Meeting Minutes

CDISC-HL7 Stage II
March 5, 2008
11:00 am – 12:00 pm (EST)

Attendees/Affiliation

Jason Rock/GlobalSubmit (Chair)
Bryan Ennis/Genzyme
Julie Evans/CDISC
Patty Garvey/FDA
Scott Getzin/Eli Lilly
Terry Hardin/IBM
Wayne Kubick/Lincoln Technologies
Mary Lenzen/Octagon
Jay Levine/FDA
Saurin Mehta/Novartis
Fred Miller/Genentech
Joyce Niland/City of Hope Medial Center
Armando Oliva/FDA

Background

FDA wishes to receive, in regulatory submissions, standard clinical study information content developed by the Clinical Data Interchange Standards Consortium (CDISC) in an Health Level 7 (HL7) message exchange format. This is key to the FDA strategic initiatives to improve public health and patient safety.

This project is currently broken in to two stages requirements analysis and message development.

The purpose of the meeting is for Regulated Clinical Research Information Management (RCRIM) members to discuss develop consensus necessary for a path forward on CDISC HL7 Stage II activities.

Discussion

- Patty provided an update on the CDISC-HL7 Project Charter. There were 8 individuals that provided comments. The charter is currently being revised to incorporate the comments. The charter will be sent to RCRIM for review early next week.

- Joyce presented the storyboards, use cases and an overview of the ASPIRE (Agreement on Standardized Protocol Inclusion Requirements for Eligibility) subproject of the CDISC Protocol Representation group. The project is striving to assemble a set of core Coded Eligibility Criteria that could be agreed upon by the research community, to ultimately extend the electronic registration of a protocol. The use cases would support a patient/ their family or physician to search for possible studies for which the patient may be eligible; a sponsor to search for a cohort of potential patients to screen further for eligibility; or a protocol author to review common use and specification of eligibility criteria. Certain eligibility criteria are "pan-disease", e.g. minimum age, maximum age, allowable genders, physiological conditions, etc, and certain criteria would be "disease-specific", e.g. for breast cancer the stage of cancer, ER/PR status, and Her2Neu status are common criteria for eligibility. The HL7 Filtered Query Service and Virtual Medical Record projects are considering the eligibility searching as use cases, and the hope is to vet the core eligibility criteria through HL7 RCRIM, CDISC, CDASH, FDA, and all related projects/communities to come to agreement, and ultimately to have the core eligibility criteria harmonized into the BRIDG model.

- Jason Rock provided a presentation on the Study Participation. Only a few slides were presented. It was noted that the starting point of the message development was BRIDG. There were questions on the scope of what a study is. Armando and Jay agreed to write up a few words.

Action Items

1. Joyce to provide more information regarding the Kick-off meeting for the CRI-WG Eligibility Standards Task Force and the forum website.

2. Jason will provide his Study Participation PowerPoint presentation.

3. Next meeting will be to finish Jason's Study Participation presentation and Joyce will present the ASPIRE Data Dictionary.

Attachments:

1. *ASPIRE: Agreement on Standardized Protocol Inclusion Requirements for Eligibility.*
2. *ASPIRE Storyboards*
3. *Forum website for CRI-WG Eligibility Standards Task Forum is located at: http://www.researchinformatics.org/component/option,com_fireboard/Itemid,111/func,showcat/catid,19/*
4. *Study Participation*

Drafted: PGarvey/3-7-2008
Approved/Final: PGarvey/4-2-2008

ASPIRE:
Agreement on Standardized Protocol Inclusion Requirements for Eligibility

Joyce C. Niland, Ph.D.
Edward & Estelle Alexander Chaired Professor
Associate Director for Information Sciences
City of Hope Cancer Center

A Critical Challenge to Advancing Biomedical Discoveries

Only a small fraction of potentially eligible subjects are enrolled in clinical trials

Among 1.2 mill new cancer diagnoses in U.S. annually:

- 12-44% are eligible for clinical trial enrollment
- Only 1-3% of eligible patients are enrolled in clinical trials

Potential Questions to be Answered via Standardized Coded Eligibility Criteria

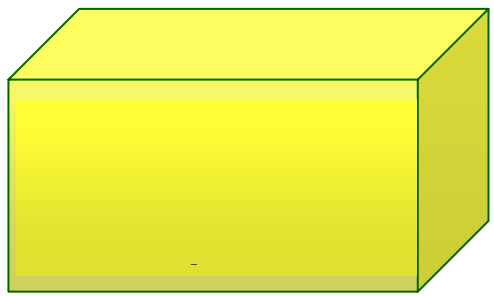
- Patients/Providers/Family Members
  - Does a specific center have an open trial for my condition?
- Sponsors
  - Where can I run my new trial so that it will have the most success of meeting its accrual goals?
- Principal Investigators
  - Which eligibility criteria are most useful / limiting in designing a clinical trial's inclusion factors?

Eligibility Screening Based on Core Criteria

International:

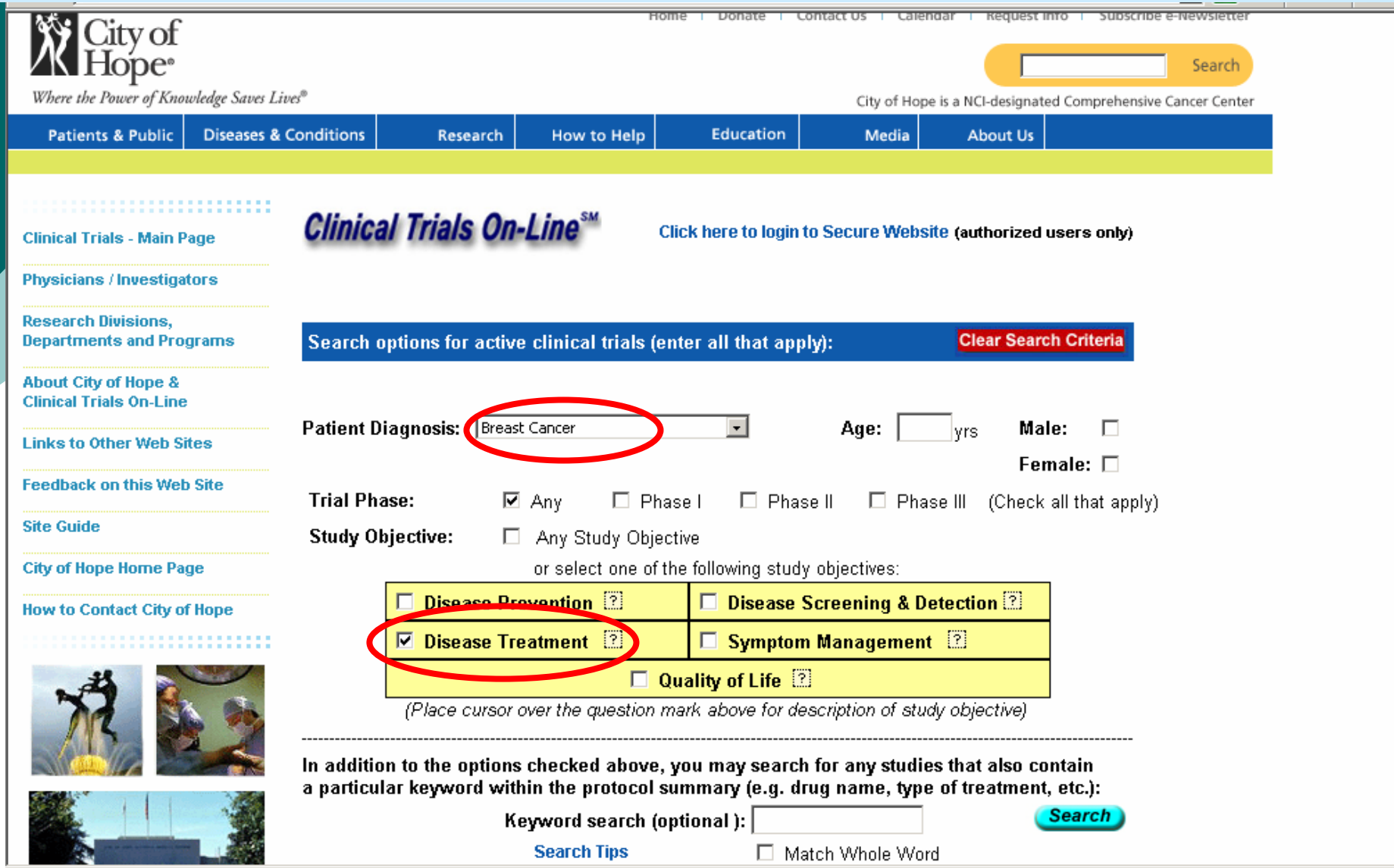
National:

City of Hope:



Sample Use Case:

City of Hope Breast Cancer-Specific Protocol Search Filter



City of Hope Clinical Trials On-Line: Physician Display - Clinical Trials On-Line (Clinical Tri - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Back Search Favorites Media

Address http://clinicaltrials.coh.org/diagnosis_search.aspx?category=1008&age=&protgroup=DT&phase=&gender=&keyword1=&frmexact= Go Links

City of Hope

Where the Power of Knowledge Saves Lives®

Home | Donate | Contact Us | Calendar | Request Info | Subscribe e-Newsletter

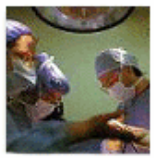
Search

City of Hope is a NCI-designated Comprehensive Cancer Center

Patients & Public | Diseases & Conditions | Research | How to Help | Education | Media | About Us

Click here to login to Secure Web Site **(authorized users only)**

- Clinical Trials - Main Page
- Physicians / Investigators
- Research Divisions, Departments and Programs
- About City of Hope & Clinical Trials On-Line
- Links to Other Web Sites
- Feedback on this Web Site
- Site Guide
- City of Hope Home Page
- How to Contact City of Hope


Click here to begin search for active clinical trials for Breast Cancer **Search**

Add additional search options: **New Search**

Stage:	☐ In Situ	☐ I	☐ II	☐ III	☐ IV (Check all that apply)
Her-2/Neu:	☐ Positive		☐ Negative		☐ Unknown
ER Status:	☐ Positive		☐ Negative		☐ Unknown
PR Status:	☐ Positive		☐ Negative		☐ Unknown
Measurable Disease?	☐ Yes		☐ No		☐ Unknown

Left Blank

Search

Done Trusted sites

Start Inbo... Micro... Solitaire City ... Prop... Prese... 4:07 PM

City of Hope Clinical Trials On-Line: Category Display - Clinical Trials On-Line (Clinical Tria - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Back Search Favorites Media

Address http://clinicaltrials.coh.org/specific_result.aspx?category=1008&age=&protgroup=DT&phase=&gender=&keyword1=&frmexact= Go Links

City of Hope
Where the Power of Knowledge Saves Lives®

Search

City of Hope is a NCI-designated Comprehensive Cancer Center

Patients & Public | Diseases & Conditions | Research | How to Help | Education | Media | About Us

Click here to login to Secure Web Site **(authorized users only)**

- Clinical Trials - Main Page
- Physicians / Investigators
- Research Divisions, Departments and Programs
- About City of Hope & Clinical Trials On-Line
- Links to Other Web Sites
- Feedback on this Web Site
- Site Guide
- City of Hope Home Page
- How to Contact City of Hope

Search results: 28 Clinical trial(s) found. (Page 1 of 6) New Search Back

[<Prev] [Next>]

Click here to generate a printer-friendly view

The following studies are available for Breast Cancer:

05085 Please select from the following options:

P.I.: Jana Portnow, M.D.

Title: SWOG S0226: Phase III Randomized Trial of Anastrozole Versus Anastrozole and Fulvestrant as First Line Therapy for Post Menopausal Women with Metastatic Breast Cancer

05042 Please select from the following options:

P.I.: George Somlo, M.D.

Title: Phase II Study of Tandem Cycle Dose-Intense Chemotherapy of Mephalan and Carboplatin, Thiotepa, and Cyclophosphamide (STMP V) followed by Helical Tomotherapy for Stage IV Metastatic and Stage IIIB Inflammatory Breast Cancer

05026 Please select from the following options:

P.I.: Lawrence Wagman, M.D.

Title: NSABP Protocol B-38: A Phase III, Adjuvant Trial Comparing Three Chemotherapy Regimens in Women With Node-Positive Breast Cancer: Docetaxel/Doxorubicin/Cyclophosphamide (TAC): Dose Dense (DD) Doxorubicin/Cyclophosphamide Followed By DD Paclitaxel (DD AC P): DD AC Followed by DD Paxlitaxel Plus Gemcitabine (DD AC PG)

05025 Please select from the following options:

P.I.: Nayana Vora, M.D.

Done Trusted sites

Start Inbo... Micr... Solit... City ... Prop... Pres... 4:10 PM

City of Hope Clinical Trials On-Line: Physician Display - Clinical Trials On-Line (Clinical Tri - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Back Search Favorites Media

Address http://clinicaltrials.coh.org/diagnosis_search.aspx?category=1008&age=&protgroup=DT&phase=&gender=&keyword1=&frmexact= Go Links

City of Hope
Where the Power of Knowledge Saves Lives®

Home | Donate | Contact Us | Calendar | Request Info | Subscribe e-Newsletter

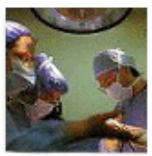
Search

City of Hope is a NCI-designated Comprehensive Cancer Center

Patients & Public | Diseases & Conditions | Research | How to Help | Education | Media | About Us

Click here to login to Secure Web Site **(authorized users only)**

- Clinical Trials - Main Page
- Physicians / Investigators
- Research Divisions, Departments and Programs
- About City of Hope & Clinical Trials On-Line
- Links to Other Web Sites
- Feedback on this Web Site
- Site Guide
- City of Hope Home Page
- How to Contact City of Hope


Click here to begin search for active clinical trials for Breast Cancer Search

Add additional search options: New Search

Stage:	☐ In Situ	☐ I	☑ II	☐ III	☐ IV (Check all that apply)
Her-2/Neu:	☑ Positive	☐ Negative	☐ Unknown		
ER Status:	☐ Positive	☑ Negative	☐ Unknown		
PR Status:	☐ Positive	☑ Negative	☐ Unknown		
Measurable Disease?	☑ Yes	☐ No	☐ Unknown		

Filled In

Search

Done Trusted sites

Start Inbo... Micr... Solit... City ... Prop... Pres... 4:10 PM

City of Hope Clinical Trials On-Line: Category Display - Clinical Trials On-Line (Clinical Tria - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Back Search Favorites Media

Address http://clinicaltrials.coh.org/specific_result.aspx?category=1008&age=&protgroup=DT&phase=&gender=&keyword1=&frmexact= Go Links

City of Hope®

Where the Power of Knowledge Saves Lives®

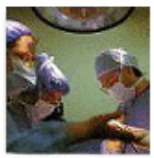
Search

City of Hope is a NCI-designated Comprehensive Cancer Center

Patients & Public | Diseases & Conditions | Research | How to Help | Education | Media | About Us

Click here to login to Secure Web Site **(authorized users only)**

- Clinical Trials - Main Page
- Physicians / Investigators
- Research Divisions, Departments and Programs
- About City of Hope & Clinical Trials On-Line
- Links to Other Web Sites
- Feedback on this Web Site
- Site Guide
- City of Hope Home Page
- How to Contact City of Hope


Search results: 7 Clinical trial(s) found. (Page 1 of 2) New Search Back

[<Prev] [Next>]

Click here to generate a printer-friendly view

The following studies are available for Breast Cancer:

05026 Please select from the following options:

P.I.: Lawrence Wagman, M.D.

Title: NSABP Protocol B-38: A Phase III, Adjuvant Trial Comparing Three Chemotherapy Regimens in Women With Node-Positive Breast Cancer: Docetaxel/Doxorubicin/Cyclophosphamide (TAC): Dose Dense (DD) Doxorubicin/Cyclophosphamide Followed By DD Paclitaxel (DD AC P): DD AC Followed by DD Paxlitaxel Plus Gemcitabine (DD AC PG)

05025 Please select from the following options:

P.I.: Nayana Vora, M.D.

Title: NSABP Protocol B-39/RTOG 0413: A Randomized Phase III Study of Conventional Whole Breast Irradiation (WBI) Versus Partial Breast Irradiation (PBI) for Women with Stage 0, I, or II Breast Cancer

05015 Please select from the following options:

P.I.: George Somlo, M.D.

Title: Randomized Phase II Study of Docetaxel, Adriamycin, and Cytoxan (TAC) Versus Adriamycin/Cytoxan, Followed By Abraxane/Carboplatin (ACAC) +/- Trastuzumab As Neoadjuvant Therapy for Patients with Stage II-III Breast Cancer

04117 Please select from the following options:

P.I.: Lawrence Wagman, M.D.

Title: NSABP B-36: A Clinical Trial of Adjuvant Therapy Comparing Six Cycles of 5-

Done Trusted sites

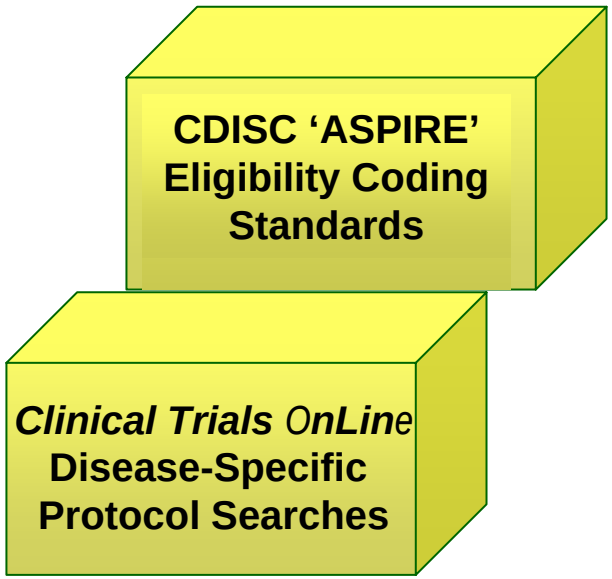
Start Inbo... Micr... Solit... City ... Prop... Pres... 4:11 PM

Eligibility Screening Based on Core Criteria

International:

National:

City of Hope:



Clinical Data Interchange Standards Consortium (CDISC)

- Open, multi-disciplinary, non-profit organization, founded in 1997
- Initial CDISC Sponsors
  - Pharma and software development companies
  - Now academic centers participating as well, e.g. City of Hope
- **Mission:** Develop global, vendor-neutral, platform independent ***standards*** to speed product development
  - Formed Protocol Representation Working Group

CDISC Protocol Representation Project

ASPIRE:

Agreement on Standardized Protocol Inclusion Requirements for Eligibility

Charter and Mission of ASPIRE Project

- Charter:
  - To develop proposed standardized method(s) of encoding protocol eligibility criteria, using accepted medical terminology / vocabulary standards as available and appropriate

- Mission:
  - To facilitate more rapid efficient ***screening*** of potential participants for available clinical trials
    - to help speed the discovery of new interventions to treat, prevent or screen for disease
    - to serve as the underpinning for various technical implementations to facilitate subject screening and recruitment

Coded *Core* Set of Eligibility Criteria

- Minimal dataset to support the following use cases:
  - Locate potential protocols for a given individual
    - Tailor the query by matching core protocol eligibility against the subject characteristics
  - Locate potential subjects for a given protocol
    - Based on coded EHR data, to then contact (with permission) and screen for full eligibility
  - Evaluate the utility and prevalence of common core eligibility criteria
    - Assist in the initial design or refinement of protocols

Coded *Core* Set of Eligibility Criteria

- *Not* an attempt to fully code or automate all inclusion/exclusion criteria for protocols
- Data elements could augment WHO protocol registration data
  - Search capabilities will be optimized with universal coverage of protocols
- Requires ‘pan-disease’ and disease-specific criteria
  - Across many diseases and study types

ASPIRE Activities to Date

- Held conference calls over past year to deliberate on core eligibility criteria
  - Completed pan-disease criteria (n=22), disease-specific criteria for breast cancer (n=15) and for diabetes (n=18)
  - Vetted elements twice with CDISC Protocol Representation Group
  - Harmonized with WHO registry elements, SDTM, and CDASH eligibility forms

Sample Core Coded Eligibility Criteria

Pan-Disease Elements:

- Min Age -Minimum allowable age on study
- Max Age -Maximum allowable age on study
- Gender -Allowable gender(s): Male, Female, Either
- Reproductive Status -Allowable status (M or F): Active, Not Active, NA
- Performance Status -Minimum allowable level among 3 global status codes* etc. (could be ECOG, Karnofsky, Lansky, SWOG scale)

* 1 - Able to carry on normal activity and to work; no special care needed

2 - Unable to work; able to live at home and care for most personal needs; varying amount of assistance needed

3 - Unable to care for self; requires equivalent of institutional or hospital care; disease may be progressing rapidly

Sample Core Coded Eligibility Criteria

Breast Cancer Specific Elements:

• Stage	-Allowable stages (code all): DCIS, I, II, III, IV
• ER Status	-Positive, Negative, Status Known, NA
• PR Status	-Positive, Negative, Status Known, NA
• Combined Hormone Status	-One Positive (ER or PR), Both Positive (ER & PR)
• Prior Chemotherapy, etc.	-Allowed, Allowed with Conditions, Required, Required with Conditions, NA*

***Examples of Prior Chemo 'Conditions':**

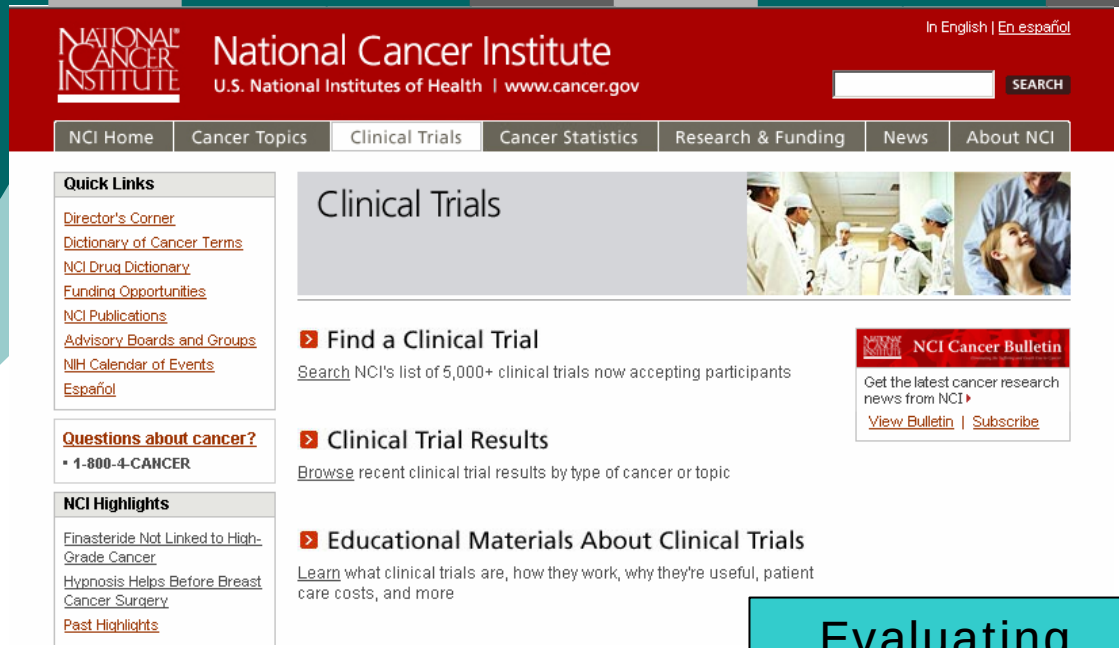
- Must not have received taxol-containing agents within past 6 months (Code as 'Allowed with Conditions')
- Must have completed at least 6 cycles of CAF regimen prior to entry (Code as 'Required with Conditions')

NOTE: Implementation of filter queries would cast "widest net", i.e. include protocols meeting eligibility 'with conditions' (but flag for further investigation)

Premise for Discussion:

- Establishing protocol “inclusion” and “exclusion” criteria generally redundant, and introduces unwanted complexity without adding value, may lead to ‘double negative’ expressions
  - Example from R. Richesson:
    - Inclusion criterion: 16 years and above
    - Exclusion criterion: Children < 16 years
- Proposed: Establish best practice of defining ‘eligibility criteria’ as uni-directional factors that will allow the subject to go on trial
  - Negation of eligibility criteria can be clearly inferred from the positively crafted statements

In Progress:
Evaluation of Eligibility Coding Utility



Compare to coded data on >25,000 women with breast cancer (pseudo EMR)

Coding ~200 PDQ breast cancer trials using ASPIRE eligibility codes

Evaluating ability of matching potential trials to patients, & utility of each coded field

Findings to Date with Respect to Standardized Eligibility Coding:

- ASPIRE team has been able to code ~130 PDQ breast cancer trials
- Process raised many issues due to non-standardized ways of describing eligibility in existing protocols:
  - Stage described in various ways, often with conditions
    - Stage III, but not inflammatory breast cancer
  - Key fields *not explicitly stated* in text
    - Stage listed in the protocol title, but nowhere in the eligibility criteria
  - **Certain criteria needed to be inferred from other information:**
    - Stage must be inferred from TNM components of staging, requiring domain knowledge to prevent errors (e.g. confusing T4 with Stage 4)
    - Gender might be inferred from ICD-9 code (female breast cancer)
    - Requirements for prior surgery in a radiotherapy trial could be inferred by domain knowledge

Findings to Date with Respect to Standardized Eligibility Coding:

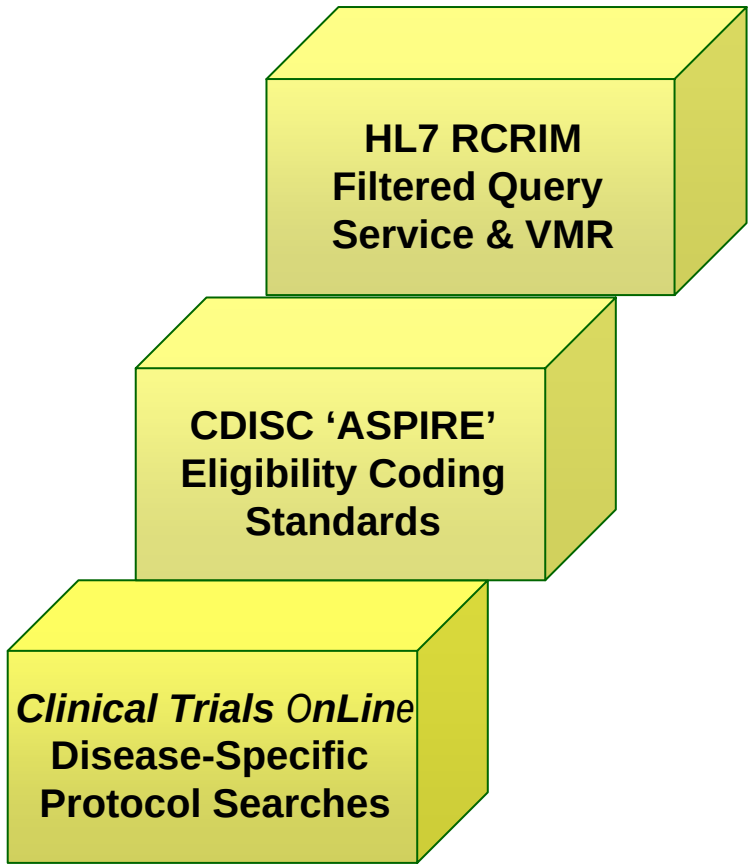
- Process raised many issues due to non-standardized ways of describing eligibility in existing protocols:
  - Certain eligibility criteria could fit into more than one rule-based category
    - Prior treatment criteria could encompass required, excluded, and allowed
    - Net result of selecting any of these ("with conditions") would be to ‘screen-in’, but need system that targets single code to accomplish other analytic goals
  - Context could be important in coding
    - Tumor size as a criterion might vary if it was related to clinical exam, imaging, or pathology

Eligibility Screening Based on Core Criteria

International:

National:

City of Hope:



Interfacing with HL7 RCRIM

Health Level 7 (HL7) Regulated Clinical Research Information Model (RCRIM)

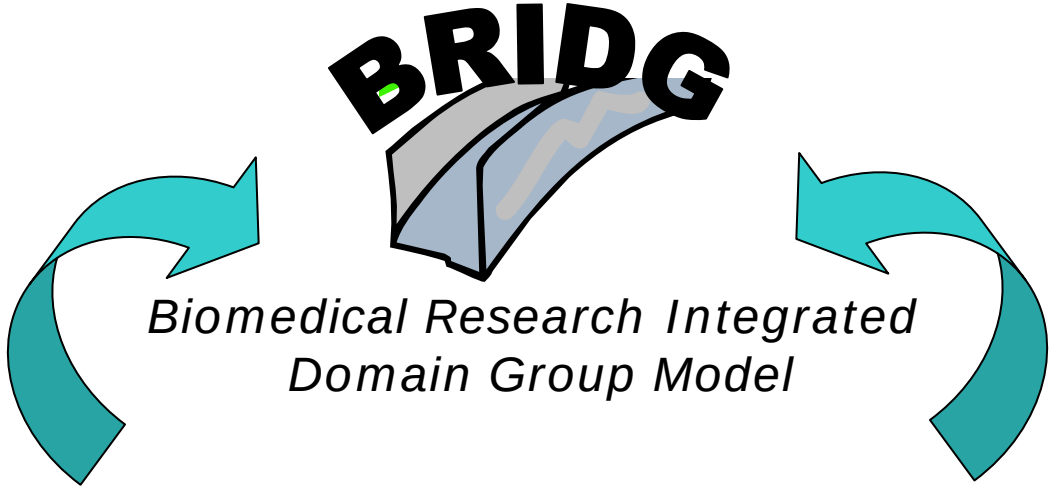
- Evolving standardized model for semantic interoperability in **research**
- ASPIRE is registered as official sub-project with HL7 RCRIM

- ASPIRE is providing primary use case for HL7 RCRIM 'Clinical Research Filtered Query' Service
  - Service to provide a set of filter capabilities in context of clinical trial protocols and associated metadata (requires existence of encoded data, e.g. eligibility criteria)

- Will provide a secondary use case for HL7 vMR project

- HL7 RCRIM–CDISC–NCI caBIG Collaboration
  - Biomedical Research Integrated Domain Group (**BRIDG**) Model

Contributing Eligibility Criteria Coding to International Standards Development



HL7 Standards

Clinical Research Filtered Query Service (CRFQ)

Virtual Medical Record (VMR)

FDA Requirements

Minimal Dataset for Therapeutic Eligibility Criteria

Components that may be included in the CDISC-FDA Integrated Safety Pilot

- Clinical trial registry elements (including the WHO 20 elements for trial registration)
- Core eligibility criteria
- Study design: TDM1
- Case report form data in ODM XML for discontinued/SAE subjects
- Standardized terminology
- Be sure that the language in human readable documentation describing the CDISC Pilot (including any advertising) conforms to the CDISC glossary
- May include other components as later stage deliverables
  - e.g TDM2, SDTM 3.1.2, Structured statistical analysis plan elements

Pros/Cons of Standardized Coded Core Eligibility Criteria

- **Pros:**
  - Facile/practical approach to code new protocols; should become part of electronic instantiation of protocol
  - Rapidly enhances patient/provider capability to identify potential trials while eliminating inappropriate studies, or data mining to ID potential subjects
    - Cast wide net, avoid “false negatives”
- **Cons:**
  - Challenging (though possible) to code from existing, non-standardly expressed protocols
  - Doesn’t automatically match patients fully to protocol (very difficult to achieve, timing of tests, experimental tests, lack of coded patient data, etc.)
  - Will require much work to cover many diseases (next ASPIRE disease = pediatric hypertension, per CDISC pilot)

ASPIRE Project Participants

Joyce Niland, Lead	City of Hope jniland@coh.org
Elly Cohen, Co-Lead	UCSF Elly.cohen@ucsfmedctr.org
Greg Eoyang	Digital Infuzion grege@digitalinfuzion.com
Lakshima Grama	NIH lgrama@mail.nih.gov
Cortney Hayflinger	GSK Cortney.d.hayflinger@gsk.com
Robert Wang	ClinTrialStat clintrialstat@yahoo.com
Jeffrey Suico	LLCR suicoje@lilly.com
Charles Barr	Roche Laboratories Inc charles_e.barr@roche.com
Allen Tien	MD Logix allen@mdlogix.com
Stanley Kaufman	Epimetics skaufman@epimetrics.com
Deborah Price	NIH Priced@mail.nih.gov
Valerie Dyer	NIH dyerv@mail.nih.gov

STORYBOARD A: Search for Potential Protocols

A woman with breast cancer is searching for possible leading-edge experimental treatment options. She goes to the Protocol Filter Query web interface, and the system asks for her "pan-disease" global characteristics (e.g. age, performance status, smoking status, pregnancy status, etc), and her diagnosis (breast cancer). Based on this last entry the system branches her to a series of disease-specific questions (e.g. stage, Her-2 Neu status, ER/PR status, prior chemotherapy, prior hormone therapy, etc).

Based upon her responses, the system searches through the set of all available protocols encoded for core eligibility criteria, eliminates all those for which the woman does *not* met the entry criteria, and returns a list of all those for which she *may* be eligible. An option to further filter for geographically close protocols is given, based on zip code and viable radius of travel miles entered, and to filter on type of intervention (e.g. primary treatment, adjunct treatment, vaccine, etc.). The returned list includes a URL linking to the full study synopsis posted on clinicaltrials.gov for each trial. The woman prints the final list to take for discussion with her physician.

STORYBOARD B: Search for Potential Subjects [1]

An academic organization has developed a new intervention for Type I diabetes and has developed a clinical trial protocol to test this new intervention. An Electronic Health Record (EHR) is available at the institution with encoded data regarding all of their current patients. The most recent patients have signed a consent form indicating they are willing to be contacted for experimental treatment should an applicable trial be available, while longstanding patients were not approached for such consent.

The PI goes to Filter Query System and enters in the global characteristics of patients who could be eligible for the study (e.g. age range, allowable gender(s), minimum performance status, allowable smoking status and history of smoking, etc), and the applicable diagnostic category (Type 1 Diabetes). Based on this last entry the system branches to a set of disease-specific queries regarding protocol entry criteria (e.g. minimum time since onset, allowable past treatment history, required organ status, etc.).

STORYBOARD B: Search for Potential Subjects [2]

The system searches through all ongoing patients in the EHR to locate those with the appropriate diagnosis, general characteristics, and disease-specific characteristics. If the patient has formally consented to further contact, they are included in an identifiable list to the PI, who will contact them with the request to pursue the protocol, and conduct further eligibility screening.

If the patient had not consented to further contact, an anonymized file is created with a unique identifier that only the "honest broker" can link back to the medical record number. A "consent agent" contacts the patient for permission to pursue the experimental study, and returns the identified list to the PI of those who agree to further screening.

STORYBOARD C: Modification of Protocol Eligibility

A drug company is conducting a protocol of a new intervention in pediatric hypertension, requiring 400 children to be studied to have sufficient power for to assess the primary objective. After one year the company has recruited only 50 children, half of the original estimated recruitment rate.

An evaluation is conducted via the Filter Query Service, to assess the typical allowable entry ranges for laboratory parameters on all available pediatric hypertension protocols encoded for eligibility. In addition, an anonymized search of the database of available potential children to be enrolled is conducted, and the median and range of the same laboratory parameters are assessed.

Through this evaluation the PI concludes that the lab parameters for the study were set to be too narrowly to allow the required enrollment of the available pediatric population. Following a safety evaluation and with IRB approval, the laboratory ranges are adjusted to be more consistent with existing good practice in other protocols and with the population data. The enrollment rate is greatly increased as a result of this protocol amendment.

AMIA symposium - CRI Working Group

Forum website for this group
http://www.researchinformatics.org/component/option,com_fireboard/Itemid,111/func,showcat/catid,19/

At the Fall 2007 AMIA symposium, a panel on "Knowledge Representation of Eligibility Criteria in Clinical Trials" was presented on behalf of the Clinical Research Informatics Working Group. The panel addressed how to create a standard approach to eligibility criteria expression and rule authoring that will provide the ability to exchange content/meaning across trials, conferring semantic interoperability. We discussed 1) mapping to standard terminologies; 2) coding 'core' eligibility criteria; 3) eligibility extraction tools; 4) eligibility rule expression; 5) decision support modules; and 6) point-of-care recruitment via Electronic Health Records.

The presentation generated much interest, and it was agreed we should continue discussing advances, collaborations, and approaches within the *CRI-WG,* and as the organizer of the panel I agreed to keep this group engaged. Accordingly, I would to call a Kick-off meeting of the proposed "Eligibility Standards Task Force". If you are interested in participating in the task force, please let my secretary, Julie Hom (jhom@coh.org) know if you're available on either of the following dates/times and we'll schedule a meeting accordingly.

March 13th: 12-1pm PST (3-4pm EST)
March 14th 12-1pm PST (3-4pm EST)

Best,
Joyce C. Niland, Ph.D.
Chair, Division of Information Sciences
Edward & Estelle Alexander Chaired Professor, Beckman Research Institute
Associate Director for Information Sciences, City of Hope Cancer Center

Study Participation

Jason Rock
Jason.Rock@GlobalSubmit.com
215-253-7474

Table of Contents

Source Information

- Started with the BRIDG
  - Need to harmonize CRO, animal, part of organism, IRB (possibly firebird), site investigators (possibly firebird), Inspection Results (site audits)
- Validated against CDISC SDTM DM and DS domains
  - Study Participation message does not include when information about the subject is recorded.
    - Will be captured in the Study Subject message

Study Participation

- Who is involved in the conduct of the study?
  - What are there roles
  - Where is there involvement
  - When are they involved

- It is probable that not all use cases will be implemented by any one party

Scope

- Studies that are performed to determine the quality, safety and efficacy of regulated products.
- Including but not limited to:
  - human clinical studies (drugs, devices, biologics, combination products)
  - animal pharmacology and toxicology studies (drugs, devices, biologics, combination products, food additives, cosmetics)
  - target animal veterinary studies
  - device performance studies
  - in vitro studies (drugs, biologics)

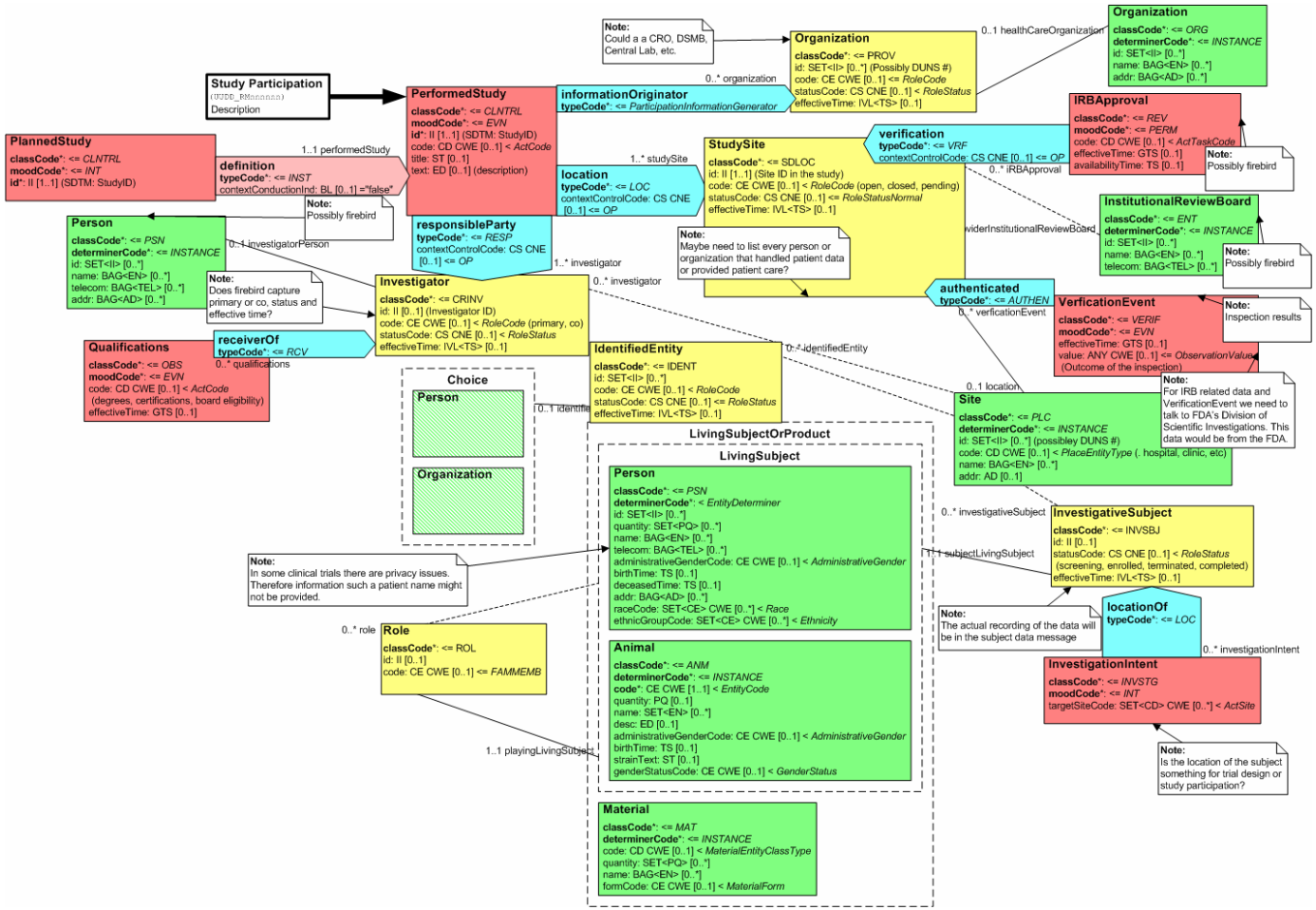
What is a Study?

- A set of observations performed in the context of testing a particular hypothesis(-es) (e.g. solving a particular problem or question)
  - Subject could be living or inanimate (device, pill, etc.)
- A study of the effects of a medical intervention, such as a comparison test of medical treatment, versus a placebo (inactive look-a-like), other medications or devices, or the standard medical treatment for a patient's condition

Model (1)

- The next slide will show a proposed model of Study Participation
- We will break down each class one by one and explain how it meets the defined requirements

Model (2)

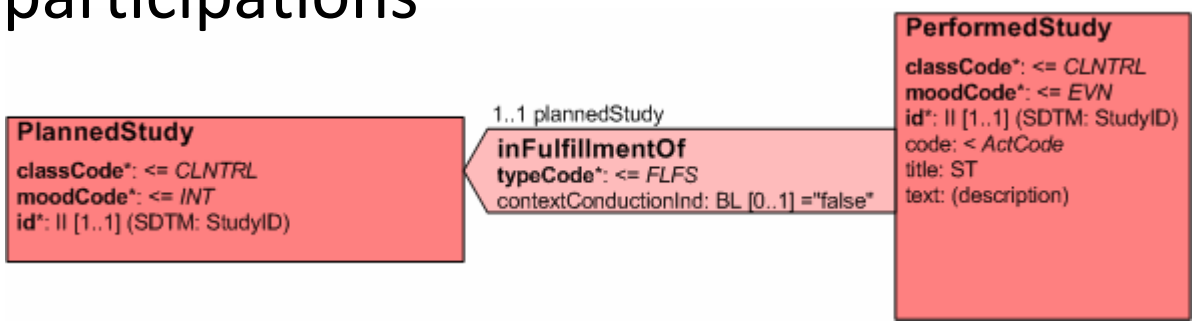

Study Participation
(UUID, RMoooooo)
Description
PerformedStudy
classCode*: <= CLNTRL
moodCode*: <= EVN
id*: II [1..1] (SDTM: StudyID)
code: CD CWE [0..1] < ActCode
title: ST [0..1]
text: ED [0..1] (description)
PlannedStudy
classCode*: <= CLNTRL
moodCode*: <= INT
id*: II [1..1] (SDTM: StudyID)
definition
typeCode*: <= INST
contextConductionInd: BL [0..1] ="false"
1..1 performedStudy
Note:
Possibly firebird
Note:
Could a a CRO, DSMB, Central Lab, etc.
Organization
classCode*: <= PROV
id: SET<II> [0..*] (Possibly DUNS #)
code: CE CWE [0..1] <= RoleCode
statusCode: CS CNE [0..1] < RoleStatus
effectiveTime: IVL<TS> [0..1]
0..* organization
informationOriginator
typeCode*: <= ParticipationInformationGenerator
0..1 healthCareOrganization
Organization
classCode*: <= ORG
determinerCode*: <= INSTANCE
id: SET<II> [0..*]
name: BAG<EN> [0..*]
addr: BAG<AD> [0..*]
IRBApproval
classCode*: <= REV
moodCode*: <= PERM
code: CD CWE [0..1] < ActTaskCode
effectiveTime: GTS [0..1]
availabilityTime: TS [0..1]
Note:
Possibly firebird
0..* IRBApproval
StudySite
classCode*: <= SDLOC
id: II [1..1] (Site ID in the study)
code: CE CWE [0..1] < RoleCode (open, closed, pending)
statusCode: CS CNE [0..1] <= RoleStatusNormal
effectiveTime: IVL<TS> [0..1]
1..* studySite
location
typeCode*: <= LOC
contextControlCode: CS CNE [0..1] <= OP
verification
typeCode*: <= VRF
contextControlCode: CS CNE [0..1] <= OP
Note:
Maybe need to list every person or organization that handled patient data or provided patient care?
responsibleParty
typeCode*: <= RESP
contextControlCode: CS CNE [0..1] <= OP
1..* investigator
Person
classCode*: <= PSN
determinerCode*: <= INSTANCE
id: SET<II> [0..*]
name: BAG<EN> [0..*]
telecom: BAG<TEL> [0..*]
addr: BAG<AD> [0..*]
0..1 investigatorPerson
Note:
Does firebird capture primary or co, status and effective time?
Investigator
classCode*: <= CRINV
id: II [0..1] (Investigator ID)
code: CE CWE [0..1] < RoleCode (primary, co)
statusCode: CS CNE [0..1] < RoleStatus
effectiveTime: IVL<TS> [0..1]
0..* investigator
receiverOf
typeCode*: <= RCV
0..* qualifications
Qualifications
classCode*: <= OBS
moodCode*: <= EVN
code: CD CWE [0..1] < ActCode
(degrees, certifications, board eligibility)
effectiveTime: GTS [0..1]
authenticated
typeCode*: <= AUTHEN
0..* verficationEvent
VerficationEvent
classCode*: <= VERIF
moodCode*: <= EVN
effectiveTime: GTS [0..1]
value: ANY CWE [0..1] <= ObservationValue
(Outcome of the inspection)
Note:
Inspection results
Note:
For IRB related data and VerificationEvent we need to talk to FDA's Division of Scientific Investigations. This data would be from the FDA.
InstitutionalReviewBoard
classCode*: <= ENT
determinerCode*: <= INSTANCE
id: SET<II> [0..*]
name: BAG<EN> [0..*]
telecom: BAG<TEL> [0..*]
Note:
Possibly firebird
widerInstitutionalReviewBoard
IdentifiedEntity
classCode*: <= IDENT
id: SET<II> [0..*]
code: CE CWE [0..1] < RoleCode
statusCode: CS CNE [0..1] <= RoleStatus
effectiveTime: IVL<TS> [0..1]
0..* identifiedEntity
Choice
Person
Organization
0..1 identifiedPerson
0..1 location
Site
classCode*: <= PLC
determinerCode*: <= INSTANCE
id: SET<II> [0..*] (possibley DUNS #)
code: CD CWE [0..1] < PlaceEntityType (. hospital, clinic, etc)
name: BAG<EN> [0..*]
addr: AD [0..1]
LivingSubjectOrProduct
LivingSubject
Person
classCode*: <= PSN
determinerCode*: < EntityDeterminer
id: SET<II> [0..*]
quantity: SET<PQ> [0..*]
name: BAG<EN> [0..*]
telecom: BAG<TEL> [0..*]
administrativeGenderCode: CE CWE [0..1] < AdministrativeGender
birthTime: TS [0..1]
deceasedTime: TS [0..1]
addr: BAG<AD> [0..*]
raceCode: SET<CE> CWE [0..*] < Race
ethnicGroupCode: SET<CE> CWE [0..*] < Ethnicity
Animal
classCode*: <= ANM
determinerCode*: <= INSTANCE
code*: CE CWE [1..1] < EntityCode
quantity: PQ [0..1]
name: SET<EN> [0..*]
desc: ED [0..1]
administrativeGenderCode: CE CWE [0..1] < AdministrativeGender
birthTime: TS [0..1]
strainText: ST [0..1]
genderStatusCode: CE CWE [0..1] < GenderStatus
Material
classCode*: <= MAT
determinerCode*: <= INSTANCE
code: CD CWE [0..1] < MaterialEntityClassType
quantity: SET<PQ> [0..*]
name: BAG<EN> [0..*]
formCode: CE CWE [0..1] < MaterialForm
Note:
In some clinical trials there are privacy issues. Therefore information such a patient name might not be provided.
0..* role
Role
classCode*: <= ROL
id: II [0..1]
code: CE CWE [0..1] <= FAMMEMB
1..1 playingLivingSubject
0..* investigativeSubject
InvestigativeSubject
classCode*: <= INVSBJ
id: II [0..1]
statusCode: CS CNE [0..1] < RoleStatus
(screening, enrolled, terminated, completed)
effectiveTime: IVL<TS> [0..1]
1..1 subjectLivingSubject
Note:
The actual recording of the data will be in the subject data message
locationOf
typeCode*: <= LOC
0..* investigationIntent
InvestigationIntent
classCode*: <= INVSTG
moodCode*: <= INT
targetSiteCode: SET<CD> CWE [0..*] < ActSite
Note:
Is the location of the subject something for trial design or study participation?

Planned and Performed Study

- Planned Study: A collector of planned activities, including a description of the planned number of subjects and the duration of their participation.
- Planned study will be further defined in the Study Design message
- Performed Studies “perform” the activates in a plan study
  - Characteristics, such as, objectives, phase, population description are in a planned study

Study Described in the RIM

- Refer to a planned study by the Id provided in a Study Design message
- Need Id to provide updates to an existing performed study
- Title is the study title (could possible get from Study Design)
- Text is a textual description about the study and their participations



Who Participated in Study?

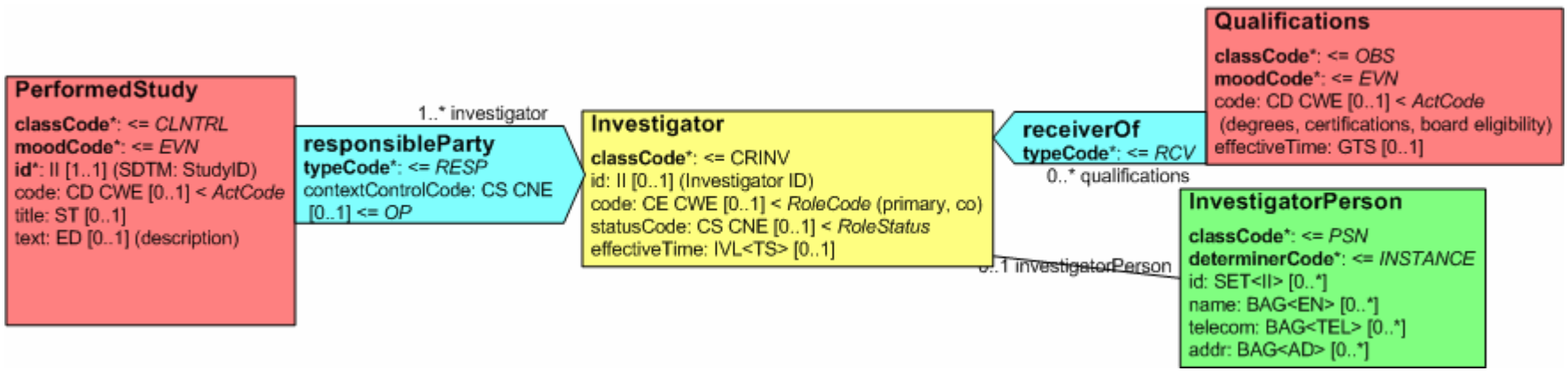
- Information about who was involved in the study and what activities occurred during the study
  - Investigators
  - Sites
  - Other Organizations
    - Sponsors, CRO's
- Site participation will be discussed in later slides

Study Investigator

- Oversees all aspects of the trial
  - such as protocol writing, IRB approval, recruitment, informed consent, analysis, etc.
- Must have one principal investigator per study
  - Can have many sub-investigators
- Investigator has qualification
  - Degrees certifications, board eligibility etc
- Investigators can be added and removed
  - Dates of the change of an investigator must be captured

Investigators described in RIM

- Investigator code describes the role of either the primary or sub investigator
  - Effective time describes when the investigator was either the primary or sub investigator
- Investigator is a person that we need to track their name, address and phone number
- We need to know are the qualified
  - code is the qualification, effective time is when the received the qualification and the time period of the qualification

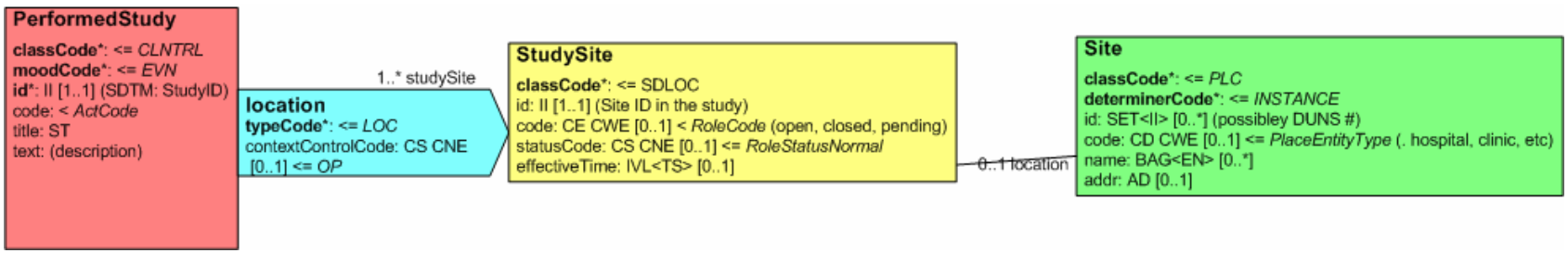


Study Site

- Where trial activities are conducted.
  - For example, the site where the subject encounter occurs or the site of the Investigator.
- There can be many sites for one study
- A site can be added or removed at any time

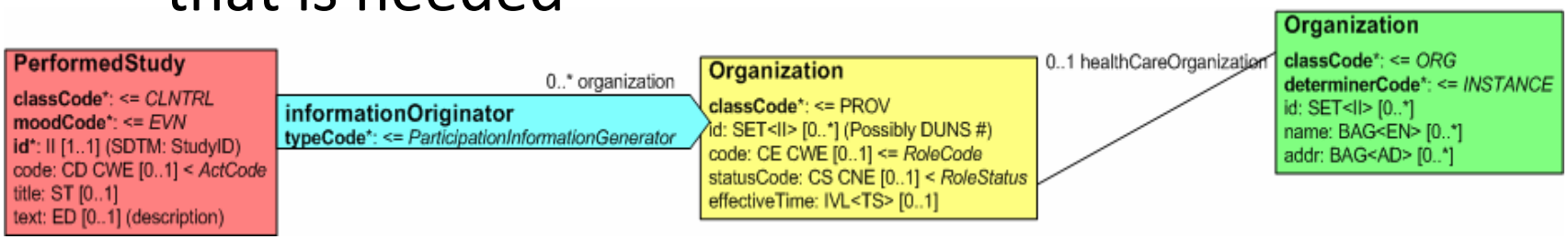
Study Site described in RIM

- Need site identifier for the study and universal identifier for the site (possibly DUNS #)
  - Need for any updates to the site
- StudySite code capture status of site in study (opened for accrual, closed for accrual, pending accrual)
  - Effective time describes when the site is in a certain status
- Site code captures type of site (hospital, clinic, etc)



Organization Described in RIM

- Any other organization that was involved in the Study
  - Code will be a pick list of organization types (e.g. CRO) – will be limited in Implementation Guide
  - Effective time when a certain organization was involved in the study
  - At this point name and Id of organization is all that is needed



What we need to know about the site?

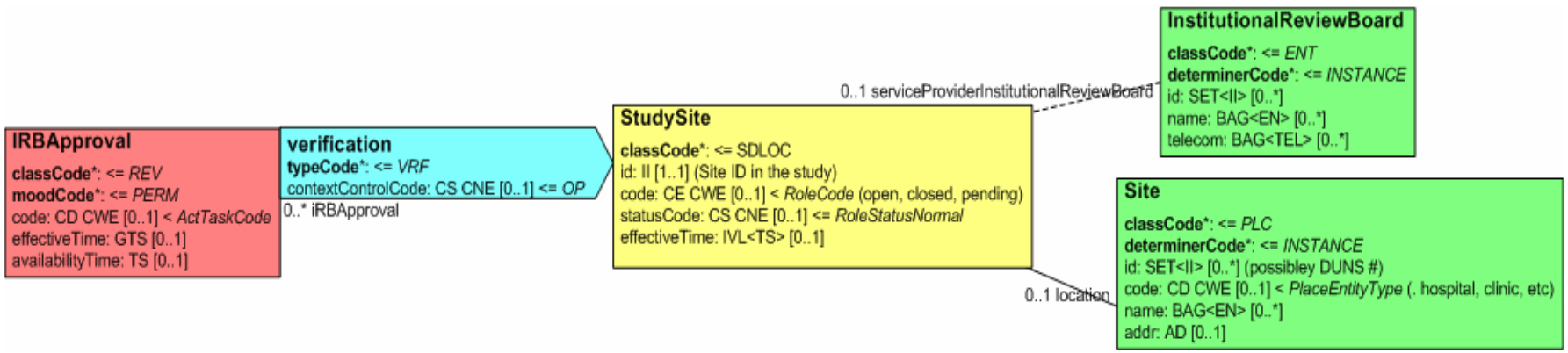
- Intuitional Review Board approvals (possibly firebird)
- Site investigators (possibly firebird)
- Subject that are involved in a study for a particular site
- Results of inspections (generated by regulators)
- Other organizations involved in the site
  - e.g. monitors

Institutional Review Board

- A board that approves, monitors and reviews biomedical research to protect the rights, safety and welfare of the subjects
- IRB approval site(s) for a specific study
- Captures when approval was recorded and effective time

IRB described in RIM

- Each site has one IRB
- IRB approval was recorded at a certain time (availability time)
- IRB approved a protocol for a specified time period (effective time)

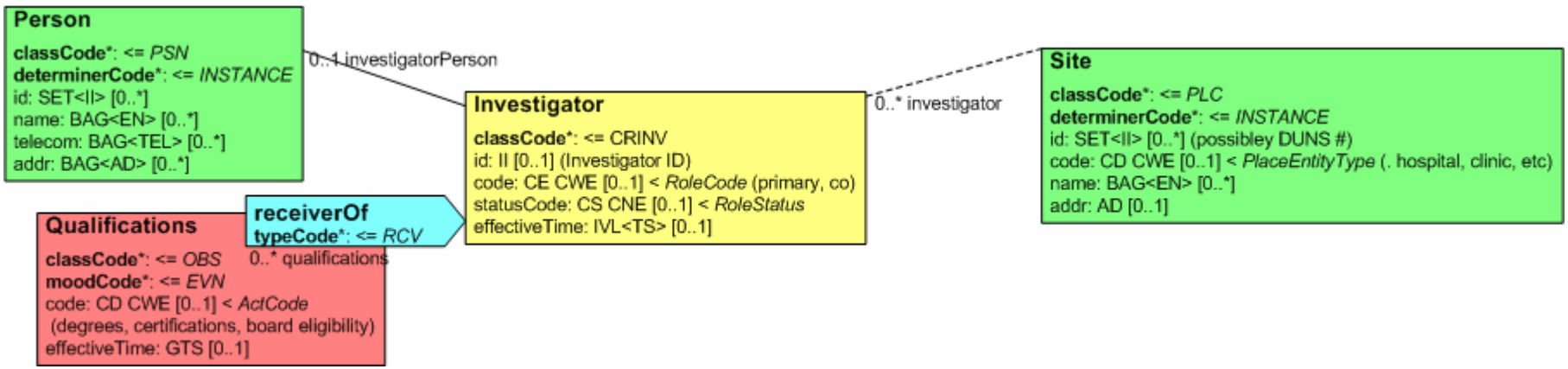


Site Investigator

- Oversees all aspects of a study at a certain site
- Must have one principal investigator per site
  - Can have many sub-investigators
- Site investigators can be added and removed
  - Dates of the change of an investigator must be captured

Site Investigator described in RIM

- Site has a relationships to investigators like study.
  - Investigators in RIM are described above

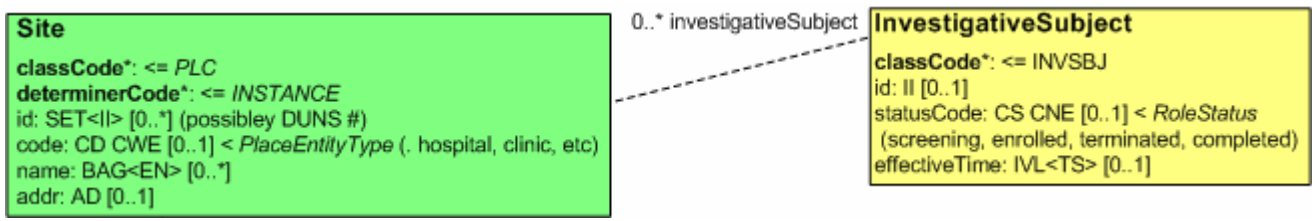


Investigative Subject

- Participates in a trials
  - a single organism (human, animal)
  - many living organisms (herds, flocks, etc.)
  - a part of an organism (artery, patch of skin, etc.) related to the organism
  - an inanimate object (pill, device, etc.)
- There could be many subjects in one trial

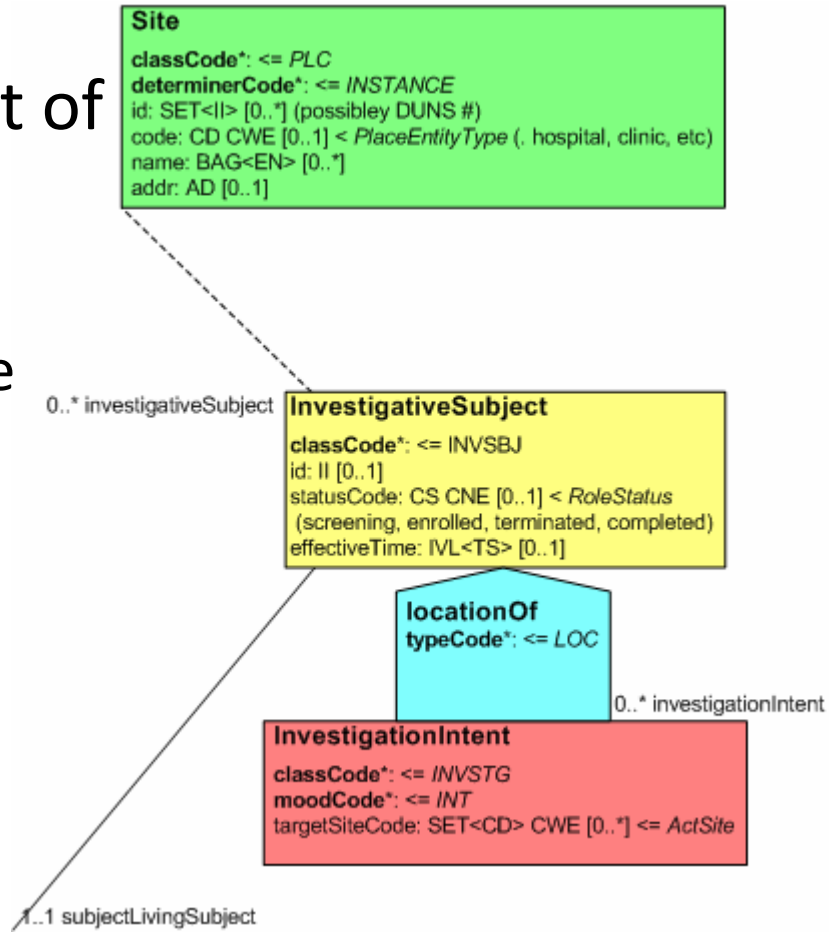
Subject described in RIM

- Id is the Id of the subject in a study
- Status code describes the state the subject is in the study
  - E.g. screening, enrolled, completed, etc.
- Effective time is the time the subject was in a certain state.



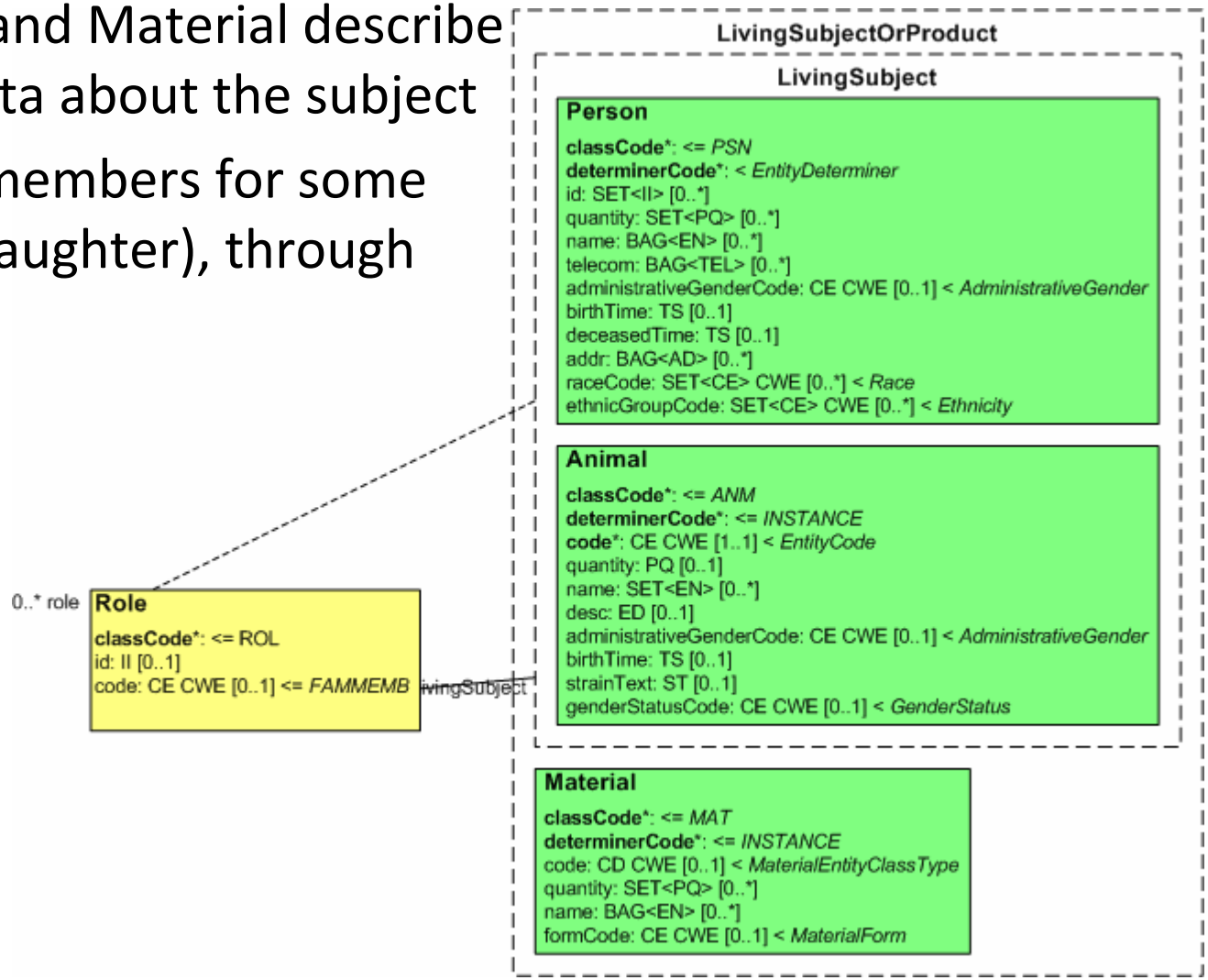
Investigative Subject Cntd.

- Could be interested in a part of the subject (Target Site)
  - Controlled vocabulary can be used to discuss the target site



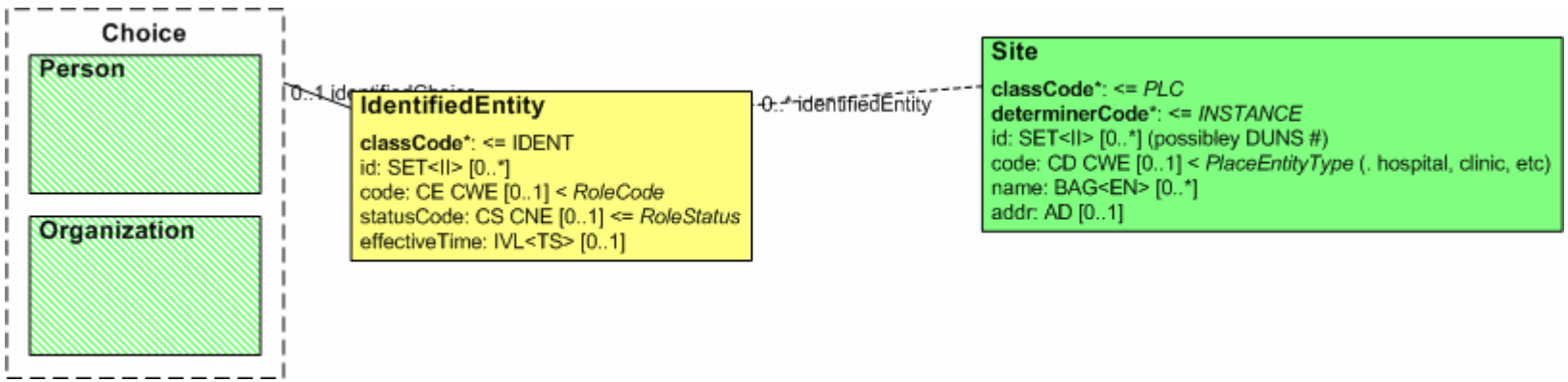
Investigative Subject Cntd.

- People, Animal and Material describe demographic data about the subject
- Capture family members for some trials (mother/daughter), through code

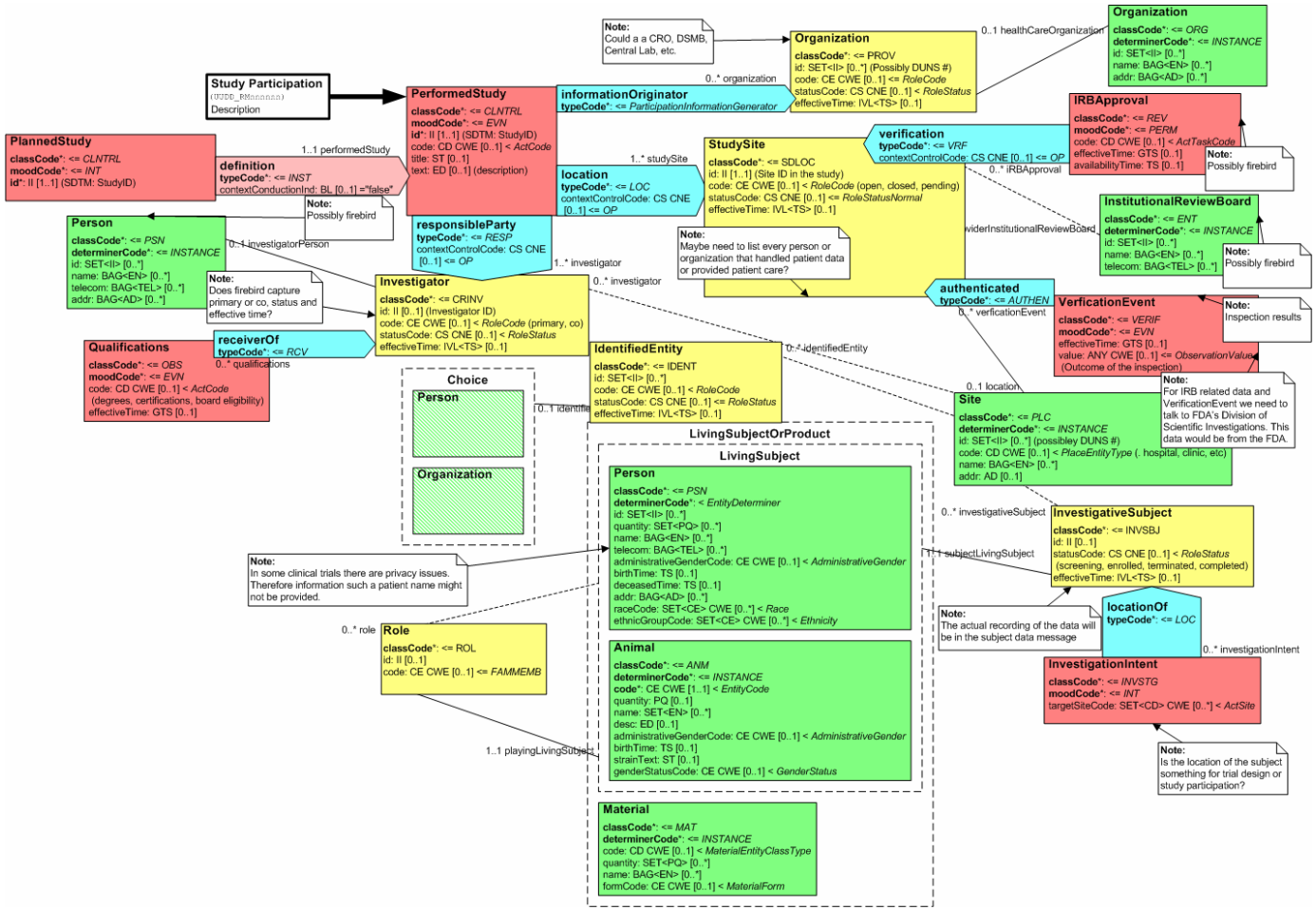


Other People or Organizations

- There could be other people or organizations involved in a site
  - Code will be a pick list of types (e.g. site monitors) – will be limited in Implementation Guide
  - Effective time when a certain organization was involved in the study
  - At this point name and Id of organization is all that is needed



Model


Study Participation
(UUID, RMoonna)
Description
PerformedStudy
classCode*: <= CLNTRL
moodCode*: <= EVN
id*: II [1..1] (SDTM: StudyID)
code: CD CWE [0..1] < ActCode
title: ST [0..1]
text: ED [0..1] (description)
PlannedStudy
classCode*: <= CLNTRL
moodCode*: <= INT
id*: II [1..1] (SDTM: StudyID)
definition
typeCode*: <= INST
contextConductionInd: BL [0..1] ="false"
1..1 performedStudy
Note:
Possibly firebird
Note:
Could a a CRO, DSMB, Central Lab, etc.
Organization
classCode*: <= PROV
id: SET<II> [0..*] (Possibly DUNS #)
code: CE CWE [0..1] <= RoleCode
statusCode: CS CNE [0..1] < RoleStatus
effectiveTime: IVL<TS> [0..1]
0..* organization
informationOriginator
typeCode*: <= ParticipationInformationGenerator
0..1 healthCareOrganization
Organization
classCode*: <= ORG
determinerCode*: <= INSTANCE
id: SET<II> [0..*]
name: BAG<EN> [0..*]
addr: BAG<AD> [0..*]
IRBApproval
classCode*: <= REV
moodCode*: <= PERM
code: CD CWE [0..1] < ActTaskCode
effectiveTime: GTS [0..1]
availabilityTime: TS [0..1]
Note:
Possibly firebird
verification
typeCode*: <= VRF
contextControlCode: CS CNE [0..1] <= OP
0..* IRBApproval
StudySite
classCode*: <= SDLOC
id: II [1..1] (Site ID in the study)
code: CE CWE [0..1] < RoleCode (open, closed, pending)
statusCode: CS CNE [0..1] <= RoleStatusNormal
effectiveTime: IVL<TS> [0..1]
1..* studySite
location
typeCode*: <= LOC
contextControlCode: CS CNE [0..1] <= OP
Note:
Maybe need to list every person or organization that handled patient data or provided patient care?
InstitutionalReviewBoard
classCode*: <= ENT
determinerCode*: <= INSTANCE
id: SET<II> [0..*]
name: BAG<EN> [0..*]
telecom: BAG<TEL> [0..*]
Note:
Possibly firebird
Person
classCode*: <= PSN
determinerCode*: <= INSTANCE
id: SET<II> [0..*]
name: BAG<EN> [0..*]
telecom: BAG<TEL> [0..*]
addr: BAG<AD> [0..*]
0..1 investigatorPerson
Note:
Does firebird capture primary or co, status and effective time?
responsibleParty
typeCode*: <= RESP
contextControlCode: CS CNE [0..1] <= OP
1..* investigator
Investigator
classCode*: <= CRINV
id: II [0..1] (Investigator ID)
code: CE CWE [0..1] < RoleCode (primary, co)
statusCode: CS CNE [0..1] < RoleStatus
effectiveTime: IVL<TS> [0..1]
0..* investigator
authenticated
typeCode*: <= AUTHEN
0..* verficationEvent
VerficationEvent
classCode*: <= VERIF
moodCode*: <= EVN
effectiveTime: GTS [0..1]
value: ANY CWE [0..1] <= ObservationValue
(Outcome of the inspection)
Note:
Inspection results
Note:
For IRB related data and VerificationEvent we need to talk to FDA's Division of Scientific Investigations. This data would be from the FDA.
Qualifications
classCode*: <= OBS
moodCode*: <= EVN
code: CD CWE [0..1] < ActCode
(degrees, certifications, board eligibility)
effectiveTime: GTS [0..1]
receiverOf
typeCode*: <= RCV
0..* qualifications
IdentifiedEntity
classCode*: <= IDENT
id: SET<II> [0..*]
code: CE CWE [0..1] < RoleCode
statusCode: CS CNE [0..1] <= RoleStatus
effectiveTime: IVL<TS> [0..1]
0..* identifiedEntity
0..1 location
Site
classCode*: <= PLC
determinerCode*: <= INSTANCE
id: SET<II> [0..*] (possibley DUNS #)
code: CD CWE [0..1] < PlaceEntityType (. hospital, clinic, etc)
name: BAG<EN> [0..*]
addr: AD [0..1]
Choice
Person
Organization
0..1 identifiedEntity
LivingSubjectOrProduct
LivingSubject
Person
classCode*: <= PSN
determinerCode*: < EntityDeterminer
id: SET<II> [0..*]
quantity: SET<PQ> [0..*]
name: BAG<EN> [0..*]
telecom: BAG<TEL> [0..*]
administrativeGenderCode: CE CWE [0..1] < AdministrativeGender
birthTime: TS [0..1]
deceasedTime: TS [0..1]
addr: BAG<AD> [0..*]
raceCode: SET<CE> CWE [0..*] < Race
ethnicGroupCode: SET<CE> CWE [0..*] < Ethnicity
Animal
classCode*: <= ANM
determinerCode*: <= INSTANCE
code*: CE CWE [1..1] < EntityCode
quantity: PQ [0..1]
name: SET<EN> [0..*]
desc: ED [0..1]
administrativeGenderCode: CE CWE [0..1] < AdministrativeGender
birthTime: TS [0..1]
strainText: ST [0..1]
genderStatusCode: CE CWE [0..1] < GenderStatus
Material
classCode*: <= MAT
determinerCode*: <= INSTANCE
code: CD CWE [0..1] < MaterialEntityClassType
quantity: SET<PQ> [0..*]
name: BAG<EN> [0..*]
formCode: CE CWE [0..1] < MaterialForm
Note:
In some clinical trials there are privacy issues. Therefore information such a patient name might not be provided.
0..* role
Role
classCode*: <= ROL
id: II [0..1]
code: CE CWE [0..1] <= FAMMEMB
1..1 playingLivingSubject
0..* investigativeSubject
InvestigativeSubject
classCode*: <= INVSBJ
id: II [0..1]
statusCode: CS CNE [0..1] < RoleStatus
(screening, enrolled, terminated, completed)
effectiveTime: IVL<TS> [0..1]
1..1 subjectLivingSubject
Note:
The actual recording of the data will be in the subject data message
locationOf
typeCode*: <= LOC
0..* investigationIntent
InvestigationIntent
classCode*: <= INVSTG
moodCode*: <= INT
targetSiteCode: SET<CD> CWE [0..*] < ActSite
Note:
Is the location of the subject something for trial design or study participation?