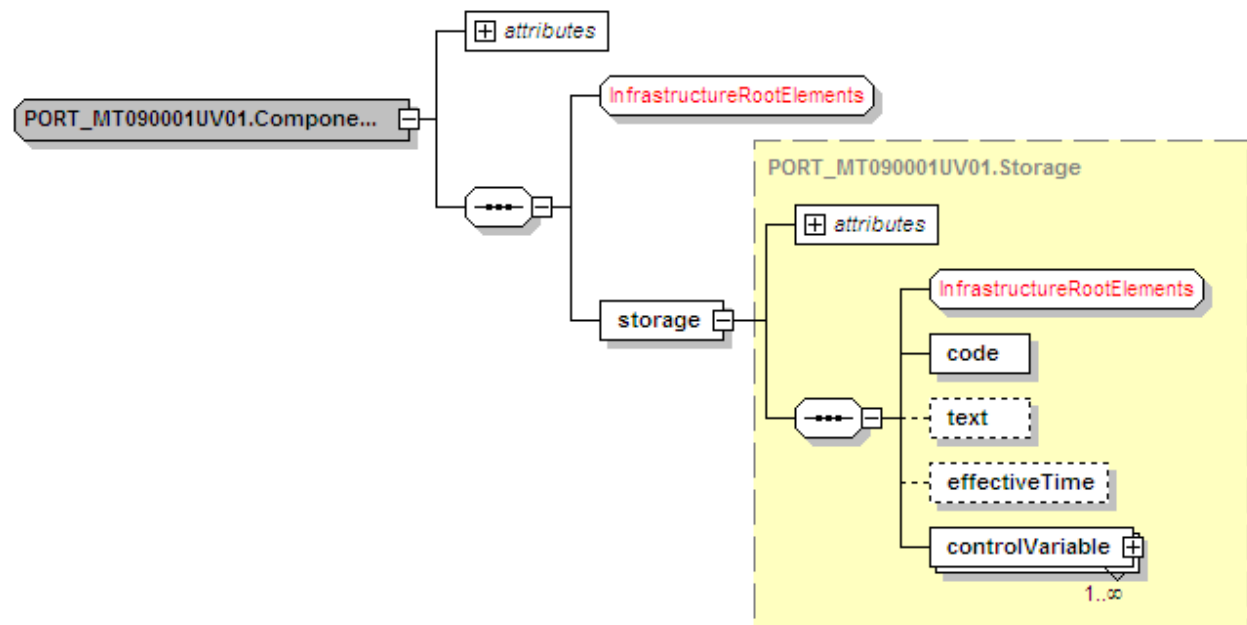
Component4				
/stabilityStudy/component/studyOnBatch/component2				
Description:				
This element represents the storage condition used for the current "studyOnBatch".				
Complex Children:				
Name	**Type**	**Description**	**H**	**F**
storage	Storage	A structure to describe the storage condition used in the study.	M	M

Storage – Element

Storage				
/stabilityStudy/component/studyOnBatch/component2/storage				
Description:				
A list of one or many storage conditions (e.g. one reference to "25°/60%" and one to "upright" – or alternatively one reference to "25°/60% upright").				
Simple Children:				
Name	**Type**	**Description**	**H**	**F**
text	ED	A textual description of this storage condition or an external reference to a PDF document to describe this storage condition.	O	O

Storage

/stabilityStudy/component/studyOnBatch/component2/storage

effectiveTime	IVL_TS	The time the product is put on stability. The date the stability storage is started for this condition, e.g. 20080412 for 12th of April 2008.	O	R

Complex Children:

Name	Type	Description	H	F
code	CE	An ACTCODE: fixed code value, may be used for other purposes in future versions.	M	M
controlVariable	ControlVariable	Reference to the predefined storage conditions (one or many may be used).	M	M

Sample Code

```xml
<storage>
  <code displayName="ICH25_60 upright"/>
  <effectiveTime>
      <high value="20080412"/>
  <effectiveTime/>
  <controlVariable>
      <storageCondition>
          <code displayName="ICH25_60"/>
          <text>Storagecondition according ICH Q1A:  25°C / 60% r.h.</text>
          <value xsi:type="ST">25°C / 60% r.h.</value>
      </storageCondition>
  </controlVariable>
  <controlVariable>
      <storageCondition>
          <code displayName="upright"/>
          <text>Storage of container in upright position</text>
          <value xsi:type="ST">upright</value>
      </storageCondition>
  </controlVariable>
</storage>
```

ControlVariable– Element

ControlVariable

/stabilityStudy/component/studyOnBatch/component2/storage/controlVariable

Description:

Intermediate element

Complex Children:

Name	Type	Description	H	F
storageCondition	StorageCondition	Intermediate element	M	M

StorageCondition– Element

StorageCondition
/stabilityStudy/component/studyOnBatch/component2/storage/controlVariable/storageCondition

Description:

A structure to describe one storage condition. Dependent of the internal company definitions this condition might be simple (e.g. 25°) or complex (e.g. 25° C/60% R.H. upright).. Complex definitions can be made up of many "ControlVariable"s referencing simple "StorageConditions".

Simple Children:

Name	Description	H	F
text	A textual description or an external reference.	O	O
value	The condition, e.g. "25°" or "25°/60%" or "25°/60% upright."	M	M
Code	An ACTCODE: Storage condition code (see page 65)	M	M

Component3 – Element
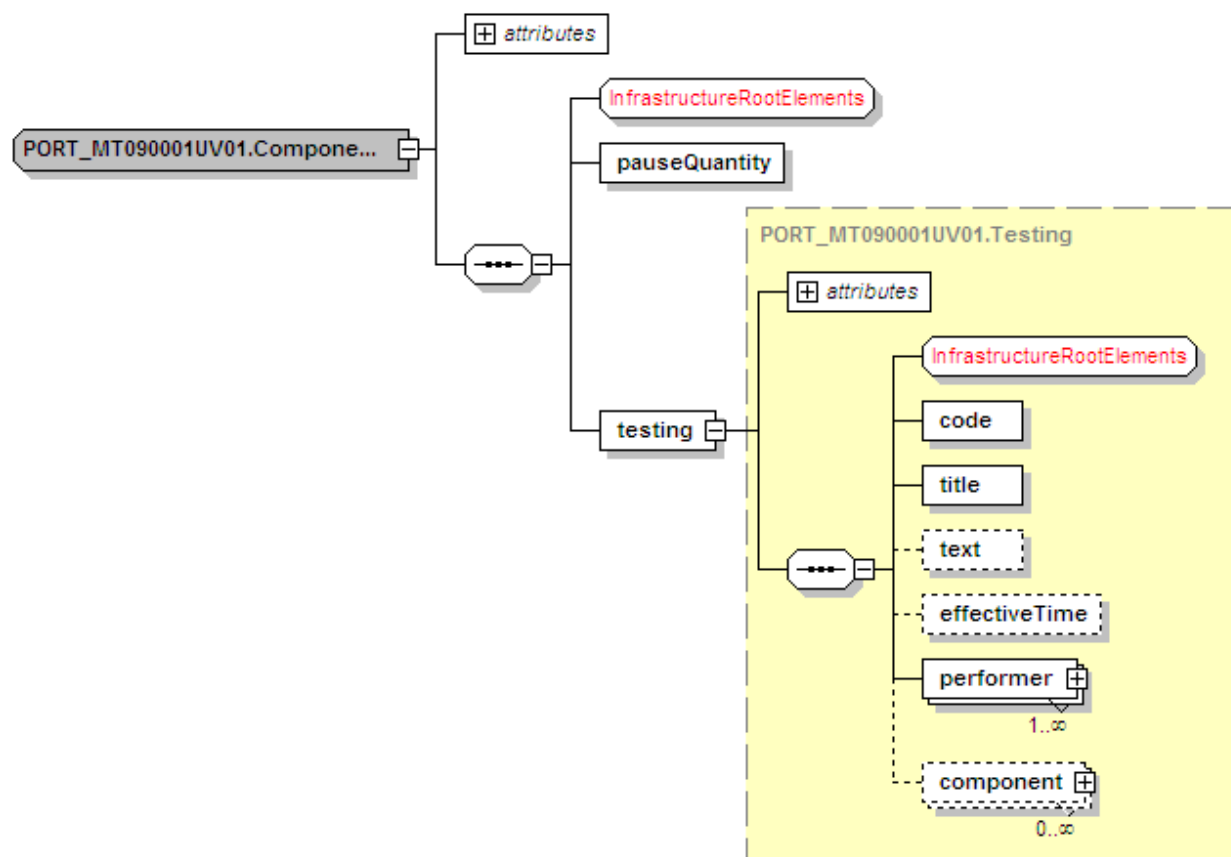
Component3
/stabilityStudy/component/studyOnBatch/component1

Description:
This element gives the results for a given storage time of a batch.

Simple Children:

Name	Type	Description	H	F
pauseQuantity	PQ	Storage time of the batch in a climatic chamber. The unit of the pauseQuantity has to be homogenous for all XML message files that are connected to this specific study, e.g. only months are used throughout the XML message files. Fractions of the unit are allowed (e.g. 0.25 months to denote a week). For more than one pauseQuanitity, the connection between the storage to the concerning testing section is done by the value of the pauseQuantity.	M	M

Complex Children:

Component3

/stabilityStudy/component/studyOnBatch/component1

Name	Type	Description	H	F
testing	Testing	A structure to store the results of measurement.	M	M

Sample Code

Only one storage condition is used in one file:

```
<component1>
  <pauseQuantity xsi:type="PQ" value="0" unit="days"/>
  <testing>
      ...
  </testing>
</component1>
<component1>
  <pauseQuantity xsi:type="PQ" value="30" unit="days"/>
  <testing>
      ...
  </testing>
</component1>
```

In the case of complex studies (e.g. cycled studies) multiple eStability data files must be used to submit the results from each "stage". These files have to use an association.

Testing – Element

Testing

/stabilityStudy/component/studyOnBatch/component1/testing

Description:

This is a representation of "pulling a sample from the climatic chamber".

Simple Children:

Name	Type	Description	H	F
title	ST	A title that labels a collection of related tests across "pauseQuantities".	M	M
text	ED	A textual description or an external reference.	O	O
effectiveTime	IVL_TS	The date the sample was pulled from the chamber (use ISO 8601 notation).	R	R

Complex Children:

Name	Type	Description	H	F
code	CE	An ACTCODE: pauseDescription. (see page 65) Something done with the sample, e.g. freeze sample.	M	M
component	Component4	A reference to the tests performed with this sample.	M	M

Testing				
/stabilityStudy/component/studyOnBatch/component1/testing				
performer	Performer1	A list of all testing sites involved in this testing.		

Sample Code

```xml
<testing>
  <code displayName="NONE"/>
  <title xsi:type="ST">Normal Testing</title>
  <effectiveTime>
      <high value="20080413"/>
  <effectiveTime/>

  <component>
      <test>
         ...
      </test>
  </component>
  <performer>
      <assignedEntity>
         ...
      </assignedEntity>
  </performer>
  <performer>
      <assignedEntity>
         ...
      </assignedEntity>
  </performer>

</testing>
```
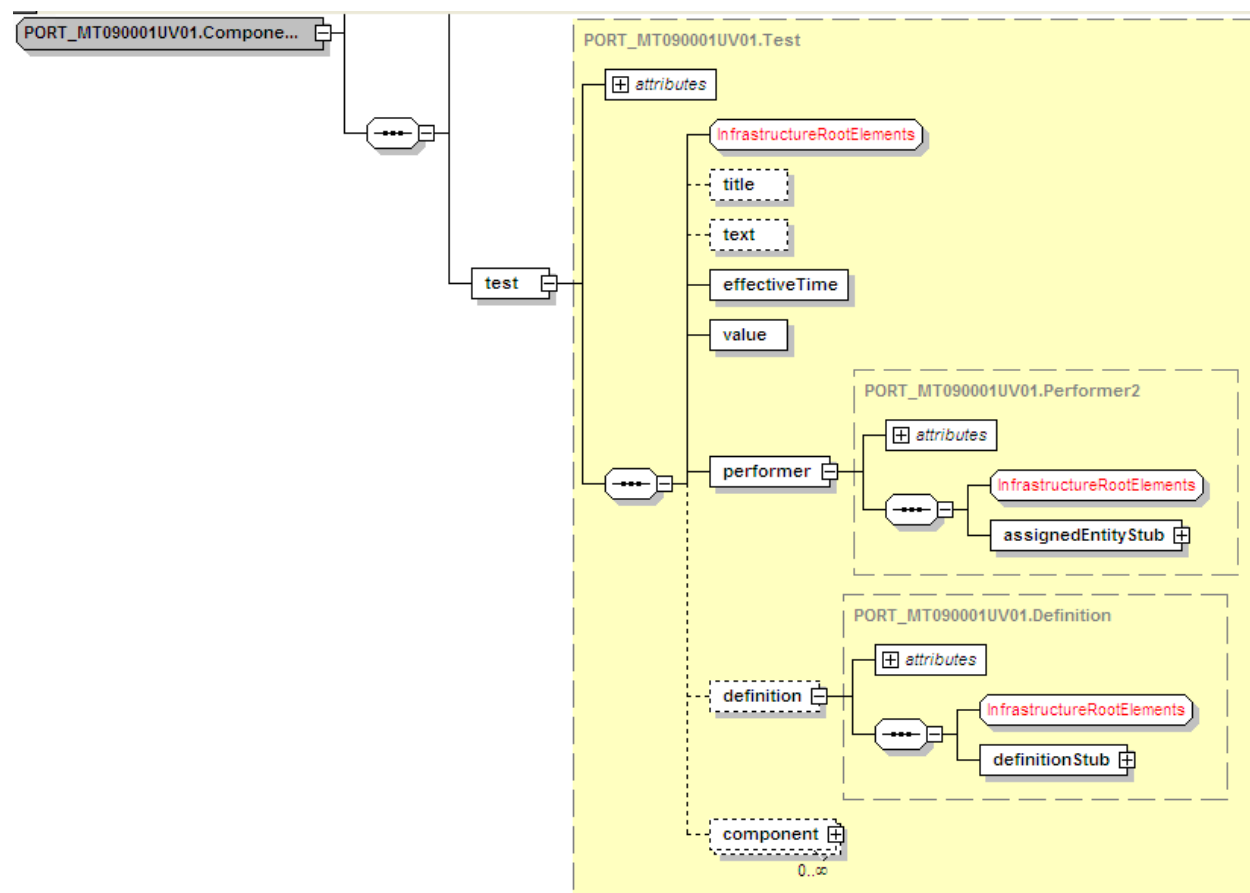
Component1 – Element

Component1
/stabilityStudy/component/studyOnBatch/component1/component/testing/component

Description:
Intermediate element

Complex Children:

Name	Type	Description	H	F
test	Test	Intermediate element	O	M

Test – Element

Test

/stabilityStudy/component/studyOnBatch/component1/testing/component/test

or

/stabilityStudy/component/studyOnBatch/component1 /testing/component/test/component/test

Description:

Representation of a test performed on a sample.

It applies the same scheme as in "TestDefinition", there might be parameters for a Test which are represented by the "Component2" reference.

Simple Children:

Name	Type	Description	H	F
title	ED	Alternative name of the measured result. This attribute can be used to identify "specified unknowns", since all of these results point to the same specification (i.e. "definition").	O	R
text	ED	A textual description or an external reference.	O	O
value	ANY	A nullFlavour has to be provided on all levels where no actual result is available.	M	M
effectiveTime	IVL_TS	A testing date that is mandatory on the first level. On the second level, a nullFlavour has to be provided where no actual result is available.	M	M

Complex Children:

Name	Type	Description	H	F
performer	Performer2	A reference to a testing site.	M	M
definition	Definition	Reference to a specification for this test.	O	M
component	Component2	Recursive reference to a "Test".	R	R

Sample Code

```xml
<test>
  <effectiveTime>
      <high value="20050628"/>
  </effectiveTime>
  <value xsi:type="PQ" nullFlavor="NA"/>
  <performer>
      ...
  </performer>
  <definition>
      ...
  </definition>
  <component>
      <test>
          ...
      </test>
  </component>
  ...
</test>
```

Performer2 – Element
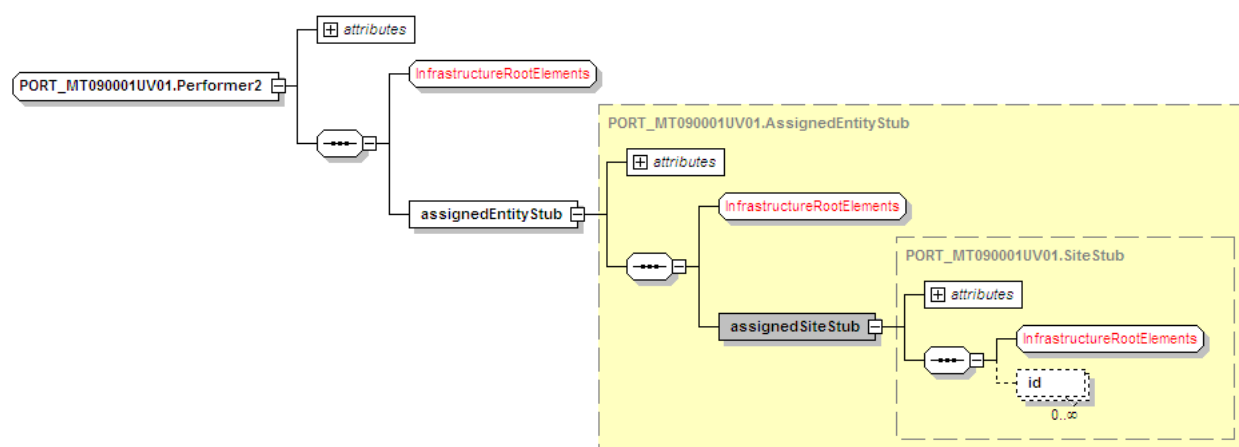
Performer2

/stabilityStudy/component/studyOnBatch/component1/testing/component/test/performer
or
/stabilityStudy/component/studyOnBatch/component1/testing/component/test/component/test/performer

Description:

Intermediate element

Complex Children:

Name	Type	Description	H	F
assignedEntityStub	AssignedEntityStub	See sample code	M	M

Sample Code

```
<performer>
  <assignedEntityStub>
    <assignedSiteStub>
      <id root="1.3.6.1.4.1.24263.2"/>
    </assignedSiteStub>
  </assignedEntityStub>
</performer>
```

Performer1 – Element
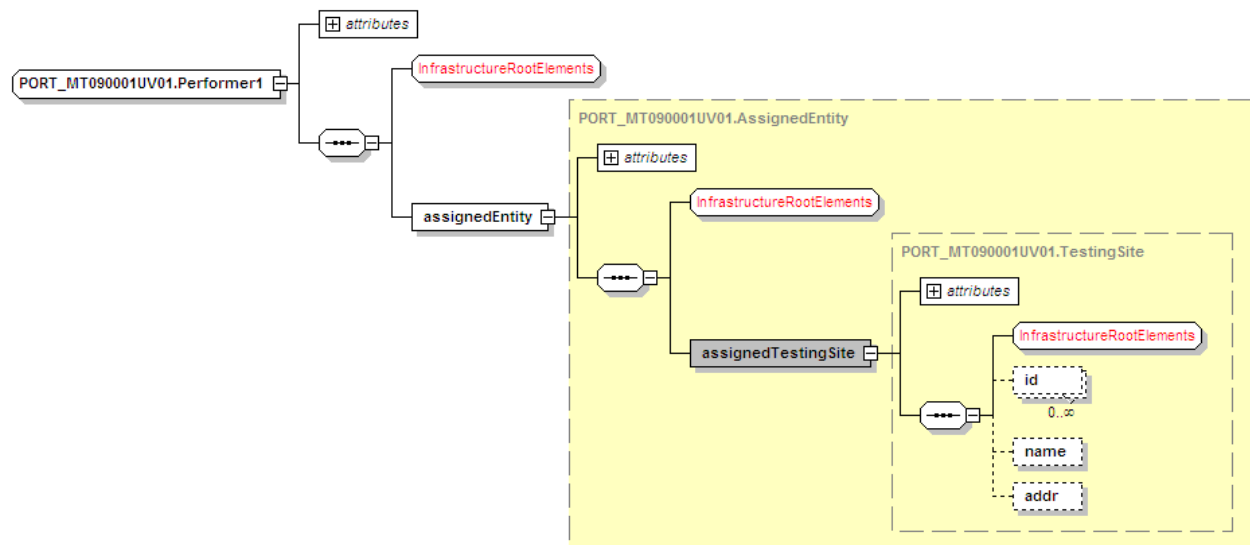
Performer1				
/stabilityStudy/component/studyOnBatch/component1/testing /performer				
Description:				
Intermediate element				
Complex Children:				
Name	**Type**	**Description**	**H**	**F**
assignedEntity	AssignedEntity	A reference to a list of testing sites involved in this testing.	M	M

AssignedEntity – Element

AssignedEntity
/stabilityStudy/component/studyOnBatch/component1/testing /performer/assignedEntity

Description:

Intermediate element, a reference to a list of testing sites involved in this testing on behalf of the ResearchSponsor.

Complex Children:

Name	Type	Description	H	F
assignedtestingSite	TestingSite	Intermediate element	M	M

TestingSite – Element

TestingSite
/stabilityStudy/component/studyOnBatch/component1/testing /performer/assignedEntity/assignedTestingSite

Description:

The details about a tester who performs the tests on behalf of the ResearchSponsor.

Simple Children:

Name	Type	Description	H	F
id	II	A set of identifiers that is used to uniquely identify the testing site. One can be the OID, a global unique identifier for the testing organization assigned by IANA. Other examples can be DUNS number or FEI number. If this site element is referencing a single person (i.e. the test performer with the testing organisation) the "id" element must be unique for this person. <table><tr><td>**Attributes**</td><td></td><td></td><td></td></tr><tr><td>Root</td><td>OID of the testing site company</td><td>M</td><td>M</td></tr><tr><td>Extension</td><td></td><td>N</td><td>N</td></tr><tr><td>assigningAuthorityName</td><td></td><td>N</td><td>N</td></tr><tr><td>Displayable</td><td></td><td>N</td><td>N</td></tr></table>	O	M
name	ON	The name of the testing site.	R	M
addr	AD	The address of the testing site. Use the "additionalLocator" to reference a single person/tester.	R	M

Sample Code

```xml
<performer>
  <assignedEntity>
    < assignedTestingSite>
      <id root="1.3.6.1.4.1.24263.1"/>
      <name>up to data professional service GmbH</name>
      <addr>
        <additionalLocator>LabPerson 1</additionalLocator>
        <country>Germany</country>
        <city>Wörrstadt</city>
        <postalCode>55286</postalCode>
        <streetAddressLine>Am Pfädchen 4</streetAddressLine>
      </addr>
    </ assignedTestingSite>
  </assignedEntity>
</performer>
<performer>
  <assignedEntity>
    < assignedTestingSite>
      <id root="1.3.6.1.4.1.24263.2"/>
      <name>up to data professional service GmbH</name>
      <addr>
        <additionalLocator>LabPerson 2</additionalLocator>
        <country>Germany</country>
        <city>Wörrstadt</city>
        <postalCode>55286</postalCode>
        <streetAddressLine>Am Pfädchen 4</streetAddressLine>
      </addr>
    </ assignedTestingSite>
  </assignedEntity>
</performer>
```
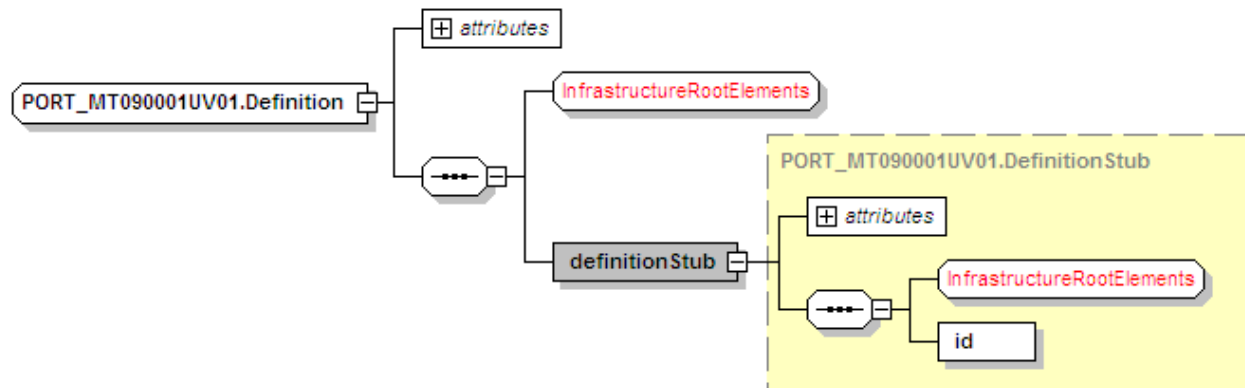
Definition - Element

Definition

/stabilityStudy/component/studyOnBatch/component1/testing/component/test/definition

or

/stabilityStudy/component/studyOnBatch/component1/testing/component/test/component/test/definition

Description:
Intermediate element which references the testdefinition.

Complex Children:

Name	Type	Description	H	F
definitionStub	DefinitionStub	Intermediate element	M	M

DefinitionStub - Element

DefinitionStub

/stabilityStudy/component/studyOnBatch/component1/testing/component/test/definition/definitionStub

or

/stabilityStudy/component/studyOnBatch/component1/testing/component/test/component/test/definition/definitionStub

Description:

Simple Children:

Name	Type	Description			H	F
Id	II	The unique identifier (id) of the referenced specification (TestDefinition).			M	M
		Attributes				
		Root	OID of the referenced specification.		M	M
		Extension			N	N
		assigningAuthorityName			N	N
		Displayable			N	N

Sample Code

```
<definition>
  <definitionStub>
      <id root="1.3.6.1.4.1.24263.4711.1.1.1"/>
  </definitionStub>
</definition>
```

Component2 - Element
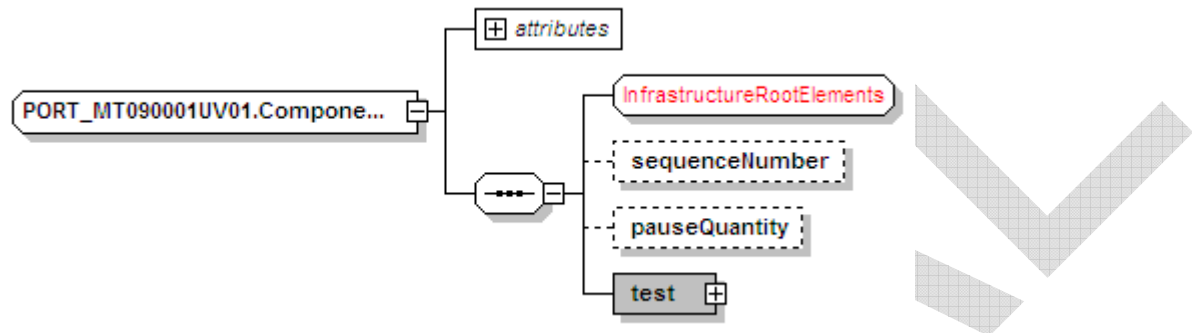
Component2

/stabilityStudy/component/studyOnBatch/component1/testing/component/test/component

Description:

If a test has parameters (e.g. Assay and ingredients) this structure is used to store the parameters and document their order ("sequenceNumber")

or

Use this structure to indicate any special handling after the sample was drawn from the chamber before the real testing took place (pauseQuantity).

Simple Children:

Name	Type	Description	H	F
sequenceNumber	INT	The sequence of parameters of the test.	O	R
pauseQuantity	PQ	To use e.g. with growth of bacteria, etc.	O	R

Complex Children:

Name	Type	Description	H	F
test	Test		O	M

Component - Element
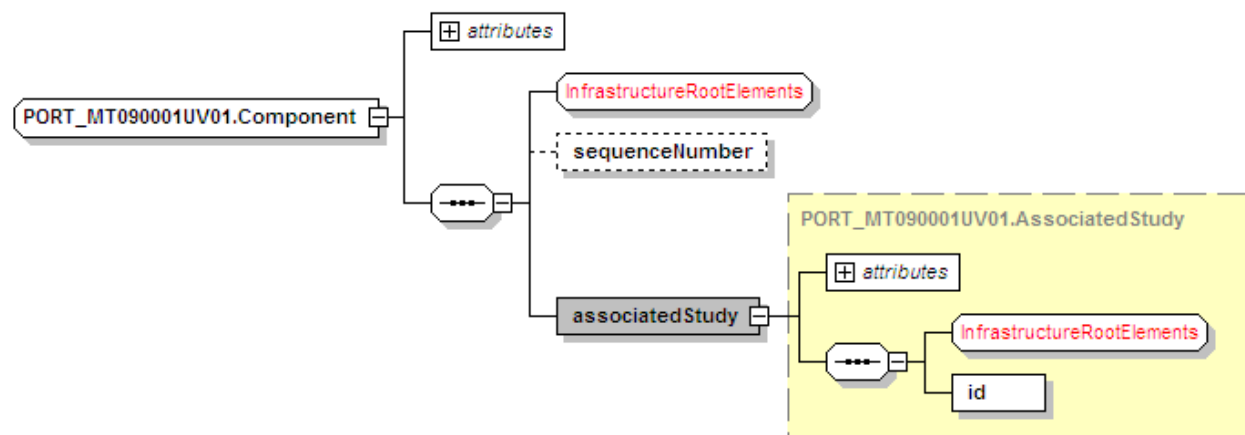
Component
/stabilityStudy/componentOf

Description:
The componentOf associates the current data file with another data file that has to be part of the same submission.

Simple Children:

Name	**Type**	**Description**	**H**	**F**
SequenceNumber	INT	Defines the sequence in which the associated files have to be interpreted.	O	R

Complex Children:

Name	**Type**	**Description**	**H**	**F**
AssociatedStudy	AssociatedStudy	The reference to the associated file.	M	M

AssociatedStudy
/stabilityStudy/componentOf/assiociatedStudy

Description:
The reference to the associated file.

Simple Children:

Name	**Description**	**H**	**F**
id	The unique id used within the "StabilityStudy" element of the associated file.	O	R

Code Lists

The implementation team intensely discussed the necessity of defining code values and agreed on the general approach that for most codes, this would be a far too complex task for this group. Instead it will be allowed to submit only descriptive text for most of the codes. After this standard has been in use, the authorities should give feedback on the submitted values and, if reasonable, standardization will be approached by the implementation team.

For those values defined (Test, Method, Container and Closure) the NCI Thesaurus will be used to map the defined code to an OID.

Companies are free to define or use their own coding system. The values submitted should be consistent throughout all submitted files of the same "ResearchSponsor" but at least for the same product.

Type of Data File

Element Name / Attribute	/stabilityStudy – code (see page 19)
Code System Name	
Code System (OID)	
This code should reflect if the file in hand is a standard data file for one storage condition or a partial file as part of a cycled study. Other file types may be possible.	

Code	Display Name	Description

Example:

```
<stabilityStudy>
    <id root="1.3.6.1.4.1.24263.4711.1.1"/>
    <code displayName="Standard"/>
…
</stabilityStudy>


<stabilityStudy>
    <id root="1.3.6.1.4.1.24263.4711.1.2"/>
    <code displayName="Cycled Study"/>
…
</stabilityStudy>
```

Reason for Data File

Element Name	/stabilityStudy – reasonCode (see page 19)
Code System Name	
Code System (OID)	

This code should reflect the reason why this data file was sent originally. An example would be "NDA" (New Drug Application), other file types may be possible

Code	Display Name	Description

Example:

```
<stabilityStudy>
    <id root="1.3.6.1.4.1.24263.4711.1.1"/>
    ….
    <reasonCode displayName="New Drug Application"/>
…
</stabilityStudy>

<stabilityStudy>
    <id root="1.3.6.1.4.1.24263.4711.3.1"/>
    ….
    <reasonCode displayName="New Active Ingedient"/>
…

<stabilityStudy>
    <id root="1.3.6.1.4.1.24263.4711.4.1"/>
    ….
    <reasonCode displayName="New Drug Application Update" />
…

</stabilityStudy>

-- Brief description of why update: e.g. opening a new facility, reference to the cover letter

<stabilityStudy>
    <id root="1.3.6.1.4.1.24263.4711.5.1"/>
    ….
    <reasonCode displayName="Annual Report"/>
…

</stabilityStudy>
```

Product Code

Element Name	/stabilityStudy/subject/researchSubject/subjectProduct – code (see page 22)
Code System Name	
Code System (OID)	

This is the code for the official product name. For FDA implementation, only the "displayName" (i.e. the product name) is mandatory, the code values might be provided if available (e.g. when used in other submissions like SPL).

For NDA this is a new identifier.

For ongoing studies the identifier should be identical to an already submitted code, so that a unique relationship can be established.

Code	Display Name	Description

Example:

```
<researchSubject>
  <subjectProduct>
    <code displayName="JBE1000"/>
    <desc>Gummi Bears 100g Bag</desc>
    …
  </subjectProduct>
```

Product Form Code

Element Name	/stabilityStudy/subject/researchSubject/subjectProduct - formCode (see page 22)
Code System Name	Dosage Form: SPL Acceptable Terms and NCI Thesaurus Codes
Code System (OID)	2.16.840.1.113883.3.26.1.1

This code describes the form of the reported product. Code values might be provided if available (e.g. when used in other submissions like SPL).

Code	Display Name	Description

Example:

```
<researchSubject>
  <subjectProduct>
    …
    <formCode code="C42897" displayName="TABLET, COATED"/>
    …
  </subjectProduct>
```

Substance Code

Element Name	/stabilityStudy/subject/researchSubject/subjectSubstance – code (see page 24) **or** /stabilityStudy/subject/researchSubject/subjectProduct/specifiedIngredient - code
Code System Name	
Code System (OID)	

The official code for a referenced substance (e.g. "acetylsalicylic acid"), as a single entity or part of a product (e.g. "aspirin"). For FDA implementation, only the "displayName" (i.e. the product name) is mandatory, the code values might be provided if available.

This code should be identical in all submissions, when referencing the same substance.

Code values might be provided if available (e.g. when used in other submissions like SPL), please refer to "Substance Registration System - Unique Ingredient Identifier (UNII)", e.g. at http://www.fda.gov/oc/datacouncil/spl.html

Code	Display Name	Description

Example:

Test Code

Element Name	/stabilityStudy/subject/researchSubject/subjectOf/specification/component/testDefinition – code (see page 28) **or** /stabilityStudy/subject/researchSubject/subjectOf/specification/component/testDefinition/component/testDefinition - code
Code System Name	
Code System (OID)	

This code describes the test performed during a study within the specification section.

Code	Display Name	Description
physical	Physical or a textual reference to the actual test or parameter	Physical measurement or determination.
chemical	Chemical or a textual reference to the actual test or parameter	Chemical measurement or determination.
biological	Biological or a textual reference to the actual test or parameter	Biological measurement or determination.

other	Other or a textual reference to the actual test or parameter	Any other measurement or determination

Example:

```
<testDefinition>
 <id root="1.3.6.1.4.1.24263.4711.1.1.1"/>
 <code code="chemical" displayName="Assay" />
 <methodCode code="proprietary" displayName="Internal Company Code XYZ" />
 <component>
    <testDefinition>
        <id root="1.3.6.1.4.1.24263.4711.1.1.2"/>
        <code code="chemical" displayName="Sodium"/>
        <methodCode code="proprietary" displayName="Internal Company Code XYZ" />
        <referenceRange>
            …
        </referenceRange>
        …
    </testDefinition>
 </component>
 ...
</testDefinition>
```

Method Type Code

Element Name	/stabilityStudy/subject/researchSubject/subjectOf/specification/component/testDefinition – methodCode (see page 28) **or** /stabilityStudy/subject/researchSubject/subjectOf/specification/component/testDefinition/component/ testDefinition - methodCode
Code System Name	
Code System (OID)	

A classification of the methods used in stability testing.

Code	Display Name	Description
compendial	Compendial	Official compendial method
proprietary	Proprietary	Company method
CFR Regulation	CFR Regulation	Method dictated by CFR
other	Other	

Example:

See. Test Code

Interpretation Code

Element Name	/stabilityStudy/subject/researchSubject/subjectOf/specification/component/testDefinition/ referenceRange/acceptanceCriterion – interpretationCode (see page 30) **or** /stabilityStudy/subject/researchSubject/subjectOf/specification/component/testDefinition/ component/testDefinition/referenceRange/acceptanceCriterion - interpretationCode
Code System Name	
Code System (OID)	

For a single acceptance criterion (i.e. limit) this code describes how to relate the given value to a measured value, e.g. a result should not be greater (not more) than the given value. The common accepted nomenclature should be used here:

NMT (not more than) – the value should not be greater than the given value and includes the given value, which is equivalent to "less than or equal to"

NLT (not less than) – the value should not be smaller than the given value and includes the given value, which is equivalent to "greater than or equal to"

MT (more than) - the value should not be smaller than the given value excluding the given value, which is equivalent to "greater than"

LT (less than) - the value should not be greater than the given value excluding the given value, which is equivalent to "less than"

Passed or Failed – if the limit has a textual structure (i.e. such as "appearance", where the limit is "white to yellow-white round tablet" and the result is complies)

Not Applicable – if a value for test has to be provided, but has no given criteria (e.g., the result is for "report only" or "monitoring")

Code	Display Name	Description
NMT	NMT	not more than
NLT	NLT	not less than
MT	MT	more than
LT	LT	less than
PASSED	Passed	This is equivalent to meets requirements
FAILED	Failed	
NA	Not Applicable	

Example:

```
<acceptanceCriterion>
    <value xsi:type="PQ" value="1900" unit="ug"/>
    <interpretationCode displayName="NLT"/>
</acceptanceCriterion>


<acceptanceCriterion>
    <value xsi:type="ST" value="Yellow" />
    <interpretationCode displayName="COMPLIES"/>
</acceptanceCriterion>
```

Remark: In the tag `<value xsi:type="PQ" value="…"  unit=" …"/>`, the qualifier xsi:type has to be used to allow schema validation, since <value> is of type "ANY".

Study Type

Element Name	/stabilityStudy/component/studyOnBatch - code (see page 32)
Code System Name	
Code System (OID)	

This code classifies the type of study performed on the given ResearchSubject, e.g. Commercial, Development, Clinical

Code	Display Name	Description

Example:

```
<studyOnBatch>
  <id root="1.3.6.1.4.1.24263.4711.1"/>
  <code displayName="Commercial"/>
  <subject>
     <instance>
        <manufacturedMaterialInstance>
           ...
        </manufacturedMaterialInstance>
     </instance>
  </subject>
  <component>
     ...
  </component>
</studyOnBatch>
```

Closure System Code

Element Name	/stabilityStudy/component/studyOnBatch/subject/instance/manufacturedMaterialInstance/asContent/container – capTypeCode (see page 38)
Code System Name	
Code System (OID)	

The closure system of the container.

No code system available currently.

Code	Display Name	Description
1	Child-resistant, Metal	Metal closure that is designed or constructed to be significantly difficult for children under five years of age to open and not difficult for normal adults to use properly.
2	Child-resistant, Plastic	Plastic closure that is designed or constructed to be significantly difficult for children under five years of age to open and not difficult for normal adults to use properly.
3	Continuous Thread, Metal	Metal closure turned onto a corresponding thread on the top or mouth of a container, whether it be glass, plastic or metal.
4	Continuous Thread, Plastic	Plastic closure turned onto a corresponding thread on the top or mouth of a container, whether it be glass, plastic or metal.
5	Tamper-evident, Metal	A closure/finish of a closure/container system designed to make it difficult to achieve the first removal of a closure from a container without it being detectable by subsequent users that the package seal has been breached (e.g., aluminum overseal).
6	Tamper-evident, Plastic	A closure that shows the package has been opened and the product has been exposed to the outside environment.
7	Tamper-evident, Composite	Composite tamper-evident closures usually consist of a metal disk with a plastic skirt. The plastic skirt is perforated or weakened in some manner so that when the closure is removed, this section is designed to break and either remain on the container or attached to the closure to indicate the package has been opened.
8	Vacuum, Metal	Metal closures used on packages where the pressure inside the package is less than atmospheric.
9	Vacuum, Plastic	Plastic closures used on packages where the pressure inside the package is less than atmospheric.
10	Vacuum, Composite	Metal/Plastic closures used on packages where the pressure inside the package is less than atmospheric.
11	Press-on/Twist-off, Metal	Closure with a stepped, skirted drawn shell with an inside curl. The closure is lined with an annular plastisol material designed to provide a proper seal along the top and side surfaces of the glass container finish. The closure uses a special plastisol material that, following application, takes a permanent impression of the glass threads ensuring cam-off and reseal.
12	Press-on, Composite	A metal/plastic composite cap composed of a plastisol lined metal disk, assembled to a plastic band. The closure requires a simple glass bead finish common on bowls, tumblers and carafes.

13	Crown, Metal	A non-threaded shallow draw metal closure that normally has 21 corrugations on the outer edge, which function to engage the container when applied. The crown is only 1/4" high when manufactured and does not have a rolled edge or wire. The crown is manufactured in 26mm worldwide and can be applied to either a threaded finish or a solid ring pry-off finish.
14	Lug, Metal	Closure with an ability to be applied and removed with a partial turn. The closure can also be produced with vacuum buttons that can clearly indicate to the packer if a vacuum has been effectively drawn following the closure application.
15	Roll-on, Metal	A tamper-evident closure produced as an unthreaded shell containing a liner. It is applied to the proper finish on a plastic or glass container by the bottler, using a roll-on capping machine that forms a thread in the closure matching the bottle thread.
16	Flip-Top (Dispensing), Plastic	A hinged single or dual flap closure for controlled product dispensing.
17	Hinged (Dispensing), Plastic	A closure with a lid that is hinged to the top of a closure and opens to expose a dispensing orifice
18	Linerless, Plastic	A closure that incorporates a specific molded-in feature such as rings, plugs or flexible sections. These features achieve a seal by conforming to one or more of the sealing surfaces on the container neck finish.
19	Pump (Dispensing), Plastic	Closure dispensing pumps are used to dispense product from containers
20	Push-pull (Dispensing), Plastic	A two-piece dispensing closure that includes a base member the lower portion of which is designed to attach and seal securely to a container finish and the upper portion of which is designed to receive a dispensing spout member. The spout member may be moved upward and downward to open and close the dispensing passageway.
21	Snap-on Cap, Plastic	A non-threaded closure that is pressed onto the package finish with a protruding feature that mates with a similar protruding feature on the closure to secure the closure to the package.
22	Snip-tip (Dispensing), Plastic	Conical closure that is turned onto a container. The tip is cut off to open the container.
23	Toggle-swing (Dispensing), Plastic	A closure with a lower part attaches securely and seals the container. The upper part provides a second movable portion which functions in a rocker-like pivotal motion between an open and a closed position.
24	Trigger Sprayer (Dispensing), Plastic	Closured designed to dispense product from containers by spraying the product when a trigger is pulled.
25	Twist Open/Close (Dispensing), Plastic	Two-piece dispensing closure that has a lower portion designed to attach and seal securely to a container finish and the upper portion of which is designed to receive a dispensing spout member. Rotating the spout member opens and closed the container.
26	Valved (Dispensing), Plastic	Dispensing closure incorporating a product-flow controlling valve within the orifice. Product will not dispense from the package until sufficient squeezing pressure is applied to the flexible container to cause the valve to open.
27	Stopper	Object used to plug opening of container.
28	Tie	Line, ribbon or cord used of fastening, or drawing the container closed.
29	Other	

Container Code

Element Name	/stabilityStudy/component/studyOnBatch/subject/instance/manufacturedMaterialInstance/asContent/container – code (see page 38)
Code System Name	Package Type: SPL Acceptable Terms and NCI Thesaurus Codes
Code System (OID)	2.16.840.1.113883.3.26.1.1

As reported entity or as part of a reported packaged product, this is the official code for a referenced package type. For FDA implementation, only the "displayName" (i.e. the product name) is mandatory, the code values might be provided if available.

This code should be identical in all submissions, when referencing the same substance.

Code values might be provided if available (e.g. when used in other submissions like SPL), please refer to "NCI Thesaurus Codes for SPL" e.g. at http://www.fda.gov/oc/datacouncil/spl.html. In other cases, you can either reference NCI or the below provided list.

Code	Display Name	Description
1	Dish, Petri	A shallow dish with a loose-fitting cover.
2	Plate, Microwell	Small volume multi-chambered plate (e.g. 96 well).
3	Canisters, lined	A type of lined can for holding a drug product.
4	Flask	Flat bottom bottle container or vessel.
5	Other	

Storage Condition Code

Element Name	/stabilityStudy/component/studyOnBatch/component1/storage/controlVariable/storageCondition – code (see page 42)
Code System Name	
Code System (OID)	

The code provided represents a storage condition.

Dependent of the internal company definitions this condition might be simple (e.g. 25°) or complex

(e.g. 25° C/60% R.H. upright).

Code	Display Name	Description

Example:

```
<storageCondition>
    <code displayName="25_60"/>
    <text>25°C / 60% r.h., upright storage</text>
</storageCondition>
```

As shown in this example, providing a "human readable" <text> element is recommended for better readability.

Pause Description Code

Element Name	/stabilityStudy/component/studyOnBatch/component2/testing – code (see page 44)
Code System Name	
Code System (OID)	

This code describes any "delay" that happened during testing, e.g. none (Immediate) or freeze sample (Delayed Frozen).

Code	Display Name	Description
Immediate		
Delayed		
Delayed Frozen		
Delayed Ambient		
Delayed Refrigerate		

Example:

```xml
<component>
  <pauseQuantity xsi:type="PQ" value="0" unit="MONTHS"/>
  <testing>
    <code displayName="NONE"/>
    <title xsi:type="ST">Normal Testing</title>
    <component>
      <test>
        <effectiveTime>
          <high value="20051115"/>
        </effectiveTime>
        <value xsi:type="PQ" nullFlavor="NA"/>
        <definition>
          <definitionStub>
            <id root="1.3.6.1.4.1.24263.4711.1.1.1"/>
          </definitionStub>
        </definition>
      …
```