Implementation Guide for Study Design Structured Document

FDA Guidance for Human Clinical Trials
Table of Contents

1 Acknowledgements ............................................................................................................................................. 1

2 Introduction ........................................................................................................................................................ 1

  2.1 Audience ...................................................................................................................................................... 1

  2.2 Approach ...................................................................................................................................................... 1

  2.3 Change process ............................................................................................................................................ 2

  2.4 Abbreviated Terms ....................................................................................................................................... 2

3 How to use this document .................................................................................................................................. 2

  3.1 Templates ..................................................................................................................................................... 2

  3.2 Embedded Data Structures .......................................................................................................................... 3

    3.2.1 Identifiers .............................................................................................................................................. 3

    3.2.2 Coded Values ......................................................................................................................................... 3

    3.2.3 Null Values ............................................................................................................................................ 4

    3.2.4 Units of Measure ................................................................................................................................... 4

4 Implementation Issues ........................................................................................................................................ 4

  4.1 Conventions ................................................................................................................................................. 4

5 Study Design Structured Document .................................................................................................................... 4

  5.1 Document Header ........................................................................................................................................ 4

  5.2 Document Sections ...................................................................................................................................... 6

    5.2.1 Unstructured Section ............................................................................................................................ 6

    5.2.2 Structured Section ................................................................................................................................ 7

5.3 Content Data Structures .............................................................................................................................. 8

  5.3.1 Study Epoch ........................................................................................................................................... 9

  5.3.2 Study Arm ............................................................................................................................................ 9

  5.3.3 Study Substance .................................................................................................................................... 9

  5.3.4 Study Element ..................................................................................................................................... 10

  5.3.5 Element in Arm ................................................................................................................................... 12

  5.3.6 Study Visit Definition ........................................................................................................................... 13

  5.3.7 Visit in Arm .......................................................................................................................................... 14

  5.3.8 Study Characteristic ............................................................................................................................ 15


1 Acknowledgements
This document is based on the Health Level Seven Study Design Structured Document, and on the CDISC SDTM Implementation Guide.

2 Introduction
This document is intended to assist organizations responsible for clinical trials in reporting the design of a study. It draws on the trial design content of the SDTM standard, and shows how to represent that content using the HL7 Specification.

The study design structured document describes what is going to be done in a study. A study in this context is any investigation performed to support the safety, effectiveness, or quality of a medical product. As such, the experimental subject of a study can be a human, other nonhuman living subjects, parts of nonhuman living subjects, groups of nonhuman living subjects, or the medical product itself. The study design structured document will transport trial design and eligibility criteria information in a standardized format. The specification is designed to allow communicating the content of a study protocol. However, it lays particular emphasis on communicating the following in a structured form: arms, epochs, subject assignment, planned encounters (visits), planned interventions, planned observations (assessments), eligibility criteria and study characteristics.

The scope of the initial release of the standard is limited to the protocol document, study plan of activities, analysis comparables and eligibility criteria. The following are out of scope: site setup, recruitment, inventory management, data management, database lock, and statistical analysis plan.

The scope of this Implementation Guide is limited to the protocol document and the trial design content defined within the SDTM Implementation Guide published by CDISC. It also leverages the standard sections of a protocol as defined by the International Conference on Harmonisation Good Clinical Practice E6 Guideline.

Further information about the Study Design Structured Document specification is available at HL7.org.

2.1 Audience
The audience for this document is software developers and development organizations who wish to produce or receive Study Design Structured Documents.

2.2 Approach
The Study Design Structured Document specification was designed to address a wide range of possible use cases for reporting or amending study protocols. This implementation guide has been designed to support an initial test of reporting protocol information using the HL7 specification. In order to ease the implementation process, the scope of the document has been restricted to only include the unstructured protocol document and content previously defined within the trial design domains of CDISC SDTM implementation guide.

1 Study Data Tabulation Model Implementation Guide: Human Clinical Trials, CDISC 2008. The document also provides a reference – Section 7 – to the structure and design of a clinical trial.
The vocabulary items that are needed to support Study Design reporting are managed by NCI within the EVS Thesaurus. NCI EVS will provide a file for the Study Design user community to be located at: http://www.cancer.gov/cancertopics/cancerlibrary/terminologyresources/fda. Material at this site will contain all pertinent CDISC terminology subsets as well as additional value sets as needed. This material is available for download 24/7 and updates to terminology will be completed by the NCI EVS team. NC EVS currently provides terminology in Excel and Text formats.

2.3 Change process
The Study Design Structured Document has been published as DSTU by HL7. It is likely that implementation experience and changes in design philosophy will lead to changes in the specification. In addition, we also expect there to be changes, possibly expansion, in the requirements to be addressed by a study design implementation guide.

Issues and new requirements should be reported to edata@fda.hhs.gov.

2.4 Abbreviated Terms
The following abbreviations appear within the document.

<table>
<thead>
<tr>
<th>Abbreviated</th>
<th>Spelled Out</th>
</tr>
</thead>
<tbody>
<tr>
<td>CDA</td>
<td>Clinical Document Architecture</td>
</tr>
<tr>
<td>CDISC</td>
<td>Clinical Data Interchange Standards Consortium</td>
</tr>
<tr>
<td>DSTU</td>
<td>Draft Standard for Trial Use</td>
</tr>
<tr>
<td>EVS</td>
<td>Enterprise Vocabulary Services</td>
</tr>
<tr>
<td>HL7</td>
<td>Health Level 7</td>
</tr>
<tr>
<td>ICH</td>
<td>International Committee on Harmonization</td>
</tr>
<tr>
<td>NCI</td>
<td>National Cancer Institute</td>
</tr>
<tr>
<td>OID</td>
<td>Object Identifier</td>
</tr>
<tr>
<td>SDTM</td>
<td>Study Data Tabulation Model</td>
</tr>
<tr>
<td>SEND</td>
<td>Standard for Exchange of Nonclinical Data</td>
</tr>
</tbody>
</table>

3 How to use this document
The Implementation Guide provides specific instructions on using the Study Design Structured Document in order to transmit the fundamental information for a planned human clinical study. It provides instruction on how to value the elements and attributes of a conformant study design document, and discusses relevant issues for managing identifiers and vocabularies.

3.1 Templates
This definition of a conformant study design document is constructed as a collection of templates. For HL7, a template is “an expression of a set of constraints on the RIM or a RIM derived model that is used to apply additional constraints to a portion of an instance of data which is expressed in terms of some other Static Model. Templates are used to further define and refine these existing models to specify a narrower and more focused scope.”³ Our templates express how the more general Study Design Structured Document specification is to be implemented for the purposes of this guide. This method of documentation is intended to ease conformance testing – we expect that instances will be tested against the constraints of these templates as a method of evaluating conformance.

---
In addition, the content in this document has been organized into templates in order to simplify presentation and to offer a reasonable and modular structure for the implementer. Whether or not template identifiers are needed within document instances will be an implementation decision.

3.2 Embedded Data Structures

Any HL7 Version 3 product is based on a common set of data types – of reusable data structures. This section discusses those for which further explanation will be useful to implementers.

3.2.1 Identifiers

The data element “id” is used for identifiers within HL7 Version 3, and is assigned the data type “II” – instance identifier. It is intended to allow unique identification of objects used within healthcare data processing. Uniqueness is assured through definition of both an identifier value and the namespace from which that identifier was drawn. HL7 offers a couple of identification schemes for ensuring the global uniqueness of the identifier namespace. Within in this guide we are assuming the use of the Object Identifier (OID). We have also simplified the implementation of this concept to meet the specific needs of implementers and of identification in the context of study design.

We do not wish to require that implementers develop the ability to manage and assign OIDs to the relevant namespaces. However it is necessary to have some method of distinguishing identifiers since it is not always possible to rely on the document content. (This is not a practical issue for Study Design, but it is one for subject data.) Therefore a generic OID will be assigned as a designator for the kind of name space that is relevant – this is equivalent to specifying the “identifier type”. The generic OIDs are used where needed, and are documented below. In addition, for those identifiers used only within the message and for which the context is always clear, the name space will not be valued. This is indicated by use of a null value indicator which signifies that a complete identifier is not being provided.

3.2.2 Coded Values

Coded values are used within this guide – as with all HL7 Version 3 products – to clearly provide the needed information (to get closer to “semantic interoperability”). You will see this in two contexts:

Structural Coherence:

HL7 has provided code sets to indicate basic structural information within a document. For example, that a structure is an observation or a substance administration, that information is being provided regarding the author of a document or the performer of an activity. These items use vocabularies provided by HL7 and are almost always constrained to a single value within implementation guides such as this.

Semantic Clarity:

Coded items constrain the set of possible included values, to allow receivers of the information to use it in more precise ways. For instance, there is a predefined set of routes of administration for medication, since different uses of the data are dependent on specific values of a particular item. These code sets are functionally meaningful, and the set of possible codes must be communicated to allow full use of the data. Within this implementation guide, those code sets (value sets) that are centrally defined, and those which are provided by study sponsors are specified in the Vocabulary section.

The data type for coded data includes properties for the code to be transmitted, for the code system used to be identified (code systems are identified with an OID), and for display text conveying the coded concept in words.

3.2.3 Null Values
HL7 allows assignment of a “null value” to any attribute. A null value “means that the information does not exist, is not available or cannot be expressed in the data type's normal value set.” The guide uses the null value assignment to indicate that a required data element cannot be provided, or that, in the case of identifiers, partial information is used.

3.2.4 Units of Measure
HL7 physical quantities use the HL7 PQ data type, in which units are expressed in the Unified Code for Units of Measure (UCUM; 2.16.840.1.113883.6.8), available at http://www.regenstrief.org. The guide calls on the representation of these units provided by CDISC and captured within the NCI Thesaurus.

4 Implementation Issues
4.1 Conventions
This document follows conventions used within HL7 CDA implementation guides. Relevant conventions are reiterated here.

The terms SHALL, SHALL NOT, SHOULD, SHOULD NOT, and MAY in this document are to be interpreted as described in the HL7 Version 3 Publishing Facilitator’s Guide. The keyword "SHALL" implies a lower cardinality of 1 but does not disallow NULL values. If NULL values are to be excluded, it will be via an additional explicit conformance statement.

5 Study Design Structured Document
The Study Design Structured Document captures the content of a study protocol as documented by the ICH and by CDISC. It contains unstructured sections that are intended to contain text based documents as well as a structured section to contain the items that are critical for subsequent transmission of information regarding the experience of study subjects.

The Study Design Structured Document Specification is a document markup standard that specifies the structure and semantics of the documentation used to describe a planned clinical or non-clinical study. This implementation guide focuses on a subset of the data that is conveyed.

5.1 Document Header
The header contains information to identify the protocol document itself and to make clear its source, and who takes responsibility for its content. The root element of the header is the Document class. The template id for the document is: FDAroot.xx.yy.01.

Its contents are specified as follows:

1. SHALL contain exactly one [1..1] @classCode="DOCCLIN"
2. SHALL contain exactly one [1..1] @moodCode="EVN"
3. SHALL contain one to many [1..*] id
   The identifier assigned to the study design must be included. It uniquely identifies the study

---

5 2.11 DataValue (ANY), Data Types: Abstract, Normative Edition of HL7 Version 3 Standards, Health Level 7, Ann Arbor MI July 2011
design/protocol.

[SDTM: STUDYID]

In addition, there may be identifiers assigned by a registry such as ct.gov.

[SDTM: Registry Identifier]

4. SHALL contain exactly one [1..1] code@code = “Cxxxx” (CodeSystem 2.16.840.1.113883.3.26.1.1 NCI Thesaurus)

5. SHOULD contain zero or one [0..1] title.
   A text name for the study
   {SDTM: TSPARMCD = TITLE}

6. SHOULD contain zero or one [0..1] effectiveTime
   The date/time on which this version of the document was released.

7. SHOULD contain zero or one [0..1] confidentiality code where @code SHALL be selected from
   (CodeSystem: 2.16.840.1.113883.5.25 Confidentiality)

8. MAY contain zero or one [0..1] languageCode (Code System 1.0.639.3 Language Codes Alpha 3)
   The language used for the document. The entry may be left out, if the language used is English.

9. May contain zero or one [0..1] realmCode (2.16.840.1.113883.5.1124)
   Identifies a country or other administrative unit that has defined particular rules for the format or
   content of the structured document. The entry may be left out if the intended realm is the United
   States.

10. SHALL contain exactly one [1..1] setID
    An identifier that remains consistent across all revisions derived from a common original. In the first
    version of the document – VersionNumber = 1, setID and id will be identical.

11. Shall contain exactly one [1..1] VersionNumber
    An integer value that designates the version of the document.

12. SHALL contain exactly one [1..1] responsibleParty
    a. The responsibleParty SHALL contain exactly one [1..1] @typeCode=“RESP”
       i. The responsibleParty SHALL contain exactly one [1..1] assignedEntity
          1. The assignedEntity SHALL contain exactly one [1..1] @classCode=“ASSIGNED”
          2. The assignedEntity SHALL contain exactly one [1..1] assignedPerson
             a. The assignedPerson SHALL contain exactly one [1..1] @classCode=“PSN”
             b. The assignedPerson SHALL contain exactly one [1..1] @determinerCode=“INSTANCE”
             c. The assignedPerson SHOULD contain zero to one [0..1] name
                A text name for the principle investigator.
                {SDTM: }
                i. The name MAY contain zero to one [0..1] prefix
                   A text entry with a name prefix, e.g., Dr.
                ii. The name SHALL contain exactly one [1..1] given
                   The given name of the person.
                iii. The name SHALL contain exactly one [1..1] family
                   The family name of the person.
3. The assignedEntity SHALL contain exactly one [1..1] representedOrganization
   a. The representedOrganization SHALL contain exactly one [1..1] @classCode="ORG"
   b. The representedOrganization SHALL contain exactly one [1..1] @determinerCode="INSTANCE"
   c. The representedOrganization SHALL contain exactly one [1..1] id
      An identifier for the study sponsor.
   d. The representedOrganization SHOULD contain zero to one [0..1] name
      A text name for the study sponsor.
      [SDTM: Appendix C3 TSPARMCD = SPONSOR]

13. SHALL contain one to many [1..*] components
    Each desired section – whose number and title may be based on advice provided by ICH – is included
    as a single component.
    a. The component SHALL contain exactly one [1..1] @typeCode="COMP"
    b. The component SHALL contain exactly one [1..1] nonXMLBody
       The nonXML body will carry an unstructured section. The list of unstructured sections should be
       drawn from the list of possible sections included below.
       i. The nonXMLBody shall contain exactly one [1..1] @classCode="DOCBODY"
       ii. The nonXMLBody shall contain exactly one [1..1] @moodCode="EVN"
       iii. The nonXMLBody shall contain exactly one [1..1] text.
           The text will contain the content of the desired protocol section

14. SHALL contain exactly one [1..1] component
    a. SHALL contain exactly one [1..1] structuredBody
       The section is defined using template FDAroot.xx.yy.02.

5.2 Document Sections
The structured document will contain structured and unstructured sections. This contains the content of the protocol
for the planned study.

5.2.1 Unstructured Section
The unstructured sections are expected to have content based on the following list.

1. Protocol Synopsis [1]
2. General Information [1]
3. Background Information [1]
4. Trial Objectives and Purpose [1]
5. Trial Design [1]
7. Assessment of Efficacy [1]
8. Assessment of Safety [1]
Study Design Structured Document Implementation Guide

10. Direct Access to Source Data/Documents [1]
11. Quality Control and Quality Assurance [1]
12. Ethics [1]
13. Data Handling and Recordkeeping [1]
14. Financing and Insurance [0..1] (if not addressed in a second document)
15. Publication Policy [0..1] (if not addressed in a second document)
16. Appendix [0..*]
17. Protocol Amendments [0..*]
18. Unspecified [0..*] (suggested for any additional information that doesn’t fit elsewhere)

5.2.2 Structured Section
The section contains the structured content for the study design. The template id for the structuredBody content is: FDAroot.xx.yy.02.

Its contents are specified as follows:

1. SHALL contain exactly one [1..1] @classCode="DOCBODY"
2. SHALL contain exactly one [1..1] @moodCode="EVN"
3. SHALL contain exactly one [1..1] component
   a. The component SHALL contain exactly one 1..1] @typeCode="COMP"
   b. The component SHALL contain exactly one 1..1] section
      i. The section SHALL contain exactly one [1..1] @classCode="DOCSEC"
      ii. The section SHALL contain exactly one [1..1] @moodCode="EVN"
      iii. The section SHALL contain exactly one [1..1] code/@code = "" (CodeSystem 2.16.840.1.113883.3.26.1.1 NCI Thesaurus)
           A code value to the section content is a planned study.
      iv. The section SHALL contain exactly one [1..1] title
      v. The section SHALL contain exactly one [1..1] subject
   1. The subject SHALL contain exactly one [1..1] @typeCode="SUBJ"
   2. The subject SHALL contain exactly one [1..1] plannedStudy
      a. The plannedStudy SHALL contain exactly one [1..1] @classCode="OBS"
      b. The plannedStudy SHALL contain exactly one [1..1] @moodCode="DEF"
      c. The plannedStudy SHALL contain exactly one [1..1] researchSubject
         i. The researchSubject SHALL contain exactly one [1..1] @classCode="RESBJ"
         ii. The researchSubject SHALL contain exactly one [1..1] subjectPersonKind
             1. The subjectPersonKind SHALL contain exactly one [1..1] @classCode="PERS"
             2. The subjectPersonKind SHALL contain exactly one [1..1] @determinerCode="KIND"
             3. The subjectPersonKind SHOULD contain zero to one [0..1] quantity@value
                The number of subjects that is planned for the study
                [SDTM: Appendix C3 TSPARMCD = PLANSUB]
            d. The plannedStudy MAY contain zero to many [0..m] precondition
               i. The precondition SHALL contain exactly one [1..1] @typeCode="PRCN"
Study Design Structured Document Implementation Guide

ii. The precondition SHALL contain exactly one [1..1] eligibilityCriterion. Information on inclusion and exclusion criteria for the study. Template ID = FDAroot.xx.yy.11

e. The plannedStudy SHALL contain one to many [1..m] component1
   i. The component1 SHALL contain exactly one [1..1] @typeCode=”COMP”
   ii. The component1 SHALL contain exactly one [1..1] epoch.
       Information on epochs defined for the study. Template ID = FDAroot.xx.yy.03

f. The plannedStudy SHALL contain one to many [1..m] component2
   i. The component2 SHALL contain exactly one [1..1] @typeCode=”COMP”
   ii. The component2 SHALL contain exactly one [1..1] arm.
       Information on arms defined for the study. Template ID = FDAroot.xx.yy.04

g. The plannedStudy SHALL contain one to many [1..m] component3
   i. The component3 SHALL contain exactly one [1..1] @typeCode=”COMP”
   ii. The component3 SHALL contain exactly one [1..1] substanceAdministration.
       Information on one or more treatment substances to be administered during the study. Template ID = FDAroot.xx.yy.05

h. The plannedStudy SHALL contain one to many [1..m] component3
   i. The component3 SHALL contain exactly one [1..1] @typeCode=”COMP”
   ii. The component3 SHALL contain exactly one [1..1] observation.
       Information on one or more locally defined value set to be used for validating subject data in reports from the study. Template ID = FDAroot.xx.yy.06

i. The plannedStudy SHALL contain one to many [1..m] component4
   i. The component4 SHALL contain exactly one [1..1] @typeCode=”COMP”
   ii. The component4 SHALL contain exactly one [1..1] timePointEventDefinition.
       Information on elements and visits defined for the study. Element information is defined within Template ID = FDAroot.xx.yy.08

j. The plannedStudy SHALL contain one to many [1..m] subjectOf
   i. The subjectOF SHALL contain exactly one [1..1] @typeCode=“SUBJ”
   ii. The subjectOF SHALL contain exactly one [1..1] studyCharacteristic
       Information on characteristics/parameters defined for the study. Study characteristic information is defined within Template ID = FDAroot.xx.yy.10.

5.3 Content Data Structures
The body of the study design is comprised of several templates that are used to represent the primary functional content of the study design.
5.3.1 Study Epoch
An epoch is “an interval of time in the planned conduct of a study during which treatment is constant.” A subject moves from one epoch to another, and can only be in one epoch at a time. The main purpose of the epoch is to organize arms for comparison purposes. The template id for the data structure is: FDAroot.xx.yy.03.

Its contents are specified as follows:

1. The epoch SHALL contain exactly one [1..1] @classCode="ACT"
2. The epoch SHALL contain exactly one [1..1] @moodCode="DEF"
3. The epoch SHALL contain exactly one [1..1] id@nullFlavor="UNK"
   The identifier is only used to provide references within the content of the study design document. A root OID to provide global uniqueness is not needed.
4. The epoch SHALL contain exactly one [1..1] id@extension
   The extension value shall be an integer, and shall be unique within the document.
5. The epoch SHALL contain exactly one [1..1] title@mediaType="text/plain"
6. The epoch SHALL contain exactly one [1..1] title
   A text description of the epoch.
[SDTM: EPOCH]

5.3.2 Study Arm
An arm is “a sequence of epochs (time intervals during which treatment is consistent) defining the course of participation for a subject in a trial.” It is a path through the study which describes what activities the subject will be involved in as they pass through the study, and is typically equivalent to a treatment group in a parallel design trial. Generally, each subject is assigned to an Arm, and the design of the study is reflected in the number and composition of the individual arms. The template id for the data structure is: FDAroot.xx.yy.04.

Its contents are specified as follows:

1. The arm SHALL contain exactly one [1..1] @classCode="ACT"
2. The arm SHALL contain exactly one [1..1] @moodCode="DEF"
3. The arm SHALL contain exactly one [1..1] id@nullFlavor="UNK"
   The identifier is only used to provide references within the content of the study design document. A root OID to provide global uniqueness is not needed.
4. The arm SHALL contain exactly one [1..1] id@extension
   The extension value shall be an integer, and shall be unique within the document.
5. The arm SHALL contain exactly one [1..1] code@code =”" (CodeSystem Arm - local)
6. The arm SHALL contain exactly one [1..1-code@displayName
   A text description of the arm.

5.3.3 Study Substance
Information on a substance to be administered during the trial, and on the manner of its administration. The template id for the data structure is: FDAroot.xx.yy.05.

Its contents are specified as follows:

1. The studySubstance SHALL contain exactly one [1..1] @classCode="SBADM"

---

2. The studySubstance SHALL contain exactly one [1..1] @moodCode="DEF"

3. The studySubstance MAY contain zero to one [0..1] effectiveTime
   a. The effectiveTime SHALL contain exactly one [1..1] @xsi:type="PIVL_TS"
   b. The effectiveTime SHALL contain exactly one [1..1] period

   Time period holds the frequency of administration. [SDTM Appendix C3 TSPARMCD = DOSFRQ]. Note that the HL7 frequency representation captures the periodicity of administrations – the scheduled time delay between two administrations.
      i. The period SHALL contain exactly one [1..1] value
      ii. The period SHALL contain exactly one [1..1] unit (CodeSystem 2.16.840.1.113883.3.26.1.1 NCI Thesaurus)

4. The studySubstance MAY contain zero to one [0..1] routeCode@code (CodeSystem 2.16.840.1.113883.3.26.1.1 NCI Thesaurus)

   The route by which the substance is administered.
   [SDTM Appendix C3 TSPARMCD = ROUTE]

5. The studySubstance MAY contain zero to one [0..1] doseQuantity@value

   The planned amount to be administered.
   [SDTM Appendix C3 TSPARMCD = DOSE]

6. The studySubstance MAY contain zero to one [0..1] doseQuantity@unit (CodeSystem 2.16.840.1.113883.3.26.1.1 NCI Thesaurus)
   [SDTM Appendix C3 TSPARMCD = DOSU]

7. The studySubstance MAY contain zero to one [0..1] consumable
   a. The consumable SHALL contain exactly one [1..1] @typeCode="CSM"
   b. The consumable SHALL contain exactly one [1..1] manufacturedProduct
      i. The manufacturedProduct SHALL contain exactly one [1..1] @classCode="MANU"
      ii. The manufacturedProduct SHALL contain exactly one [1..1] manufacturedMaterial
         1. The manufacturedMaterial SHALL contain exactly one [1..1] @classCode="MMAT"
         2. The manufacturedMaterial SHALL contain exactly one [1..1] @determinerCode="KIND"
         3. The manufacturedMaterial may contain zero to one [0..1] code@code
         4. The manufacturedMaterial may contain zero to one [0..1] name

   Information on the substance to be administered. Either the name or code may be provided.
   [SDTM Appendix C3 TSPARMCD = PLANSUB]
   [SDTM Appendix C3 TSPARMCD = TRT]

5.3.4 Study Element

An element is a building block that is used to organize activity within the trial. It represents a cluster of activities that may be assigned to one or more arms within the study. Note, study design provides information about the individual elements of the study, and about an elements assignment to a particular arm. It would be possible to define a list of activities that would be expected to be performed as part of an element. However, that level of detail is beyond the scope of this implementation guide. The template id for the data structure is: FDAroot.xx.yy.06.

Its contents are specified as follows:

1. The timePointEventDefinition SHALL contain exactly one [1..1] @classCode="CTTEVENT"
2. The timePointEventDefinition SHALL contain exactly one [1..1] @moodCode="DEF"
3. The timePointEventDefinition SHALL contain exactly one \([1..1]\) id@nullFlavor=“UNK”
   Presence of the identifier is required by the schema, but is not functionally required.
4. The timePointEventDefinition SHALL contain exactly one \([1..1]\) code@code (CodeSystem = Element Code Local)
   A code to indicate the nature of the element.
   [SDTM: ETCD]
5. The timePointEventDefinition SHALL contain exactly one \([1..1]\) code@displayText
   [SDTM: ELEMENT]
6. The timePointEventDefinition MAY contain zero to one \([0..1]\) effectiveTime@xsi:type="IVL_TS"
   a. The effectiveTime SHALL contain exactly one \([1..1]\) width@value
   b. The effectiveTime SHALL contain exactly one \([1..1]\) width@unit
      The expected duration of the activities included within the element.
   [SDTM: TEDUR]
7. The timePointEventDefinition MAY contain zero to one \([0..1]\) precondition
   a. The precondition SHALL contain exactly one \([1..1]\) @typeCode=“PRCN”
   b. The precondition SHALL contain exactly one \([1..1]\) checkpointCode@code=“B”
      The checkpoint code “B” indicates the criterion is evaluated before the activities included within
      the element begin.
      i. The timePointEventCriterion SHALL contain exactly one \([1..1]\) @classCode=“OBS”
      ii. The timePointEventCriterion SHALL contain exactly one \([1..1]\) @moodCode=“CRT”
      iii. The timePointEventCriterion SHALL contain exactly one \([1..1]\) code@code = “CXXXXX”
            (CodeSystem 2.16.840.1.113883.3.26.1.1 NCI Thesaurus)
            The code value indicates the observation is an element performance rule.
      iv. The timePointEventCriterion SHALL contain exactly one \([1..1]\) value@xsi:type=“ED”
      v. The timePointEventCriterion SHALL contain exactly one \([1..1]\) value@mediaType=“text/plain”
      vi. The timePointEventCriterion SHALL contain exactly one \([1..1]\) value
         A rule describing the condition under which the element is to start.
   [SDTM: TESTRL]
8. The timePointEventDefinition MAY contain zero to one \([0..1]\) precondition
   a. The precondition SHALL contain exactly one \([1..1]\) @typeCode=“PRCN”
   b. The precondition SHALL contain exactly one \([1..1]\) checkpointCode@code=“E”
      The checkpoint code “E” indicates the criterion is evaluated in order to allow the activities within
      the element to end.
      i. The timePointEventCriterion SHALL contain exactly one \([1..1]\) @classCode=“OBS”
      ii. The timePointEventCriterion SHALL contain exactly one \([1..1]\) @moodCode=“CRT”
      iii. The timePointEventCriterion SHALL contain exactly one \([1..1]\) code@code = “CXXXXX”
            (CodeSystem 2.16.840.1.113883.3.26.1.1 NCI Thesaurus)
            The code value indicates the observation is an element performance rule.
      iv. The timePointEventCriterion SHALL contain exactly one \([1..1]\) value@xsi:type=“ED”
      v. The timePointEventCriterion SHALL contain exactly one \([1..1]\) value@mediaType=“text/plain”
      vi. The timePointEventCriterion SHALL contain exactly one \([1..1]\) value
         A rule describing the condition under which the element is to end.
   [SDTM: TEENRL]
9. The timePointEventDefinition SHALL contain one to many \([1..*]\) component2
   a. The component2 SHALL contain exactly one \([1..1]\) @typeCode=“COMP”
b. The component2 SHALL contain exactly one [1..1] timePointEventDefinition

Information on an element’s positioning within a particular study arm. Element in Arm information is defined within Template ID = FDAroot.xx.yy.07

5.3.5 Element in Arm

The element defines a collection of activities to be performed during a study. However this collection can take place in different contexts – through being situated in different arms of the study. The “element in arm” template captures an element’s assignment to an arm, as well as allowing the definition of particular rules that apply when the element occurs within the arm. The template id for the data structure is: FDAroot.xx.yy.07.

Its contents are specified as follows:

1. The timePointEventDefinition SHALL contain exactly one [1..1] @classCode=“CTTEVENT”
2. The timePointEventDefinition SHALL contain exactly one [1..1] @moodCode=“DEF”
3. The timePointEventDefinition SHALL contain exactly one [1..1] id@nullFlavor=“UNK”

   Presence of the identifier is required by the schema, but is not functionally required.
4. The timePointEventDefinition SHALL contain exactly one [1..1] code@code (CodeSystem = Element Code Local)

   A code to indicate the nature of the element. For the element in arm, the value is used as reference to the parent element.
   [SDTM: ETCD]
5. The timePointEventDefinition MAY contain zero to one [0..1] precondition

   a. The precondition SHALL contain exactly one [1..1] @typeCode=“PRCN”

   b. The precondition SHALL contain exactly one [1..1] checkpointCode@code=“X”

      The checkpoint code “X” indicates the criterion is evaluated at the point the element is exited.

      i. The timePointEventCriterion SHALL contain exactly one [1..1] @classCode=“OBS”

      ii. The timePointEventCriterion SHALL contain exactly one [1..1] @moodCode=“CRT”

      iii. The timePointEventCriterion SHALL contain exactly one [1..1] code@code = “CXXXXX”

         (CodeSystem 2.16.840.1.113883.3.26.1.1 NCI Thesaurus)

         The code value indicates the observation is a branching rule applying to the element’s presence in the arm.

      iv. The timePointEventCriterion SHALL contain exactly one [1..1] value@xsi:type=“ED”

      v. The timePointEventCriterion SHALL contain exactly one [1..1] value@mediaType=“text/plain”

      vi. The timePointEventCriterion SHALL contain exactly one [1..1] value

         A rule describing the condition that, during the performance of the element, would lead a subject to be assigned to this arm of the study..
         [SDTM: TABRANCH]
6. The timePointEventDefinition MAY contain zero to one [0..1] precondition

   a. The precondition SHALL contain exactly one [1..1] @typeCode=“PRCN”

   b. The precondition SHALL contain exactly one [1..1] checkpointCode@code=“E”

      The checkpoint code “E” indicates the criterion is evaluated at the point that the activities within the element end.

      i. The timePointEventCriterion SHALL contain exactly one [1..1] @classCode=“OBS”

      ii. The timePointEventCriterion SHALL contain exactly one [1..1] @moodCode=“CRT”

      iii. The timePointEventCriterion SHALL contain exactly one [1..1] code@code = “CXXXXX”

         (CodeSystem 2.16.840.1.113883.3.26.1.1 NCI Thesaurus)

         The code value indicates the observation is an element performance rule.
iv. The timePointEventCriterion SHALL contain exactly one 
   \[1..1\] value\[@\text{xsi:type=}\text{“ED”}\]

v. The timePointEventCriterion SHALL contain exactly one 
   \[1..1\] value\[@\text{mediaType=}\text{“text/plain”}\]

vi. The timePointEventCriterion SHALL contain exactly one \[1..1\] value
   A rule describing the next element to be performed for the subject.

[SDTM: TATRANS]

7. The timePointEventDefinition MAY contain exactly one 
   \[1..1\]componentOf1
   a. The componentOf1 SHALL contain exactly one \[1..1\] @typeCode=“COMP”
   b. The componentOf1 SHALL contain exactly one \[1..1\] epochReference
      i. The epochReference SHALL contain exactly one \[1..1\] @classCode=“ACT”
      ii. The epochReference SHALL contain exactly one \[1..1\] @moodCode=“EVN”
      iii. The epochReference SHALL contain exactly one \[1..1\] id\[@nullFlavor=“NI”\]
      iv. The epochReference SHALL contain exactly one \[1..1\] id\[@extension\]
         The extension includes the identifier assigned to the epoch for the element.

8. The timePointEventDefinition MAY contain exactly one \[1..1\]componentOf2
   a. The componentOf2 SHALL contain exactly one \[1..1\] @typeCode=“COMP”
   b. The componentOf2 SHALL contain exactly one \[1..1\] sequenceNumber
      The sequence number indicates the order of the element within the arm.
      [SDTM: TAETORD]
   c. The componentOf2 SHALL contain exactly one \[1..1\] armReference
      i. The armReference SHALL contain exactly one \[1..1\] @classCode=“ACT”
      ii. The armReference SHALL contain exactly one \[1..1\] @moodCode=“EVN”
      iii. The armReference SHALL contain exactly one \[1..1\] id\[@nullFlavor=“NI”\]
      iv. The armReference SHALL contain exactly one \[1..1\] id\[@extension\]
         The extension includes the identifier assigned to the arm for the element.

5.3.6 Study Visit Definition

Visits are defined for a study as a way of grouping elements and activities within elements for performance by participants within the study or the study subject. The CDISC glossary notes that a visit is “A clinical encounter for a subject in a trail. Visits are frequently referred to as occurring on Day X or during Week Y; there may be gaps between visits, which can take place within an epoch or span an epoch.” Note, a visit does not have to be a face to face encounter, but could be a telephone call. The template id for the data structure is: FDAroot.xx.yy.08.

Its contents are specified as follows:

1. The timePointEventDefinition SHALL contain exactly one \[1..1\] @classCode=“CTTEVENT”
2. The timePointEventDefinition SHALL contain exactly one \[1..1\] @moodCode=“DEF”
3. The timePointEventDefinition SHALL contain exactly one \[1..1\] id\[@nullFlavor=“UNK”\]
   The identifier is only used to provide references within the content of the study design document. A root OID to provide global uniqueness is not needed
4. The timePointEventDefinition SHALL contain exactly one \[1..1\] id\[@extension\]
   The extension value shall be an integer, and shall be unique within the document. It is used to identify a particular visit.
   [SDTM: VISITNUM]
5. The timePointEventDefinition SHALL contain exactly one \[1..1\] code\[@code=“visit”\](CodeSystem = Element Code Local)

---

A code value is needed to indicate the time point event definition refers to a visit as opposed to a particular element.

6. The timePointEventDefinition MAY contain zero to one [0..1] title@mediaType="textPlan"

7. The timePointEventDefinition MAY contain zero to one [0..1] title
   The title contains a text description of the visit.
   [SDTM: VISIT]

8. The timePointEventDefinition SHALL contain one to many [1..*] component2
   a. The component2 SHALL contain exactly one [1..1] @typeCode="COMP"
   b. The component2 SHALL contain exactly one [1..1] timePointEventDefinition
      Information on a visit’s positioning within a particular study arm. Visit in Arm information is defined
      within Template ID = FDAroot.xx.yy.09.

9. The timePointEventDefinition MAY contain zero to one [0..1] subjectOf
   a. The subjectOf SHALL contain exactly one [1..1] @typeCode="SUBJ"
   b. The subjectOf SHALL contain exactly one [1..1] timePointEventCharacteristic
      i. The timePointEventCharacteristic SHALL contain exactly one [1..1] @classCode="OBS"
      ii. The timePointEventCharacteristic SHALL contain exactly one [1..1] @moodCode="EVN"
      iii. The timePointEventCharacteristic SHALL contain exactly one [1..1] code@code = “CXXXXX”
           (CodeSystem 2.16.840.1.113883.3.26.1.1 NCI Thesaurus)
           The code value indicates the observation is a planned study day for the visit.
      iv. The timePointEventCharacteristic SHALL contain exactly one [1..1] value@xsi:type="INT"
      v. The timePointEventCharacteristic SHALL contain exactly one [1..1] value@value
         The planned study day for the visit.
         [SDTM: VISTDY]

5.3.7 Visit in Arm
A visit defines a contact or group of contacts with the study subject. However, the rules associated with a visit may vary depending on the arm a subject is assigned to. The visit in arm structure supports the representation of these rules. The template id for the data structure is: FDAroot.xx.yy.09.

Its contents are specified as follows:

1. The timePointEventDefinition SHALL contain exactly one [1..1] @classCode="CTTEVENT"
2. The timePointEventDefinition SHALL contain exactly one [1..1] @moodCode="DEF"
3. The timePointEventDefinition SHALL contain exactly one [1..1] id@extension
   The extension contains the same value of VISITNUM as does the “parent” visit.
4. The timePointEventDefinition MAY contain zero to one [0..1] precondition
   a. The precondition SHALL contain exactly one [1..1] @typeCode="PRCN"
   b. The precondition SHALL contain exactly one [1..1] checkpointCode@code="B" ()
      The checkpoint code “B” indicates the criterion is to be evaluated at the beginning of the visit.
      i. The timePointEventCriterion SHALL contain exactly one [1..1] @classCode="OBS"
      ii. The timePointEventCriterion SHALL contain exactly one [1..1] @moodCode="CRT"
      iii. The timePointEventCriterion SHALL contain exactly one [1..1] code@code = “CXXXXX”
           (CodeSystem 2.16.840.1.113883.3.26.1.1 NCI Thesaurus)
           The code value indicates the observation is a performance rule applying to the visit’s presence in
           the arm.
      iv. The timePointEventCriterion SHALL contain exactly one [1..1] value@xsi:type="ED"
5. The timePointEventDefinition MAY contain zero to one [0..1] precondition
   a. The precondition SHALL contain exactly one [1..1] @typeCode="PRCN"
   b. The precondition SHALL contain exactly one [1..1] checkpointCode@code="E"
      The checkpoint code “E” indicates the criterion is evaluated at the point that the activities within the visit end.
      i. The timePointEventCriterion SHALL contain exactly one [1..1] @classCode="OBS"
      ii. The timePointEventCriterion SHALL contain exactly one [1..1] @moodCode="CRT"
      iii. The timePointEventCriterion SHALL contain exactly one [1..1] code@code = “CXXXXX”
            (CodeSystem 2.16.840.1.113883.3.26.1.1 NCI Thesaurus)
            The code value indicates the observation is a visit performance rule.
      iv. The timePointEventCriterion SHALL contain exactly one [1..1] value@xsi:type="ED"
   v. The timePointEventCriterion SHALL contain exactly one [1..1] CONTENT
      The element during which the visit ends –if different from the start one.
      [SDTM: TVENRL]

6. The timePointEventDefinition MAY contain exactly one [1..1] componentOf2
   a. The componentOf2 SHALL contain exactly one [1..1] @typeCode="COMP"
   b. The componentOf2 SHALL contain exactly one [1..1] armReference
      i. The armReference SHALL contain exactly one [1..1] @classCode="ACT"
      ii. The armReference SHALL contain exactly one [1..1] @moodCode="EVN"
      iii. The armReference SHALL contain exactly one [1..1] id@nullFlavor="NI"
      iv. The armReference SHALL contain exactly one [1..1] id@extension
         The extension includes the identifier assigned to the arm for the visit.

5.3.8 Study Characteristic
The design for a study includes a number of relevant items that are customarily carried as a collection of name value pairs within the SDTM Trial Summary domain. Some of this information – that which can be directly modeled within the Study Design Structured Document structure – is carried elsewhere in the implementation guide. The rest is captured as a collection of study characteristics. The template id for the data structure is: FDAroot.xx.yy.10.

Its contents are specified as follows:

1. The studyCharacteristic SHALL contain exactly one [1..1] @classCode="OBS"
2. The studyCharacteristic SHALL contain exactly one [1..1] @moodCode="EVN"
3. The studyCharacteristic SHALL contain exactly one [1..1] code@code =””(CodeSystem 2.16.840.1.113883.3.26.1.1 NCI Thesaurus)
   A code to indicate the nature of the study characteristic. Note, it is expected that a predefined set of study characteristic types will be used.
   [SDTM: TSPARMCD]
4. The studyCharacteristic SHALL contain exactly one [1..1] code@displayText
   A text description of the characteristic
   [SDTM: TSPARM]
5. The studyCharacteristic SHALL contain exactly one [1..1] value
   The content of the characteristic. The data type to be used will vary with the nature of the characteristic.

5.3.9 Study Eligibility Criterion
Definition of the criteria for enrolling subjects is a feature of many study designs. These criteria are captured as eligibility criteria. The template id for the data structure is: FDAroot.xx.yy.11.

Its contents are specified as follows:

1. The eligibilityCriterion SHALL contain exactly one [1..1] @classCode="OBS"
2. The eligibilityCriterion SHALL contain exactly one [1..1] @moodCode="CRT"
3. The eligibilityCriterion MAY contain zero to one [0..1] id@nullFlavor="UNK"
   The identifier is only used to provide references within the content of the study design document. A root OID to provide global uniqueness is not needed
4. The eligibilityCriterion MAY contain zero to one [0..1] id@extension
   An identifier is needed when a criterion is a replacement of a previous criteria or criterion. In this case, the identifier will be used to indicate the version of the criterion.
   [SDTM: TIVERS]
5. The eligibilityCriterion SHALL contain exactly one [1..1] code@code =""(CodeSystem Local)
   A code to indicate the nature of the eligibility criterion.
   [SDTM: IETESTCD]
6. The eligibilityCriterion SHALL contain exactly one [1..1] code@displayText
   A text description of the criterion.
   [SDTM: IETST]
7. The eligibilityCriterion SHALL contain exactly one [1..1] value@xsi:Type="ED"
8. The eligibilityCriterion SHALL contain exactly one [1..1] value@mediaType="text/plan"
9. The eligibilityCriterion SHALL contain exactly one [1..1] value CONTENT
   The content of the criterion. Since the criteria are defined locally, it is assumed that text data will be uniformly provided.
10. The eligibilityCriterion SHALL contain exactly one [1..1] valueNegationIndicator@value
    Indicates whether the criterion provides rules for including or for excluding study subjects. If Negation = True, it is an exclusion indicator. If Negation = False, it is an inclusion indicator.
    [SDTM: IECAT (we assume that IECAT is restricted to only take on the values inclusion and exclusion.)]
11. The eligibilityCriterion MAY contain zero to many [0..*] replacementOf
    The structure supports the possibility that an amended study may designate one or more eligibility criteria as replacements for a previous one.
    a. The replacementOf SHALL contain exactly one [1..1] @typeCode="RPLC"
    b. The replacement Of SHALL contain exactly one [1..1] eligibilityCriterion.
    Information on inclusion and exclusion criteria for the study. Template ID = FDAroot.xx.yy.11

5.3.10 Study Sponsor Vocabulary
Many of the coded items that are included within subject data reports draw their values from locally defined value sets. [Such a value set may or may not draw its values from a standard code system, although the likelihood is that the code system will be sponsor defined as well.] This information is currently carried in a separate file known as define.xml. This structure makes it possible to define as many value sets as needed, and to include the allowable values for each. The template id for the data structure is: FDAroot.xx.yy.14.
1. The organizer SHALL contain exactly one \([1..1]\) @classCode="CLUSTER"
2. The organizer SHALL contain exactly one \([1..1]\) @moodCode="DEF"

1. The organizer SHALL contain exactly one \([1..1]\) code@code ="" "" (CodeSystem 2.16.840.1.113883.3.26.1.1 NCI Thesaurus)
   A code that indicates the nature of the value set. Section A.4.3 provides a list of the locally defined value sets currently recognized for human subject data reporting.
2. The organizer SHALL contain exactly one \([1..1]\) code@displayName
   A text description of the locally defined valueset

3. The organizer SHALL contain one to many \([1..\ast]\) component
   a. The component SHALL contain exactly one \([1..1]\) @typeCode="COMP"
   a. The component SHALL contain exactly one \([1..1]\) observation
      Each observation contains a single member of the value set.
      i. The observation SHALL contain exactly one \([1..1]\) @classCode="OBS"
      ii. The observation SHALL contain exactly one \([1..1]\) @moodCode="DEF"
      iii. The observation SHALL contain exactly one \([1..1]\) value@xsi:type="CD"
      iv. The observation SHALL contain exactly one \([1..1]\) value@code
          A code value defined within the local value set.
      v. The observation SHALL contain exactly one \([1..1]\) value@displayName
          The text name associated with the code.
      vi. The observation SHALL contain exactly one \([1..1]\) value@codeSystem
          Use the code system OID for the locally defined value set as provided above.

A Appendices

A.1: Templates

The following templates are referred to within this document. Templates have been created as a way of partitioning the definition of the document. In addition, use of templates greatly eases the task of creating this content within tooling designed for capturing CDA specifications, e.g., the MDHT tooling. Also, template identifiers in document instances may be required for some implementers.

<table>
<thead>
<tr>
<th>Template ID</th>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>FDAroot.xx.yy.01</td>
<td>Study Design Structured Document</td>
</tr>
<tr>
<td>FDAroot.xx.yy.02</td>
<td>Study Design Structured Document Body</td>
</tr>
<tr>
<td>FDAroot.xx.yy.03</td>
<td>Study Epoch Definition</td>
</tr>
<tr>
<td>FDAroot.xx.yy.04</td>
<td>Study Arm Definition</td>
</tr>
<tr>
<td>FDAroot.xx.yy.05</td>
<td>Study Substance</td>
</tr>
<tr>
<td>FDAroot.xx.yy.06</td>
<td>Study Element Definition</td>
</tr>
<tr>
<td>FDAroot.xx.yy.07</td>
<td>Element in Arm</td>
</tr>
<tr>
<td>FDAroot.xx.yy.08</td>
<td>Study Visit Definition</td>
</tr>
<tr>
<td>FDAroot.xx.yy.09</td>
<td>Visit in Arm</td>
</tr>
</tbody>
</table>

\(^{9}\) The object identifier for a template needs to be created as an FDA assigned OID. For convenience it is reasonable to include a value used to prefix all templates, and a second value to indicate study design templates.
A2. Identifiers

<table>
<thead>
<tr>
<th>Identifier</th>
<th>Default Namespace</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Document ID, set ID</td>
<td>FDAroot.xx.zz.01</td>
<td></td>
</tr>
<tr>
<td>Represented Organization ID</td>
<td>FDAroot.xx.zz.02</td>
<td></td>
</tr>
<tr>
<td>Epoch ID</td>
<td>Unnecessary</td>
<td>Used for reference within the document.</td>
</tr>
<tr>
<td>Arm ID</td>
<td>Unnecessary</td>
<td>Used for reference within the document.</td>
</tr>
<tr>
<td>Element ID</td>
<td>FDAroot.xx.zz.03</td>
<td>Only used for visits. Provides a reference between the study design and reported subject data</td>
</tr>
<tr>
<td>Eligibility Criterion ID</td>
<td>Unnecessary</td>
<td>Used for reference within the document.</td>
</tr>
</tbody>
</table>

A3. Vocabulary: Act Codes

Any HL7 Version 3 structure uses generic classes within HL7’s RIM to represent more specific concepts that are relevant to it. This Implementation Guide uses specific act code assignments – most of these are observations – to clarify the structure of the document, but also – more specifically – to convey items that are modeled generically within the CDISC implementation guide. These code values are documented below.

A3.1 Structural Code Values

There are several places within the study design data structure in which a specific code value needs to be assigned to clarify the meaning of an act or observation. Each of these has been defined within NCI EVS, and provided with a concept ID. Here is a list of those code values.

<table>
<thead>
<tr>
<th>Attribute</th>
<th>Concept ID</th>
<th>Class within the IG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Act.code</td>
<td></td>
<td>Document (indicates a human clinical study design)</td>
</tr>
<tr>
<td>Act.code</td>
<td></td>
<td>Document Section (indicates the structured data for a human clinical study design)</td>
</tr>
<tr>
<td>Act.code</td>
<td></td>
<td>Epoch</td>
</tr>
<tr>
<td>Act.code</td>
<td></td>
<td>Arm</td>
</tr>
<tr>
<td>Observation.code</td>
<td></td>
<td>Time Point Event Criterion</td>
</tr>
<tr>
<td>Observation code</td>
<td></td>
<td>Planned Study Day (for a visit)</td>
</tr>
</tbody>
</table>

A3.2 Study Characteristic Code Values

A number of important information items for the study are carried within generic observation based structures within this guide. Creation of this list of value sets both reflects the design created by CDISC, and the fact that creating specific models for a disparate range of important information items can become a burdensome way to model the necessary data. The list below includes those code values that have been created to define salient features of the study – modeled in the Study Characteristic template. In some cases, the data item is supported directly within the Study Design Structured Document structure to facilitate processing by receivers. Over time, more of the content may move into this area.
Here is a list of the code values used to define Study Characteristic.¹⁰

<table>
<thead>
<tr>
<th>Description</th>
<th>Concept ID</th>
<th>Data Type</th>
<th>Value Set</th>
<th>IG Placement</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adaptive Design</td>
<td>C98704</td>
<td>ED</td>
<td>Study Characteristics</td>
<td></td>
<td>Indicate if the study includes a prospectively planned opportunity for modification of one or more specified aspects of the study design and hypotheses based on analysis of data (usually interim data) from subjects in the study.</td>
</tr>
<tr>
<td>Added on to Existing Treatment</td>
<td>C49703</td>
<td>BL</td>
<td>Study Characteristics</td>
<td></td>
<td>The addition of a therapeutic product to the existing regimen in a clinical trial, where both entities remain as discrete products.</td>
</tr>
<tr>
<td>Age</td>
<td>C49703</td>
<td>BL</td>
<td>Study Characteristics</td>
<td></td>
<td>Age and age unit will be captured as a single item.</td>
</tr>
<tr>
<td>Age Span</td>
<td>C66738</td>
<td>CD</td>
<td>Study Characteristic</td>
<td></td>
<td>Age and age unit will be captured as a single item.</td>
</tr>
<tr>
<td>Age Unit</td>
<td>C66738</td>
<td>CD</td>
<td>Study Characteristic</td>
<td></td>
<td>Age and age unit will be captured as a single item.</td>
</tr>
<tr>
<td>Clinical Study Sponsor</td>
<td>C70793</td>
<td>ED</td>
<td>Header</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Comparative Treatment Name</td>
<td>C68612</td>
<td>ED</td>
<td>Study Characteristic</td>
<td></td>
<td>A therapeutically active agent that is intended to provide reference measurements for the experimental protocol of a clinical trial. (could be managed as a study substance)</td>
</tr>
<tr>
<td>Confirmed Response Minimum Duration</td>
<td>C98715</td>
<td>PQ</td>
<td>Study Characteristic</td>
<td></td>
<td>The protocol specified minimum amount of time needed to meet the definition of a confirmed response to treatment.</td>
</tr>
<tr>
<td>Control Type</td>
<td>C49647</td>
<td>CD</td>
<td>Study Control Type</td>
<td>Study Characteristic</td>
<td>Comparator against which the study treatment is evaluated (e.g., concurrent (placebo, no treatment, dose-response, active), external (historical, published literature).</td>
</tr>
<tr>
<td>Current Therapy or Treatment</td>
<td>C85582</td>
<td>CD</td>
<td>Substance Code</td>
<td>Study Substance</td>
<td>The literal identifier of the therapy or medication that is currently being given per protocol. This does not include treatment that has been given in the past. (Does this belong in Subject Data?)</td>
</tr>
<tr>
<td>Diagnosis Group</td>
<td>C49650</td>
<td>CD</td>
<td>Diagnosis Type</td>
<td>Study Characteristic</td>
<td>Note, this could be modeled directly as an eligibility criterion.</td>
</tr>
<tr>
<td>Dose per administration</td>
<td>C25488</td>
<td>PQ</td>
<td>Study Substance</td>
<td>Study Substance</td>
<td>Dose and unit are captured as a single item.</td>
</tr>
<tr>
<td>Dose Units</td>
<td>C73558</td>
<td>PQ</td>
<td>Study Substance</td>
<td>Study Substance</td>
<td>Dose and unit are captured as a single item.</td>
</tr>
</tbody>
</table>

¹⁰The content of the table is drawn from 7.63 Trial Summary Codes, Standard for Exchange of Nonclinical Data Implementation Guides: Nonclinical Studies, CDISC, 2011
<table>
<thead>
<tr>
<th>Description</th>
<th>Concept ID</th>
<th>Data Type</th>
<th>Value Set</th>
<th>IG Placement</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dosing Frequency</td>
<td>C89081</td>
<td>PIVL&lt;TS&gt;</td>
<td></td>
<td>Study Substance</td>
<td></td>
</tr>
<tr>
<td>Existing Treatment Addition</td>
<td>C49703</td>
<td>CD</td>
<td>Treatment Addition Type</td>
<td>Study Characteristic</td>
<td></td>
</tr>
<tr>
<td>Exploratory Outcome Measure</td>
<td>C98724</td>
<td>ED</td>
<td></td>
<td>Study Characteristic</td>
<td>Exploratory measures that will be used to evaluate the intervention(s) or, for observational studies, that are exploratory of the study.</td>
</tr>
<tr>
<td>Healthy Subject Indicator</td>
<td>C98737</td>
<td>BL</td>
<td></td>
<td>Study Characteristic</td>
<td>Indicate if persons who have not had the condition(s) being studied or otherwise related conditions or symptoms, as specified in the eligibility requirements, may participate in the study.</td>
</tr>
<tr>
<td>Intervention Model</td>
<td>C98746</td>
<td>ED</td>
<td></td>
<td>Study Characteristic</td>
<td>The trial design developed to compare treatment groups.</td>
</tr>
<tr>
<td>Intervention Type</td>
<td>C98747</td>
<td>ED</td>
<td></td>
<td>Study Characteristic</td>
<td>The kind of product or procedure studied in a trial.</td>
</tr>
<tr>
<td>Investigational Therapy or Treatment</td>
<td>C41161</td>
<td>ED</td>
<td></td>
<td>Study Substance</td>
<td></td>
</tr>
<tr>
<td>Planned Maximum Age of Subjects</td>
<td>C49694</td>
<td>PQ</td>
<td></td>
<td>Study Characteristic</td>
<td>Age and age unit will be captured as a single item. This could be captured as an eligibility characteristic.</td>
</tr>
<tr>
<td>Planned Minimum Age of Subjects</td>
<td>C49693</td>
<td>PQ</td>
<td></td>
<td>Study Characteristic</td>
<td>Age and age unit will be captured as a single item. This could be captured as an eligibility characteristic.</td>
</tr>
<tr>
<td>Pharmacological Class of Investigational Therapy</td>
<td>C98768</td>
<td>CD</td>
<td></td>
<td>Study Substance</td>
<td></td>
</tr>
<tr>
<td>Planned Number of Arms</td>
<td>C98771</td>
<td>INT</td>
<td></td>
<td>Study Characteristic</td>
<td>The planned number of intervention groups.</td>
</tr>
<tr>
<td>Planned Number of Subjects</td>
<td>C49692</td>
<td>INT</td>
<td>Structured Section; Record Target</td>
<td>Study Characteristic</td>
<td></td>
</tr>
<tr>
<td>Primary Outcome Measure</td>
<td>C98772</td>
<td>ED</td>
<td></td>
<td>Study Characteristic</td>
<td>The primary measurement(s) or observation(s) used to measure the effect of experimental variables in a study, or for observational studies, to describe patterns of diseases or traits or associations with exposures, risk factors or treatment. These are the outcome measures used to assess the primary objective(s).</td>
</tr>
<tr>
<td>Randomization Character</td>
<td>CD</td>
<td>Randomization Type</td>
<td>Study Characteristic</td>
<td>Indicates the manner of randomization.</td>
<td></td>
</tr>
<tr>
<td>Description</td>
<td>Concept ID</td>
<td>Data Type</td>
<td>Value Set</td>
<td>IG Placement</td>
<td>Comment</td>
</tr>
<tr>
<td>------------------------------------------</td>
<td>------------</td>
<td>-----------</td>
<td>--------------------</td>
<td>-----------------------</td>
<td>--------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Randomization Quotient</td>
<td>C98775</td>
<td>INT</td>
<td>Value Set</td>
<td>Study Characteristic</td>
<td>The randomization quotient is the number of planned subjects to be exposed to investigational therapy, independent of dose or other factors, divided by the total number of planned subjects.</td>
</tr>
<tr>
<td>Registry Identifier</td>
<td>C98714</td>
<td>II</td>
<td>Header</td>
<td></td>
<td>Identification numbers assigned to the protocol by ct.gov, EudraCT, or other registries.</td>
</tr>
<tr>
<td>Route of Administration</td>
<td>C38114</td>
<td>CD</td>
<td>Route of Administration</td>
<td>Study Substance</td>
<td></td>
</tr>
<tr>
<td>Secondary Outcome Measure</td>
<td>C98781</td>
<td>ED</td>
<td>Study Substance</td>
<td></td>
<td>Other key measures that will be used to evaluate the intervention(s) or, for observational studies, that are a focus of the study. These are the outcome measures used to assess the secondary objective(s).</td>
</tr>
<tr>
<td>Sex of Participants</td>
<td>C49696</td>
<td>CD</td>
<td>Sex of Participants Type</td>
<td>Study Characteristic</td>
<td>Note, this could be modeled directly as an eligibility criterion.</td>
</tr>
<tr>
<td>Stable Disease Minimum Duration</td>
<td>C98783</td>
<td>PQ</td>
<td>Study Characteristic</td>
<td></td>
<td>The protocol specified minimum amount of time needed to meet the definition of stable disease.</td>
</tr>
<tr>
<td>Study Stop Rules</td>
<td>C49698</td>
<td>CD</td>
<td>Stop Rule Type</td>
<td>Study Characteristic</td>
<td>Describes the role the study plays in determining the interventions a subject receives.</td>
</tr>
<tr>
<td>Study Type</td>
<td>C15320</td>
<td>ED</td>
<td>Study Characteristic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trial Blinding Schema</td>
<td>C49658</td>
<td>CD</td>
<td>Blinding Schema Type</td>
<td>Study Characteristic</td>
<td>The basis for initiation of a treatment for a disease or of a diagnostic test (causal, or symptomatic, or disease-specific indication).</td>
</tr>
<tr>
<td>Trial Indication</td>
<td>C41184</td>
<td>ED</td>
<td>Study Characteristic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trial Indication Type</td>
<td>C49652</td>
<td>CD</td>
<td>Indication Type</td>
<td>Study Characteristic</td>
<td>The name of a code list that contains terms to define the type of trial, e.g. cure or prevention. (NCI)</td>
</tr>
<tr>
<td>Trial is Randomized</td>
<td>C25196</td>
<td>ED</td>
<td>Study Characteristic</td>
<td></td>
<td>This appears to be a description as opposed to a Boolean indicator.</td>
</tr>
<tr>
<td>Trial Length</td>
<td>PQ</td>
<td></td>
<td>Study Characteristic</td>
<td></td>
<td>The expected duration of a subject’s participation in the trial.</td>
</tr>
<tr>
<td>Trial Phase Classification</td>
<td>C48281</td>
<td>CD</td>
<td>Trial Phase Type</td>
<td>Study Characteristic</td>
<td></td>
</tr>
<tr>
<td>Trial Primary Objective</td>
<td>C85826</td>
<td>ED</td>
<td>Study Characteristic</td>
<td></td>
<td>This may become a controlled list.</td>
</tr>
<tr>
<td>Trial Secondary Objective</td>
<td>C85827</td>
<td>ED</td>
<td>Study Characteristic</td>
<td></td>
<td>This may become a controlled list.</td>
</tr>
<tr>
<td>Trial Title</td>
<td>C49802</td>
<td>ED</td>
<td>Header</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
A.4 Vocabulary: Value Sets

Submission of a study design includes a number of coded elements – elements whose values are drawn from defined value set. These are organized into three categories:

- HL7 Defined
- Centrally Defined
- Sponsor Defined.

A.4.1 HL7 Defined Value Sets

These value sets are defined by the Health Level 7 Organization. For the most part they function as structural elements within the document structure. A few additional value sets provide general codes to define the context of the report.

<table>
<thead>
<tr>
<th>Value Set Name</th>
<th>Description</th>
<th>Local?</th>
<th>OID &amp; Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>ActClass</td>
<td>The set of valid act types defined by HL7.  (^{11})</td>
<td>No</td>
<td>2.16.840.1.113883.5.6 HL7</td>
</tr>
<tr>
<td>ActMood</td>
<td>The set of valid act moods defined by HL7.</td>
<td>No</td>
<td>2.16.840.1.113883.5.1001 HL7</td>
</tr>
<tr>
<td>ParticipationType</td>
<td>The set of valid participation types (associations between an act and a role) defined by HL7.</td>
<td>No</td>
<td>2.16.840.1.113883.5.90 HL7</td>
</tr>
<tr>
<td>ActRelationshipType</td>
<td>The set of valid act relationship types (associations between two acts) defined by HL7.</td>
<td>No</td>
<td>2.16.840.1.113883.5.1002 HL7</td>
</tr>
<tr>
<td>RoleClass</td>
<td>The set of valid role types defined by HL7.</td>
<td>No</td>
<td>2.16.840.1.113883.5.110</td>
</tr>
<tr>
<td>EntityClass</td>
<td>The set of valid entity types defined by HL7.</td>
<td>No</td>
<td>2.16.840.1.113883.5.41 HL7</td>
</tr>
<tr>
<td>EntityDeterminer</td>
<td>The set of valid entity determiner values defined by HL7.</td>
<td>No</td>
<td>2.16.840.1.113883.5.30 HL7</td>
</tr>
<tr>
<td>Confidentiality</td>
<td>The set of values used to control disclosure of information.</td>
<td>No</td>
<td>2.16.840.1.113883.5.25 HL7</td>
</tr>
<tr>
<td>Language</td>
<td>The set of valid language codes maintained by ISO</td>
<td>No</td>
<td>1.0.639.3 ISO</td>
</tr>
<tr>
<td>HL7 Realm</td>
<td>The list of HL7 affiliate countries used to define the expected usage of the implementation guide.</td>
<td>No</td>
<td>2.16.840.1.113883.5.1124 HL7</td>
</tr>
<tr>
<td>Act Relationship</td>
<td>A set of codes used to indicate when, during the course of an act’s performance, to check a rule that will be used to determine the next step in processing</td>
<td>No</td>
<td>2.16.840.1.113883.5.10</td>
</tr>
</tbody>
</table>

\(^{11}\) Refer to documentation of the HL7 Reference Information Model for more information on the HL7 “structural codes. Implementers should note that these coded elements use the data type CS, and that code system information does not need to be included within a document instance.
A.4.2 Centrally Defined Value Sets

These value sets are defined centrally for use by all submitters of this Implementation Guide. They cover key concepts for which generally agreed upon codes have been created. The use of centrally defined value sets make it easier to process the data, and to compare the design of studies generated by different sponsors. The codes within these value sets are maintained within the NCI EVS. Note, a single OID – that which identifies the NCI Thesaurus is used for each of these value sets. In a document instance, the value that is passed will be an NCI concept ID. For conformance purposes, that value should be tested to ensure it is a member of the set of concepts that is valid within the named value set.

<table>
<thead>
<tr>
<th>Value Set Name</th>
<th>Concept ID</th>
<th>Description</th>
<th>OID &amp; Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Units of Measure</td>
<td></td>
<td>A unit, whether of time, mass or other physical quantity that is required to</td>
<td>2.16.840.1.113883.3.26.1.1 NCI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>add context to a measure.</td>
<td>Thesaurus</td>
</tr>
<tr>
<td>Route of administration</td>
<td></td>
<td>The path taken by an administered substance to get into the body, or to</td>
<td>2.16.840.1.113883.3.26.1.1 NCI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>come in contact with the body</td>
<td>Thesaurus</td>
</tr>
<tr>
<td>Study Characteristic</td>
<td></td>
<td>A set of codes to define possible relevant characteristics of a study. (aka</td>
<td>2.16.840.1.113883.3.26.1.1 NCI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>trial summary parameter)</td>
<td>Thesaurus</td>
</tr>
<tr>
<td>Study Component Rule</td>
<td></td>
<td>A set of rules that specify, at least, the rules for initiating or ending an</td>
<td>2.16.840.1.113883.3.26.1.1 NCI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>element, for branching from one element to another, or for initiating or</td>
<td>Thesaurus</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ending a visit.</td>
<td></td>
</tr>
<tr>
<td>Treatment Addition Type</td>
<td></td>
<td>A set of types of treatment that may be added on to existing treatments</td>
<td>2.16.840.1.113883.3.26.1.1 NCI</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Thesaurus</td>
</tr>
<tr>
<td>Age Group Type</td>
<td></td>
<td>A set of age groupings used to organize age ranges into categories.</td>
<td>2.16.840.1.113883.3.26.1.1 NCI</td>
</tr>
<tr>
<td>Randomization Type</td>
<td>C66742</td>
<td>A set of methods for randomizing the treatment of subjects within a study.</td>
<td>2.16.840.1.113883.3.26.1.1 NCI</td>
</tr>
<tr>
<td>Sex of Participants Type</td>
<td>C66732</td>
<td>The collection of different combinations of sex that would be eligible to be</td>
<td>2.16.840.1.113883.3.26.1.1 NCI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>study subjects. (Can Administrative Gender be used?)</td>
<td>Thesaurus</td>
</tr>
<tr>
<td>Stop Rule Type</td>
<td></td>
<td>The set of rules that define the conditions under which a study will be</td>
<td>2.16.840.1.113883.3.26.1.1 NCI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>stopped.</td>
<td>Thesaurus</td>
</tr>
<tr>
<td>Blinding Schema Type</td>
<td>C66735</td>
<td>The set of methods by which a study is blinded.</td>
<td>2.16.840.1.113883.3.26.1.1 NCI</td>
</tr>
<tr>
<td>Indication Type</td>
<td>C66736</td>
<td>The set of different indications for providing mitigation of the adverse</td>
<td>2.16.840.1.113883.3.26.1.1 NCI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>effect of a study treatment.</td>
<td>Thesaurus</td>
</tr>
<tr>
<td>Study Control Type</td>
<td>C66785</td>
<td>A set of different roles that a group of subjects may perform as controls</td>
<td>2.16.840.1.113883.3.26.1.1 NCI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>within a study. E.g., vehicle control, positive control</td>
<td>Thesaurus</td>
</tr>
<tr>
<td>Diagnosis Type</td>
<td>C66787</td>
<td>A set of diagnoses that may appear as indications for enrollment in a study.</td>
<td>2.16.840.1.113883.3.26.1.1 NCI</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Thesaurus</td>
</tr>
<tr>
<td>Trial Phase Type</td>
<td>C66737</td>
<td>A set of values that describe the different phases of a trial.</td>
<td>2.16.840.1.113883.3.26.1.1 NCI</td>
</tr>
<tr>
<td>Trial Type</td>
<td>C66739</td>
<td>A set of values that define the possible types of study.</td>
<td>2.16.840.1.113883.3.26.1.1 NCI</td>
</tr>
<tr>
<td>Pharmaceutical Class</td>
<td></td>
<td>The collection of drug classes that are used to characterize the study</td>
<td>2.16.840.1.113883.3.26.1.1 NCI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>treatment</td>
<td>Thesaurus</td>
</tr>
</tbody>
</table>
A.4.3 Locally Defined Value Sets

In an ideal world, all the value sets used for study design would be shared across all study sponsors. However, the wide range of circumstances in which studies take place, as well as the different histories of the organizations carrying out studies make that impractical. This table lists those value sets that are locally defined. For each, the sponsor needs to define the allowable values, and to provide that set of values along with the submitted study design.

<table>
<thead>
<tr>
<th>Locally Defined Value Sets</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Value Set Name</strong></td>
</tr>
<tr>
<td>Substance Code</td>
</tr>
<tr>
<td>Study Element</td>
</tr>
<tr>
<td>Eligibility Criteria</td>
</tr>
<tr>
<td>Study Time Point</td>
</tr>
</tbody>
</table>

A.4.4 Subject Data Locally Defined Value Sets

The table provides a list of locally defined value sets. These are value sets needed for evaluating coded values within subject data reports, which are defined by the study sponsor since no generally agreed upon and maintained set of values exists.

The list of the value sets that need definition to fully support subject data reporting is included within the Subject Data Implementation Guide.
A.4 Sample Messages

A sample message has been devised that uses a publicly available data set to illustrate the content of this guide.

```xml
<?xml version="1.0" encoding="UTF-8"?>
<Document xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance" xmlns="urn:hl7-org:v3"
xmlns:ctm="http://clinicalTrialMaterial" xsi:schemaLocation="urn:hl7-org:v3 ../StudyDesignSchemas/StudyDesign.xsd"
classCode="DOCLIN" moodCode="EVN">
  <!-- this sample message is drawn from a public SDTM dataset - study1_sdtm_define -->
  <realmCode code="US"/>
  <typeId root="2.16.840.1.113883.1.3" extension="POCD_HD000040"/>
  <templateId root="2.16.840.1.113883.10.20.25.1"/>
  <id nullFlavor="UNK" extension="STUDY1"/>
  <code code="TBD" codeSystem="2.16.840.1.113883.6.1" codeSystemName="LOINC"/>
  <title>A 29 Day, Placebo Washout, Double Blind Randomization, Dose Escalation, Randomized Washout, Placebo or continued active treatment.</title>
  <effectiveTime value="20120704"/>
  <confidentialityCode code="N" codeSystem="2.16.840.1.113883.5.25"/>
  <languageCode/>
  <setId nullFlavor="UNK" extension="2388747"/>
  <versionNumber>1</versionNumber>
  <responsibleParty typeCode="RESP">
    <assignedEntity classCode="ASSIGNED">
      <representedOrganization classCode="ORG" determinerCode="INSTANCE">
        <id nullFlavor="UNK" extension="GSB234455"/>
      </representedOrganization>
    </assignedEntity>
  </responsibleParty>
  <!-- XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX
        Unstructured Text Content - to handle text protocol material
        The sample content does not include the text material for the protocol.
        XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX-->
  <component typeCode="COMP">
    <structuredBody classCode="DOCBODY" moodCode="EVN">
      <!-- The Planned Study Content is here. -->
      XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX
      <component typeCode="COMP">
        <section classCode="DOCSECT" moodCode="EVN">
          <!-- XXXXXXXXXXXXXXXXXXXXXXXXXXXXX
                Epoch Information
                XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX-->
          <component1 typeCode="COMP">
            <epoch classCode="ACT" moodCode="DEF">
              <id nullFlavor="UNK" extension="1"/>
            </epoch>
          </component1>
        </section>
        <plannedStudy classCode="CLNTRL" moodCode="DEF">
          <!-- XXXXXXXXXXXXXXXXXXXXXXXXXXXXX
                Epoch Information
                XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX-->
          <component1 typeCode="COMP">
            <epoch classCode="ACT" moodCode="DEF">
              <id nullFlavor="UNK" extension="1"/>
            </epoch>
          </component1>
        </plannedStudy>
      </component>
    </structuredBody>
  </component>
</Document>
```

(-- The ID is assigned to serve as a pointer later. --)
<code code="xxx" displayName="PLACEBO WASHOUT" codeSystem="1.22.3.1"/>
</code>

<code code="xxx" displayName="DOUBLE BLIND" codeSystem="1.22.3.1"/>
</code>

<code code="xxx" displayName="RANDOMIZED WASHOUT" codeSystem="1.22.3.1"/>
</code>

<!-- XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX
Arm Information
XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX-->
<code code="HIGHHIGH" displayName="HIGHDOSE/HIGHDOSE" codeSystem="1.22.3.2"/>
</code>

<code code="HIGHPBO" displayName="HIGHDOSE/PLACEBO" codeSystem="1.22.3.2"/>
</code>

<code code="LOWLOW" displayName="LOWDOSE/LOWDOSE" codeSystem="1.22.3.2"/>
</code>

<code code="LOWPBO" displayName="LOWDOSE/PLACEBO" codeSystem="1.22.3.2"/>
</code>

<code code="MIDDMIDD" displayName="MIDDLEDOSE/DOSE/MIDDLEDOSE" codeSystem="1.22.3.2"/>
</code>
Study Design Structured Document Implementation Guide

<id nullFlavor="UNK" extension="6"/>
<!-- The ID is assigned to serve as a pointer later. -->
<code code="MIDDPOB" displayName="MIDDLEDOSE/PLACEBO" codeSystem="1.22.3.2"/>
</arm>
<!-- XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX
Study Substance Information -
In SDTM terms, this is drawn from the Trial Summary domain.

<br/>&lt;component3 typeCode="COMP">
  <substanceAdministration classCode="SBADM" moodCode="DEF">
    <effectiveTime xsi:type="PIVL_TS">
      <period value="1" unit="day"/>
    </effectiveTime>
    <routeCode code="xxxx" displayName="ORAL" codeSystem="1.22.3.3"/>
    <doseQuantity value="0.625" unit="mg"/>
    <consumable typeCode="CSM" xsi:nil="true"/>
  </substanceAdministration>
</component3>
<br/>&lt;component3 typeCode="COMP">
  <substanceAdministration classCode="SBADM" moodCode="DEF">
    <effectiveTime xsi:type="PIVL_TS">
      <period value="1" unit="day"/>
    </effectiveTime>
    <routeCode code="xxxx" displayName="ORAL" codeSystem="1.22.3.3"/>
    <doseQuantity value="1.25" unit="mg"/>
    <consumable typeCode="CSM" xsi:nil="true"/>
  </substanceAdministration>
</component3>
<br/>&lt;component3 typeCode="COMP">
  <substanceAdministration classCode="SBADM" moodCode="DEF">
    <effectiveTime xsi:type="PIVL_TS">
      <period value="1" unit="day"/>
    </effectiveTime>
    <routeCode code="xxxx" displayName="ORAL" codeSystem="1.22.3.3"/>
    <doseQuantity value="2.5" unit="mg"/>
    <consumable typeCode="CSM" xsi:nil="true"/>
  </substanceAdministration>
</component3>
<br/>&lt;component3 typeCode="COMP">
  <substanceAdministration classCode="SBADM" moodCode="DEF">
    <effectiveTime xsi:type="PIVL_TS">
      <period value="1" unit="day"/>
    </effectiveTime>
    <routeCode code="xxxx" displayName="ORAL" codeSystem="1.22.3.3"/>
    <doseQuantity value="5" unit="mg"/>
    <consumable typeCode="CSM" xsi:nil="true"/>
  </substanceAdministration>
</component3>
<br/>
Study Design Structured Document Implementation Guide

<moodCode>DEF</moodCode>

<substanceAdministration classCode="SBADM">
<effectiveTime xsi:type="PIVL_TS">
<period value="1" unit="day"/>
</effectiveTime>
<routeCode code="xxxx" displayName="ORAL" codeSystem="1.22.3.3"/>
<doseQuantity value="10" unit="mg"/>
<consumable typeCode="CSM" xsi:nil="true"/>
</substanceAdministration>
</component3>
<component3 typeCode="COMP">
<substanceAdministration classCode="SBADM">
<effectiveTime xsi:type="PIVL_TS">
<period value="1" unit="day"/>
</effectiveTime>
<routeCode code="xxxx" displayName="ORAL" codeSystem="1.22.3.3"/>
<doseQuantity value="20" unit="mg"/>
<consumable typeCode="CSM" xsi:nil="true"/>
</substanceAdministration>
</component3>
<component3 typeCode="COMP">
<substanceAdministration classCode="SBADM">
<effectiveTime xsi:type="PIVL_TS">
<period value="1" unit="day"/>
</effectiveTime>
<routeCode code="xxxx" displayName="ORAL" codeSystem="1.22.3.3"/>
<doseQuantity value="40" unit="mg"/>
<consumable typeCode="CSM" xsi:nil="true"/>
</substanceAdministration>
</component3>
<!-- XXXXXXXXXXXXXXXXXXXXXXXXXXX
Study Element Information
[I have included the first six elements.]
Element # 1
XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX-->

<component4 typeCode="COMP">
<timePointEventDefinition classCode="CTTEVENT">
<id nullFlavor="UNK"/>
<code code="HWH1" displayName="High Dose 20mg D1-2" codeSystem="1.22.3.4"/>
<effectiveTime xsi:type="IVL_TS">
<width value="2" unit="day"/>
</effectiveTime>
<precondition typeCode="PRCN">
<checkpointCode code="B"/>
<timePointEventCriterion classCode="OBS" moodCode="CRT">
<code code="CXXXXX" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
<value xsi:type="ED" mediaType="text/plain">First dose of Double Blind medication</value>
</timePointEventCriterion>
</precondition>
</timePointEventDefinition>
</component4>

moodCode="DEF">

<id nullFlavor="UNK"/>
<code code="HWH1" displayName="High Dose 20mg D1-2" codeSystem="1.22.3.4"/>
<effectiveTime xsi:type="IVL_TS">
<width value="2" unit="day"/>
</effectiveTime>
<precondition typeCode="PRCN">
<checkpointCode code="B"/>
<timePointEventCriterion classCode="OBS" moodCode="CRT">
<code code="CXXXXX" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
<value xsi:type="ED" mediaType="text/plain">First dose of Double Blind medication</value>
</timePointEventCriterion>
</precondition>
</component4>
classCode="OBS" moodCode="CRT">

codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
is an element performance rule. -->

mediaType="text/plain">Prior to Dose Escalation Start</value>

<timePointEventCriterion>
</precondition>
</timePointEventCriterior>

</precondition>
<checkpointCode code="E"/>

<timePointEventCriterion>
</precondition>
<value xsi:type="ED" mediaType="text/plain">Prior to Dose Escalation Start</value>
</timePointEventCriterior>

<!-- xxxxxxxxxxxxxxxxxxxxxxxxx
Element in Arm information
xxxxxxxxxxxxxxxxxxxxxxxxx-->

<component2 typeCode="COMP">
<timePointEventDefinition>
<id nullFlavor="NI"/>
<code code="HWH1"/>
<value xsi:type="ED" mediaType="text/plain">Dose Escalation to 40mg on Day 3 unless limited by as AE or excessive hypotension</value>
</timePointEventDefinition>

as the element this is part of. -->

typeCode="PRCN">

<timePointEventCriterion classCode="OBS" moodCode="CRT"> <!-- Indicate that the observation is a transition rule applying to the element's presence in an arm. -->
<code code="CXXXXXX" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
</timePointEventCriterion>

<checkPointCode code="E"/>

<timePointEventCriterion classCode="OBS" moodCode="CRT">
<code code="CXXXXXX" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
</timePointEventCriterion>

<value xsi:type="ED">Dose Escalation to 40mg on Day 3 unless limited by as AE or excessive hypotension</value>

<!-- TAETORD. Can we rely on this being an integer? No, we cannot, the sample has 2.2. -->

<sequenceNumber>
<value="22"/>
</sequenceNumber>

<armReference>
<id nullFlavor="NI" extension="1"/>
</armReference>

<armReference>
<id nullFlavor="NI" extension="2"/>
</armReference>

<armReference>
<id nullFlavor="NI" extension="2"/>
</armReference>

we rely on this being an integer? No, we cannot, the sample has 2.2. -->

classCode="ACT" moodCode="DEF">

nullFlavor="NI" extension="2"/>

<epochReference>
<id nullFlavor="NI" extension="2"/>
</epochReference>

<epochReference>
<id nullFlavor="NI" extension="1"/>
</epochReference>

<sequenceNumber>
<value="22"/>
</sequenceNumber>

<armReference>
<id nullFlavor="NI" extension="1"/>
</armReference>

<armReference>
<id nullFlavor="NI" extension="2"/>
</armReference>

<componentOf1 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf1>

<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf2>

<componentOf1 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf1>

<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf2>

<componentOf1 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf1>

<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf2>

<componentOf1 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf1>

<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf2>

<componentOf1 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf1>

<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf2>

<componentOf1 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf1>

<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf2>

<componentOf1 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf1>

<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf2>

<componentOf1 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf1>

<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf2>

<componentOf1 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf1>

<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf2>

<componentOf1 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf1>

<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf2>

<componentOf1 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf1>

<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf2>

<componentOf1 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf1>

<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf2>

<componentOf1 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf1>

<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf2>

<componentOf1 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf1>

<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf2>

<componentOf1 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf1>

<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf2>

<componentOf1 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf1>

<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf2>

<componentOf1 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf1>

<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf2>

<componentOf1 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf1>

<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf2>

<componentOf1 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf1>

<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf2>

<componentOf1 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf1>

<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf2>

<componentOf1 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf1>

<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf2>

<componentOf1 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf1>

<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf2>

<componentOf1 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf1>

<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf2>

<componentOf1 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf1>

<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf2>

<componentOf1 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf1>

<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf2>

<componentOf1 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf1>

<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf2>

<componentOf1 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf1>

<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf2>

<componentOf1 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf1>

<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf2>

<componentOf1 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf1>

<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf2>

<componentOf1 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf1>

<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf2>

<componentOf1 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf1>

<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf2>

<componentOf1 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf1>

<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf2>

<componentOf1 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf1>

<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf2>

<componentOf1 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf1>

<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf2>

<componentOf1 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf1>

<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf2>

<componentOf1 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf1>

<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf2>

<componentOf1 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf1>

<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf2>

<componentOf1 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf1>

<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf2>

<componentOf1 typeCode="COMP">
<sequenceNumber value="22"/>
</componentOf1>

<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
classCode="CTTEVENT" moodCode="DEF">
  <id nullFlavor="NI"/>
  <code code="HWH1"/>
  <precondition>
    <code code="E"/>
    <timePointEventCriterion classCode="OBS" moodCode="CRT">
      <code code="CXXXXXX" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
      <!-- Indicate that the observation is a transition rule applying to the element's presence in an arm. -->
      <value xsi:type="ED" mediaType="text/plain">Dose Escalation to 40mg on Day 3 unless limited by as AE or excessive hypotension</value>
    </timePointEventCriterion>
  </precondition>
</component2>

<componentOf1 typeCode="COMP">
  <epochReference classCode="ACT" moodCode="DEF">
    <id nullFlavor="NI" extension="2"/>
  </epochReference>
</componentOf1>

<componentOf2 typeCode="COMP">
  <sequenceNumber value="22"/>
  <armReference classCode="ACT" moodCode="DEF">
    <id nullFlavor="NI" extension="2"/>
  </armReference>
</componentOf2>
</timePointEventDefinition>

<!-- XXXXXXXXXXXXXXXXXXXXXXXXXXX
Study Element Information
Element # 2
XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX
Study Element Information
Element # 2
XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX-->

<component4 typeCode="COMP">
  <timePointEventDefinition classCode="CTTEVENT">
    <id nullFlavor="UNK"/>
    <code code="HWH2" displayName="High Dose 40mg D3-14 E" codeSystem="1.22.3.4"/>
    <effectiveTime xsi:type="IVL_TS">
      <width value="12" unit="day"/>
    </effectiveTime>
    <precondition typeCode="PRCN">
      <checkpointCode code="B"/>
      <timePointEventCriterion/>
    </precondition>
  </timePointEventDefinition>
</component4>

moodCode="DEF">
  <id nullFlavor="UNK"/>
  <code code="HWH2" displayCode="High Dose 40mg D3-14 E" codeSystem="1.22.3.4"/>
  <effectiveTime xsi:type="IVL_TS">
    <width value="12" unit="day"/>
  </effectiveTime>
  <precondition typeCode="PRCN">
    <checkpointCode code="B"/>
    <timePointEventCriterion/>
  </precondition>
</component4>

classCode="OBS" moodCode="CRT">
  <id nullFlavor="UNK"/>
  <code code="HWH2" displayCode="High Dose 40mg D3-14 E" codeSystem="1.22.3.4"/>
  <effectiveTime xsi:type="IVL_TS">
    <width value="12" unit="day"/>
  </effectiveTime>
  <precondition typeCode="PRCN">
    <checkpointCode code="B"/>
    <timePointEventCriterion/>
  </precondition>
</component4>
Study Design Structured Document Implementation Guide

codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>

is an element performance rule. -->

mediaType="text/plain">First dose of Double Blind Dose Escalation</value>

<timePointEventCriterion>
<precondition typeCode="PRCN">
<checkpointCode code="E"/>
<timePointEventCriterion

classCode="OBS" moodCode="CRT">

is an element performance rule. -->

mediaType="text/plain">Prior to Randomized Washout dose start</value>

</timePointEventCriterion>
</precondition>
</timePointEventDefinition>

classCode="CTTEVENT" moodCode="DEF">

typeCode="PRCN">

code="X"/>

<timePointEventCriterion classCode="OBS" moodCode="CRT">

<code code="CXXXXXXX" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>

that the observation is a branching rule applying to the element's presence in an arm. -->

value xsi:type="ED" mediaType="text/plain">Randomization at the end of day 14: RW High Dose 40 mg E</value>

</timePointEventCriterion>
</precondition>
<componentOf1

typeCode="COMP">

classCode="ACT" moodCode="DEF">

nullFlavor="NI" extension="2"/>

<sequenceNumber>
<armReference

value="32"/>

classCode="ACT" moodCode="DEF">

nullFlavor="NI" extension="1"/>
Study Design Structured Document Implementation Guide

<component2 typeCode="COMP">
  <timePointEventDefinition classCode="CTTEVENT" moodCode="DEF">
    <id nullFlavor="NI"/>
    <code code="HWH2"/>
    <precondition typeCode="PRCN">
      <checkpointCode code="X"/>
      <timePointEventCriterion classCode="OBS" moodCode="CRT">
        <code code="CXXXXXX" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
        <!-- Indicate that the observation is a branching rule applying to the element's presence in an arm. -->
        <value xsi:type="ED" mediaType="text/plain">Randomization at the end of day 14. RW Placebo</value>
      </timePointEventCriterion>
    </precondition>
    <componentOf1 typeCode="COMP">
      <epochReference classCode="ACT" moodCode="DEF">
        <id nullFlavor="NI" extension="2"/>
      </epochReference>
    </componentOf1>
    <componentOf2 typeCode="COMP">
      <sequenceNumber value="32"/>
      <armReference classCode="ACT" moodCode="DEF">
        <id nullFlavor="NI" extension="2"/>
      </armReference>
    </componentOf2>
  </timePointEventDefinition>
</component2>

<!-- XXXXXXXXXXXXXXXXXXXXXXXXXXX
Study Element Information
Element # 3
XXXXXXXXXXXXXXXXXXXXXXXXXXXX-->

<component4 typeCode="COMP">
  <timePointEventDefinition classCode="CTTEVENT" moodCode="DEF">
    <id nullFlavor="UNK"/>
    <code code="HWL1" displayName="High Dose 10mg D1-2 E" codeSystem="1.22.3.4"/>
    <effectiveTime xsi:type="IVL_TS">
      <width value="2" unit="day"/>
    </effectiveTime>
    <precondition typeCode="PRCN">
      <checkpointCode code="B"/>
    </precondition>
  </timePointEventDefinition>
</component4>

<component2>
  <timePointEventDefinition classCode="CTTEVENT" moodCode="DEF">
    <id nullFlavor="NI"/>
    <code code="HWH2"/>
    <precondition typeCode="PRCN">
      <checkpointCode code="X"/>
      <timePointEventCriterion classCode="OBS" moodCode="CRT">
        <code code="CXXXXXX" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
        <!-- Indicate that the observation is a branching rule applying to the element's presence in an arm. -->
        <value xsi:type="ED" mediaType="text/plain">Randomization at the end of day 14. RW Placebo</value>
      </timePointEventCriterion>
    </precondition>
    <componentOf1 typeCode="COMP">
      <epochReference classCode="ACT" moodCode="DEF">
        <id nullFlavor="NI" extension="2"/>
      </epochReference>
    </componentOf1>
    <componentOf2 typeCode="COMP">
      <sequenceNumber value="32"/>
      <armReference classCode="ACT" moodCode="DEF">
        <id nullFlavor="NI" extension="2"/>
      </armReference>
    </componentOf2>
  </timePointEventDefinition>
</component2>
</timePointEventDefinition>

<component4>
  <!-- XXXXXXXXXXXXXXXXXXXXXXXXXXX
  Study Element Information
  Element # 3
  XXXXXXXXXXXXXXXXXXXXXXXXXXXX
  -->
  <timePointEventDefinition classCode="CTTEVENT" moodCode="DEF">
    <id nullFlavor="UNK"/>
    <code code="HWL1" displayName="High Dose 10mg D1-2 E" codeSystem="1.22.3.4"/>
    <effectiveTime xsi:type="IVL_TS">
      <width value="2" unit="day"/>
    </effectiveTime>
    <precondition typeCode="PRCN">
      <checkpointCode code="B"/>
    </precondition>
  </timePointEventDefinition>
</component4>
codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>

is a performance rule.  

mediaType="text/plain">First dose of Double Blind medication</value>

<timePointEventCriterion>
<precondition>
<precondition typeCode="PRCN">
<checkpointCode code="E"/>
<timePointEventCriterion>

classCode="OBS" moodCode="CRT">
<codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>

is a performance rule.  

mediaType="text/plain">Prior to Dose Escalation Start</value>

<timePointEventCriterion>
<precondition>
<precondition typeCode="PRCN">
<checkpointCode code="E"/>
<timePointEventCriterion>

classCode="CTTEVENT" moodCode="DEF">

typeCode="PRCN">

code="E"/>

<timePointEventCriterion classCode="OBS" moodCode="CRT">
<code code="CXXXXXX" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>

that the observation is a transition rule applying to the element's presence in an arm.  

xsi:type="ED" mediaType="text/plain">Dose escalation to 20mg on Day 3 unless limited by as AE or excessive hypotension</value>

</timePointEventCriterion>

typeCode="COMP">

classCode="ACT" moodCode="DEF">

nullFlavor="NI" extension="2"/>

<sequenceNumber value="21"/>

classCode="ACT" moodCode="DEF">

nullFlavor="NI" extension="1"/>
classCode="CTTEVENT" moodCode="DEF">
<id nullFlavor="NI"/>
<code code="HWL1"/>
<precondition>
<checkpointCode code="E"/>
<timePointEventCriterion classCode="OBS" moodCode="CRT">
<code code="CXXXXXX" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
<!-- Indicate that the observation is a transition rule applying to the element's presence in an arm. -->
value xsi:type="ED" mediaType="text/plain">Dose escalation to 20mg on Day 3 unless limited by an AE or excessive hypotension</value>
</timePointEventCriterion>
</precondition>
classCode="ACT" moodCode="DEF">
<sequenceNumber value="21"/>
<armReference>
<id nullFlavor="NI" extension="2"/>
</armReference>
</timePointEventDefinition>
</component2>
</timePointEventDefinition>
</component4>
</timePointEventDefinition>
</component2>
</component4>
</timePointEventDefinition>
</component2>
</timePointEventDefinition>
</timePointEventDefinition>
</component4>
</timePointEventDefinition>
</component2>
</timePointEventDefinition>
</component4>
</timePointEventDefinition>
</component2>
</timePointEventDefinition>
</timePointEventDefinition>
</component4>
</timePointEventDefinition>
</component2>
</timePointEventDefinition>
</timePointEventDefinition>
</component4>
</timePointEventDefinition>
<id nullFlavor="UNK"/>
code code="HWL2" displayName="High Dose"
<effectiveTime xsi:type="IVL_TS">
<width value="12" unit="day"/>
</effectiveTime>
<precondition typeCode="PRCN">
<checkpointCode code="B"/>
<timePointEventCriterion classCode="OBS" moodCode="CRT">
<code code="CXXXXXX" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
<!-- Indicate that the observation is an element performance rule. -->
<value xsi:type="ED" mediaType="text/plain">First dose of Double Blind medication</value>
</timePointEventCriterion>

<timePointEventCriterion classCode="OBS" moodCode="CRT">
<code code="CXXXXXX" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
<!-- Indicate that the observation is an element performance rule. -->
<value xsi:type="ED" mediaType="text/plain">Prior to Randomized Washout dose Start</value>
</timePointEventCriterion>

<timePointEventDefinition classCode="CTTEVENT" moodCode="DEF">
<id nullFlavor="NI"/>
<code code="HWL2"/>
<precondition typeCode="PRCN">
<checkpointCode code="X"/>
<timePointEventCriterion classCode="OBS" moodCode="CRT">
<code code="CXXXXXX" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
<!-- Indicate that the observation is a branching rule applying to the element's presence in an arm. -->
<value xsi:type="ED" mediaType="text/plain">Randomization at the end of day 14: RW High Dose 20mg E</value>
</timePointEventCriterion>
</precondition>
</timePointEventDefinition>

<timePointEventCriterion classCode="OBS" moodCode="CRT">
<code code="CXXXXXX" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
<!-- Indicate that the observation is an element performance rule. -->
<value xsi:type="ED" mediaType="text/plain">Prior to Randomized Washout dose Start</value>
</timePointEventCriterion>

<timePointEventDefinition classCode="CTTEVENT" moodCode="DEF">
<id nullFlavor="NI"/>
<code code="HWL2"/>
<precondition typeCode="PRCN">
<checkpointCode code="X"/>
<timePointEventCriterion classCode="OBS" moodCode="CRT">
<code code="CXXXXXX" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
<!-- Indicate that the observation is a branching rule applying to the element's presence in an arm. -->
<value xsi:type="ED" mediaType="text/plain">Randomization at the end of day 14: RW High Dose 20mg E</value>
</timePointEventCriterion>
</precondition>
</timePointEventDefinition>

<timePointEventCriterion classCode="OBS" moodCode="CRT">
<code code="CXXXXXX" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
<!-- Indicate that the observation is an element performance rule. -->
<value xsi:type="ED" mediaType="text/plain">Prior to Randomized Washout dose Start</value>
</timePointEventCriterion>

<timePointEventDefinition classCode="CTTEVENT" moodCode="DEF">
<id nullFlavor="NI"/>
<code code="HWL2"/>
<precondition typeCode="PRCN">
<checkpointCode code="X"/>
<timePointEventCriterion classCode="OBS" moodCode="CRT">
<code code="CXXXXXX" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
<!-- Indicate that the observation is a branching rule applying to the element's presence in an arm. -->
<value xsi:type="ED" mediaType="text/plain">Randomization at the end of day 14: RW High Dose 20mg E</value>
</timePointEventCriterion>
</precondition>
</timePointEventDefinition>

<timePointEventCriterion classCode="OBS" moodCode="CRT">
<code code="CXXXXXX" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
<!-- Indicate that the observation is an element performance rule. -->
<value xsi:type="ED" mediaType="text/plain">Prior to Randomized Washout dose Start</value>
</timePointEventCriterion>

<timePointEventDefinition classCode="CTTEVENT" moodCode="DEF">
<id nullFlavor="NI"/>
<code code="HWL2"/>
<precondition typeCode="PRCN">
<checkpointCode code="X"/>
<timePointEventCriterion classCode="OBS" moodCode="CRT">
<code code="CXXXXXX" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
<!-- Indicate that the observation is a branching rule applying to the element's presence in an arm. -->
<value xsi:type="ED" mediaType="text/plain">Randomization at the end of day 14: RW High Dose 20mg E</value>
</timePointEventCriterion>
</precondition>
</timePointEventDefinition>
Study Element Information
Element # 5

1.25mg D1-2 codeSystem="1.22.3.4"
<timePointEventCriterion classCode="OBS" moodCode="CRT">
  codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
  is an element performance rule. -->
  mediaType="text/plain">First dose of Double Blind medication</value>
</timePointEventCriterion>

<timePointEventCriterion classCode="OBS" moodCode="CRT">
  codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
  is an element performance rule. -->
  mediaType="text/plain">Prior to Dose Escalation Start</value>
</timePointEventCriterion>

<timePointEventDefinition classCode="CTTEVENT" moodCode="DEF">
  <id nullFlavor="NI"/>
  <code code="LWH1"/>
  <precondition typeCode="PRCN"> checkpointCode code="E"/>
  <timePointEventCriterion classCode="OBS" moodCode="CRT">
    code="CXXXXXX" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
    <!-- Indicate that the observation is an element performance rule. -->
    <value xsi:type="ED" mediaType="text/plain">Dose escalation to 1.25mg on Day 3 unless limited by as AE or excessive hypotension</value>
  </timePointEventCriterion>
</timePointEventDefinition>

<epochReference classCode="ACT" moodCode="DEF">
  <id nullFlavor="NI" extension="2"/>
</epochReference>

<componentOf1 typeCode="COMP">
  <sequenceNumber value="22"/>
  <armReference classCode="ACT" moodCode="DEF">
  <componentOf1 typeCode="COMP">
  <epochReference classCode="ACT" moodCode="DEF">
  <id nullFlavor="NI" extension="2"/>
</epochReference>

<componentOf2 typeCode="COMP">
  <sequenceNumber value="22"/>
  <armReference classCode="ACT" moodCode="DEF">

nullFlavor="NI" extension="3"/>

<timePointEventDefinition>
<id nullFlavor="NI"/>
<code code="LWH1"/>
<precondition typeCode="PRCN">}
code="E"/>
<timePointEventCriterion classCode="OBS" moodCode="CRT">
<code code="CXXXXXX" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
<!-- Indicate that the observation is a transition rule applying to the element's presence in an arm. -->
<value xsi:type="ED" mediaType="text/plain">Dose escalation to 1.25mg on Day 3 unless limited by as AE or excessive hypotension</value>
</timePointEventCriterion>
</precondition>
<componentOf1 typeCode="COMP">
<epochReference classCode="ACT" moodCode="DEF">
:id nullFlavor="NI" extension="2"/>
</epochReference>
</componentOf1>
<componentOf2 typeCode="COMP">
<sequenceNumber value="22"/>
<armReference classCode="ACT" moodCode="DEF">
:id nullFlavor="NI" extension="4"/>
</armReference>
</componentOf2>
</timePointEventDefinition>
</timePointEventDefinition>

<!-- XXXXXXXXXXXXXXXXXXXXXXXXXXX
Study Element Information
Element # 6
XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX
Study Element Information
Element # 6
XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX-->
<component4 typeCode="COMP">
<moodCode="DEF ">
1.25mg D3-14E" codeSystem="1.22.3.4"/>
First dose of Double Blind medication

Prior to Randomized Washout dose Start

Randomization at the end of day 14: Lowe Dose 1.25mg
Study Design Structured Document Implementation Guide

classCode="ACT" moodCode="DEF">
<armReference>
<id
nullFlavor="NI" extension="3"/>

</armReference>
</componentOf2>
</timePointEventDefinition>
</component2>
</timePointEventDefinition>
</component4>
<!-- XXXXXXXXXXXXXXXXXXXXXXXXX
Study visit Information
XXXXXXXXXXXXXXXXXXXXXXXXX-->
<!-- Visit #1 -->
<component4 typeCode="COMP">
<timePointEventDefinition classCode="CTTEVENT" moodCode="DEF">
<id nullFlavor="NI"/>
<code code="LWH2"/>
<precondition typeCode="PRCN">
<checkpointCode code="X"/>
<timePointEventCriterion classCode="OBS" moodCode="CRT">
<code code="CXXXXXX" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
<!-- Indicate that the observation is a branching rule applying to the element's presence in an arm. -->
<xsi:type="ED" mediaType="text/plain">randomization at the end of day 14: RW Placebo</value>
</timePointEventCriterion>
</precondition>
<componentOf1 typeCode="COMP">
<epochReference classCode="ACT" moodCode="DEF">
<id
nullFlavor="NI" extension="2"/>
</epochReference>
</componentOf1>
<componentOf2 typeCode="COMP">
<sequenceNumber value="32"/>
<armReference classCode="ACT" moodCode="DEF">
<id
nullFlavor="NI" extension="4"/>
</armReference>
</componentOf2>
</timePointEventDefinition>
</component4>
<!-- We need a code for visit in the code system. -->
is not needed because there is no arm referred to.

```xml
<component2 typeCode="COMP">
  <timePointEventDefinition classCode="CTTEVENT" moodCode="DEF">
    <id nullFlavor="UNK" extension="1"/>
    <precondition typeCode="PRCN">
      <checkpointCode code="B"/>
      <timePointEventCriterion classCode="OBS" moodCode="CRT">
        <code codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
        <!-- Indicate that the observation is a visit performance rule applying to the visit's presence in an arm. -->
        <value xsi:type="ED" mediaType="text/plain">Days prior to Double Blind Randomization</value>
      </timePointEventCriterion>
      <precondition typeCode="PRCN">
        <checkpointCode code="E"/>
        <timePointEventCriterion classCode="OBS" moodCode="CRT">
          <code codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
          <!-- Indicate that the observation is a visit performance rule applying to the visit's presence in an arm. -->
          <value xsi:type="ED" mediaType="text/plain">Prior to first dose of Double Blind Randomization</value>
        </timePointEventCriterion>
      </precondition>
    </precondition>
    <componentOf2 typeCode="COMP" xsi:nil="true"/>
  </timePointEventDefinition>
</component2>
```

As noted, the ARM designation is blank. -->

```xml
<timePointEventDefinition classCode="OBS" moodCode="EVN">
  <code codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
  <!-- Planned Study Day -->
  <value xsi:type="INT" value="-7"/>
</timePointEventDefinition>
```

<!-- Study visit Information -->

```xml
<subjectOf typeCode="SUBJ">
  <timePointEventCharacteristic classCode="OBS" moodCode="EVN">
    <code code="C83450"/>
    <!-- VISITDY -->
    <value xsi:type="INT" value="-7"/>
  </timePointEventCharacteristic>
</subjectOf>
```

41
<timePointEventDefinition classCode="CTTEVENT" moodCode="DEF">
    <id nullFlavor="UNK" extension="3"/>
    <code code="Visit" codeSystem="1.22.3.4"/>
    <title mediaType="text/plain">Day 3</title>
</timePointEventDefinition>

<component2 typeCode="COMP">
    <timePointEventDefinition classCode="CTTEVENT" moodCode="DEF">
        <id nullFlavor="UNK" extension="3"/>
        <precondition typeCode="PRCN">
            <checkpointCode code="B"/>
            <timePointEventCriterion classCode="OBS" moodCode="CRT">
                <code code="C83450" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
                <value xsi:type="INT" value="3"/>
            </timePointEventCriterion>
        </precondition>
        <precondition typeCode="PRCN">
            <checkpointCode code="E"/>
            <timePointEventCriterion classCode="OBS" moodCode="CRT">
                <code code="C83450" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
                <value xsi:type="INT" value="3"/>
            </timePointEventCriterion>
        </precondition>
    </timePointEventDefinition>

    <subjectOf typeCode="SUBJ">
        <timePointEventCharacteristic classCode="OBS" moodCode="EVN">
            <code code="C83450" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
            <value xsi:type="INT" value="3"/>
        </timePointEventCharacteristic>
    </subjectOf>
</component2>
<timePointEventDefinition classCode="CTTEVENT" moodCode="DEF">
  <id nullFlavor="UNK" extension="4"/>
  <code code="Visit" codeSystem="1.22.3.4"/>
  <title mediaType="text/plain">Day 7</title>
  <!-- XXXXXXXXXXXXXXXXXXXXX
  Visit within Arm Information
  XXXXXXXXXXXXXXXXXXXXXXXXXXX-->
  <component2 typeCode="COMP">
    <timePointEventDefinition classCode="CTTEVENT" moodCode="DEF">
      <id nullFlavor="UNK" extension="3"/>
      <precondition typeCode="PRCN">
        <checkpointCode code="B"/>
        <timePointEventCriterion classCode="OBS" moodCode="CRT">
          <code code="CXXXXXX" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
          <value xsi:type="ED" mediaType="text/plain">The 7th day after visit 2 (Day 1)</value>
        </timePointEventCriterion>
        <precondition typeCode="PRCN">
          <checkpointCode code="E"/>
          <timePointEventCriterion classCode="OBS" moodCode="CRT">
            <code code="CXXXXXX" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
            <value xsi:type="ED" mediaType="text/plain">6 days after visit 2 (Day 1)</value>
          </timePointEventCriterion>
        </precondition>
      </precondition>
    </timePointEventDefinition>
  </component2>
  <subjectOf typeCode="SUBJ">
    <timePointEventCharacteristic classCode="OBS" moodCode="EVN">
      <code code="C83450" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
      <!-- Planned Study Day -->
      <value xsi:type="INT" value="7"/>
    </timePointEventCharacteristic>
  </subjectOf typeCode="SUBJ">
</timePointEventDefinition>
<component typeCode="COMP">
  <timePointEventDefinition classCode="CTTEVENT" moodCode="DEF">
    <id nullFlavor="UNK" extension="5"/>
    <code code="Visit" codeSystem="1.22.3.4"/>
    <title mediaType="text/plain">Day 15</title>
    <!-- XXXXXXXXXXXXXXXXXXXXX
    Visit within Arm Information
    XXXXXXXXXXXXXXXXXXXXXXXXXXX-->
    <componentOf typeCode="COMP" xsi:nil="true"/>
  </timePointEventDefinition>
  <subjectOf typeCode="SUBJ">
    <timePointEventCharacteristic classCode="OBS" moodCode="EVN">
      <code code="C83450" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
      <!-- Planned Study Day -->
      <value xsi:type="INT" value="15"/>
    </timePointEventCharacteristic>
  </subjectOf>
  <timePointEventDefinition>
    <id nullFlavor="UNK"/>
    <precondition typeCode="PRCN">
      <checkpointCode code="B"/>
      <timePointEventCriterion classCode="OBS" moodCode="CRT">
        <code code="CXXXXXX" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
        <!-- Indicate that the observation is a visit performance rule applying to the visit's presence in an arm. -->
        <value xsi:type="ED" mediaType="text/plain">The 15th day after visit 2 (Day 1)</value>
      </timePointEventCriterion>
      <precondition typeCode="PRCN">
        <checkpointCode code="E"/>
        <timePointEventCriterion classCode="OBS" moodCode="CRT">
          <code code="CXXXXXX" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
          <!-- Indicate that the observation is a visit performance rule applying to the visit's presence in an arm. -->
          <value xsi:type="ED" mediaType="text/plain">14 days after visit 2 (Day 1)</value>
        </timePointEventCriterion>
      </precondition>
    </precondition>
    <typeCode="PRCN"/>
    <checkpointCode code="B"/>
    <timePointEventCriterion classCode="OBS" moodCode="CRT">
      <code code="CXXXXXX" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
      <!-- Indicate that the observation is a visit performance rule applying to the visit's presence in an arm. -->
      <value xsi:type="ED" mediaType="text/plain">The 15th day after visit 2 (Day 1)</value>
    </timePointEventCriterion>
    <precondition typeCode="PRCN">
      <checkpointCode code="E"/>
      <timePointEventCriterion classCode="OBS" moodCode="CRT">
        <code code="CXXXXXX" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
        <!-- Indicate that the observation is a visit performance rule applying to the visit's presence in an arm. -->
        <value xsi:type="ED" mediaType="text/plain">14 days after visit 2 (Day 1)</value>
      </timePointEventCriterion>
    </precondition>
    <!-- Study visit Information -->
    <xsi:type="ED" mediaType="text/plain">The 15th day after visit 2 (Day 1)</xsi:type>
  </timePointEventDefinition>
</component>
<component4 typeCode="COMP">
<timePointEventDefinition classCode="CTTEVENT" moodCode="DEF ">
  <id nullFlavor="UNK" extension="6"/>
  <title mediaType="text/plain">Day 22</title>
  <!-- XXXXXXXXXXXXXXXXXXXXX
  Visit within Arm Information
  XXXXXXXXXXXXXXXXXXXXXXXXXXX-->
  <component2 typeCode="COMP">
    <timePointEventDefinition classCode="CTTEVENT" moodCode="DEF ">
      <id nullFlavor="UNK" extension="3"/>
      <precondition typeCode="PRCN">
        <checkpointCode code="B"/>
        <timePointEventCriterion classCode="OBS" moodCode="CRT">
          <code code="CXXXXXX" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
          <!-- Indicate that the observation is a visit performance rule applying to the visit's presence in an arm. -->
          <value xsi:type="ED" mediaType="text/plain">The 22nd day after visit 2 (Day 1)</value>
        </timePointEventCriterion>
      </precondition>
      <precondition typeCode="PRCN">
        <checkpointCode code="E"/>
        <timePointEventCriterion classCode="OBS" moodCode="CRT">
          <code code="CXXXXXX" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
          <!-- Indicate that the observation is a visit performance rule applying to the visit's presence in an arm. -->
          <value xsi:type="ED" mediaType="text/plain">21 days after visit 2 (Day 1)</value>
        </timePointEventCriterion>
      </precondition>
      <componentOf2 typeCode="COMP" xsi:nil="true"/>
    </timePointEventDefinition>
    <!-- As noted, the ARM designation is blank. -->
  </component2>
</timePointEventDefinition>
</component4>
<value xsi:type="INT" value="22"/>
</timePointEventCharacteristic>
</subjectOf>
</timePointEventDefinition>
</component4>
<!-- Visit #7 -->
<component4 typeCode="COMP">
<timePointEventDefinition classCode="CTTEVENT" moodCode="DEF ">
<id nullFlavor="UNK" extension="7"/>
<code code="Visit" codeSystem="1.22.3.4"/>
<title mediaType="text/plain">Day 29 OR EARLY WITHDRAWAL</title>
<!-- XXXXXXXXXXXXXXXXXXXXX
Visit within Arm Information
XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX-->
<component2 typeCode="COMP">
<timePointEventDefinition classCode="CTTEVENT" moodCode="DEF ">
<id nullFlavor="UNK" extension="3"/>
<precondition typeCode="PRCN">
<checkpointCode code="B"/>
<timePointEventCriterion classCode="OBS" moodCode="CRT">
<code code="C" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
<!-- Indicate that the observation is a visit performance rule applying to the visit's presence in an arm. -->
<xsi:type="ED" mediaType="text/plain">The 29th day after visit 2 (Day 1)</xsi:type>
</timePointEventCriterion>
</precondition>
<precondition typeCode="PRCN">
<checkpointCode code="E"/>
<timePointEventCriterion classCode="OBS" moodCode="CRT">
<code code="C" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
<!-- Indicate that the observation is a visit performance rule applying to the visit's presence in an arm. -->
<xsi:type="ED" mediaType="text/plain">28 days after visit 2 (Day 1)</xsi:type>
</timePointEventCriterion>
</precondition>
</timePointEventDefinition>
</component2>
</component4>
<!-- Study visit Information -->
<subjectOf typeCode="SUBJ"/>
Study Design Structured Document Implementation Guide

classCode="OBS" moodCode="EVN">
<timePointEventCharacteristic>
<code code="C83450">
<!-- Planned Study Day -->

<value xsi:type="INT" value="29"/>
</timePointEventCharacteristic>
</subjectOf>
</timePointEventDefinition>
</component4>

<!-- XXXXXXXXXXXXXXXXXXXX
Study Summary Information
XXXXXXXXXXXXXXXXXXXXXXXX-->

<subjectOf typeCode="SUBJ">
<studyCharacteristic classCode="OBS" moodCode="EVN">
<code code="AGESPAN" displayName="Age Span" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>

<value xsi:type="ED">Pediatrics</value>
</studyCharacteristic>
</subjectOf>
<subjectOf typeCode="SUBJ">
<studyCharacteristic classCode="OBS" moodCode="EVN">
<code code="DESIGN" displayName="Description of Trial Design" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>

<value xsi:type="ED">Double-Blind Pediatrics randomized to low, middle, and high dose, Dose Escalation on Day 3, Randomize Washout on Day 14 to placebo or continued active treatment</value>
</studyCharacteristic>
</subjectOf>
<subjectOf typeCode="SUBJ">
<studyCharacteristic classCode="OBS" moodCode="EVN">
<code code="INDIC" displayName="Indication" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>

<value xsi:type="ED">Hypertensive Medication</value>
</studyCharacteristic>
</subjectOf>
<subjectOf typeCode="SUBJ">
<studyCharacteristic classCode="OBS" moodCode="EVN">
<code code="LENGTH" displayName="Trial Duration" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>

<value xsi:type="IVL_TS">
<width value="29" unit="day"/>
</value>
</studyCharacteristic>
</subjectOf>
<subjectOf typeCode="SUBJ">
<studyCharacteristic classCode="OBS" moodCode="EVN">
<code code="RANDOM" displayName="Randomized" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>

<value xsi:type="BL" value="true"/>
</studyCharacteristic>
</subjectOf>
</subjectOf>

48
<studyCharacteristic classCode="OBS" moodCode="EVN">
<code code="SEXPOP" display_name="Sex of Participants" codeSystem="1.22.3.3"/>
<value xsi:type="CD" code="CXXXXXX" display_name="Both" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
</studyCharacteristic>

<studyCharacteristic classCode="OBS" moodCode="EVN">
<code code="TBLIND" display_name="Trial Blinding Schema" codeSystem="1.22.3.3"/>
<value xsi:type="CD" code="CXXXXX" display_name="DOUBLE BLIND" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
</studyCharacteristic>

<studyCharacteristic classCode="OBS" moodCode="EVN">
<code code="TBLIND" display_name="Trial Blinding Schema" codeSystem="1.22.3.3"/>
<value xsi:type="CD" code="CXXXXX" display_name="RANDOMIZED WASHOUT" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
</studyCharacteristic>

<studyCharacteristic classCode="OBS" moodCode="EVN">
<code code="TDIGRP" display_name="Diagnosis Group" codeSystem="1.22.3.3"/>
<value xsi:type="CD" code="CXXXXX" display_name="Subjects Diagnosis with Hypertensive Children" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
</studyCharacteristic>

<studyCharacteristic classCode="OBS" moodCode="EVN">
<code code="TINDTP" display_name="Trial Indication Type" codeSystem="1.22.3.3"/>
<value xsi:type="CD" code="CXXXXX" display_name="TREATMENT" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
</studyCharacteristic>

<studyCharacteristic classCode="OBS" moodCode="EVN">
<code code="TPHASE" display_name="Trial Phase Classification" codeSystem="1.22.3.3"/>
<value xsi:type="CD" code="CXXXXX" display_name="Phase 1 Trial" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
</studyCharacteristic>

<studyCharacteristic classCode="OBS" moodCode="EVN">
<code code="TRT" display_name="Reported Name of Test Product" codeSystem="1.22.3.3"/>
Study Design Structured Document Implementation Guide

mediaType="text/plain">DRUGA</value>
</studyCharacteristic>
</subjectOf>
<subjectOf typeCode="SUBJ">
<studyCharacteristic classCode="OBS">
<moodCode="EVN">
<code code="TTYPE" displayName="Trial Type" codeSystem="1.22.3.3"/>
<value xsi:type="CD" code="CXXXXX" displayName="SAFETY" codeSystem="2.16.840.1.113883.3.26.1.1" codeSystemName="NCI Thesaurus"/>
</studyCharacteristic>
</subjectOf>
</subjectOf typeCode="SUBJ">
<studyCharacteristic classCode="OBS">
<moodCode="EVN">
<code code="WTSPAN" displayName="Weight Span" codeSystem="1.22.3.3"/>
<!-- Note, the code does not appear on the list I have published in the SDTM IG. -->
<value xsi:type="IVL_PQ" inclusive="false">
<low value="50" unit="kg"/>
</value>
</studyCharacteristic>
</subjectOf>
</subjectOf typeCode="SUBJ">
<studyCharacteristic classCode="OBS">
<moodCode="EVN">
<code code="WTSPAN" displayName="Weight Span" codeSystem="1.22.3.3"/>
<!-- Note, the code does not appear on the list I have published in the SDTM IG. -->
<value xsi:type="IVL_PQ" inclusive="true">
<high value="50" unit="kg"/>
</value>
</studyCharacteristic>
</subjectOf>
</subjectOf typeCode="SUBJ">
<studyCharacteristic classCode="OBS">
<moodCode="EVN">
<code code="WTSPAN" displayName="Weight Span" codeSystem="1.22.3.3"/>
<!-- Note, the code does not appear on the list I have published in the SDTM IG. -->
</value>
</studyCharacteristic>
</subjectOf>
</subjectOf typeCode="SUBJ">
<studyCharacteristic classCode="OBS">
<moodCode="EVN">
<code code="WTSPAN" displayName="Weight Span" codeSystem="1.22.3.3"/>
<!-- Note, the code does not appear on the list I have published in the SDTM IG. -->
</value>
</studyCharacteristic>
</subjectOf>
</subjectOf typeCode="SUBJ">
<studyCharacteristic classCode="OBS">
<!-- XXXXXXXXXXXXXXXXXXXXX 
Inclusion/Exclusion Information 
The sample data set does not include any. 
XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX -->
</plannedStudy>
</section>
</component>
</structuredBody>
</component>
</Document>