Proposal for SPL Release 2

Scope and Content

Document Revision 1.39

Gunther Schadow

Regenstrief Institute, Inc.

1 Introduction

1.1 Purpose

The purpose of this document is to set a basis for discussion of further SPL developments. This is not the specification draft itself but an explanation what material such draft might contain, what changes and what additions from the previous release 1 of SPL might be committed to the specification draft.

1.2 Scope

The scope of further SPL development at this time is set by the U.S. Food and Drug Authority (FDA) in its mission to support existing and future drug labeling and drug listing regulations in the U.S. The most important scope-setter for major current SPL development is the so called "Physicians' Labeling Rule," that was announced as NPRM in 2000 and for which the release of the final rule is now imminent.

This document primarily discussed information model updates rather than Narrative Block updates which are assumed to be handled through HL7 SDTC (CDA).

1.3 Approach

The approach of this document is to show the continuity between the present release of SPL and the next release. We begin with a recount of the status quo in terms of information model diagrams and then discuss how these might be further developed. We further break the SPL specification up into the features of SPL as a document specification on the one hand and SPL as a structured drug-knowledge specification on the other hand.

As a general principle, this proposal for SPL release 2 is cast as an extension of SPL release 1 such that present SPL content would not have to change. A few minor changes have been found necessary through the work of the SPL Implementation Guide and pilot project. Finally, since the work on SPL release 1 was completed the work of the Pharmacy SIG of the Orders and Observations Technical Committee in HL7, who has primary responsibility for defining medication-related information models in HL7, has progressed, this proposal entertains the possibility of a few (generally insubstantial) changes to improve the alignment between the two work specifications.

2 SPL v1 – Status Quo

In this section we quickly present the status quo of SPL. This is mainly done as a convenience to the reader, but also in order to familiarize the reader with a changed layout of the information models such that reading the proposed extended models will be easier.

2.1 Overview

The following diagram is all of SPL v1. This diagram is very small and may not be suitable for detailed reading. The reader should not be worried about this but only focus on the general impression. If this document is read in color the reader will immediately see three regions in this diagram: a mostly red area in the center with a small blue, yellow and green are on the left, and finally a larger yellow and green area covering almost the entire right half of the diagram.
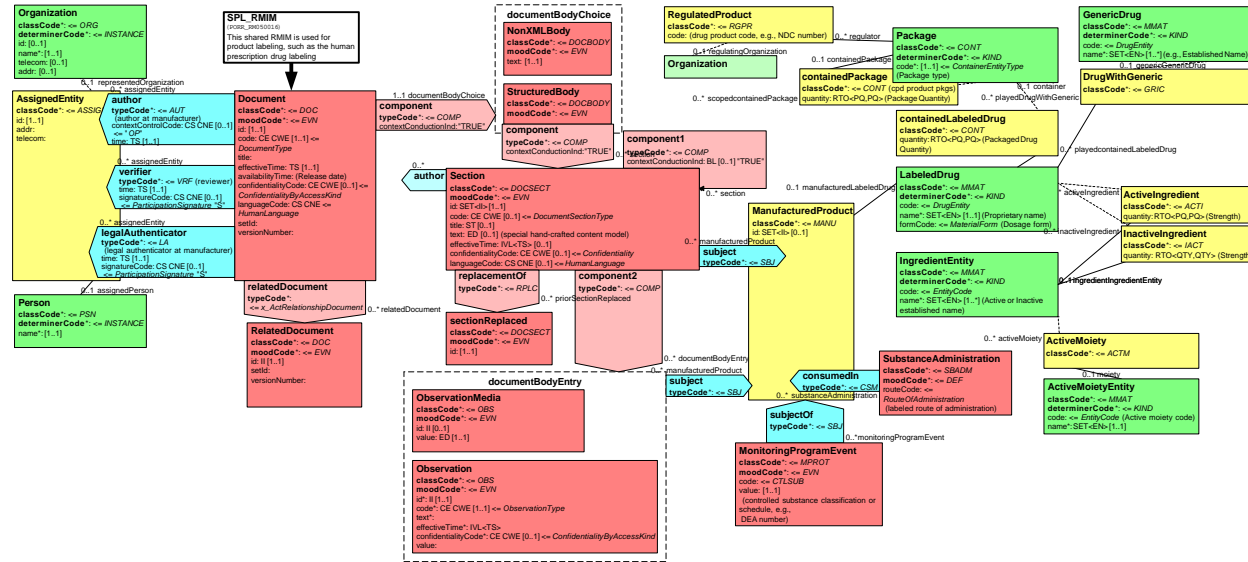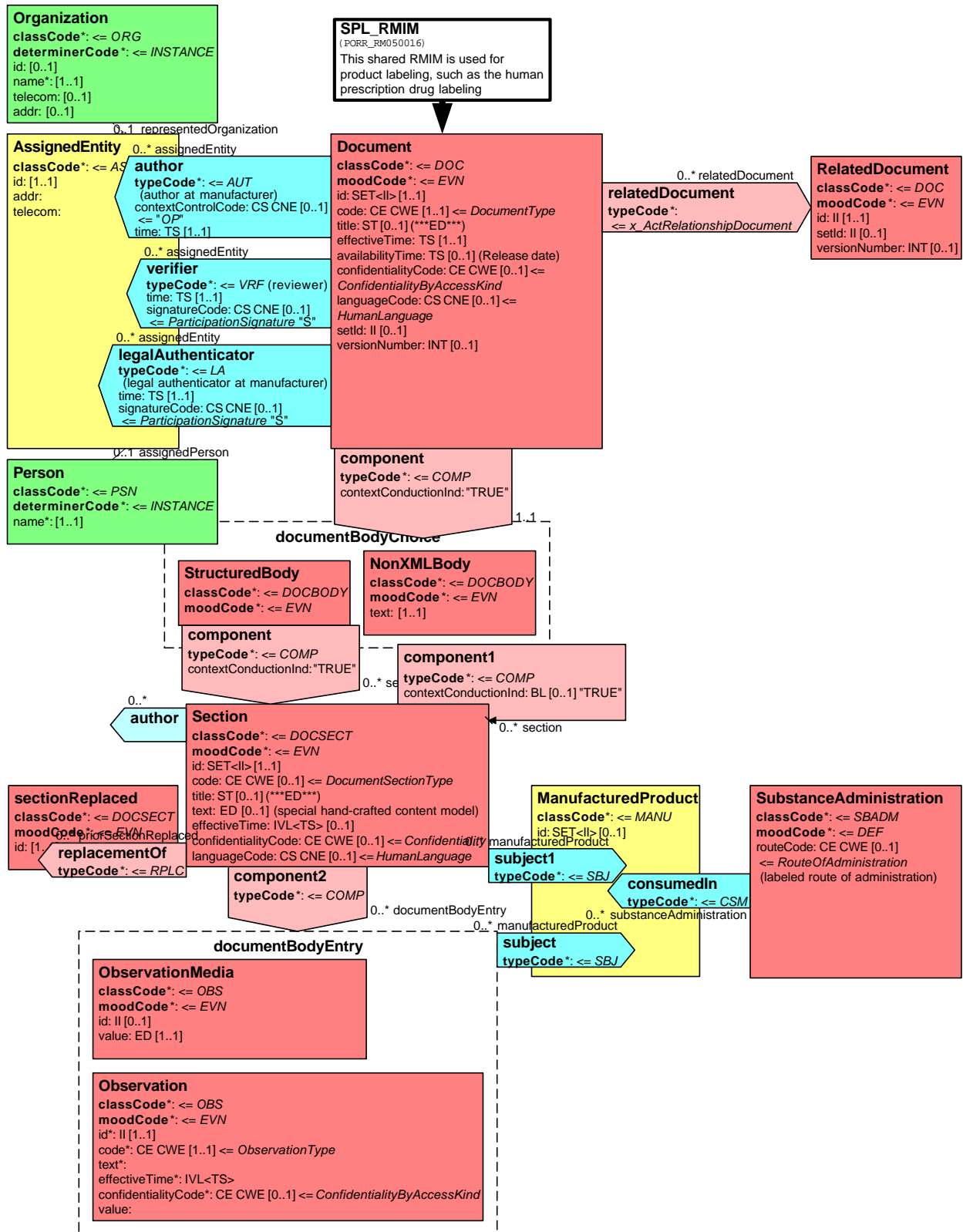
The right half contains the structured information that in SPL 1 covers mostly drug-description and drug listing information. Since this information details the product as a material with ingredients and packaging, most of this model is made up of Entities (green) and Roles (yellow). Conversely the left half of the diagram is about Documents and Sections, which in HL7 are modeled as Acts (red). The small blue yellow and green area on the far left is about document authors and other participants.

The SPL documents themselves consist of a substantial amount of free text. This text is assigned to the Section.text attributes in this information mode. The text is marked up according to the CDA "Narrative Block" schema. Motivated by the needs of the SPL Implementation Guide and pilot team, the Structured Document Technical Committee (SDTC) of HL7 has decided to make some changes and additions to the Narrative Block schema. These modifications are not being discussed in this document.

2.2 Document Model

The document model is about a product label as a Document that contains Sections. The document has authors and other participants. This structure is entirely borrowed from the HL7 Clinical Document Architecture. The only SPL specific modifications to the CDA document model are the removal of patient information (which would have no purpose in SPL) and the difference in structured data. In CDA the structured content is called "entries" and consists of clinical information about patients. Conversely in SPL the structured content is entirely different. In SPL 1 the structured content was mainly a "LabeledDrug" Entity as a ManufacturedProduct

(even though a manufacturer wasn't actually specified for it. This content is linked to the Section as the "subject" of the Section. Another kind of structured content – again borrowed from CDA – are characteristics (Observation) of the drug such as color, shape, scoring, etc.

Organization
classCode* <= ORG
determinerCode* <= INSTANCE
id: [0..1]
name*: [1..1]
telecom: [0..1]
addr: [0..1]

SPL_RMIM
(PORR_RM050016)
This shared RMIM is used for product labeling, such as the human prescription drug labeling

0..1 representedOrganization

AssignedEntity
classCode* <= AS
id: [1..1]
addr:
telecom:

0..* assignedEntity

author
typeCode* <= AUT
(author at manufacturer)
contextControlCode: CS CNE [0..1] <= "OP"
time: TS [1..1]

0..* assignedEntity

verifier
typeCode* <= VRF (reviewer)
time: TS [1..1]
signatureCode: CS CNE [0..1] <= ParticipationSignature "S"

0..* assignedEntity

legalAuthenticator
typeCode* <= LA
(legal authenticator at manufacturer)
time: TS [1..1]
signatureCode: CS CNE [0..1] <= ParticipationSignature "S"

Document
classCode* <= DOC
moodCode* <= EVN
id: SET<II> [1..1]
code: CE CWE [1..1] <= DocumentType
title: ST [0..1] (***ED***)
effectiveTime: TS [1..1]
availabilityTime: TS [0..1] (Release date)
confidentialityCode: CE CWE [0..1] <= ConfidentialityByAccessKind
languageCode: CS CNE [0..1] <= HumanLanguage
setId: II [0..1]
versionNumber: INT [0..1]

0..* relatedDocument

relatedDocument
typeCode*:
<= x_ActRelationshipDocument

0..* relatedDocument

RelatedDocument
classCode* <= DOC
moodCode* <= EVN
id: II [1..1]
setId: II [0..1]
versionNumber: INT [0..1]

component
typeCode* <= COMP
contextConductionInd: "TRUE"

0..1 assignedPerson

Person
classCode* <= PSN
determinerCode* <= INSTANCE
name*: [1..1]

1..1

documentBodyChoice

StructuredBody
classCode* <= DOCBODY
moodCode* <= EVN

NonXMLBody
classCode* <= DOCBODY
moodCode* <= EVN
text: [1..1]

component
typeCode* <= COMP
contextConductionInd: "TRUE"

component1
typeCode* <= COMP
contextConductionInd: BL [0..1] "TRUE"

0..* se

0..* section

0..*

author

Section
classCode* <= DOCSECT
moodCode* <= EVN
id: SET<II> [1..1]
code: CE CWE [0..1] <= DocumentSectionType
title: ST [0..1] (***ED***)
text: ED [0..1] (special hand-crafted content model)
effectiveTime: IVL<TS> [0..1]
confidentialityCode: CE CWE [0..1] <= Confidentiality
languageCode: CS CNE [0..1] <= HumanLanguage

sectionReplaced
classCode* <= DOCSECT
moodCode* <= EVN
id: [1..

0..* priorSectionReplaced

replacementOf
typeCode* <= RPLC

ManufacturedProduct
classCode* <= MANU
id: SET<II> [0..1]

SubstanceAdministration
classCode* <= SBADM
moodCode* <= DEF
routeCode: CE CWE [0..1] <= RouteOfAdministration
(labeled route of administration)

manufacturedProduct

subject1
typeCode* <= SBJ

consumedIn
typeCode* <= CSM

0..* substanceAdministration

component2
typeCode* <= COMP

0..* documentBodyEntry

0..* manufacturedProduct

subject
typeCode* <= SBJ

documentBodyEntry

ObservationMedia
classCode* <= OBS
moodCode* <= EVN
id: II [0..1]
value: ED [1..1]

Observation
classCode* <= OBS
moodCode* <= EVN
id*: II [1..1]
code*: CE CWE [1..1] <= ObservationType
text*:
effectiveTime*: IVL<TS>
confidentialityCode*: CE CWE [0..1] <= ConfidentialityByAccessKind
value:

2.3   Structured Information Model

The SPL release 1 structured information model is shown in the following diagram.

RegulatedProduct
classCode*: <= *RGPR*
code: CE CWE [0..1] (drug product code, e.g., NDC number)

0..* regulator

GenericDrug
classCode*: <= *MMAT*
determinerCode*: <= *KIND*
code: CE CWE [0..1] <= *DrugEntity*
name*: BAG<EN> [1..*]
((e.g., Established Name)

0..1 genericGenericDrug

DrugWithGeneric
classCode*: <= *GRIC*

containedPackage
classCode*: <= *CONT*
(cpd product pkgs)
quantity: RTO<PQ,PQ> [0..1] (Package Quantity)

0..* scopedcontainedPackage   0..* playedDrugWithGeneric

0..1 containedPackage
0..1 container

Package
classCode*: <= *CONT*
determinerCode*: <= *KIND*
code*: CE CWE [1..1] <= *ContainerEntityType* (Package type)

LabeledDrug
classCode*: <= *MMAT*
determinerCode*: <= *KIND*
code: CE CWE [0..1] <= *DrugEntity*
name*: BAG<EN> [1..1] (Proprietary name)
formCode: CE CWE [0..1] <= *MaterialForm* (Dosage form)

IngredientEntity
classCode*: <= *MMAT*
determinerCode*: <= *KIND*
code: CE CWE [0..1] <= *EntityCode*
name*: BAG<EN> [1..*]
(Active or Inactive established name)

ActiveMoietyEntity
classCode*: <= *MMAT*
determinerCode*: <= *KIND*
code: CE CWE [0..1] <= *EntityCode*
(Active moiety code)
name*: BAG<EN> [1..1]

containedLabeledDrug
classCode*: <= *CONT*
quantity: RTO<PQ,PQ> [0..1] (Packaged Drug Quantity)

0..* playedcontainedLabeledDrug

0..1 manufacturedLabeledDrug   InactiveIngredientEntity

InactiveIngredient
classCode*: <= *IACT*

0..* inactiveIngredient
0..* inactiveIngredient

0..1 moiety

ActiveMoiety
classCode*: <= *ACTM*

0..* activeMoiety

SectionSubject
(UUDD_RMnnnnnn)
Description

ManufacturedProduct
classCode*: <= *MANU*
id: II [0..1]

ActiveIngredient
classCode*: <= *ACTI*
quantity: RTO<PQ,PQ> [0..1] (Strength)

0..* activeIngredient

subjectOf
typeCode*: <= *SBJ*

0..*monitoringProgramEvent

consumedIn
typeCode*: <= *CSM*

0..* substanceAdministration

MonitoringProgramEvent
classCode*: <= *MPROT*
moodCode*: <= *EVN*
code: <= *CTLSUB*
value: [1..1]
(controlled substance classification or schedule, e.g., DEA number)

SubstanceAdministration
classCode*: <= *SBADM*
moodCode*: <= *DEF*
routeCode: CE CWE [0..1] <= *RouteOfAdministration*
(labeled route of administration)

This part of the model is entered through the ManufacturedProduct role, which is a Role of the LabeledDrug Entity for which description and listing information is being provided. Active and Inactive ingredients are listed through the respective Roles. Packaged product information and NDC codes are given through the Package class.

2.4   Outstanding Issues

This is a summary of issues with the present SPL model that could be addressed in the forthcoming ballot aside from adding the extensions that are essential for SPL release 2.

Issue 1 – Product Characteristics: During the implementation guide and pilot phase the SPL team had to struggle with the fact that the drug characteristics (color, shape, scoring) were placed in a different area in the section and were not related at all to the product that is to be characterized.

Issue 2 – Titles: the Implementation Guide and pilot team found that Document titles need some markup. Since the SDTC has resolved to change the data types of the Act.title element from ST to ED subject to a pending RIM harmonization proposal.

Issue 3 – DEA Schedule: a ballot comment against SPL v1 concerning the MonitoringProgramEvent had been resolved by deferring the actual implementation to the Implementation Guide that has intentionally not made any use of this feature yet. The MonitoringProgramEvent was to be a method to assign the DEA schedule (controlled substance schedule) to the labeled drug. The point of the comment was that the use of an Observation in this form is conceptually wrong (DEA number would be Act.code not Observation.value). This

is being discussed in the Pharmacy SIG and probably can be resolved in a relatively minor change.

Issue 4 – Alignment with Pharmacy SIG: It is the purpose of the SPL release 2 to improve electronic prescribing. Therefore a close alignment of the SPL Medication model with the overall HL7 Medication model as created by the Pharmacy SIG is desirable. The two models are already relatively close and therefore some small insubstantial changes (possibly name changes) might be entertained.

Issue 5 – Combination Products: The present approach to combination products, or kits, is through the packaging structures. A kit with multiple drug products is represented as the kit being a LabeledDrug and the components of the kit also represented as LabeledDrugs. These components are then connected through the containedPackage role with the kit. For instance, Prevpac containing Prevacid and Trimox will be represented as Prevpac as a LabeledDrug without any ingredients but with a Packaging with NDC code for Prevpac which in turn has contained Packages for Prevacid and Trimox as individually packaged products. The problem with this approach is that it is assumed that the components of the kit are individually packaged (which in this example they are not).

Issue 6 – Package Code and NDC Code: The present approach uses Container.code to specify the general type of packaging (e.g., whether it is a box or a bottle). The NDC code for the packaged product hangs from the Package as a special Role "regulated product". The Pharmacy SIG has since determined that the RIM Class Container is assumed to stand for the combination of a Container with its Content (just as it is assumed in SPL), but that the Container.code should be the specific code for the Product in its Container (or "packaged product"). Furthermore, the kind of container should be specified in the Container.formCode attribute.

Issue 7 – Entity Names: the Entity.name attributes are taken unconstrained from the RIM as BAG<EN>, which is multiple names, each of which can have multiple name parts. This feature is mostly there for Person names with given and last names, maiden names, etc. For drugs, names would be unstructured, basically just strings. For this purpose the EN data type should be constrained to the TN (trivial name) type, which is simply a string. Also, while LabeledDrug (aka Medication) and ActiveMoietyEntity (aka, Moiety) have the multiplicity constrained to at most one name, IngredientEntity (aka. Substance) is allowed multiple names. This might also be constrained to at most 1 name.

Issue 8 – Mandatory Constraints: for SPL, or at least the FDA implementation of it, a lot more mandatory constraints could be added. Most all of the attributes could be turned to mandatory or at least required.

Issue 9 – Need the ability to communicate specific changes to a label. This was an outstanding ballot comment that was withdrawn on the promise that it would be addressed in next release of SPL. Presently the insert and delete tags in the NarrativeBlock allow to mark up changes from prior versions of a label, and there is the ability to reference prior revision of Sections and Documents.

One could argue that change management works as follows: labeler sends an updated SPL document. It references the unique document id of the prior version of the updated document, and within updated sections, will reference the unique section id of the prior version of the

section so updated. The insert and delete tags are used to show the actual changes to the text. It is unclear whether the SPL specification needs to change in order to support the use case or whether a clarification in the specification text might suffice.

Issue 10 – Need a way to place general annotations into the text to support negotiations.
Presently proprietary word-processor files are sent back and forth between the labeler and the agency to which comments and tracked changes are applied. A comment/annotation feature might be useful to avoid having to use proprietary word-processor files for negotiations that would have to be converted to SPL in a costly after-process that could potentially introduce errors and thus cause a prolonged negotiation.

Issue 11 – Need to supply literature reference as evidence for specific statements in the label. For example if you have a dosing statement such as 1 tablet every 12 hours, there would be text with a link that would take you to a dosing study that concludes the dosing should be 1 tablet every 12 hours. If SPL can be modified to accommodate annotations with links to other files, then a version of the SPL file we would submit could replace the need to generate a PDF with extra space in the margins to accommodate the annotations.

3   SPL v2 – Quo Vadis?

The proposed changes for SPL release 2 are presented first regarding SPL as Document and then regarding SPL as a Drug Information model.
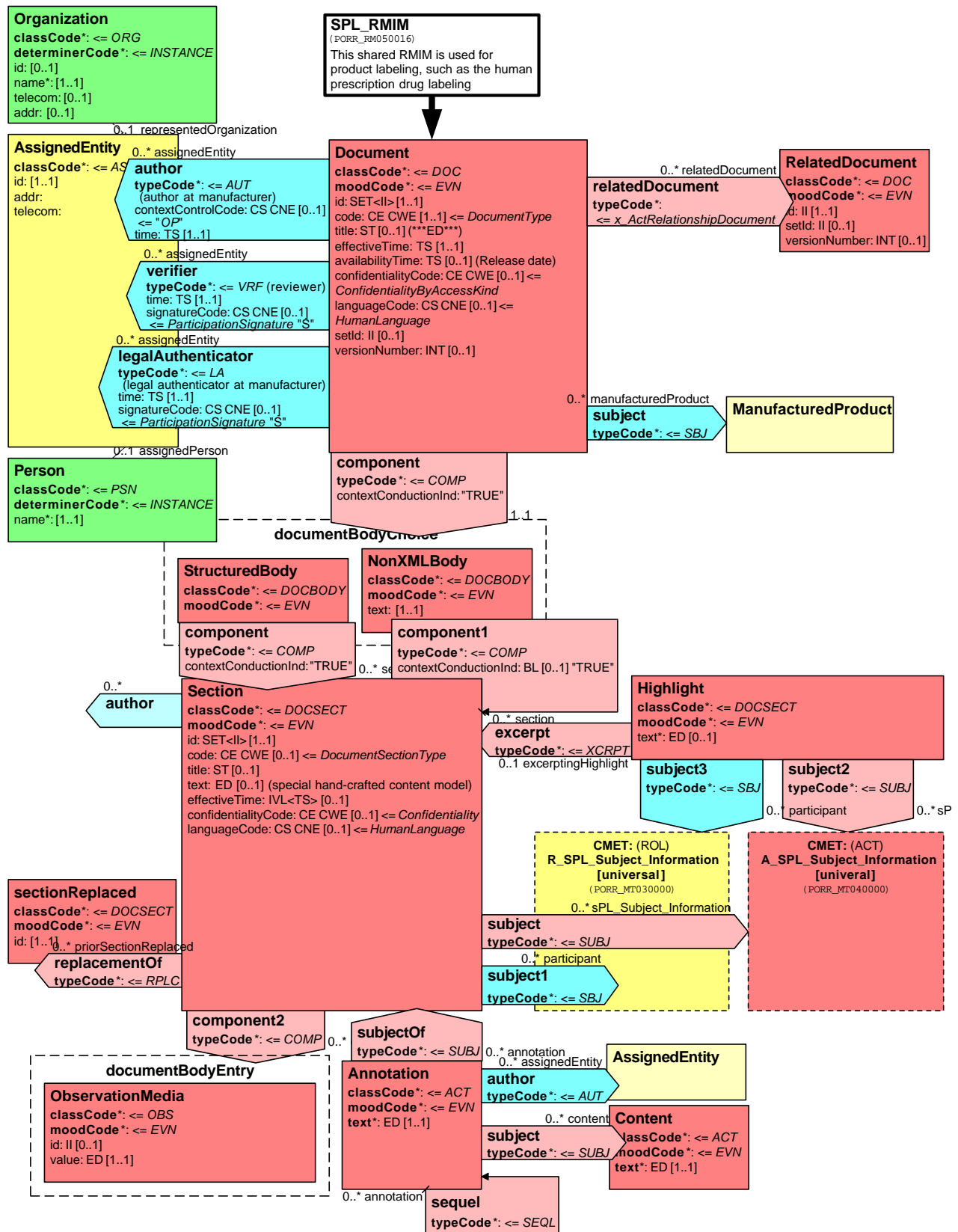
3.1   Document Model

The major change to the Document module is be the addition of the Highlights, which is a feature set forth in the 2000 Physicians' Labeling Rule NPRM. The rule requires that the most important features of the label be summarized in concise bullet points on a half page at the beginning of the label document. This section is called Highlights. The highlights are structured in major sections parallel to the comprehensive prescribing information. Each bullet point refers to the sub-section in the comprehensive prescribing information where it is described in detail.

We propose that the highlights section would not be present in the SPL as a section on its own, but instead would be compiled from highlights elements found in their respective sub-section to which they apply. The appropriate HL7 RIM concept for a highlight is the ActRelationship of type extract that connects Sections to their Highlight.

The Highlight has a text element containing a text "snippet" that makes up the bullet point in the highlights section. The highlights are also the point at which we propose to place the extended structured information for SPL release 2. The structured information of current SPL is placed as a subject of the Section directly. In SPL 2 the same could be done, but we propose to use the Highlights as the primary hook into structured information mostly because the highlights provide a good criterion to pair down the amount of information that could be captured as structured. We represent structured information in the Document model as two very general hooks depending on whether we refer to information about physical entities (yellow Role box) or usage information (red Act box). Presently in SPL any Section can contain any structured information and there is no rule which structured information may or must appear in which section. This is carried forward into SPL 2, however, we could propose specific constraints in FDA implementation

guides that would trim down the variability such that specific structured information could appear (and must appear) only in specific Sections' Highlights.

Organization
classCode* <= *ORG*
determinerCode* <= *INSTANCE*
id: [0..1]
name*: [1..1]
telecom: [0..1]
addr: [0..1]

SPL_RMIM
(PORR_RM050016)
This shared RMIM is used for
product labeling, such as the human
prescription drug labeling

0..1 representedOrganization

AssignedEntity
classCode* <= *AS*
id: [1..1]
addr:
telecom:

0..* assignedEntity

author
typeCode* <= *AUT*
  (author at manufacturer)
contextControlCode: CS CNE [0..1]
  <= "*OP*"
time: TS [1..1]

0..* assignedEntity

verifier
typeCode* <= *VRF* (reviewer)
time: TS [1..1]
signatureCode: CS CNE [0..1]
  <= *ParticipationSignature* "S"

0..* assignedEntity

legalAuthenticator
typeCode* <= *LA*
  (legal authenticator at manufacturer)
time: TS [1..1]
signatureCode: CS CNE [0..1]
  <= *ParticipationSignature* "S"

0..1 assignedPerson

Document
classCode* <= *DOC*
moodCode* <= *EVN*
id: SET<II> [1..1]
code: CE CWE [1..1] <= *DocumentType*
title: ST [0..1] (***ED***)
effectiveTime: TS [1..1]
availabilityTime: TS [0..1] (Release date)
confidentialityCode: CE CWE [0..1] <=
ConfidentialityByAccessKind
languageCode: CS CNE [0..1] <=
HumanLanguage
setId: II [0..1]
versionNumber: INT [0..1]

0..* relatedDocument

relatedDocument
typeCode*:
  <= *x_ActRelationshipDocument*

RelatedDocument
classCode* <= *DOC*
moodCode* <= *EVN*
id: II [1..1]
setId: II [0..1]
versionNumber: INT [0..1]

0..* manufacturedProduct

subject
typeCode* <= *SBJ*

ManufacturedProduct

Person
classCode* <= *PSN*
determinerCode* <= *INSTANCE*
name*: [1..1]

component
typeCode* <= *COMP*
contextConductionInd: "TRUE"

1..1

documentBodyChoice

StructuredBody
classCode* <= *DOCBODY*
moodCode* <= *EVN*

NonXMLBody
classCode* <= *DOCBODY*
moodCode* <= *EVN*
text: [1..1]

component
typeCode* <= *COMP*
contextConductionInd: "TRUE"

component1
typeCode* <= *COMP*
contextConductionInd: BL [0..1] "TRUE"

0..* se

author

0..*

Section
classCode* <= *DOCSECT*
moodCode* <= *EVN*
id: SET<II> [1..1]
code: CE CWE [0..1] <= *DocumentSectionType*
title: ST [0..1]
text: ED [0..1] (special hand-crafted content model)
effectiveTime: IVL<TS> [0..1]
confidentialityCode: CE CWE [0..1] <= *Confidentiality*
languageCode: CS CNE [0..1] <= *HumanLanguage*

0..* section

excerpt
typeCode* <= *XCRPT*

0..1 excerptingHighlight

Highlight
classCode* <= *DOCSECT*
moodCode* <= *EVN*
text*: ED [0..1]

subject3
typeCode* <= *SBJ*

subject2
typeCode* <= *SUBJ*

0..\ participant   0..* sP

CMET: (ROL)
R_SPL_Subject_Information
[universal]
(PORR_MT030000)

CMET: (ACT)
A_SPL_Subject_Information
[univeral]
(PORR_MT040000)

sectionReplaced
classCode* <= *DOCSECT*
moodCode* <= *EVN*
id: [1..1]

0..* priorSectionReplaced

replacementOf
typeCode* <= *RPLC*

0..* sPL_Subject_Information

subject
typeCode* <= *SUBJ*

0..* participant

subject1
typeCode* <= *SBJ*

component2
typeCode* <= *COMP*

0..*

documentBodyEntry

ObservationMedia
classCode* <= *OBS*
moodCode* <= *EVN*
id: II [0..1]
value: ED [1..1]

subjectOf
typeCode* <= *SUBJ*

0..* annotation
0..* assignedEntity

Annotation
classCode* <= *ACT*
moodCode* <= *EVN*
text*: ED [1..1]

author
typeCode* <= *AUT*

AssignedEntity

0..* content

subject
typeCode* <= *SUBJ*

Content
classCode* <= *ACT*
moodCode* <= *EVN*
text*: ED [1..1]

0..* annotation

sequel
typeCode* <= *SEQL*

Issue 10 – Need a way to place general annotations into the text to support negotiations.
Presently proprietary word-processor files are sent back and forth between the labeler and the agency to which comments and tracked changes are applied. A comment/annotation feature might be useful to avoid having to use proprietary word-processor files for negotiations that would have to be converted to SPL in a costly after-process that could potentially introduce errors and thus cause a prolonged negotiation.

Therefore it is proposed to add an Annotation act, whose subject is the Section, and whose detailed subject can be specifically named content-element within the section. An annotation carries text and is attributed to a specific author. Furthermore, annotations could be added in response to other annotations.

Issue 11 – Need to supply literature reference as evidence for specific statements in the label. For example if you have a dosing statement such as 1 tablet every 12 hours, there would be text with a link that would take you to a dosing study that concludes the dosing should be 1 tablet every 12 hours. If SPL can be modified to accommodate annotations with links to other files, then a version of the SPL file we would submit could replace the need to generate a PDF with extra space in the margins to accommodate the annotations.

[Proposed change not shown in diagram yet.] Therefore it is proposed to add external document cross-references into the document model. These references could be from the structured data or from the document text or both. It might be a similar if not common feature to the Annotations. The general pattern would use a RIM Document class clone which can be referenced by URL or by bibliorgaphicDesignation attribute.
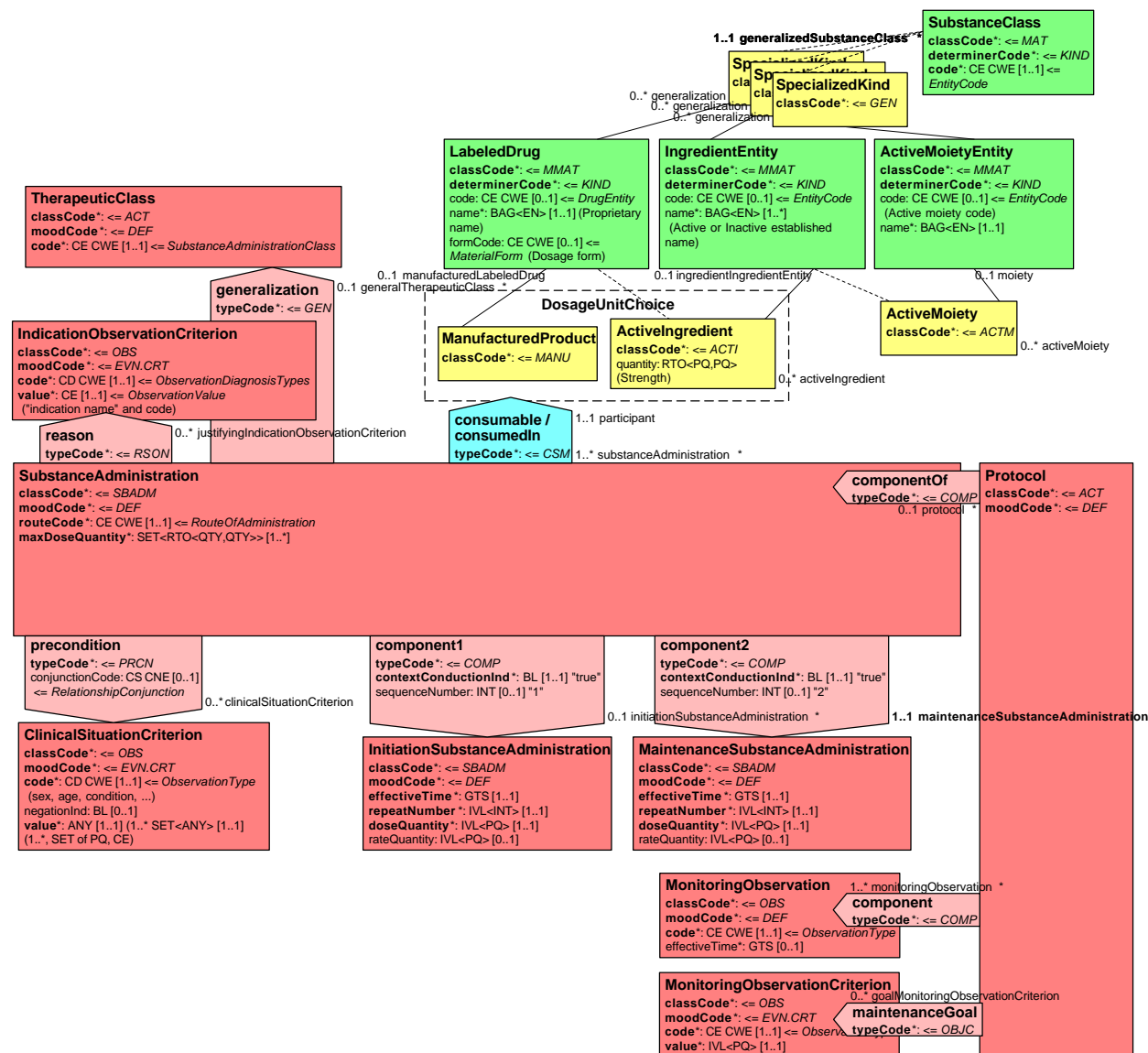
3.2   Structured Information Model Overview

The following diagram presents the complete overview of the proposed structured information content for SPL release 2. This includes the content presently in SPL 1. Rather than discussing all of this content at once we divide the discussion into 3 sub-sections or "modules". These modules could reasonably be proposed as HL7 common model elements which would help constrain the variability of SPL content.

The three modules include the current SPL 1 content, which is drug description and listing information, plus two new modules (1) Indication and Usage and (2) Adverse Events, Contraindications, Interactions and other Issues requiring special caution. We will first present the two new modules and then conclude by revisiting the current SPL 1 content module.

GenericDrug
classCode *: <= MMAT
determinerCode*: <= KIND
code: CE CWE [0..1] <= DrugEntity
name*: BAG<EN> [1..*] ((e.g., Established Name)

0..1 genericGenericDrug

DrugWithGeneric
classCode *: <= GRIC

0..* playedDrugWithGeneric

1..1 generalizedSubstanceClass

SubstanceClass
classCode *: <= MAT
determinerCode*: <= KIND
code *: CE CWE [1..1] <= EntityCode

SpecializedKind
classCode *: <= GEN

0..* generalization
0..* generalization

containedPackage
classCode *: <= CONT
(cpd product pkgs)
quantity: RTO<PQ,PQ>
[0..1] (Package Quantity)

0..* scopedcontainedPackage

Package
classCode *: <= CONT
determinerCode*: <= KIND
code*: CE CWE [1..1]
<= ContainerEntityType
(Package type)

LabeledDrug
classCode *: <= MMAT
determinerCode*: <= KIND
code: CE CWE [0..1] <= DrugEntity
name*: BAG<EN> [1..1] (Proprietary name)
formCode: CE CWE [0..1] <= MaterialForm (Dosage form)

IngredientEntity
classCode *: <= MMAT
determinerCode*: <= KIND
code: CE CWE [0..1] <= EntityCode
name*: BAG<EN> [1..*]
(Active or Inactive established name)

ActiveMoietyEntity
classCode *: <= MMAT
determinerCode*: <= KIND
code: CE CWE [0..1] <= EntityCode
(Active moiety code)
name*: BAG<EN> [1..1]

0..1 container
0..1 containedPackage

containedLabeledDrug
classCode *: <= CONT
quantity: RTO<PQ,PQ> [0..1]
(Packaged Drug Quantity)

0..* playedcontainedLabeledDrug

0..1 manufacturedLabeledDrug

InactiveIngredient
classCode *: <= IACT

0..* inactiveIngredient

0..1 moiety

ActiveMoiety
classCode *: <= ACTM

0..* activeMoiety

DosageUnitChoice

ManufacturedProduct
classCode *: <= MANU

ActiveIngredient
classCode *: <= ACTI
quantity: RTO<PQ,PQ> (Strength)

0..* activeIngredient

TherapeuticClass
classCode *: <= ACT
moodCode *: <= DEF
code *: CE CWE [1..1] <= SubstanceAdministrationClass

**consumable /
consumedIn**
typeCode*: <= CSM

1..1 participant

subjectOf
typeCode*: <= SBJ

0..*additionalInformation

AdditionalInformation

Policy
classCode *: <= ACT
moodCode *: <= EVN
code *: CE CNE [1..1]
<= RegulationPolicyActCode
(DEA schedule, Rx vs. OTC)

Observation
classCode *: <= OBS
moodCode *: <= EVN
code*: CE CWE [1..1] <= ObservationType
text*: ED [0..1]
value: ANY [0..*]

generalization
typeCode*: <= GEN

0..1 generalTherapeuticClass

IndicationObservationCriterion
classCode *: <= OBS
moodCode *: <= EVN.CRT
code *: CD CWE [1..1] <= ObservationDiagnosisTypes
value *: CE [1..1] <= ObservationValue
("indication name" and code)

reason
typeCode*: <= RSON

0..* justifyingIndicationObservationCriterion

1..* substanceAdministration *

componentOf
typeCode*: <= COMP

0..1 protocol *

Protocol
classCode *: <= ACT
moodCode *: <= DEF

SubstanceAdministration
classCode *: <= SBADM
moodCode *: <= DEF
routeCode *: CE CWE [1..1] <= RouteOfAdministration
maxDoseQuantity *: SET<RTO<QTY,QTY>> [1..*]

ClinicalSituationCriterion

precondition
typeCode*: <= PRCN
conjunctionCode: CS CNE [0..1]
<= RelationshipConjunction

0..*clinicalSituationCriterion

subjectOf
typeCode*: <= SUBJ 0..* issue

component1
typeCode*: <= COMP
contextConductionInd *: BL [1..1] "true"
sequenceNumber: INT [0..1] "1"

component2
typeCode*: <= COMP
contextConductionInd *: BL [1..1] "true"
sequenceNumber: INT [0..1] "2"

Issue
classCode *: <= ALRT
moodCode *: <= DEF
code *: CD CWE [1..1] <= x_ClinicalEffectsCategory
(adverse event, interaction with drug or food, caution, ...)

0..1 initiationSubstanceAdministration *
1..1 maintenanceSubstanceAdm

subject
typeCode*: <= SUBJ
conjunctionCode: CS CNE [0..1] <= RelationshipConjunction

risk
typeCode

InitiationSubstanceAdministration
classCode *: <= SBADM
moodCode*: <= DEF
effectiveTime *: GTS [1..1]
repeatNumber *: IVL<INT> [1..1]
doseQuantity *: IVL<PQ> [1..1]
rateQuantity: IVL<PQ> [0..1]

MaintenanceSubstanceAdministration
classCode *: <= SBADM
moodCode *: <= DEF
effectiveTime *: GTS [1..1]
repeatNumber *: IVL<INT> [1..1]
doseQuantity *: IVL<PQ> [1..1]
rateQuantity: IVL<PQ> [0..1]

causeOf
typeCode*: <= CAUS *

0..* causedConsequenceObservation

OtherIssueSubject

ClinicalSituationCriterion
classCode *: <= OBS
moodCode *: <= EVN.CRT
code *: CD CWE [1..1] <= ObservationType
(sex, age, condition, ...)
negationInd: BL [0..1]
value *: ANY [1..1] (1..* SET<ANY> [1..1]
(1..*, SET OF PQ, CE)

ConsequenceObservation
classCode *: <= OBS
moodCode *: <= EVN.CRT
code *: CD CWE [1..1]
<= ObservationDiagnosisTypes
text: ST [0..1]
value *: CE CWE [1..1] <= ObservationValue

MonitoringObservation
classCode *: <= OBS
moodCode *: <= DEF
code *: CE CWE [1..1] <= ObservationType
effectiveTime*: GTS [0..1]

1..* monitoringObservation *

component
typeCode*: <= COMP

subjectOf5
typeCode*: <= SUBJ

subjectOf3
typeCode*: <= SUBJ

0..1 severity

SubstanceAdministrationCriterion
classCode *: <= SBADM
moodCode *: <= EVN.CRT
routeCode: CE CWE [0..1] <= RouteOfAdministration
(labeled route of administration)

Severity
classCode *: <= OBS
moodCode *: <= EVN.CRT
code *: CD CWE [1..1] <= "SEV"
value *: CE [1..1] <= SeverityObservationValue
(mild, moderate, severe)

MonitoringObservationCriterion
classCode *: <= OBS
moodCode *: <= EVN.CRT
code *: CE CWE [1..1] <= Observa
value *: IVL<PQ> [1..1]

0..* goalMonitoringObservationCriterion

maintenanceGoal
typeCode*: <= OBJC

consumable
typeCode*: <= CSM 1..1 participant

MaterialKind
classCode *: <= MAT
determinerCode *: <= KIND
code *: [1..1] <= EntityCode
(specific or general type of drug or food that interacts)

aRole
classCode *: <= ROL

1..1 playingMaterialKind *

1..1 frequency *

Frequency
classCode *: <= OBS
moodCode *: <= EVN
code *: CD CWE [1..1] <= ActCode (fixed)
value *: CE [1..1] <= SymptomFrequency
(e.g., frequent, infrequent)

3.2.1   Indication and Usage Module

The Indication and Usage module covers the common labeling section "Indications" and "Dosage and Administration" as well as Monitoring, in short anything that describes the proper usage of the drug. Since this module is all about appropriate and save use of the drug, the use of the drug, i.e., the SubstanceAdministration Act is in the center of this module.

Indication: is the ObservationCriterion linked through the ActRelationship of type "reason" to the SubstanceAdministration. The observation criteria consist of an Observation.code to indicate that we have a diagnoses, symptoms, conditions, etc. and the Observation.value, a code representing the specific indication, e.g. hypertension, etc.

Special populations and other clinical situations: The use can be limited to special populations or clinical situations by the ClinicalSituationCriterion which can be stated positively as requirements (e.g. patient over 12 years of age) or negatively as limitations (e.g., not for patient under 12 years of age.) The clinical situations criterion is similar to the

IndicationCriterion with Observation.code and Observation.value, but the value can include both coded and quantitative value types to express clinical conditions as well as age ranges.

Classifications of drugs and their use: Two mechanisms are proposed to represent grouping or classifications of the drug substances on the one hand and their use on the other hand. Pharmacologic class (e.g., aminopenicillin, aminoglycosides, etc.) or mechanism of action (e.g., MAO inhibitor, ACE inhibitor, Ca-channel blocker, beta-2-blocker, etc.) is a classification of drug substances, either of drug products, their active ingredients or active moiety, and all represented by generalization Roles to a MaterialKind. Classification of treatment intent (e.g., antihypertensive, antiphlogistic, antiinferctive, etc.) are classifications of the SubstanceAdministration act, and represented as a generalization of this Act.

Dosing: the full scope of detail available for specifying recommended dosage in SPL release 2 might not have been fully determined. The HL7 Pharmacy model can represent a wide variety of dosage instructions but in SPL it might be useful to limit these to only a few very common patterns. In this proposal the dosage amount is specified by basically 3 attributes: maximum amount per any time interval (e.g., 4 g in any 24-hour period), usual dose amount, and initiation dosage. Timing patterns (e.g., twice a day, every 8 hours) and timing boundaries (e.g., for 10 days) can be specified differently for usual dosage an initiation. This is done by having a required ManintenanceSubstanceAdministration with dosage amount and timing and an optional InitiationSubstanceAdministration with the same attributes both a components of the overall SubstanceAdministration.

Monitoring is understood as additional measures required to embed the drug use itself (SubstanceAdministration) in a Protocol of safe and effective treatment. This Protocol contains monitoring observation steps represented as Observation plan steps, with Observation.codes detailing the kind of tests that should be performed and effectiveTime to specify the recommended frequency of these tests in the same way as the frequency of drug administration is specified. In addition the Protocol can have maintenance goals for effective and save drug levels. This addresses two different use cases. (1) Recommendation to check for liver enzymes once a month, where the normal ranges are used to interpret the test results. (2) Levels of the drug or metabolites or any measurement of the drug's effect to establish safe and effective doses. In the latter case specific low and high limits should be provided.

3.2.2   Adverse Events, Contraindications, Interactions and other Issues
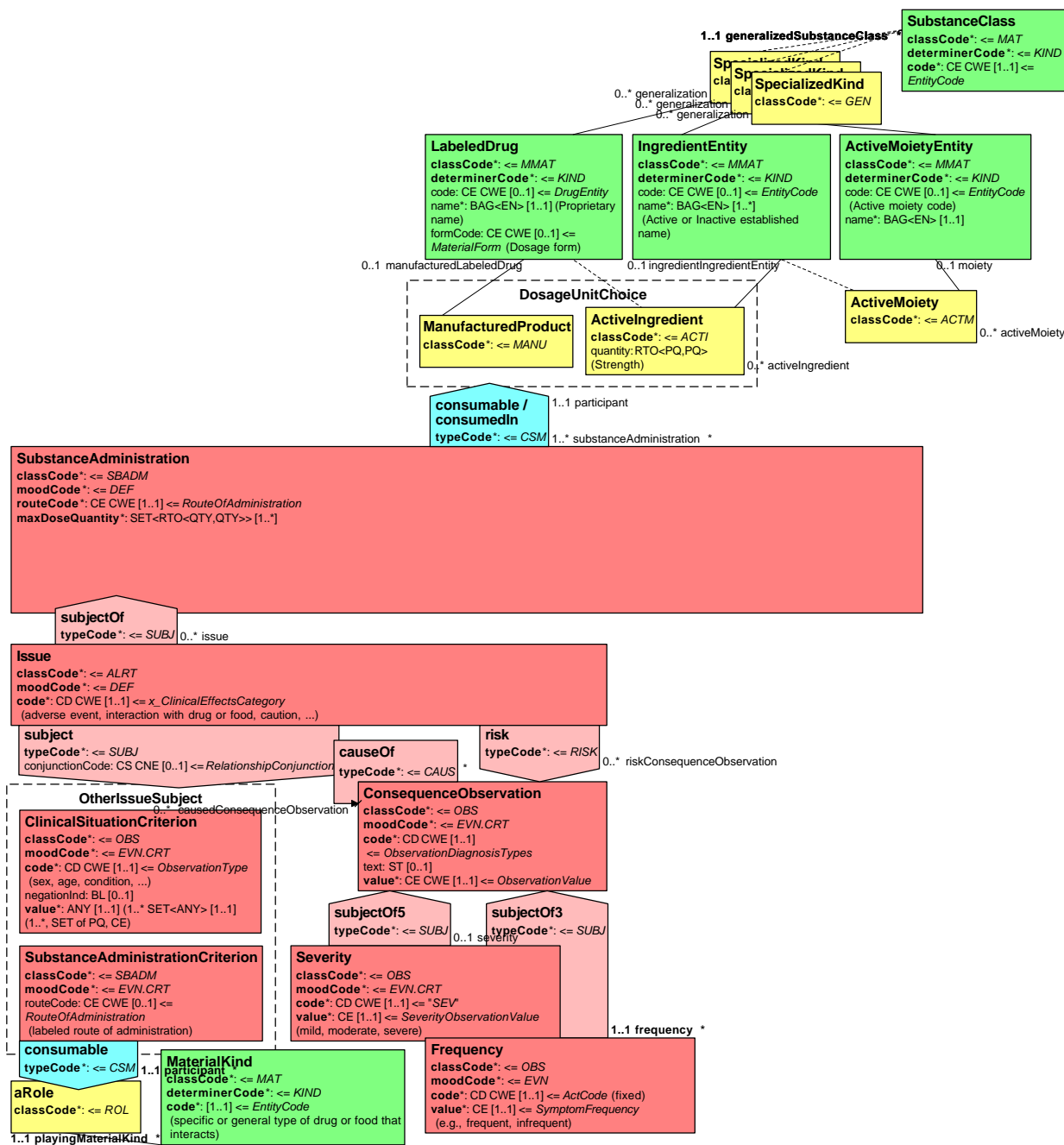
Adverse events, interactions, contraindications and other issues of special note are represented in one uniform structure. The Pharmacy SIG has established a special kind of Act, called Issue for this purpose. An Issue has one or more other Acts as subjects and indicate that there is a certain problem requiring special note and care with its subject Acts. In the case of drug labels, the subject is the SubstanceAdministration described in the label. One or more additional subjects can be used to specify additional ClinicalSituationCriteria or SubstanceAdministrationCriteria. The latter is used to represent interactions which is an Issue involving the administration of two substances.

An Issue should specify a risk, as a coded Observation criterion with information about severity and frequency of the undesired outcome. The description of the risk can nest to refine to a level of specificity that makes the adverse event actually recognizable. For example, a risk may be specified as a "hypersensitivity syndrome" but then specific manifestations may be given including "rash," or "Guillain-Barré Syndrome", or even quantitative measures as "leukopenia with WBC below 1000/mm^3.

3.2.3   Description and Drug-Listing Module
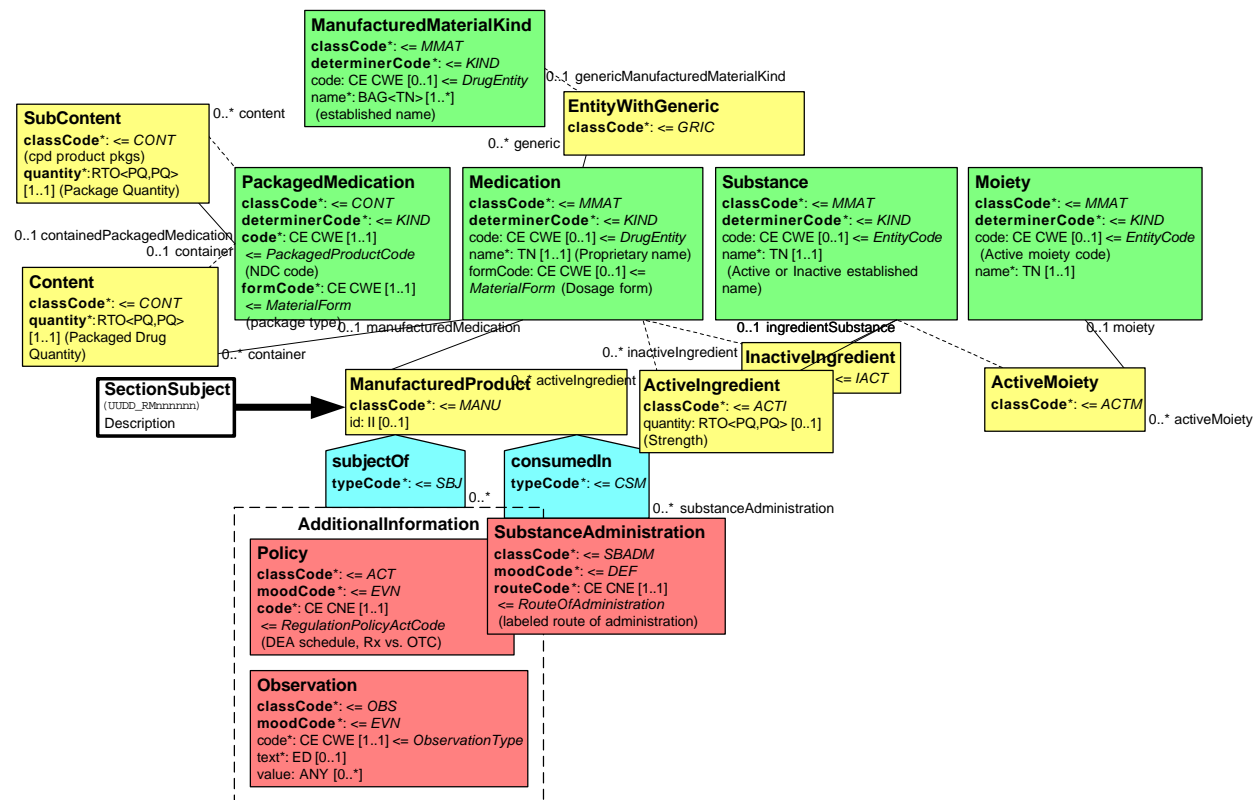
The drug description and listing data module is the contents of present SPL release 1. As stated in the introduction, this module could be left completely unchanged for SPL release 2. However, here we give a proposal in what way this module *could* be changed (ever so slightly) to address the Issues noted above. We will repeat those issues here and discuss briefly how this module diagram proposes to address them.

This is a summary of issues with the present SPL model that could be addressed in the forthcoming ballot aside from adding the extensions that are essential for SPL release 2.

Issue 1 – Product Characteristics: During the implementation guide and pilot phase the SPL team had to struggle with the fact that the drug characteristics (color, shape, scoring, etc.) were placed in a different area in the section and were not related at all to the product that is to be characterized.

It is therefore proposed to introduce an Observation that is reachable from the drug itself rather than from a different component of the Section in which the drug is described. Basically this will

make the "subject" participation in the diagram navigable from the ManufacturedProduct to the Observation.

Issue 2 – Titles: the Implementation Guide and pilot team found that Document titles need some markup. Since the SDTC has resolved to change the data types of the Act.title element from ST to ED subject to a pending RIM harmonization proposal.

Issue 3 – DEA Schedule: a ballot comment against SPL v1 concerning the MonitoringProgramEvent had been resolved by deferring the actual implementation to the Implementation Guide that has intentionally not made any use of this feature yet. The MonitoringProgramEvent was to be a method to assign the DEA schedule (controlled substance schedule) to the labeled drug. The point of the comment was that the use of an Observation in this form is conceptually wrong (DEA number would be Act.code not Observation.value). This is being discussed in the Pharmacy SIG and probably can be resolved in a relatively minor change.

It is therefore proposed to use a general Policy Act where the Act.code represents the DEA schedule. In the same manner, other policies can be represented, such as whether a drug is a prescription drug or an over-the-counter drug.

Issue 4 – Alignment with Pharmacy SIG: It is the purpose of the SPL release 2 to improve electronic prescribing. Therefore a close alignment of the SPL Medication model with the overall HL7 Medication model as created by the Pharmacy SIG is desirable. The two models are already relatively close and therefore some small insubstantial changes (possibly name changes) might be entertained.

It is therefore proposed to rename: LabeledDrug to Medication, containedLabeledDrug to Content, containedPackage to SubContent.

These changes are not critical but would aim not only at Alignment but also at reducing the number of quite awkward tag names in the XML instances (e.g., ingredientIngredientEntity or playedcontainedLabeledDrug).

Issue 5 – Combination Products: The present approach to combination products, or kits, is through the packaging structures. A kit with multiple drug products is represented as the kit being a LabeledDrug and the components of the kit also represented as LabeledDrugs. These components are then connected through the containedPackage role with the kit. For instance, Prevpac containing Prevacid and Trimox will be represented as Prevpac as a LabeledDrug without any ingredients but with a Packaging with NDC code for Prevpac which in turn has contained Packages for Prevacid and Trimox as individually packaged products. The problem with this approach is that it is assumed that the components of the kit are individually packaged (which in this example they are not).

This issue has not been addressed in the diagram above.

Issue 6 – Package Code and NDC Code: The present approach uses Container.code to specify the general type of packaging (e.g., whether it is a box or a bottle). The NDC code for the packaged product hangs from the Package as a special Role "regulated product". The Pharmacy SIG has since determined that the RIM Class Container is assumed to stand for the combination

of a Container with its Content (just as it is assumed in SPL), but that the Container.code should be the specific code for the Product in its Container (or "packaged product"). Furthermore, the kind of container should be specified in the Container.formCode attribute.

It is therefore proposed to add the formCode attribute into the Package clone to represent the Package type and to use the Package.code for the NDC code representing the package product.

Issue 7 – Entity Names: the Entity.name attributes are taken unconstrained from the RIM as BAG<EN>, which is multiple names, each of which can have multiple name parts. This feature is mostly there for Person names with given and last names, maiden names, etc. For drugs, names would be unstructured, basically just strings. For this purpose the EN data type should be constrained to the TN (trivial name) type, which is simply a string. Also, while LabeledDrug (aka Medication) and ActiveMoietyEntity (aka, Moiety) have the multiplicity constrained to at most one name, IngredientEntity (aka. Substance) is allowed multiple names. This might also be constrained to at most 1 name.

Issue 8 – Mandatory Constraints: for SPL, or at least the FDA implementation of it, a lot more mandatory constraints could be added. Most all of the attributes could be turned to mandatory or at least required.

4   Example

An approximate example for the present proposals can be examined at
http://aurora.regenstrief.org/spl/captopril.xml