Integrating the Healthcare Enterprise

IHE QRPH
Technical Framework Supplement

Clinical Research Process Content (CRPC)

Trial Implementation

Date: August 27, 2012

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Foreword

This is a supplement to the IHE Quality, Research and Public Health Technical Framework V0.1. Each supplement undergoes a process of public comment and trial implementation before being incorporated into the volumes of the Technical Frameworks.

This supplement is published for Trial Implementation on August 27, 2012 and may be available for testing at subsequent IHE Connectathons. The supplement may be amended based on the results of testing. Following successful testing it will be incorporated into the Quality, Research and Public Health Technical Framework (QRPH). Comments are invited and may be submitted at http://www.ihe.net/qrph/qrphcomments.cfm.

This supplement describes changes to the existing technical framework documents and where indicated amends text by addition (**bold underline**) or removal (~~**bold strikethrough**~~), as well as addition of new sections introduced by editor's instructions to "add new text" or similar, which for readability are not bolded or underlined.

"Boxed" instructions like the sample below indicate to the Volume Editor how to integrate the relevant section(s) into the relevant Technical Framework volume:

Replace Section X.X by the following:

General information about IHE can be found at: www.ihe.net

Information about the IHE QRPH domain can be found at:
http://www.ihe.net/Domains/index.cfm

Information about the structure of IHE Technical Frameworks and Supplements can be found at:
http://www.ihe.net/About/process.cfm and http://www.ihe.net/profiles/index.cfm

The current version of the IHE Technical Framework can be found at:
http://www.ihe.net/Technical_Framework/index.cfm

CONTENTS

Introduction to this Supplement

This proposal is to specify content, which is appropriate to help automate the sharing of information among systems during the clinical research process. Using the transactions from the Retrieve Process for Execution (RPE) profile, the proposed content profiles will improve the recruitment for, setup, and performance of clinical trials.

Open Issues and Questions

1. Currently we assume that the CTMS will implement both the Process Definition manager and Process State Manager Actors from RPE (see figure X-1.1). Is this a realistic assumption? Do we need to consider cases where there are more than the CTMS (Research Protocol Source) and EMR (Research Protocol Consumer) systems involved?
2. Use case 2 (patient recruitment at the point of care) assumes that the matching of patient to study includes any screening performed as per the study definition, and the Initiate Process transaction occurs after the information is collected and will contain the corresponding patient data as necessary. Is that a valid assumption? Answer: There is patient pre-enrollment screening that may be done in use case 2. This is to be distinguished from a separate use case, where enrollment is done on the healthcare side, and so there is no need to send any additional information besides the information that the patient has been enrolled.
3. It is not clear where the boundaries for de-identification of patient data and for patient confidentiality lie. The questions that come up are: is it appropriate to include the study subject ID as part of the patient's list of identifiers? Where is de-identified data expected?
4. In the Initiate Process transaction we need to specify which study is associated with the patient. What information is needed to identify the study?

Closed Issues

None

Volume 1 – Profiles

Copyright Permission

Not applicable

Domain-specific additions

Not applicable

Add to Section X

X Clinical Research Process Content (CRPC) Profile

The US clinical research industry has difficulty in gaining participants for research studies, as shown by the increasing use of off-shore sites. One revealing statistic is that 66% of site-based investigators participate in one, and only one, study. A common complaint of site-based researchers is the difficulty of participating in studies, particularly managing the multiple systems required, often one for each study.

Research protocols are complex documents that guide the conduct of trials. Subsets of the protocol, the trial design model and schedule of activities, represent the planned sequence of events and interventions pertaining to a study, activities that are typically performed at the healthcare provider site that participates in the trial. The existing IHE profile Retrieve Process for Execution acts as a general framework which provides messaging interactions, which could be used to convey the necessary information. The proposed Research Content profiles utilize RPE as a framework and solve the issues of exchanging detailed content specific to the research domain.

X.1 CRPC Actors, Transactions, and Content Modules

Figure X.1-1 shows the actors directly involved in the CRPC Profile and the relevant **transactions between them. If needed for context, other actors that may be indirectly involved** due to their participation in other related profiles are shown in dotted lines. Actors which have a mandatory grouping are shown in conjoined boxes.

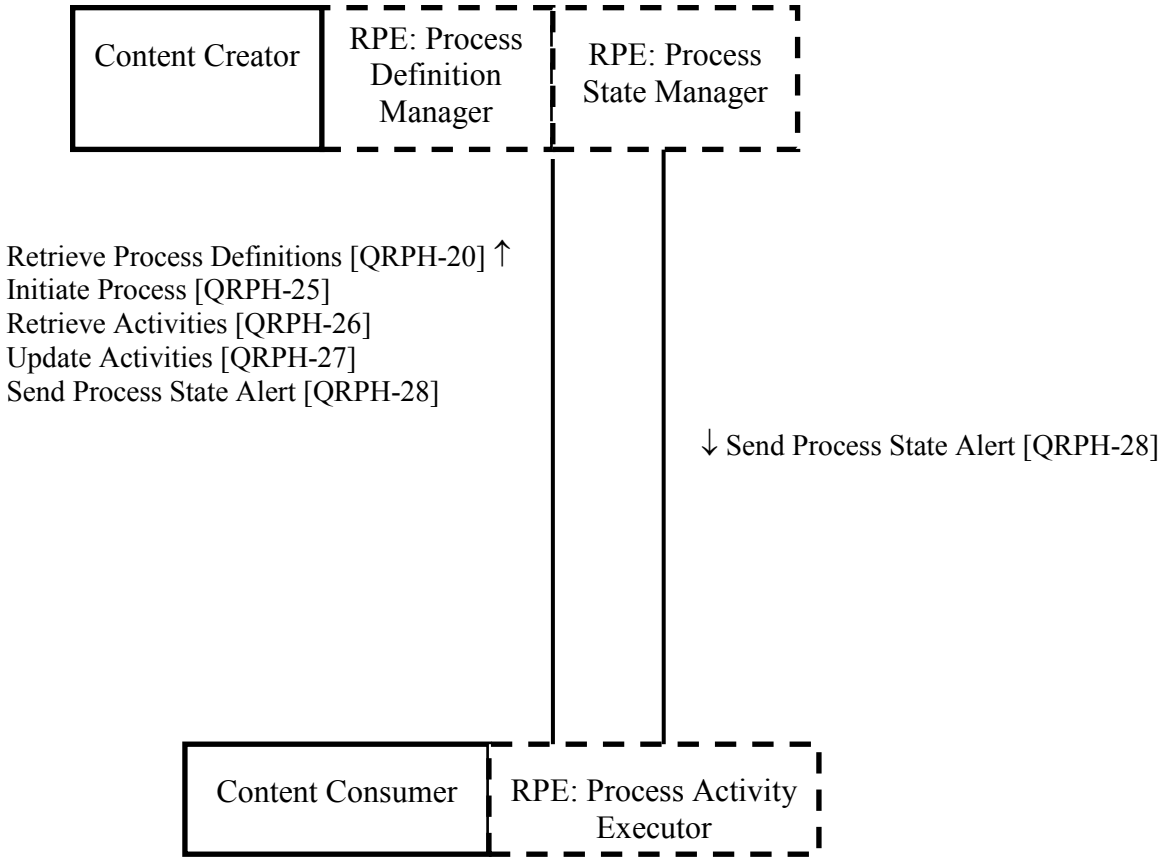


Figure X.1-1: CRPC Actor Diagram

Table X.1-1 lists the transactions for each actor directly involved in the CRPC Profile. In order to claim support of this Profile, an implementation of an actor must perform the required transactions (labeled "R") and may support the optional transactions (labeled "O"). Actor groupings are further described in Section X.3.

Table X.1-1: CRPC Profile - Actors and Content Modules

Actors	Content Module	Optionality	Section in Vol. 3?
Content Creator	Initiate Process Content Module	R	8.3.1.C1
	Protocol Definition Content Module	R	8.3.1.C2
	Activities Content Module	O	
	Process State Content Module	O	
Content Consumer	Initiate Process Content Module	R	8.3.1.C1
	Process Definition Content Module	R	8.3.1.C2

Actors	Content Module	Optionality	Section in Vol. 3?
	Activities Content Module	O	
	Process State Content Module	O	

X.1.1 Actor Descriptions and Actor Profile Requirements

Normative requirements are typically documented in Volume 2 (Transactions) and Volume 3 (Content Modules). Some Integration Profiles, however, contain requirements which link transactions, data, and/or behavior. Those Profile requirements are documented in this section as normative requirements ("shall").

X.1.1.1 Content Creator

The Research Protocol Source Actor shall be grouped with the RPE Process Definition Manager Actor, and the RPE Process State Manager Actor. The Research Protocol Source Actor shall support generating the Protocol Definition content, and shall understand the Initiate Process content. This actor may also support the Activities content, and/or the Process State content.

X.1.1.2 Content Consumer

The Research Protocol Consumer Actor shall be grouped with the RPE Process Activity Executor Actor. This actor shall understand the content of a Protocol Definition. When participating in point of care enrollment use case, this actor shall generate the Initiate Process content. Optionally, this actor may understand the Activities content, and/or the Process State content.

X.1.2 CRPC Document Content Modules

The CRPC profile contains four different content modules, as described below.

X.1.2.1 Study Definition Content Module

This content module represents the following information about a research protocol:

- NCT number
- IRB number
- Short Name
- Study Name
- Study Code
- Study Description
- Protocol Definition Version

- Study Type
- Study Status
- Study start date
- Study closed date
- Study Principle Investigator
- Key Staff identifiers

X.1.2.2 Initiate Process Content Module

This content module represents the following information about a candidate for enrollment in a research study:

- Information about the research protocol, as presented in the Protocol Definition Content Module
- Patient Demographics
- Patient ID
- Optionally, clinically relevant information based on pre-screening activities

X.1.2.3 Activities Content Module

This content module represents the following information about the activities in a research study:

The generic (i.e., not linked to particular date) study schedule of events, and their chargeable information. This would get translated into the EMR's study protocol configuration. It is important to make sure that if we can get information about what gets covered by the study and what is handled as standard of care (with a modifier) to patient/insurance account, there is a way to represent that.

X.1.2.4 Process State Content Module

This content module represents the following information about the state of a particular research study:

- Current stage (epoch), indicating at what point a patient is in the study timeline
- Possible changes to the study timeline due to unexpected events
- Clinical information if applicable

X.2 CRPC Actor Options

Options that may be selected for this Profile are listed in the table X.2-1 along with the actors to which they apply. Dependencies between options when applicable are specified in notes.

Table X.2-1: CRPC - Actors and Options

Actor	Options	Volume & Section
Content Creator	Activities Content Module	TBD
	Process State Content Module	TBD
Content Consumer	Activities Content Module	TBD
	Process State Content Module	TBD

X.3 CRPC Required Actor Groupings

Actor(s) which are required to be grouped with another actor(s) are listed in this section. The grouped actor may be from this profile or a different domain/profile. These mandatory required groupings, plus further descriptions if necessary, are given in the table below.

An actor from this profile (Column 1) must implement all of the required transactions in this profile in addition to all of the required transactions for the grouped profile/actor listed (Column 2).

Table X.3-1: Clinical Research Process Content - Actors Required Groups

CRPC Actor	Actor to be Grouped with	Technical Framework Reference	Content Bindings Reference
Content Creator	RPE Process Definition Manager	QRPH TF1: 12.1.1.1	
Content Creator	RPE Process State Manager	QRPH TF1: 12.1.1.2	
Content Consumer	RPE Process Activity Executor	QRPH TF1: 12.1.1.3	

X.4 CRPC Overview

X.4.1 Concepts

Not applicable

X.4.2 Use Case #1: Study Definition Sharing

X.4.2.1 Study Definition Sharing Use Case Description

A researcher at a health system is planning to conduct a clinical research study (Study X). A number of pre-approval steps are being tracked in the clinical trial management system (CTMS). A member of the study support staff creates a study in the clinical trials management system in order to start tracking these preparatory activities for the potential study. One of the typical steps will be to specify the definition of the study schedule of events, a labor intensive step. Once the study has received all necessary approvals, study information must also be made available to the

EMR to support activities that are inherently tied the provisioning of services to patients being treated within their organization (e.g., research-appropriate scheduling, ordering, billing).

Currently most study definition information, including basic information such as NCT#, Study Code, study type, and advanced information such as the study schedule of events, must be built and maintained manually in both the CTMS and the EMR. This profile will allow the study definition to be shared in a machine processable format.

X.4.2.2 Study Definition Sharing Process Flow

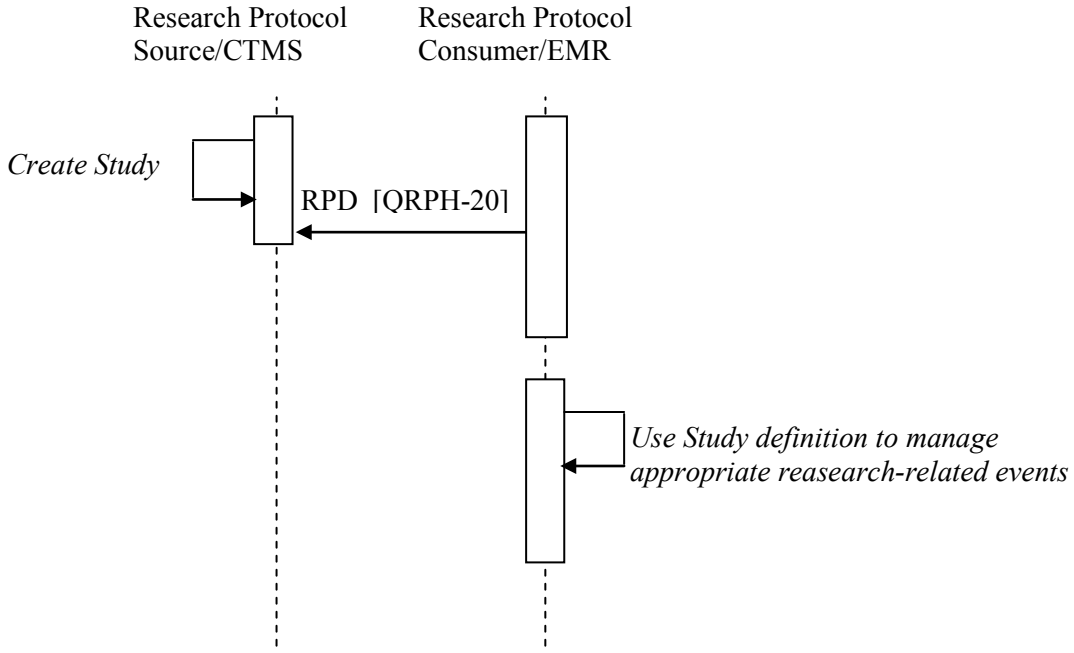


Figure X.4.2.2-1: Basic Process Flow in CRPC Profile

X.4.3 Use Case #2: Recruitment at the Point of Care

X.4.3.1 Recruitment at the Point of Care Use Case Description

The healthcare organization is using the decision support engine of its EMR to help identify patients at the point of care who may be eligible for the study. Evidence and experience indicate that recruitment at the point of care can greatly improve recruitment efficiency. A patient, not currently involved in Study X, is seen by her PCP at the healthcare organization. Information in her medical record, in addition to new information added by her PCP during the course of her

visit triggers a notification in the PCP's workflow she may be a candidate for study X. The PCP can indicate without leaving the clinical workflow if the patient is willing to be contacted to learn more and the EMR can automatically notify the study. If the information about study X available in the EMR doesn't include the specific inclusion and exclusion criteria, the information is obtained from the research system. As any expected pre-enrollment actions are completed in the EMR, it is important to know that that there is now an association between the patient and Study X (e.g., an association status of 'interested') to facilitate desired system and workflow functionality. Knowledge of this pre-enrollment association between the patient and the study may also be desired in the research system.

Currently it is typically assumed that recruitment happens outside the EMR and that the EMR is always the recipient on information about which patients are associated with which studies. When the EMR initiates the association, there needs to be a mechanism for exchanging the appropriate research participant information at the appropriate points in time. If a patient is accepted by the research system as a screening candidate, the research system will issue an identifier. This screening identifier might persist as the subject identifier if the patient is subsequently enrolled in the study. Or a new subject identifier might be issued at the point of enrollment.

X.4.3.2 Recruitment at the Point of Care Process Flow

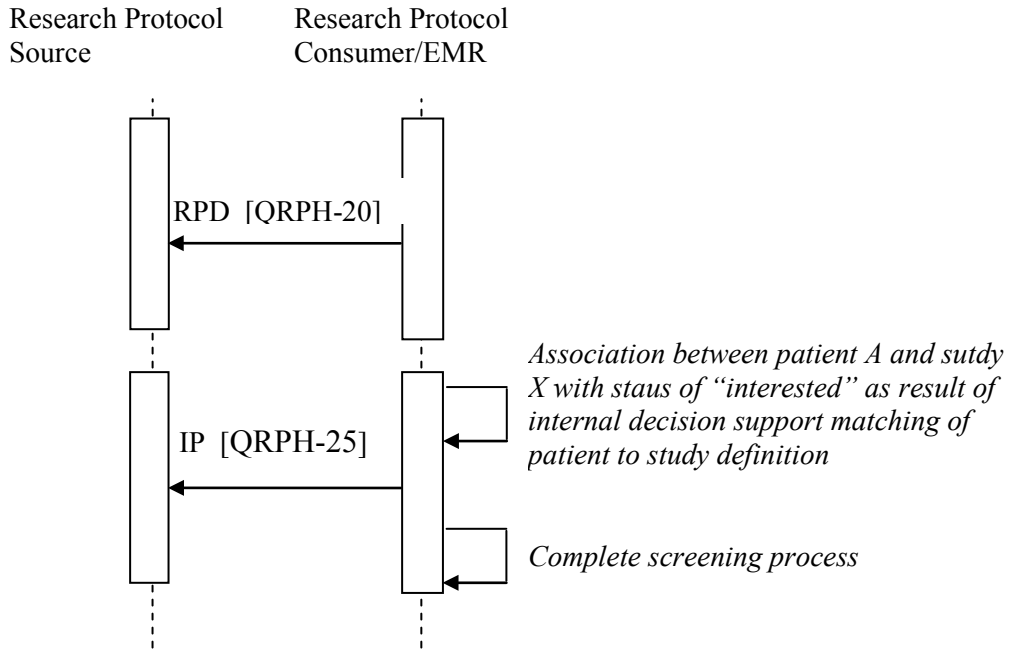


Figure X.4.3.2-1: Basic Process Flow in CRPC Profile

X.4.4 Use Case #3: Enrollment through the EMR

X.4.4.1 Enrollment through the EMR Use Case Description

Once the patient has been identified as a candidate, and any pre-enrollment steps completed in the EMR (screening tests done, necessary consents have been signed), the EMR will send information to the research system with a request to enroll the patient as a subject in the study. The enrollment task is fulfilled by the Research Protocol Source. The research system assigns a study identifier to the subject, and returns a notification to the Research Protocol Consumer that the patient is now part of the study. This notification includes either the patient's MRN as known by the EMR, or the subject identifier, which constitutes the pseudonymous identifier for the subject. In the case where the patient was assigned a screening identifier, this identifier can persist as subject id.

X.4.4.2 Enrollment through the EMR Process Flow

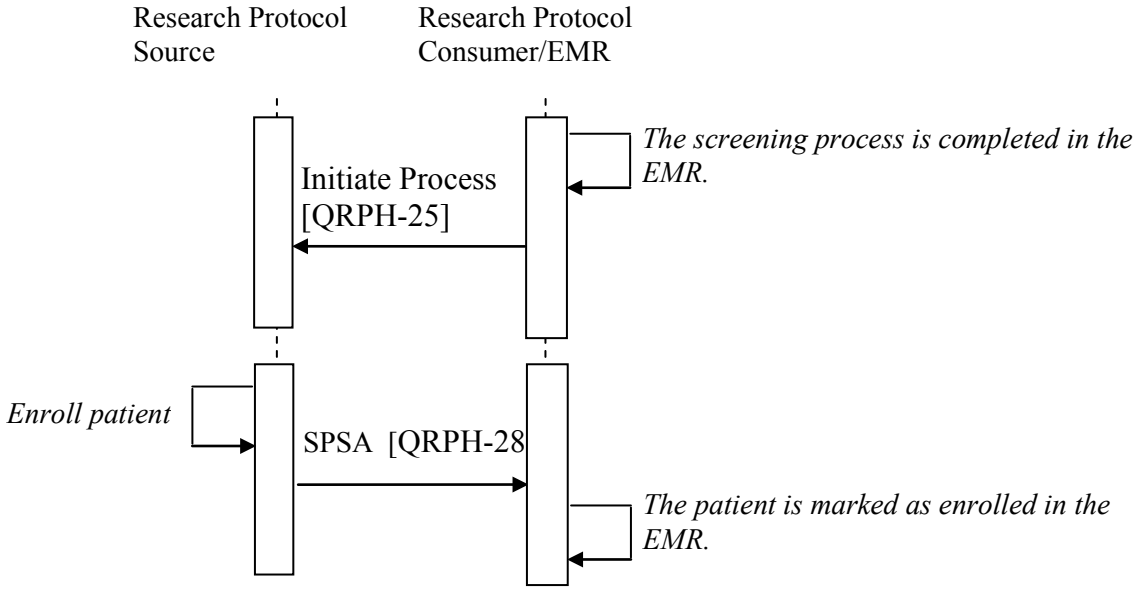


Figure X.4.4.2-1: Basic Process Flow in CRPC Profile

X.4.5 Use Case #4: Generation of Patient-specific Timeline of Study Events

X.4.5.1 Generation of Patient-specific Timeline of Study Events Use Case Description

Once the patient has been enrolled, the study coordinator will indicate the start date for the patient. It is possible that this information could instead be entered initially through the EMR. In either case, both systems require not only the status update, but also the patient's start date.

Based on the start date, and the study's standard calendar of events, subsequent study visit dates will be calculated in both the research system and the EMR. This is critical information in the EMR to appropriately manage clinical activities related to the patient and the study, as well as to support the requisite billing requirements.

Today, information related to patient timelines must be maintained manually in both systems.

X.4.5.2 Generation of Patient-specific Timeline of Study Events Process Flow

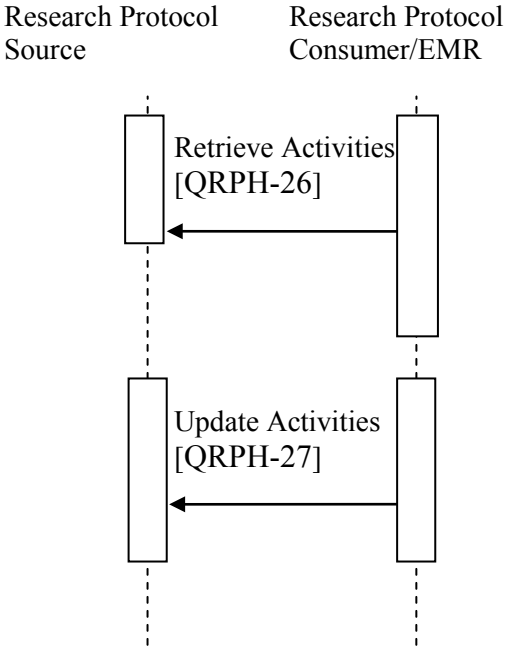


Figure X.4.5.2-1: Basic Process Flow in CRPC Profile

X.4.6 Use Case #5: Adjustment of Patient-specific Timeline of Study Events

X.4.6.1 Adjustment of Patient-specific Timeline of Study Events Use Case Description

Based on the study calendar, and the patient start date, an extensive series of appointments is likely to be scheduled for a patient. The actual scheduling of appointments that take place at the healthcare organization is not done in the research system, but rather in a healthcare system that is tightly integrated with, if not part of, the EMR. If an appointment tied to a specific study is cancelled/rescheduled/no-show/completed, information needs to be sent back to the research system for tracking purposes. As a consequence of the appointment change, any changes to the patient timeline that is done in the research system needs to be sent to the EMR.

Today, scheduling of research-related services relies extensively on manual workflows and human communication. Changes to patient timelines in one system, if not communicated and adjusted in the other system, can create confusion, at best, and potentially patient disqualification from a study if requisite timelines are not adjusted.

X.4.6.2 Adjustment of Patient-specific Timeline of Study Events Process Flow

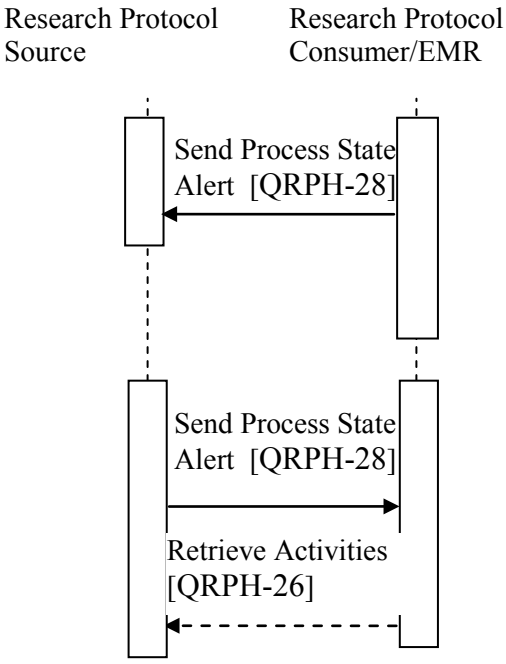


Figure X.4.6.2-1: Basic Process Flow in CRPC Profile

X.5 CRPC Security Considerations

None.

X.6 CRPC Cross Profile Considerations

Not applicable

Appendix A Actor Summary Definitions

No new actors defined by this profile.

Appendix B Transaction Summary Definitions

No new transactions defined by this profile.

Glossary

No new glossary terms defined by this profile.

Volume 2 – Transactions

Add section 4.B1

4.B1 RPE Bindings for the CRPC content profile

4.B1.1 Binding with the Study Definition Content Module

This content module may be used in various interoperability use cases. The bindings below describe the specific requirements for known use cases.

4.B1.1.1 Binding with RPE Request Process Definition

Include the complete Study Definition content module (8.3.1.C1)

4.B1.1.2 Binding with RPE Request Activities

Retrieve set of activities based on current state and some input information

4.B1.1.3 Binding with RPE Update Activities

Volume 3 – Content Modules

5 Namespaces and Vocabularies

None.

8 Content Modules

8.3.1 HL7 V3 Content Modules

This section defines each IHE QRPH content module in detail, specifying the standards used and the information transferred.

8.3.1.C1 Study Definition Content Module

The Study Definition Content Module describes a clinical research study in a machine readable format.

8.3.1.C1.1 Format Code

N/A

8.3.1.C1.2 LOINC Code

N/A

8.3.1.C1.3 Standards

RCRIM HL7 V3 Study Design Topic

SDM CDISC Study Design Model

8.3.1.C1.4 Specification

This section references content modules using IHE Specification Headers as the key identifier. Definitions of the modules are found in either:

- This supplement
- IHE QRPH Retrieve Process for Execution (RPE) Trial Implementation supplement

Data Element Name	Opt	Content Module
Study Description	R	8.3.4.S1
Eligibility Criteria	O	8.3.4.S2

Data Element Name	Opt	Content Module
Study Schedule	O	8.3.4.S3

8.3.1.C1.5 Conformance

HL7 V3 XML structures that conform to the requirements of this content module shall indicate their conformance by the inclusion of the appropriate templateId elements at the top level of the structure. A content module may conform to more than one template. The example below describes the overall structure of the Study Definition Content Module.


```
<clinicalStudyDefinition xmlns="urn:hl7-org:v3"
    xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance"
        classCode="CLNTRL" moodCode="DEF">
    <templateId><item root="1.2.3.4.5.6"/></templateId>
    <!-- Study Description Content Module -->
    <id>
        <item root="1.2.3.4" extension="ABCD"/>
    </id>
    <title value="Study Title"/>
    <text value="Study Description"/>
    <!-- Eligibility criteria -->
    <precondition typeCode="PRCN">
        <conjunctionCode code="AND"/>
        <eligibilityCriterion classCode="CLNTRL" moodCode="CRT">
            <id>
                <item root="6.2.3.4.5" extension="234"/>
            </id>
            <code code="DIAG" valueSet="3.3.4.5"/>
            <text value="Diagnosis of Diabetes"/>
            <value xsi:type="CD" code="E10-E14" codeSystem="2.16.840.1.113883.6.90"/>
            <precondition typeCode="PRCN">
                <conjunctionCode code="AND_NOT"/>
                <eligibilityCriterion classCode="CLNTRL" moodCode="CRT">
                    <code code="DIAG" codeSystem="3.3.4.5"/>
                    <text value="Not blind"/>
                    <value xsi:type="CD" code="H54.0" codeSystem="2.16.840.1.113883.6.90"/>
                </eligibilityCriterion>
            </precondition>
        </eligibilityCriterion>
    </precondition>
    <!-- Definition of the different epochs of the study -->
    <component1 typeCode="COMP">
        <sequenceNumber value="1"/>
        <epoch classCode="CLNTRL" moodCode="DEF">
            <id extension="ABDC" root="1.2.3.4"/>
            <code code="Treatment" valueSet="2.3.4.5"/>
            <title value="First Treatment Epoch"/>
        </epoch>
    </component1>
    <component1 typeCode="COMP">
        <sequenceNumber value="2"/>
        <epoch classCode="CLNTRL" moodCode="DEF">
            <id root="2.3.4.5" extension="ABLMN"/>
            <code code="Treatment" valueSet="2.3.4.5"/>
            <title value="Second treatment epoch"/>
        </epoch>
    </component1>
    <!-- Definition of the different arms of the study -->
    <component2 typeCode="COMP">
        <arm classCode="CLNTRL" moodCode="DEF">
            <id>
                <item root="2.3.4.6" extension="MLNOP"/>
            </id>
            <title value="Arm 1"/>
        </arm>
    </component2>
    <component2 typeCode="COMP">
        <arm classCode="CLNTRL" moodCode="DEF">
            <id>
                <item root="2.3.4.6" extension="MLNOQ"/>
            </id>
            <title value="Arm 2"/>
        </arm>
    </component2>
    <!-- Possible reasons to revise the study -->
```

```
    <component3 typeCode="COMP">
        <controlActEvent classCode="ACTN" moodCode="EVN">
            <text value="Timing events in the protocol refined"/>
            <reasonCode validTimeHigh="20120411">
                <item code="eventsRefined" valueSet="3.2.5.6"/>
            </reasonCode>
        </controlActEvent>
    </component3>
    <!-- Timing events -->
    <component4 typeCode="COMP">
        <timePointEventDefinition classCode="CTTEVENT" moodCode="DEF">
           <templateId><item root=""/></templateId>
               <!-- Study schedule content module -->
           <id root=""/>
        </timePointEventDefinition>
    </component4>
    <!-- Study characteristics -->
    <subjectOf typeCode="SUBJ">
        <studyCharacteristic classCode="CLNTRL" moodCode="EVN">
            <!-- type of characteristic -->
            <code code="Duration" valueSet="7.6.5.4"/>
            <statusCode code="active"/>
            <value xsi:type="IVL_TS">
                <low value="20120325"/>
                <high value="20120825"/>
            </value>
        </studyCharacteristic>
    </subjectOf>
    <subjectOf typeCode="SUBJ">
        <studyCharacteristic classCode="CLNTRL" moodCode="EVN">
            <!-- type of characteristic -->
            <code code="Phase" valueSet="7.6.5.4"/>
            <statusCode code="active"/>
            <value xsi:type="INT" value="4"/>
        </studyCharacteristic>
    </subjectOf>
</clinicalStudyDefinition>
```

Figure 8.3.1.C1-1 Sample Study Definition Structure

8.3.1.C1.6 Bindings

This content module may be used in various interoperability use cases. The bindings below describe the specific requirements for known use cases.

8.3.1.C1.6.1 Binding with RPE Request Process Definition

8.3.1.C1.6.2 Binding with RPE Request Activities

8.3.1.C1.6.3 Binding with RPE Update Activities

8.3.1.C2 Initiate Process Content Module

The Initiate Process Content Module describes the initiation of a clinical research study in a machine readable format.

8.3.1.C2.1 Format Code

N/A

8.3.1.C2.2 LOINC Code

N/A

8.3.1.C2.3 Standards

RPE IHE Retrieve Process for Execution

8.3.1.C2.4 Specification

This section references content modules using IHE Specification Headers as the key identifier. Definitions of the modules are found in either:

- This supplement
- IHE CDA Content Modules Supplement

Data Element Name	Opt	Content Module
Study Description	R	8.3.4.S1
Patient Demographics	C	8.3.4.S3

Note: Patient Demographics is optional when an identifier is already known by both systems.

8.3.4.S1 Study Description

This entry content module describes the general structure of a research study description. At its most general applicability, the model can describe an action plan for a formal investigation to assess the utility, impact, pharmacological, physiological, and psychological effects of a particular treatment, procedure, drug, device, biologic, food product, cosmetic, care plan, or subject characteristic. The definitions presented here are constrained for the most common clinical research studies.

8.3.4.S1.1 Specification


```
<clinicalStudyDefinition xmlns="urn:hl7-org:v3"
    xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance"
        classCode="CLNTRL" moodCode="DEF">
    <templateId><item root="1.2.3.4.5.6"/></templateId>
    <!-- Study Description Content Module -->
    <!-- Multiple IDs can describe the various IDs associated with the study -->
    <id>
        <item root="1.2.3.4" extension="ABCD"/>
    </id>
    <title value="Study Title"/>
    <text value="Study Description"/>
    <!-- Eligibility criteria -->
    <precondition typeCode="PRCN">
        <conjunctionCode code="AND"/>
        <eligibilityCriterion classCode="CLNTRL" moodCode="CRT">
            <templateId><item root=""/></templateId>
            <!-- Eligibility Criterion Content Module -->
        </eligibilityCriterion>
    </precondition>
    <!-- Definition of the different epochs of the study -->
    <component1 typeCode="COMP">
        <sequenceNumber value="1"/>
        <epoch classCode="CLNTRL" moodCode="DEF">
            <id extension="ABDC" root="1.2.3.4"/>
            <code code="Treatment" valueSet="2.3.4.5"/>
            <title value="First Treatment Epoch"/>
        </epoch>
    </component1>
    <component1 typeCode="COMP">
        <sequenceNumber value="2"/>
        <epoch classCode="CLNTRL" moodCode="DEF">
            <id root="2.3.4.5" extension="ABLMN"/>
            <code code="Treatment" valueSet="2.3.4.5"/>
            <title value="Second treatment epoch"/>
        </epoch>
    </component1>
    <!-- Definition of the different arms of the study -->
    <component2 typeCode="COMP">
        <arm classCode="CLNTRL" moodCode="DEF">
            <id>
                <item root="2.3.4.6" extension="MLNOP"/>
            </id>
            <title value="Arm 1"/>
        </arm>
    </component2>
    <component2 typeCode="COMP">
        <arm classCode="CLNTRL" moodCode="DEF">
            <id>
                <item root="2.3.4.6" extension="MLNOQ"/>
            </id>
            <title value="Arm 2"/>
        </arm>
    </component2>
    <!-- Possible reasons to revise the study -->
    <component3 typeCode="COMP">
        <controlActEvent classCode="ACTN" moodCode="EVN">
            <text value="Timing events in the protocol refined"/>
            <reasonCode validTimeHigh="20120411">
                <item code="eventsRefined" valueSet="3.2.5.6"/>
            </reasonCode>
        </controlActEvent>
    </component3>
    <!-- Timing events -->
    <component4 typeCode="COMP">
```

```
        <timePointEventDefinition classCode="CTTEVENT" moodCode="DEF">
           <templateId><item root=""/></templateId>
               <!-- Study schedule content module -->
           <id root=""/>
        </timePointEventDefinition>
    </component4>
    <!-- Study characteristics -->
    <subjectOf typeCode="SUBJ">
        <studyCharacteristic classCode="CLNTRL" moodCode="EVN">
            <!-- type of characteristic -->
            <code code="VERSION" valueSet="7.6.5.4">
                <displayName value="Version of the study"/>
            </code>
            <statusCode code="active"/>
            <value xsi:type="ST" value="V1.3"/>
        </studyCharacteristic>
    </subjectOf>
    <subjectOf typeCode="SUBJ">
        <studyCharacteristic classCode="CLNTRL" moodCode="EVN">
            <!-- type of characteristic -->
            <code code="Duration" valueSet="7.6.5.4"/>
            <statusCode code="active"/>
            <value xsi:type="IVL_TS">
                <low value="20120325"/>
                <high value="20120825"/>
            </value>
        </studyCharacteristic>
    </subjectOf>
    <subjectOf typeCode="SUBJ">
        <studyCharacteristic classCode="CLNTRL" moodCode="EVN">
            <!-- type of characteristic -->
            <code code="Phase" valueSet="7.6.5.4"/>
            <statusCode code="active"/>
            <value xsi:type="INT" value="4"/>
        </studyCharacteristic>
    </subjectOf>
</clinicalStudyDefinition>
```

Figure 8.3.4.S1-1: Sample Study Definition Structure

The Study Definition Content module contains the definitions of a study arm or arms, the study epochs, and the set of characteristics for the study. The eligibility criteria and the schedule of events are represented by the corresponding entry content modules.

8.3.4.S1.1.1 Study Definition Fields

Field	Opt.	XML Tag	Description
Study Characteristics	R	<subjectOf> <studyCharacteristic/> </subjectOf>	There are several attributes of the study. Each attribute is used to describe the study. One possible list of Study Characteristics can be found at the Characteristics identified by the CT.gov trial registration Data specification.
Epoch Definition	R2	<conponent1> <sequenceNumber/> <epoch/> </component1>	A subject moves from one Epoch to another and can only be in one epoch at a time. The subject can only move to an Epoch with a greater sequenceNumber. The main purpose of the Epoch is to organize the Arms for comparison purposes. Activities in the same Epoch but a different Arm need not be similar in time and pattern.
Arm Definition	R2	<component2> <arm/> </component2>	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.

Field	Opt.	XML Tag	Description
			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. This intended path the subject progresses in a trial is composed of a time point events (study cell) for each Epoch of the study. Each time point events, in turn, has a pattern of child time points through which the subject would pass. This planned path thus describes how subjects assigned to the Arm will be treated.
Reason for Revision	O	<component3> <controlActEvent/> </component3>	The reason why the study protocol was revised
Subjects			
Eligibility Criteria	R2	<precondition> <conjunctionCode/> <eligibilityCriterion/> </precondition>	Eligibility criteria are a set of conditions that a subject must meet in order to participate in a study. Because eligibility criteria affect recruitment into a study, they are often the subject of protocol amendments, and one criterion may be superseded by another. The most commonly occurring types of criteria involve age, sex, the type and stage of a disease, treatment history, and other medical conditions.
Timing Events	R2	<component4> <timePointEventDefinitio n/> </component4>	TimePoint has exit and entry criteria and uses workflow control suite of attributes. Each TimePointEventCriteria has a precondition Act relationship with a priority number. If there are multiple TimePointEventDefinitions with the same sequence number, the priority number determines which criteria to evaluate first. Before each step is executed preconditions are tested. If the test is positive, the activities have clearance for execution. At that time the pauseQuantity timer is started and the activities are executed after the pauseQuantity has elapsed. Pause quantity is allowed to be negative provided that it is possible to predict the occurrence of the target condition (e.g. administer 3 hours prior to surgery).

8.3.4.S1.1.2 Study Definition IDs

8.3.4.S1.1.3 Study Definition Title

690 #### 8.3.4.S1.1.4 Study Definition Description

8.3.4.S1.1.5 Study Definition Eligibility Criteria

The study definition timing events are described in the Eligibility Criteria content module section (8.3.4.S2)

8.3.4.S1.1.6 Study Definition Epoch Sequence Number

8.3.4.S1.1.7 Study Definition Epoch ID

8.3.4.S1.1.8 Study Definition Epoch Code

8.3.4.S1.1.9 Study Definition Epoch Title

8.3.4.S1.1.10 Study Definition Epoch Description

8.3.4.S1.1.11 Study Definition Arm IDs

8.3.4.S1.1.12 Study Definition Arm Title

8.3.4.S1.1.13 Study Definition Reason For Revision Description

8.3.4.S1.1.14 Study Definition Reason For Revision Codes

8.3.4.S1.1.15 Study Definition Timing Events

The study definition timing events are described in the Timing Events content module section (8.3.4.S3)

8.3.4.S1.1.16 Study Definition Characteristic Code

8.3.4.S1.1.17 Study Definition Characteristic Status

8.3.4.S1.1.18 Study Definition Characteristic Value

8.3.4.S2 Eligibility Criterion

This entry content module describes the structure of eligibility criteria, including the building of complex criteria.

8.3.4.S2.1 Specification

```
    <!-- Eligibility criteria -->
    <!-- Adults age 18-55, with Diabetes Mellitus, and not blind, coded in ICD-10 -->
    <precondition typeCode="PRCN">
        <conjunctionCode code="AND"/>
        <eligibilityCriterion classCode="CLNTRL" moodCode="CRT">
            <id>
                <item root="6.2.3.4.5" extension="218"/>
            </id>
            <code code="AGE" valueSet="3.3.4.5"/>
            <text value="Adults between 18 and 55"/>
            <value xsi:type="IVL_PQ">
                <low value="18" unit="year"/>
                <high value="55" unit="year"/>
            </value>
        </eligibilityCriterion>
    </precondition>
    <precondition typeCode="PRCN">
        <conjunctionCode code="AND"/>
        <eligibilityCriterion classCode="CLNTRL" moodCode="CRT">
            <id>
                <item root="6.2.3.4.5" extension="234"/>
            </id>
            <code code="DIAG" valueSet="3.3.4.5"/>
            <text value="Diagnosis of Diabetes"/>
            <value xsi:type="CD" code="E10-E14" codeSystem="2.16.840.1.113883.6.90"/>
            <precondition typeCode="PRCN">
                <conjunctionCode code="AND"/>
                <eligibilityCriterion classCode="CLNTRL" moodCode="CRT">
                    <code code="DIAG" codeSystem="3.3.4.5"/>
                    <negationInd value="true"/>
                    <text value="Not blind"/>
                    <value xsi:type="CD" code="H54.0" codeSystem="2.16.840.1.113883.6.90"/>
                </eligibilityCriterion>
            </precondition>
        </eligibilityCriterion>
    </precondition>
```

Figure 8.3.4.S2-1: Sample Eligibility Criteria Structure

The Eligibility Criteria content module is a list of pre-conditions, combined with a conjunction code. Complex criteria can be expressed using the recursive structure of pre-conditions.

765 **8.3.4.S2.1.1 Eligibility Criterion Fields**

Field	Opt.	XML Tag	Description
Conjunction Code	R	<conjunctionCode code=""/>	One of "AND", "OR", or "XOR"
Nested condition	O	<eligibilityCriterion> <precondition/> </eligibilityCriterion>	When eligibility criteria are on the same level, they are evaluated in sequence. The nesting of eligibility criteria is used to group conditional expressions, e.g. A AND (B OR C)

8.3.4.S2.1.2 Eligibility Criterion IDs

8.3.4.S2.1.3 Eligibility Criterion Fields

770 **8.3.4.S2.1.4 Eligibility Criterion Code**

8.3.4.S2.1.5 Eligibility Criterion Negation

8.3.4.S2.1.6 Eligibility Criterion Description

775

8.3.4.S2.1.7 Eligibility Criterion Value

8.3.4.S3 Time Point Event Definition

This entry content module describes the structure of timing events. Both a study cell and a study
780 segment are Time Point Events. Since every study segment is contained wholly within an epoch, there are, within an arm, at least as many Time Point Events as a there are epochs.

8.3.4.S3.1 Specification


```
<clinicalStudyDefinition xmlns="urn:hl7-org:v3"
    xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance"
        classCode="CLNTRL" moodCode="DEF">
    <templateId><item root="1.2.3.4.5.6"/></templateId>
    <id>
        <item root="1.2.3.4" extension="ABCD"/>
    </id>
    <title value="Study Title"/>
    <text value="Study Description"/>
    <!-- Eligibility criteria -->
     …
    <!-- Timing events -->
    <!-- Cells -->
    <!-- Screening Cell -->
    <component4 typeCode="COMP">
        <timePointEventDefinition classCode="CTTEVENT" moodCode="DEF">
            <!-- Time Event Content Module -->
            <templateId>
                <item root=""/>
            </templateId>
            <id root="3.2.4.4.5" extension="CELL.SCREEN"/>
            <code code="CELL.SCREEN" codeSystem="1.2.3.4.8.2">
                <displayName value="Screening Cell"/>
            </code>
            <effectiveTime xsi:type="IVL_TS">
                <low value="20120317"/>
                <high value="20120517"/>
            </effectiveTime>
            <component1 typeCode="COMP">
                <splitCode code=""/>
                <joinCode code=""/>
                <timePointEventDefinition classCode="CTTEVENT" moodCode="DEF">
                    <!-- Screening Segment -->
                    <id root="1.2.3.4.8.2" extension="SCREENSEG"/>
                    <code code="SCREENSEG" codeSystem="1.2.3.4.8.2">
                        <displayName value="Screening Segment"/>
                    </code>
                    <!-- Activities in this segment -->
                    <component1 typeCode="COMP">
                        <sequenceNumber value="1"/>
                        <timePointEventDefinition classCode="CTTEVENT" moodCode="DEF">
                            <id root="1.2.3.4.8.2" extension="ACT.INFORMEDCONSENT"/>
                        </timePointEventDefinition>
                    </component1>
                    <component1 typeCode="COMP">
                        <sequenceNumber value="2"/>
                        <timePointEventDefinition classCode="CTTEVENT" moodCode="DEF">
                            <id root="1.2.3.4.8.2" extension="ACT.PATIENTNUMBERASSIGNMENT"/>
                        </timePointEventDefinition>
                    </component1>
                    <component1 typeCode="COMP">
                        <sequenceNumber value="3"/>
                        <timePointEventDefinition classCode="CTTEVENT" moodCode="DEF">
                            <id root="1.2.3.4.8.2" extension="ACT.MEDICALHISTORY_01"/>
                        </timePointEventDefinition>
                    </component1>
                    <component1 typeCode="COMP">
                        <sequenceNumber value="4"/>
                        <timePointEventDefinition classCode="CTTEVENT" moodCode="DEF">
                            <id root="1.2.3.4.8.2" extension="ACT.VITALSIGNS_01"/>
                        </timePointEventDefinition>
                    </component1>
                    <component1 typeCode="COMP">
                        <sequenceNumber value="5"/>
                        <timePointEventDefinition classCode="CTTEVENT" moodCode="DEF">
```

```
                        <id root="1.2.3.4.8.2" extension="ACT.AMB_ECG_PLACEMENT_01"/>
                    </timePointEventDefinition>
                </component1>
                <component1 typeCode="COMP">
                    <sequenceNumber value="6"/>
                    <timePointEventDefinition classCode="CTTEVENT" moodCode="DEF">
                        <id root="1.2.3.4.8.2" extension="ACT.AMB_ECG_REMOVAL_01"/>
                    </timePointEventDefinition>
                </component1>
                <component1 typeCode="COMP">
                    <sequenceNumber value="7"/>
                    <pauseQuantity value="7" unit="day">
                        <uncertainRange>
                            <low xsi:type="PQ" value="-24" unit="hours"/>
                            <high xsi:type="PQ" value="48" unit="hours"/>
                        </uncertainRange>
                    </pauseQuantity>
                    <timePointEventDefinition classCode="CTTEVENT" moodCode="DEF">
                        <id root="1.2.3.4.8.2" extension="ACT.VITALSIGNS_02"/>
                    </timePointEventDefinition>
                </component1>
                <component1 typeCode="COMP">
                    <sequenceNumber value="8"/>
                    <timePointEventDefinition classCode="CTTEVENT" moodCode="DEF">
                        <id root="1.2.3.4.8.2" extension="ACT.PATIENTRANDOMIZATION"/>
                    </timePointEventDefinition>
                </component1>
                <component1 typeCode="COMP">
                    <sequenceNumber value="9"/>
                    <timePointEventDefinition classCode="CTTEVENT" moodCode="DEF">
                        <id root="1.2.3.4.8.2" extension="ACT.HACHINSKI"/>
                    </timePointEventDefinition>
                </component1>
            </timePointEventDefinition>
        </component1>
        <!-- The screening part of the study is not blinded with respect to the arms -->
        <subjectOf typeCode="SUBJ">
            <timePointEventCharacteristic classCode="CLNTRL" moodCode="EVN">
                <code code="BLINDED" codeSystem="1.2.3.4.8.2"/>
                <value xsi:type="BL" value="false"/>
            </timePointEventCharacteristic>
        </subjectOf>
        <!-- Links to the epoch and Arm(s) of the study -->
        <componentOf1 typeCode="COMP">
            <epochStub classCode="CLNTRL" moodCode="DEF">
                <id extension="EP.SCREPOCH" root="1.2.3.4"/>
            </epochStub>
        </componentOf1>
        <componentOf2 typeCode="COMP">
            <armStub classCode="CLNTRL" moodCode="DEF">
                <id>
                    <item root="2.3.4.6" extension="ARM.PLACEBO"/>
                </id>
            </armStub>
        </componentOf2>
        <componentOf2 typeCode="COMP">
            <armStub classCode="CLNTRL" moodCode="DEF">
                <id>
                    <item root="2.3.4.6" extension="ARM.LOWDOSE"/>
                </id>
            </armStub>
        </componentOf2>
        <componentOf2 typeCode="COMP">
            <armStub classCode="CLNTRL" moodCode="DEF">
                <id>
```

```
                    <item root="2.3.4.6" extension="ARM.HIGHDOSE"/>
                </id>
            </armStub>
        </componentOf2>
    </timePointEventDefinition>
</component4>
<!-- Treatment Cell -->
<component4 typeCode="COMP">
    <timePointEventDefinition classCode="CTTEVENT" moodCode="DEF">
        <templateId>
            <item root=""/>
        </templateId>
        <id root="3.2.4.4.5" extension="CELL.TREATMENT"/>
        <code code="CELL.TREATMENT" codeSystem="1.2.3.4.8.2">
            <displayName value="Treatment Cell"/>
        </code>
        <!-- The treatment part of the study is blinded with respect to the arms -->
        <subjectOf typeCode="SUBJ">
            <timePointEventCharacteristic classCode="CLNTRL" moodCode="EVN">
                <code code="BLINDED" codeSystem="1.2.3.4.8.2"/>
                <value xsi:type="BL" value="true"/>
            </timePointEventCharacteristic>
        </subjectOf>
        <!-- Links to the epoch and Arm(s) of the study -->
        <componentOf1 typeCode="COMP">
            <epochStub classCode="CLNTRL" moodCode="DEF">
                <id extension="EP.TREPOCH" root="1.2.3.4"/>
            </epochStub>
        </componentOf1>
        <componentOf2 typeCode="COMP">
            <armStub classCode="CLNTRL" moodCode="DEF">
                <id>
                    <item root="2.3.4.6" extension="ARM.PLACEBO"/>
                </id>
            </armStub>
        </componentOf2>
        <componentOf2 typeCode="COMP">
            <armStub classCode="CLNTRL" moodCode="DEF">
                <id>
                    <item root="2.3.4.6" extension="ARM.LOWDOSE"/>
                </id>
            </armStub>
        </componentOf2>
        <componentOf2 typeCode="COMP">
            <armStub classCode="CLNTRL" moodCode="DEF">
                <id>
                    <item root="2.3.4.6" extension="ARM.HIGHDOSE"/>
                </id>
            </armStub>
        </componentOf2>
    </timePointEventDefinition>
</component4>
<!-- Followup Cell -->
<component4 typeCode="COMP">
    <timePointEventDefinition classCode="CTTEVENT" moodCode="DEF">
        <templateId>
            <item root=""/>
        </templateId>
        <id root="3.2.4.4.5" extension="CELL.FOLLOWUP"/>
        <code code="CELL.FOLLOWUP" codeSystem="1.2.3.4.8.2">
            <displayName value="Follow-up Cell"/>
        </code>
        <!-- The followup part of the study is blinded with respect to the arms -->
        <subjectOf typeCode="SUBJ">
            <timePointEventCharacteristic classCode="CLNTRL" moodCode="EVN">
```

```
                    <code code="BLINDED" codeSystem="1.2.3.4.8.2"/>
                    <value xsi:type="BL" value="true"/>
                </timePointEventCharacteristic>
            </subjectOf>
            <!-- Links to the epoch and Arm(s) of the study -->
            <componentOf1 typeCode="COMP">
                <epochStub classCode="CLNTRL" moodCode="DEF">
                    <id extension="EP.FUPEPOCH" root="1.2.3.4"/>
                </epochStub>
            </componentOf1>
            <componentOf2 typeCode="COMP">
                <armStub classCode="CLNTRL" moodCode="DEF">
                    <id>
                        <item root="2.3.4.6" extension="ARM.PLACEBO"/>
                    </id>
                </armStub>
            </componentOf2>
            <componentOf2 typeCode="COMP">
                <armStub classCode="CLNTRL" moodCode="DEF">
                    <id>
                        <item root="2.3.4.6" extension="ARM.LOWDOSE"/>
                    </id>
                </armStub>
            </componentOf2>
            <componentOf2 typeCode="COMP">
                <armStub classCode="CLNTRL" moodCode="DEF">
                    <id>
                        <item root="2.3.4.6" extension="ARM.HIGHDOSE"/>
                    </id>
                </armStub>
            </componentOf2>
        </timePointEventDefinition>
    </component4>
    <!-- Activity Events -->
    <!-- Informed Consent -->
    <component4 typeCode="COMP">
        <timePointEventDefinition classCode="CTTEVENT" moodCode="DEF">
            <id root="3.2.4.4.5" extension="ACT.INFORMEDCONSENT"/>
            <code code="ACT.INFORMEDCONSENT" codeSystem="1.2.3.4.8.2">
                <displayName value="Informed Consent"/>
            </code>
            <subjectOf typeCode="SUBJ">
                <timePointEventCharacteristic classCode="VERIF" moodCode="EVN">
                    <!-- Form ID -->
                    <id>
                        <item root="1.2.3.4.5" extension="form1ID"/>
                    </id>
                    <code code="FO.INFORMEDCONSENT" codeSystem="1.2.3.4.8.2" />
                    <value xsi:type="TEL" value="https://some.formmanager.addr/forms/"/>
                </timePointEventCharacteristic>
            </subjectOf>
        </timePointEventDefinition>
    </component4>
    <!-- Study characteristics -->
    …
</clinicalStudyDefinition>
```

Figure 8.3.4.S3-1: Time Point Event Definition Structure

The Time Point Event Definition Content module contains the definitions of a study cells, segments, and activities. Each time point event may have various characteristics, entry and exit conditions, and links to other activities. The general structure of the time point event definitions is as follows:

Study Cell
Link to Epoch
Link(s) to Arm(s)
Study Segment
Link(s) to Activity in the segment
Study Segment
…
Study Cell
…
…
Activity
…

Activity
…

Study cells are recognized by the links to the Epoch and Arm or Arms they belong to, while Activities inherit these links from the segments from which they are referenced. The pause quantity in the links to the activities in a given segment represents the relative time between them, with the uncertainty range representing an interval, during which the activity can still be performed while staying within the parameters of the study.

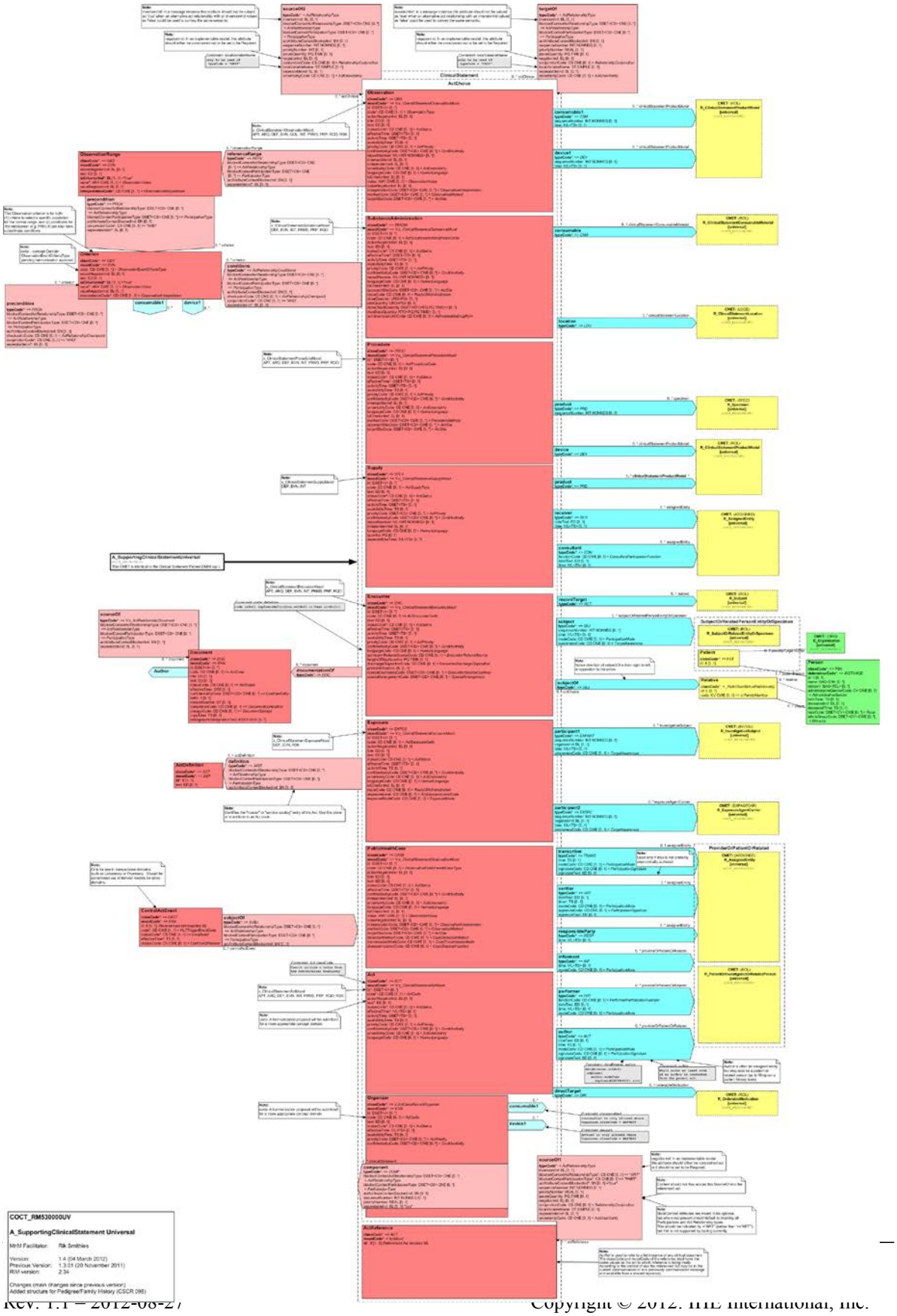
8.3.4.S3.1.1 Time Point Event Definition Fields

Field	Opt.	XML Tag	Description
Study Cell	R	<component4> <timePointEventDefinition> <!-- ……. --> <componentOf1> <epochStub> <id/> </epochStub> </componentOf1> <compnentOf2> <armStub> <id/> </armStub> </componentOf2> <!-- ……. --> </timePointEventDefinition> </component4>	A study cell is a Time Point Event Definition, which is linked to an Epoch, and to one or more Arms via their corresponding IDs
Study Segment	R	<component4> <timePointEventDefinition> <component1> <timePointEventDefinition/> </component1> <componentOf1/> <componentOf2/> </timePointEventDefinition>	A study segment is a Time Point Event Definition contained inside a study cell. It contains a list of links to study activities, which are part of the segment.

Field	Opt.	XML Tag	Description
		</component4>	
Study Activity	R	<component4> <timePointEventDefinition> <id/> <code/> <subjectOf> <timePointEventCharacteristic/> </subjectOf> </timePointEventDefinition> </component4>	A study activity or study event is a Time Point Event Definition which may have various characteristics, and may refer to clinical acts. It may also contain a list of references to other study activities or events.
Activity Form	O	<component4> <timePointEventDefinition> <subjectOf> <timePointEventCharacteristic classCode="VERIF" moodCode="EVN"> <!-- Form ID --> <id> <item root="1.2.3.4.5" extension="form1ID"/> </id> <code code="FO.INFORMEDCONSENT" codeSystem="1.2.3.4.8.2" /> <value xsi:type="TEL" value=https://some.formmanager.addr/forms//> </timePointEventCharacteristic> </subjectOf> </timePointEventDefinition> </component4>	When an activity has a characteristic designated with class code "VERIF", it contains information about a specific form to be used to document this activity. The characteristic ID is the form ID, and the value is the URL where the form can be accessed via RFD.

8.3.4.S4 Supporting Clinical Statement Definition

This entry content module describes the structure of supporting clinical statements with respect to a specific activity. The Clinical Statement CMET is used to define the supporting clinical statement module of a timing event. While a clinical statement in general can be as complicated as a full patient clinical record, in this profile we only present how to specify a visit (encounter), a procedure, and an observation.



8.3.4.S4.1 Specification


```
<clinicalStudyDefinition xmlns="urn:hl7-org:v3"
    xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance"
        classCode="CLNTRL" moodCode="DEF">
    <templateId><item root="1.2.3.4.5.6"/></templateId>
    <id>
        <item root="1.2.3.4" extension="ABCD"/>
    </id>
    <title value="Study Title"/>
    <text value="Study Description"/>
    <!-- Eligibility criteria -->
     …
    <!-- Timing events -->
    <!-- Cells -->
    <!-- Screening Cell -->
     …
    <!-- Activity Events -->
    <!-- Informed Consent -->
    <component4 typeCode="COMP">
        <timePointEventDefinition classCode="CTTEVENT" moodCode="DEF">
            <id root="3.2.4.4.5" extension="ACT.INFORMEDCONSENT"/>
            <code code="ACT.INFORMEDCONSENT" codeSystem="1.2.3.4.8.2">
                <displayName value="Informed Consent"/>
            </code>
            <subjectOf typeCode="SUBJ">
                <timePointEventCharacteristic classCode="VERIF" moodCode="EVN">
                    <!-- Form ID -->
                    <id>
                        <item root="1.2.3.4.5" extension="form1ID"/>
                    </id>
                    <code code="FO.INFORMEDCONSENT" codeSystem="1.2.3.4.8.2" />
                    <value xsi:type="TEL" value="https://some.formmanager.addr/forms/"/>
                </timePointEventCharacteristic>
            </subjectOf>
        </timePointEventDefinition>
    </component4>
    <!-- Visit Activity -->
    <component4 typeCode="COMP">
        <timePointEventDefinition classCode="CTTEVENT" moodCode="DEF">
            <id root="3.2.4.4.5" extension="VisitDefinitionID"/>
            <code code="ACT.VISIT" codeSystem="1.2.3.4.8.2"/>
            <component2 typeCode="COMP">
                <encounter classCode="ENC" moodCode="DEF">
                    <code code="Visit1" codeSystem="1.2.3.4.8.2"/>
                    <effectiveTime xsi:type="IVL_TS">
                        <low value="201206110900"/>
                        <high value="201206140900"/>
                    </effectiveTime>
                    <activityTime xsi:type="TS" value="201206120900"/>
                </encounter>
            </component2>
            <subjectOf typeCode="SUBJ">
                <timePointEventCharacteristic classCode="VERIF" moodCode="EVN">
                    <!-- Form ID -->
                    <id>
                        <item root="1.2.3.4.5" extension="form2ID"/>
                    </id>
                    <code code="FO.VISIT" codeSystem="1.2.3.4.8.2" />
                    <value xsi:type="TEL" value="https://some.formmanager.addr/forms/"/>
                </timePointEventCharacteristic>
            </subjectOf>
        </timePointEventDefinition>
    </component4>
    <!-- Vital Signs activity -->
    <component4 typeCode="COMP">
        <timePointEventDefinition classCode="CTTEVENT" moodCode="DEF">
```

```
            <id root="1.2.3.4.8.2" extension="ACT.VITALSIGNS_01"/>
            <code code="ACT.VISIT" codeSystem="1.2.3.4.8.2"/>
            <component2 typeCode="COMP">
                <observation classCode="CLNTRL" moodCode="EVN">
                    <code code="Observation1" codeSystem="3.4.2.3.5"/>
                </observation>
            </component2>
            <subjectOf typeCode="SUBJ">
                <timePointEventCharacteristic classCode="VERIF" moodCode="EVN">
                    <!-- Form ID -->
                    <id>
                        <item root="1.2.3.4.5" extension="form3ID"/>
                    </id>
                    <code code="FO.VITALS" codeSystem="1.2.3.4.8.2" />
                    <value xsi:type="TEL" value="https://some.formmanager.addr/forms/"/>
                </timePointEventCharacteristic>
            </subjectOf>
            <!-- This Characteristic indicates that this is billed to regular care, and not to
Clinical Trial -->
            <subjectOf typeCode="SUBJ">
                <timePointEventCharacteristic classCode="VERIF" moodCode="EVN">
                    <code code="BILL_TO_TRIAL" codeSystem="1.2.3.4.8.2" />
                    <value xsi:type="BL" value="false"/>
                </timePointEventCharacteristic>
            </subjectOf>
        </timePointEventDefinition>
    </component4>
    <!-- ECG activity -->
    <component4 typeCode="COMP">
        <timePointEventDefinition classCode="CTTEVENT" moodCode="DEF">
            <id root="1.2.3.4.8.2" extension="ACT.AMB_ECG_PLACEMENT_01"/>
            <code code="ACT.AMB_ECG_PLACEMENT_01" codeSystem="1.2.3.4.8.2"/>
            <!-- Patient is in this activity -->
            <subject typeCode="SBJ">
                <experimentalUnit classCode="RESBJ">
                    <subjectPersonKind classCode="PSN" determinerCode="KIND">
                        <id extension="patID" root="2.1.3.4.5.9"/>
                    </subjectPersonKind>
                </experimentalUnit>
            </subject>
            <component2 typeCode="COMP">
                <procedure classCode="PROC" moodCode="EVN">
                    <code code="Procedure1" codeSystem="3.4.2.3.5"/>
                </procedure>
            </component2>
            <subjectOf typeCode="SUBJ">
                <timePointEventCharacteristic classCode="VERIF" moodCode="EVN">
                    <!-- Form ID -->
                    <id>
                        <item root="1.2.3.4.5" extension="form3ID"/>
                    </id>
                    <code code="FO.VITALS" codeSystem="1.2.3.4.8.2" />
                    <value xsi:type="TEL" value="https://some.formmanager.addr/forms/"/>
                </timePointEventCharacteristic>
            </subjectOf>
        </timePointEventDefinition>
    </component4>
    <!-- Study characteristics -->
    …
</clinicalStudyDefinition>
```

Figure 8.3.4.S4-1: Supporting Clinical Statement Definition Structure

The Clinical Statement components used to describe the corresponding activities (encounter, observation, or procedure) contain the attributes effective time and activity time. The activity time designates the point in time when the activity is supposed to occur (or has already occurred, if the mood code is EVN). The effective time describes an interval around the activity time during which the activity can still be performed while staying within the parameters of the study. The effective time in an instantiated protocol for a specific patient directly corresponds to the uncertainty range in the protocol definition.

8.5 CRPC Value Sets

None

Volume 4 – National Extensions

Add appropriate Country section

Not applicable