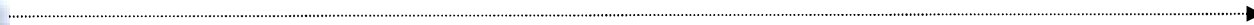


OECD Workshop on Pharmacogenetics

Development of international data standards to support the acquisition, exchange, submission and archiving of clinical-genomic data

CG



EHR

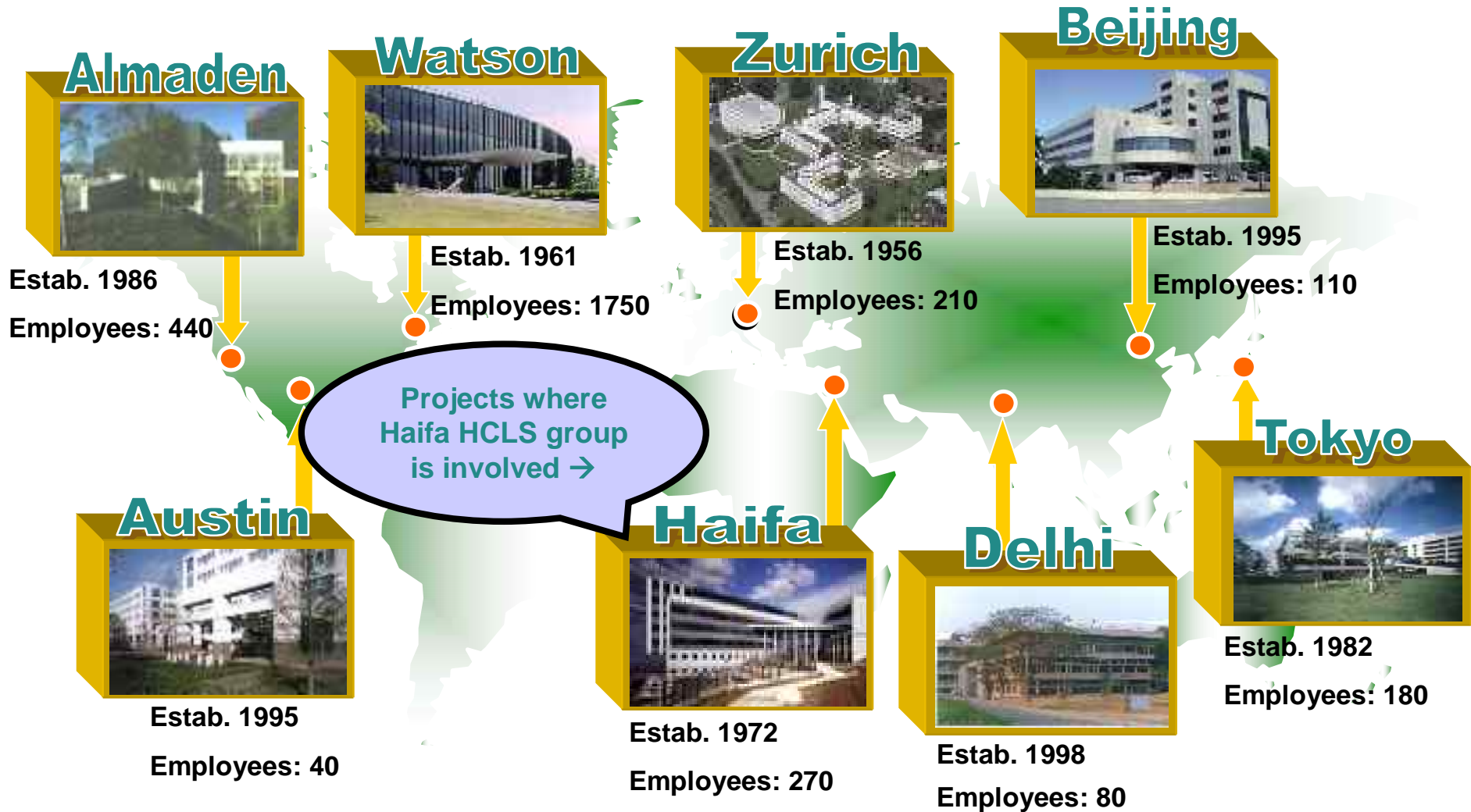


**Rome, Italy
October 17, 2005**

**Amnon Shabo (Shvo), PhD
IBM Research Lab in Haifa**



IBM Research Worldwide

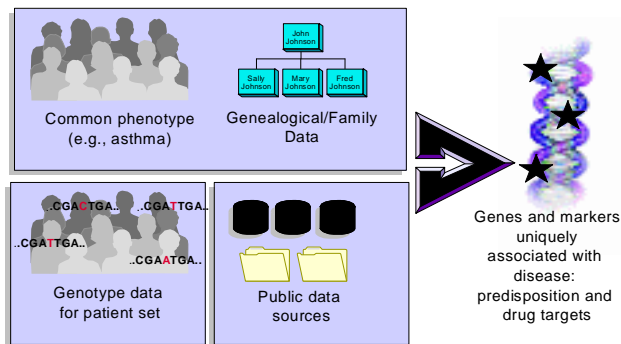




Haifa Research Lab HCLS Focal Areas

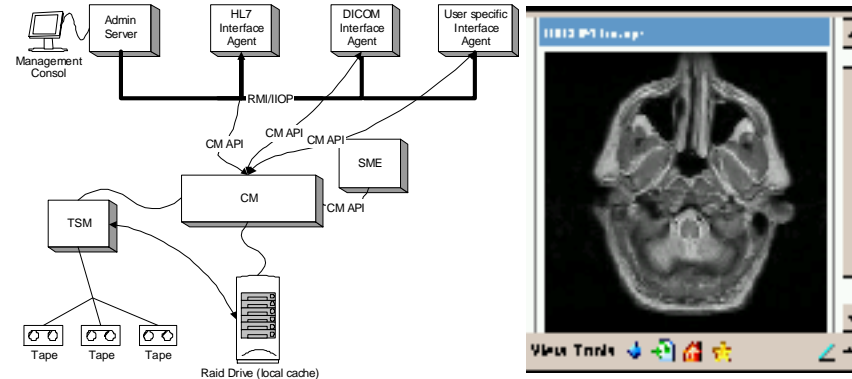
CGv2

Clinical Genomics Solutions



MCM

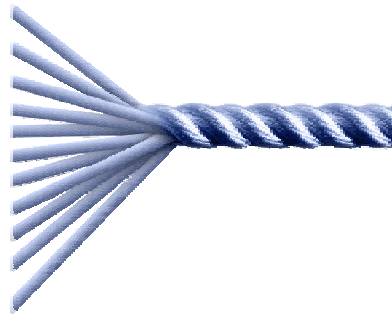
Medical Content Manager



IHII

Interoperable Health Information Infrastructure

- Targeted at regional and national EHR initiatives
- In collaboration with Almaden Research Center and HCLS



Health Standards Practice

HL7 / IHE / CEN / DICOM / HIPAA

Offering Education & Services

My HL7 roles:

- Co-chair and facilitator of Clinical Genomics SIG
- Co-editor of CDA Release Two (Clinical document)





Agenda / Key Points

◆ **Health Information Standards**

- should be based on a central Health Reference Information Model (RIM)

◆ **Clinical Genomics & Clinical Trials Standards**

- should implement the *'encapsulate & bubble-up'* paradigm

◆ **The Final Frontier: EHR – Electronic Health Record**

- personalized longitudinal and cross-institutional EHR
- personal genetic data should be part of the EHR
- inter/national Health Information Infrastructure is focused on EHR
- the inevitable sustainability model:
'Independent Health Records Banks'



Types of Health Informatics Standard Artifacts

- ◆ **Codes & Identifiers** (SNOMED, ICD, LOINC, CPT, GenBank, etc.)
- ◆ **Messages** (HL7, DICOM, X12)
- ◆ **Clinical Documents** (HL7-CDA)
- ◆ **Records** (CEN, ISO, OpenEHR, HL7-Functional Model)
- ◆ **Integration profiles** (IHE: implement best-practice workflows)
- ◆ **Claims** (HIPAA / X12, HL7-Attachments)
- ◆ **Others**: Knowledge Representation (e.g., Clinical Guidelines - GLIF);
Context Synchronization (CCOW)



HL7 – The Dominant SDO



- ◆ Focus on the 7th layer in ISO OSI (Open Systems Interconnection)

- ◆ **V2→V3: Quantum Leap** like the shift from 'structured' to OO programming

V2 allows site-specific impl.

- ◆ V2 messaging specifications – ANSI standard for ADT, Billing, Observations, Medications, etc.
- ◆ V2.XML is under ballot (XML Encoding Framework)



V3 specifications

- ◆ Dedicated Data Types (e.g., CD – Concept Codes)
- ◆ Mandatory & Central RIM – Reference Information Model
- ◆ New specs: CDA, Public Health Reporting, Clinical Trials, Clin. Genom.



HL7's mission is clinical interoperability

- ◆ “To provide standards for the **exchange, management** and **integration** of data that supports clinical patient care and the management, delivery and evaluation of healthcare services.”

Source: HL7 Mission statement (1997)

- ◆ **interoperability**

: ability of two or more systems or components to exchange information and to use the information that has been exchanged.

Source: IEEE Standard Computer Dictionary: A Compilation of IEEE Standard Computer Glossaries, IEEE, 1990]

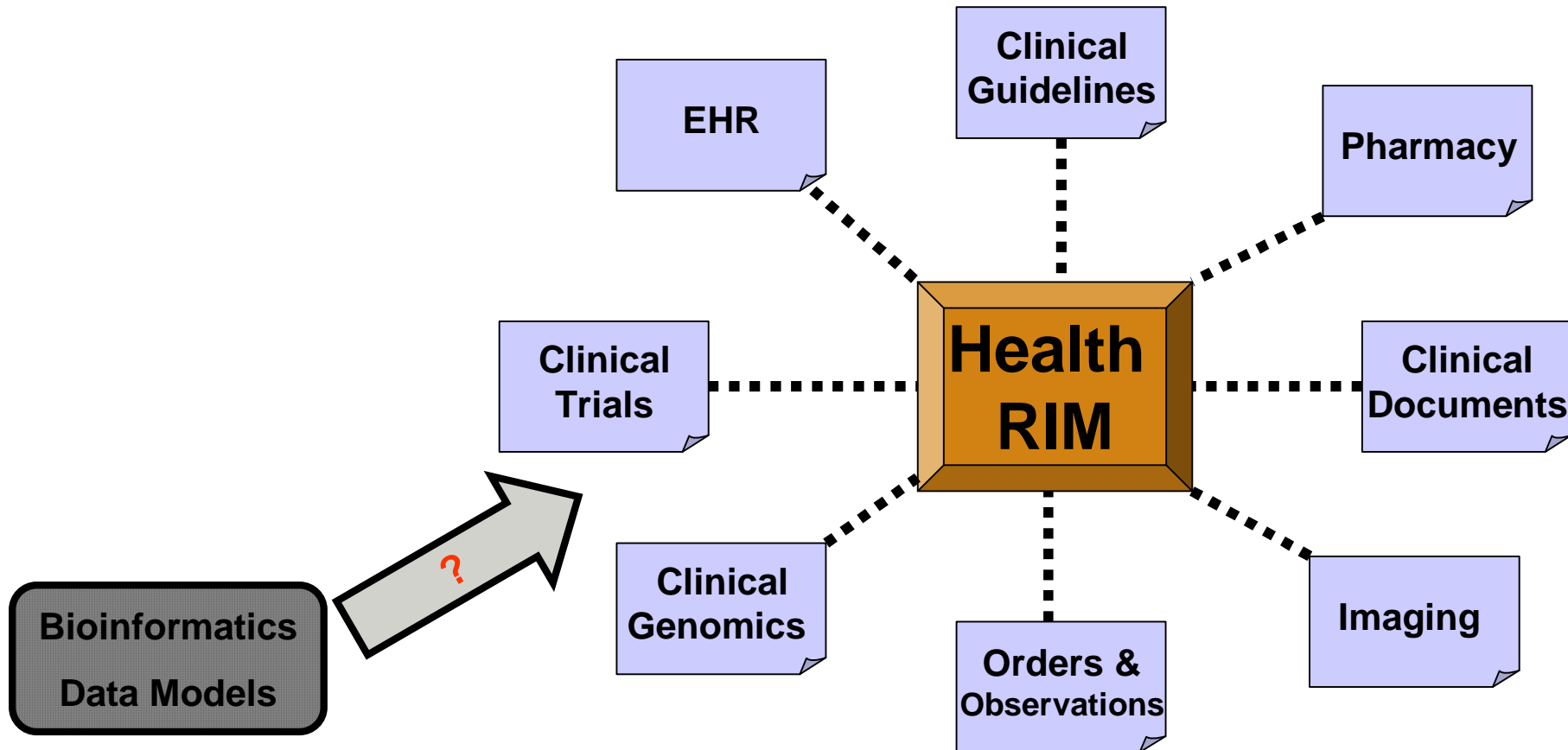
Functional interoperability

Semantic interoperability

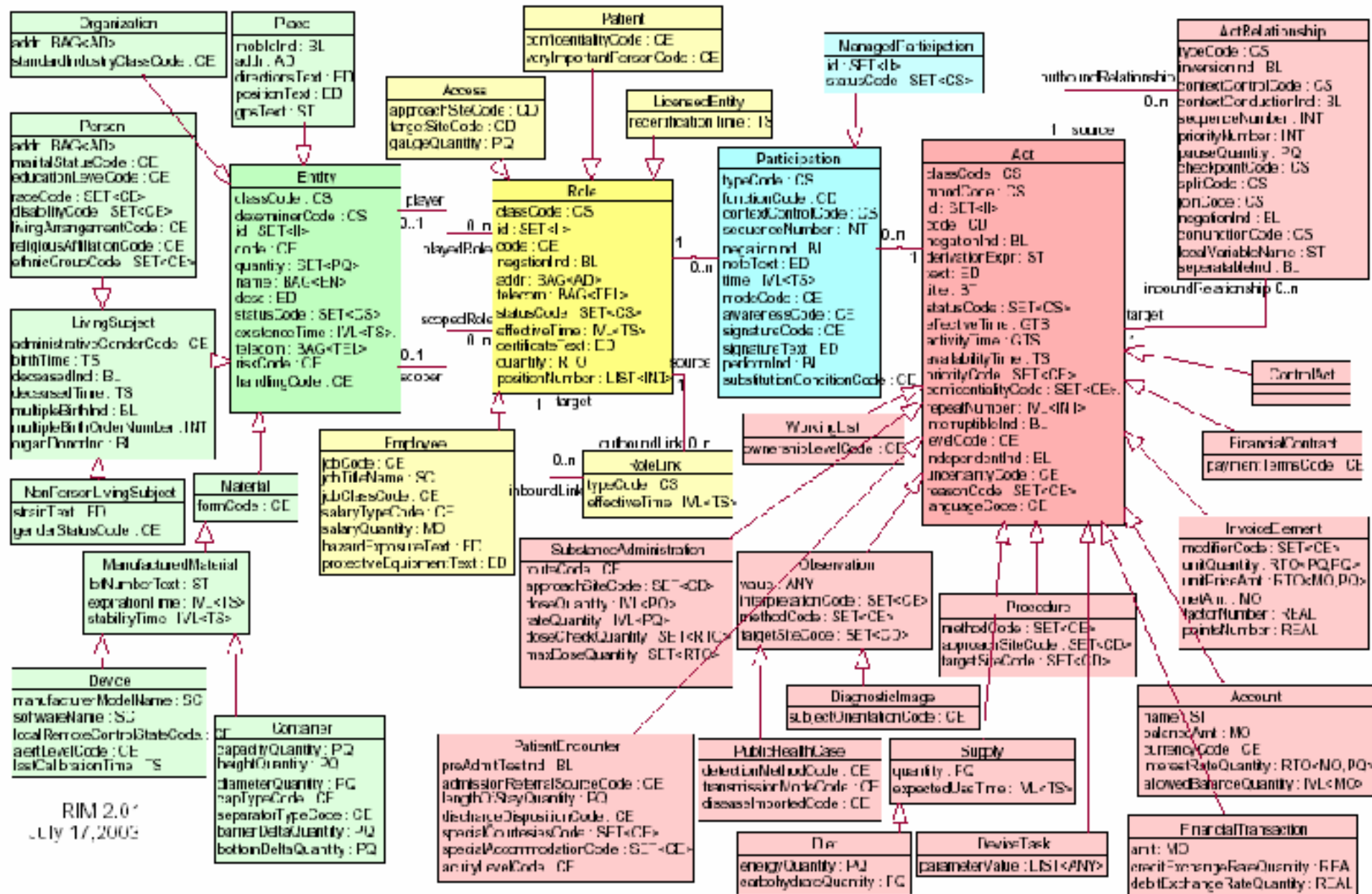


To achieve semantic interoperability...

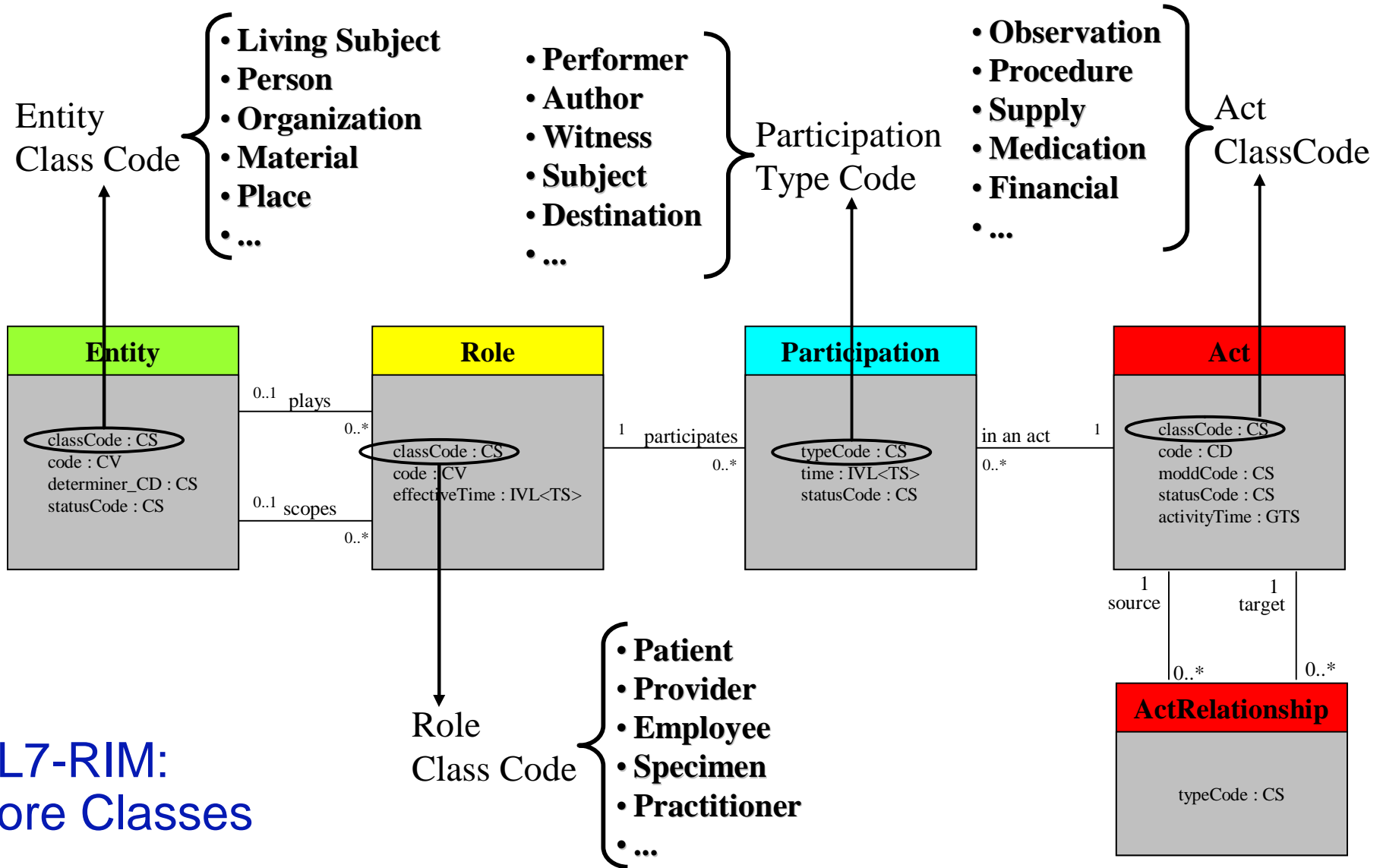
...we need standard specs derived from a **Central Health RIM**:



**Central Health RIM (e.g., an extended HL7 V3 Reference Information Model):
Bio- & medical-informatics standard specs are derived from the same RIM**

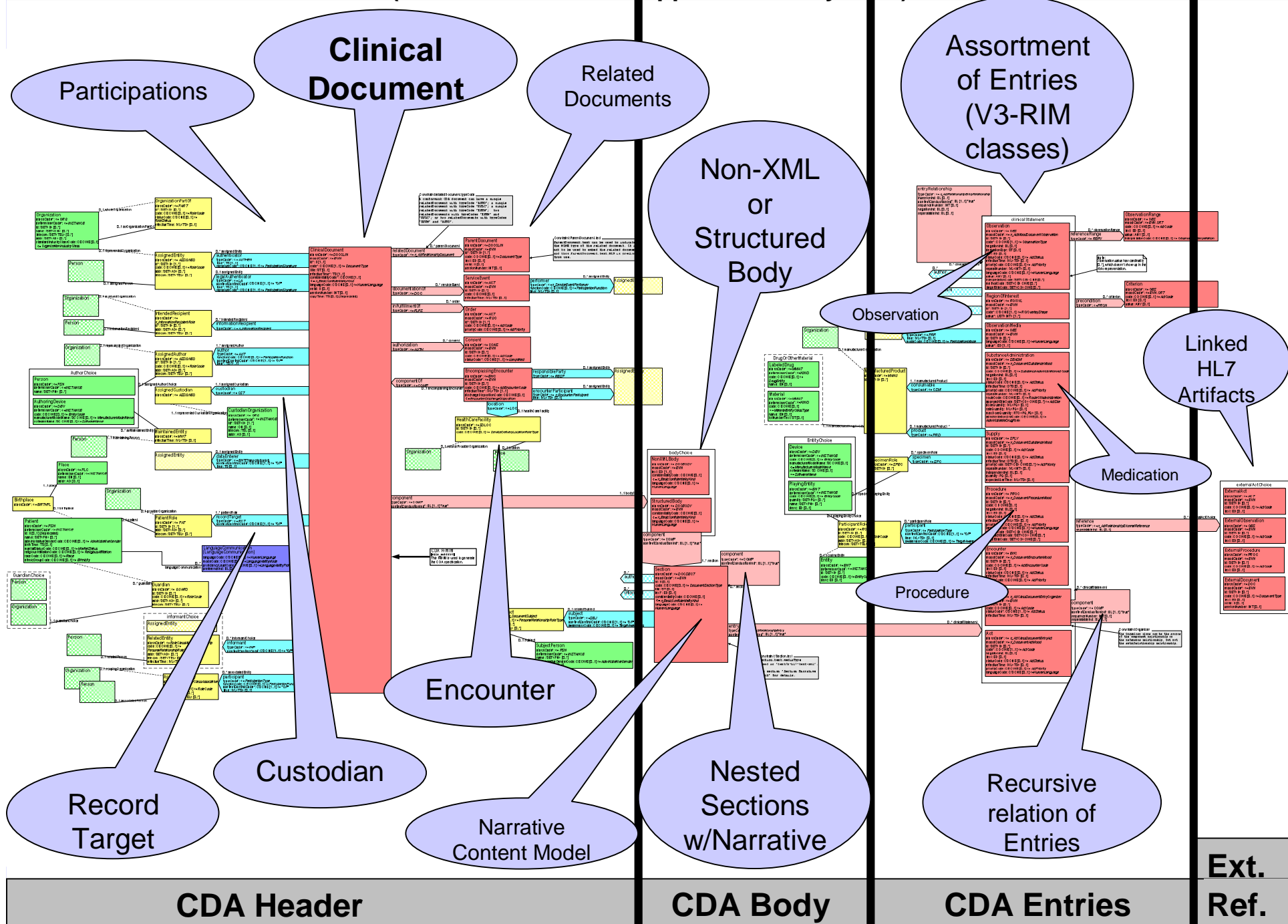


RIM 2.0
July 17, 2003



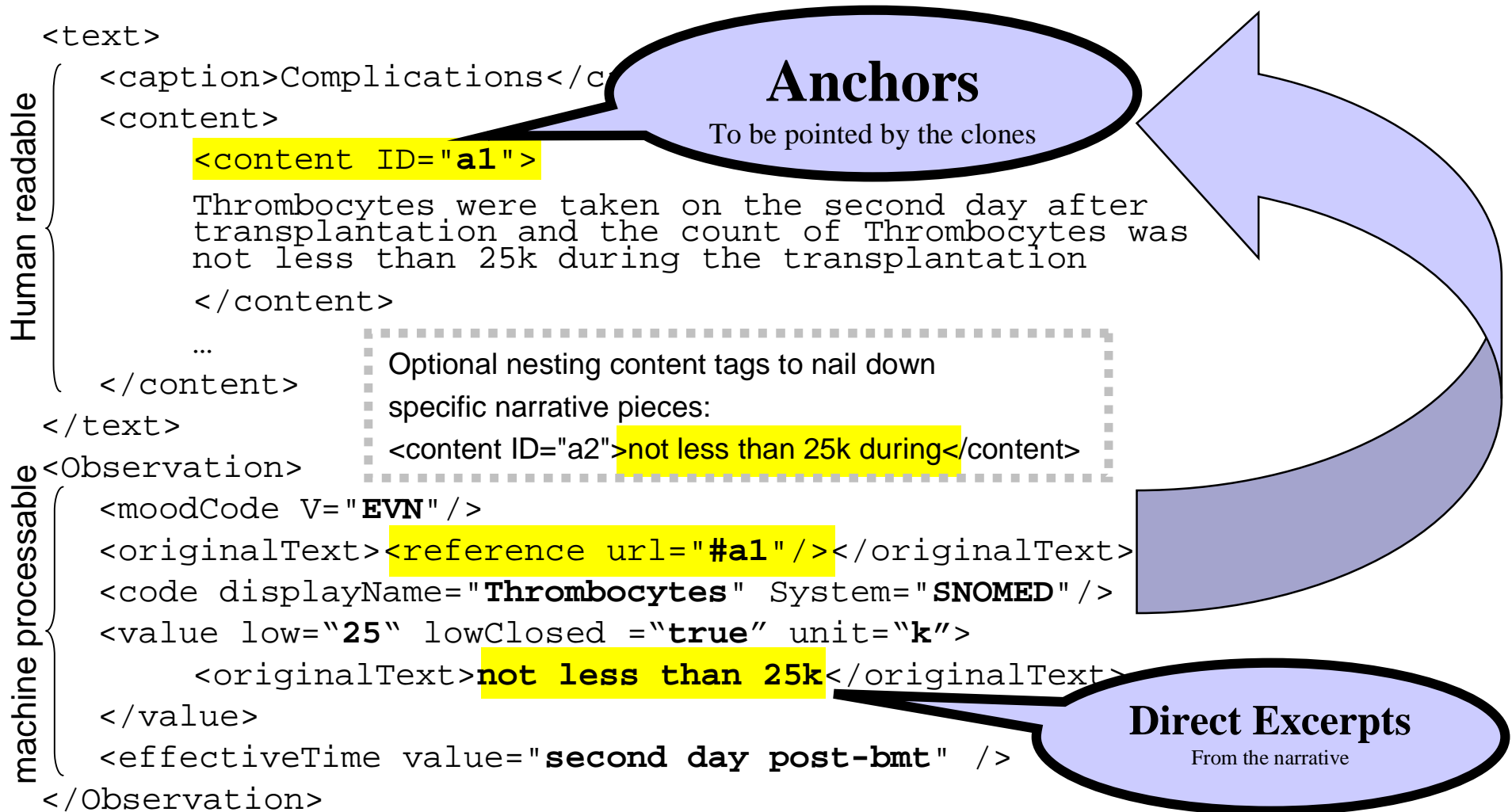
HL7-RIM: Core Classes

CDA Information Model (Release Two – ANSI approved in May 2005)





Clinical Document – Structured to Narrative Links





Agenda / Key Points

◆ Health Information Standards

- should be based on a central Health Reference Information Model (RIM)

◆ **Clinical Genomics & Clinical Trials Standards**

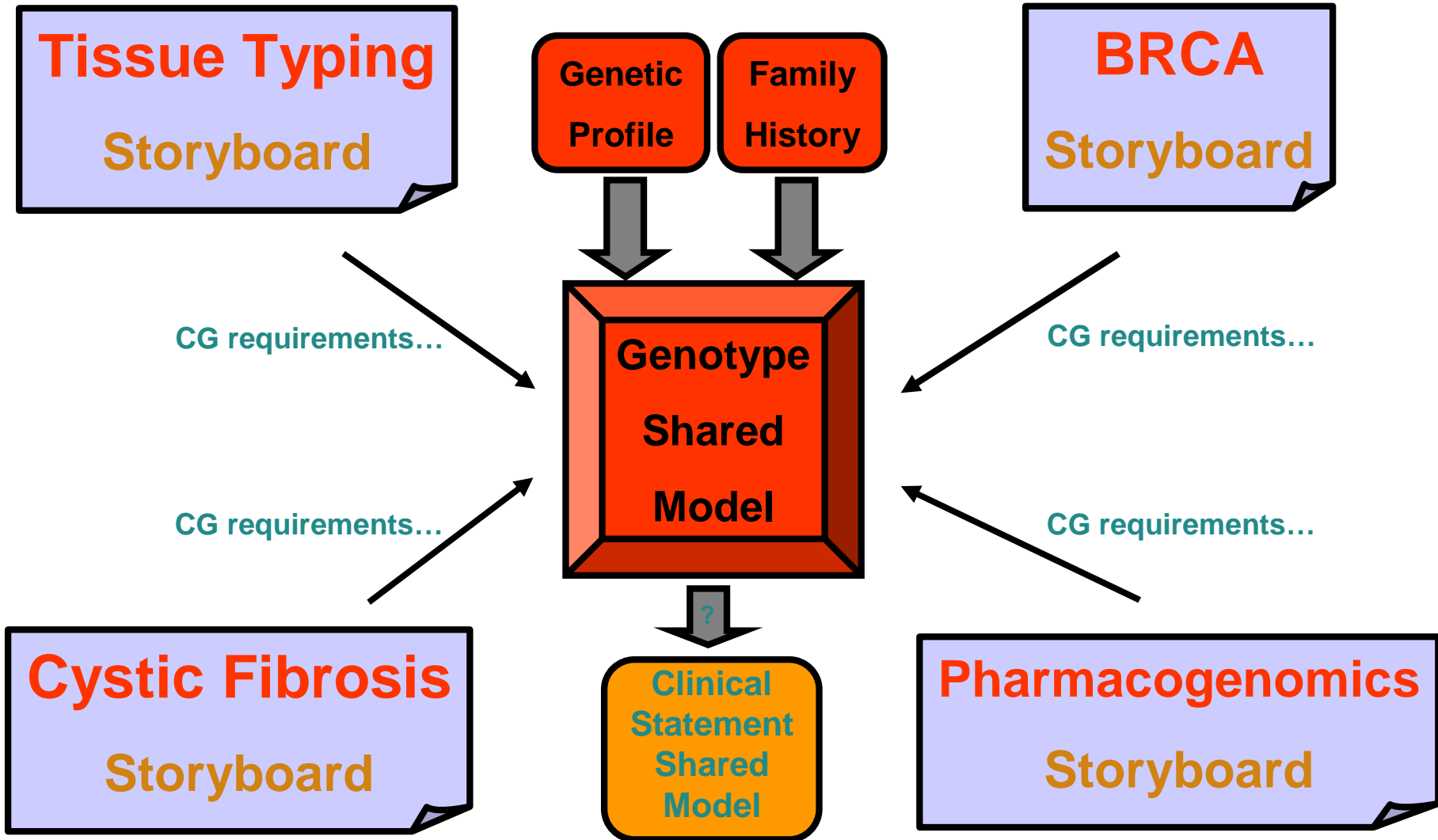
- **should implement the 'encapsulate & bubble-up' paradigm**

◆ The Final Frontier: EHR – Electronic Health Record

- personalized longitudinal and cross-institutional EHR
- personal genetic data should be part of the EHR
- inter/national Health Information Infrastructure is focused on EHR
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The HL7 Clinical Genomics SIG Efforts





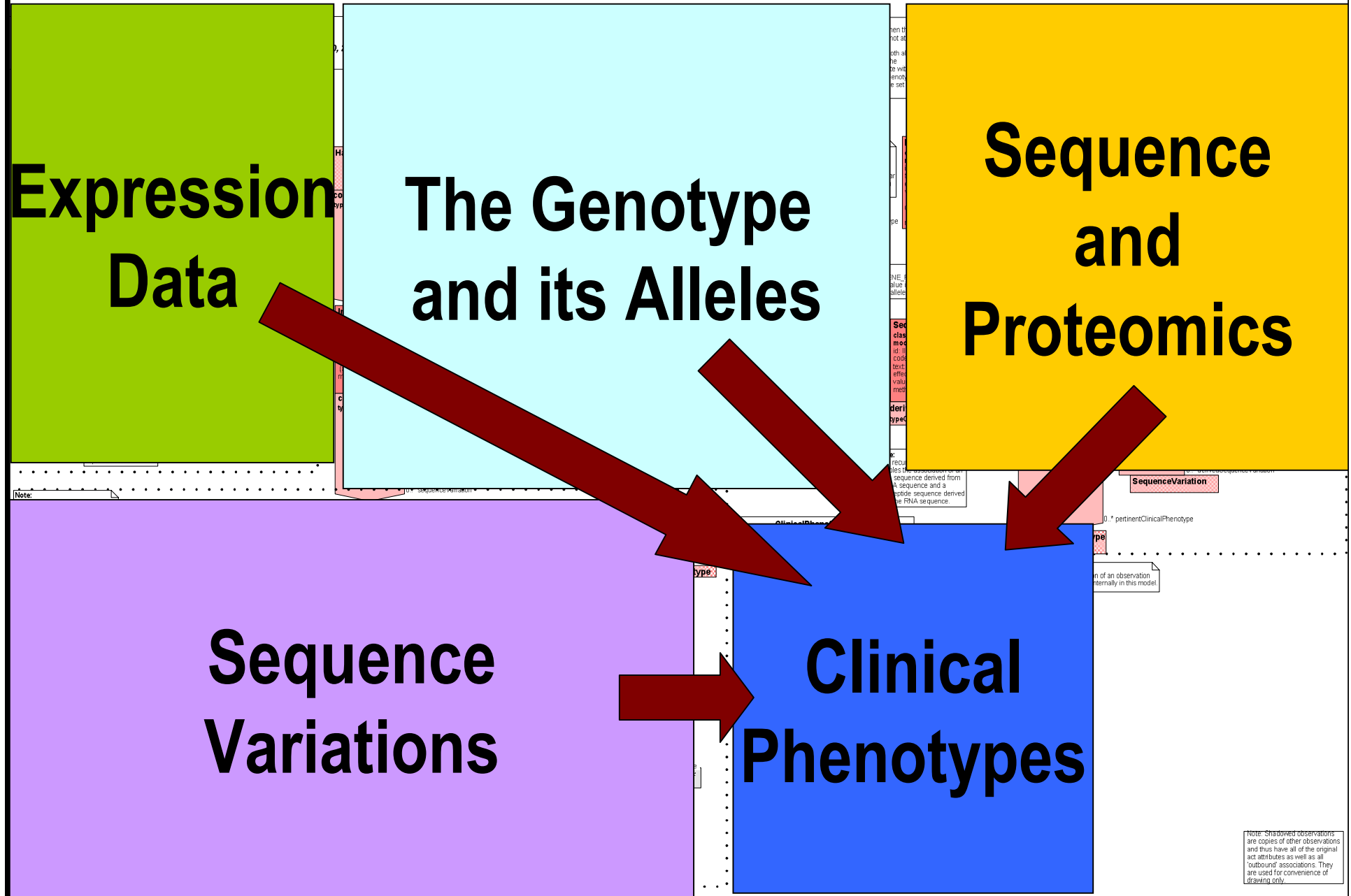
HL7 Clinical Genomics Specs (DSTU)

- ◆ DSTU = Draft Standard for Trial Use
(collaborations with early adopters)

- ◆ The Genotype / Genetic Profile Model
 - ◆ “Encapsulate & Bubble-Up” paradigm...
 - ◆ Bridging HL7 and bio-informatics markups

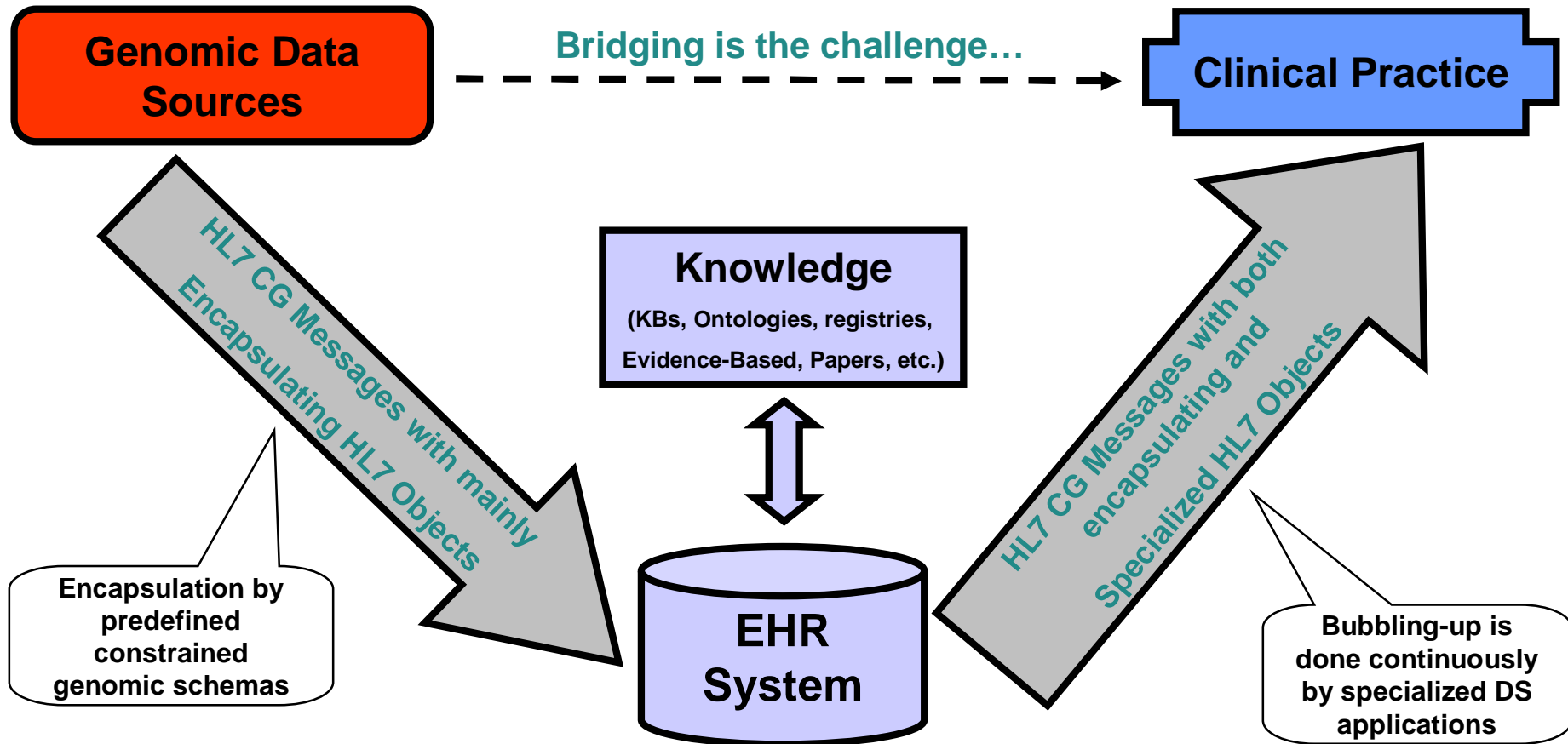
- ◆ Family History
 - ◆ Standardization of Patient’s Pedigree for risk assessment of cancer patient

The Genotype Model - Focal Areas:





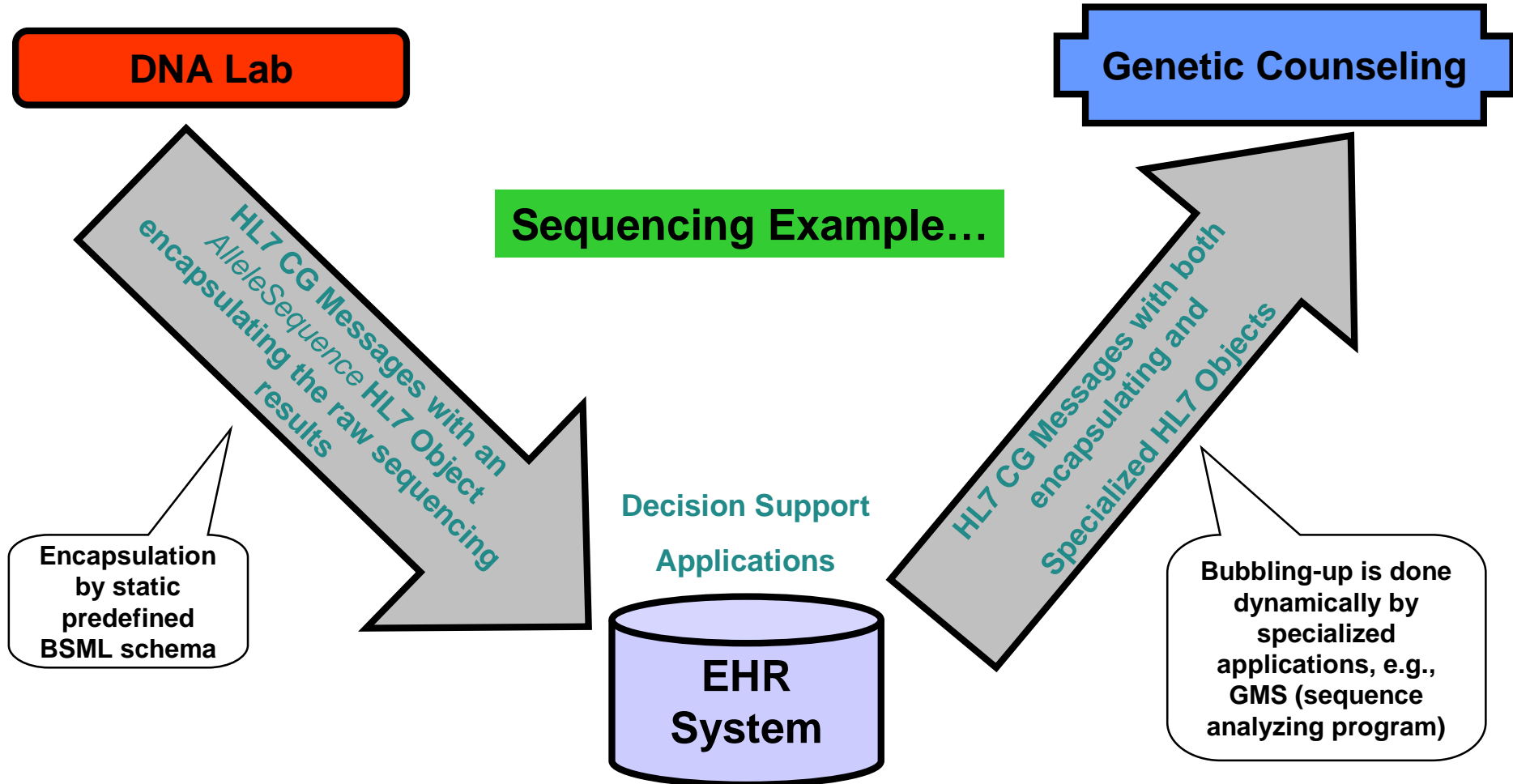
Coexistence of HL7 schemas and Bioinformatics Markup: Enabling the “**Encapsulate & Bubble-up**” paradigm



Bubbling up the clinically-significant raw genomic data into specialized HL7 objects and link them with clinical data from the patient EHR



Encapsulate & bubble-up (cont.)



**Bubbling up the clinically-significant SNP data into
HL7 SNP and Mutation objects and
link them with clinical data from the patient EHR**



The Genotype Model

Entry Point:
Locus

Encapsulating Obj.
Bubbled-up Obj.

Individual Allele

Determinant Polypeptide

Bio Sequence

Expression Attributes

Expression Data

Related Allele

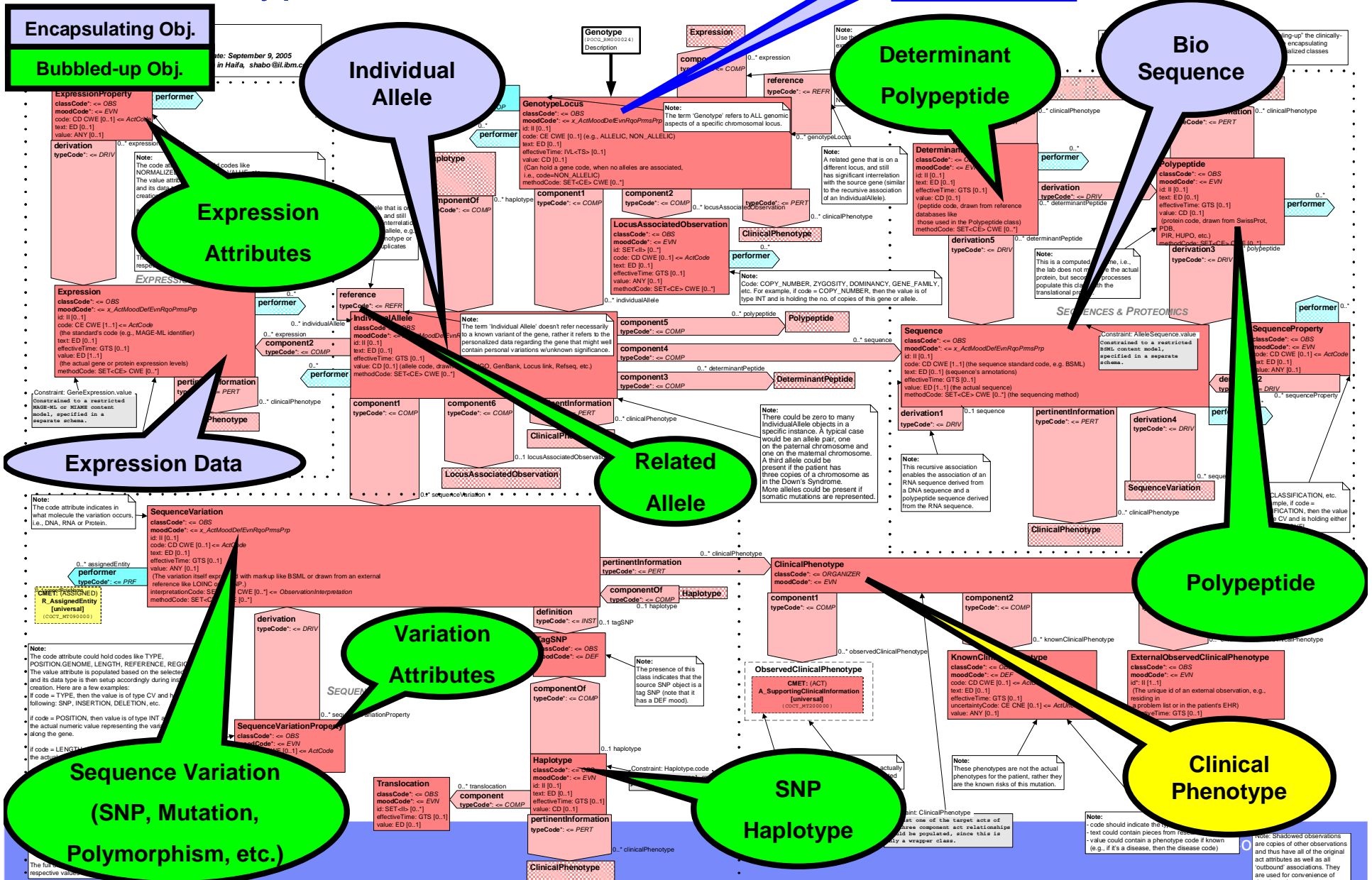
Variation Attributes

Sequence Variation (SNP, Mutation, Polymorphism, etc.)

SNP Haplotype

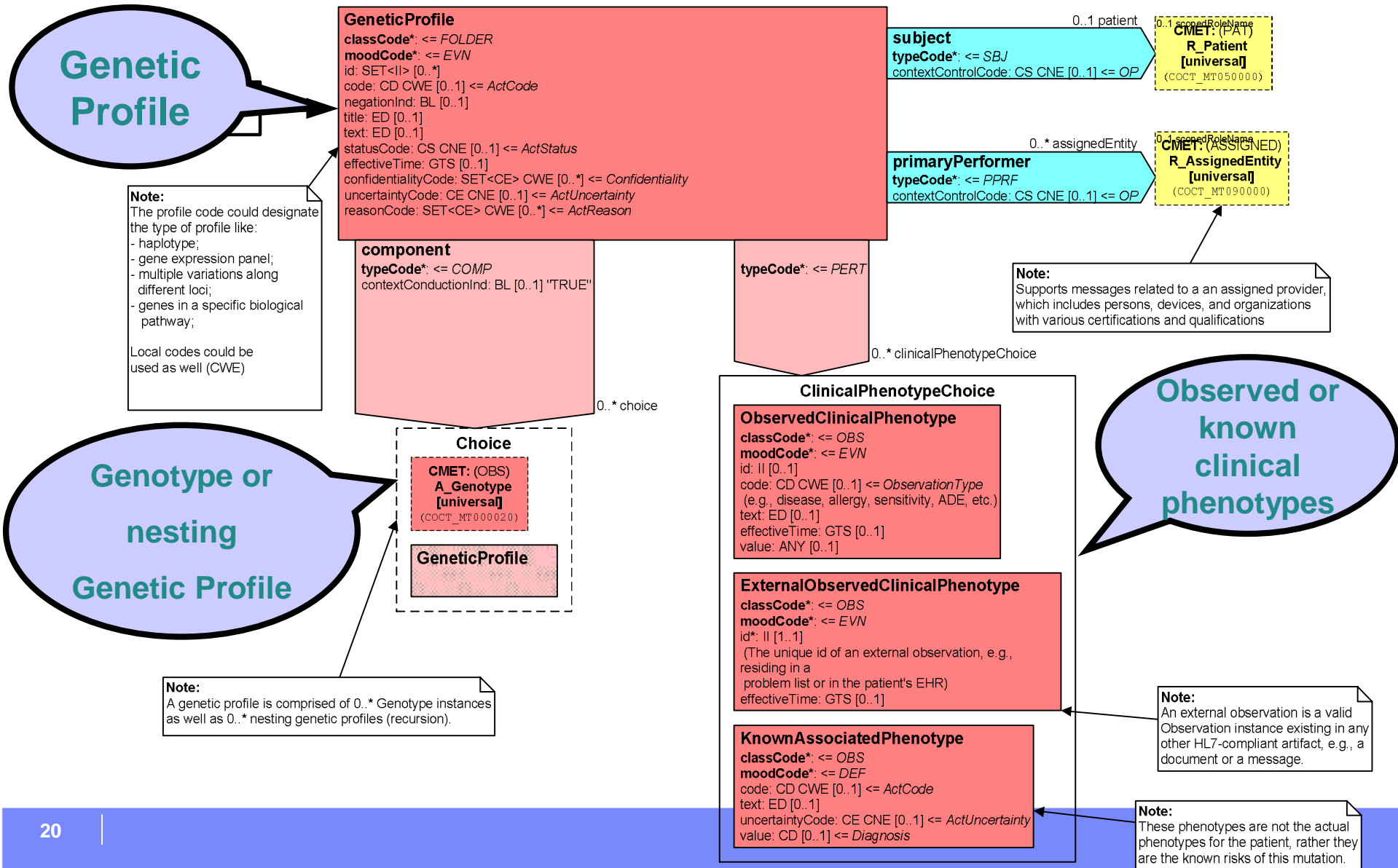
Polypeptide

Clinical Phenotype



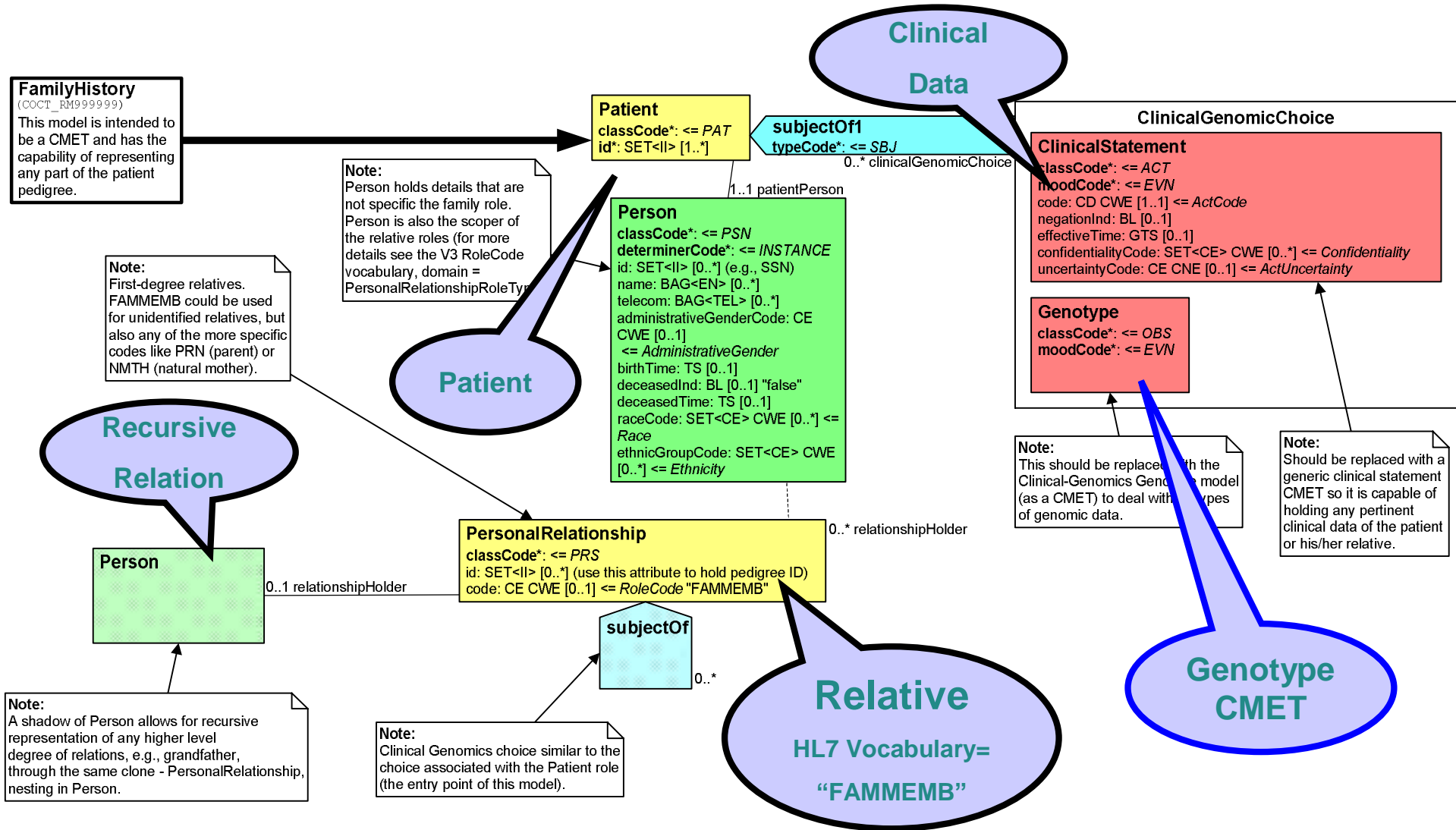


The Genetic Profile Model (since ballot #10)





The Family History Model (initial version)





How the Genotype fits in a F.Hx XML?

```

<!-- DAUGHTER -->
- <relationshipHolder>
  <id extension="555.011" />
  <code code="DAU" />
+ <relationshipHolder>
  <!-- GENOMIC DATA -->
- <subjectOf>
  <clinicalGenomicChoice>
    <clinicalGenomicChoiceGenotype>
      <Genotype>
        - <individualAllele>
          <code code="BRCA1" codeSystem="[insert GenBank OID]"
            codeSystemName="GenBank" />
          <text>Homo sapiens breast and ovarian cancer susceptibility (BRCA1)
            complete cds.</text>
          + <AlleleSequence>
          + <SequenceVariation>
          </individualAllele>
        </Genotype>
      </clinicalGenomicChoiceGenotype>
    </clinicalGenomicChoice>
  </subjectOf>
  <!-- CLINICAL DATA -->
+ <subjectOf>
</relationshipHolder>
<!-- end of DAUGHTER data -->

```

Taken from a patient pedigree, the portion related to patient's daughter (in collaboration with Partners HealthCare & other HL7 CG SIG members)

Bubble up...
To phenotype and beyond....

Point back...

Need to assure uniqueness across the various type encapsulated data

Click [here](#) to browse the entire XML...

Click [here](#) for the same sample with sequence data...



Sequence Sample XML

```
<sequence>
  <code code="BSMLcon3"/>
  <effectiveTime value="20050901"/>
  <value>
    <Definitions>
      <Sequences>
        <Sequence id="seq1" molecule="dna" title="EGFR - Homo sapiens epidermal growth factor
receptor" length="5616" representation="raw">
          <Seq-data>
            1 ccccggcgca gcgcggccgc agcagcctcc gccccccgca cgggtgtgagc gcccgacgcg
            61 gccgaggcgg ccggagtccc gagctagccc cggcggccgc cgccgcccag accggacgac
            121 aggccacctc gtcggcgtcc gcccgagtec ccgcctcgcc gccaacgcca caaccaccgc
          -----
          </Seq-data>
        </Sequence>
      </Sequences>
      <Isoforms>
        <Isoform-set>
          <Isoform id="snp1" seqref="seq1" location="190" change="T"/>
          <Isoform id="snp2" seqref="seq1" location="1099" change="G"/>
          <Isoform id="snp3" seqref="seq1" location="2418" change="C"/>
          <Isoform id="snp4" seqref="seq1" location="3721" change="T"/>
          <Isoform id="snp5" seqref="seq1" location="4982" change="G"/>
        </Isoform-set>
      </Isoforms>
    </Definitions>
  </value>
</sequence>
```

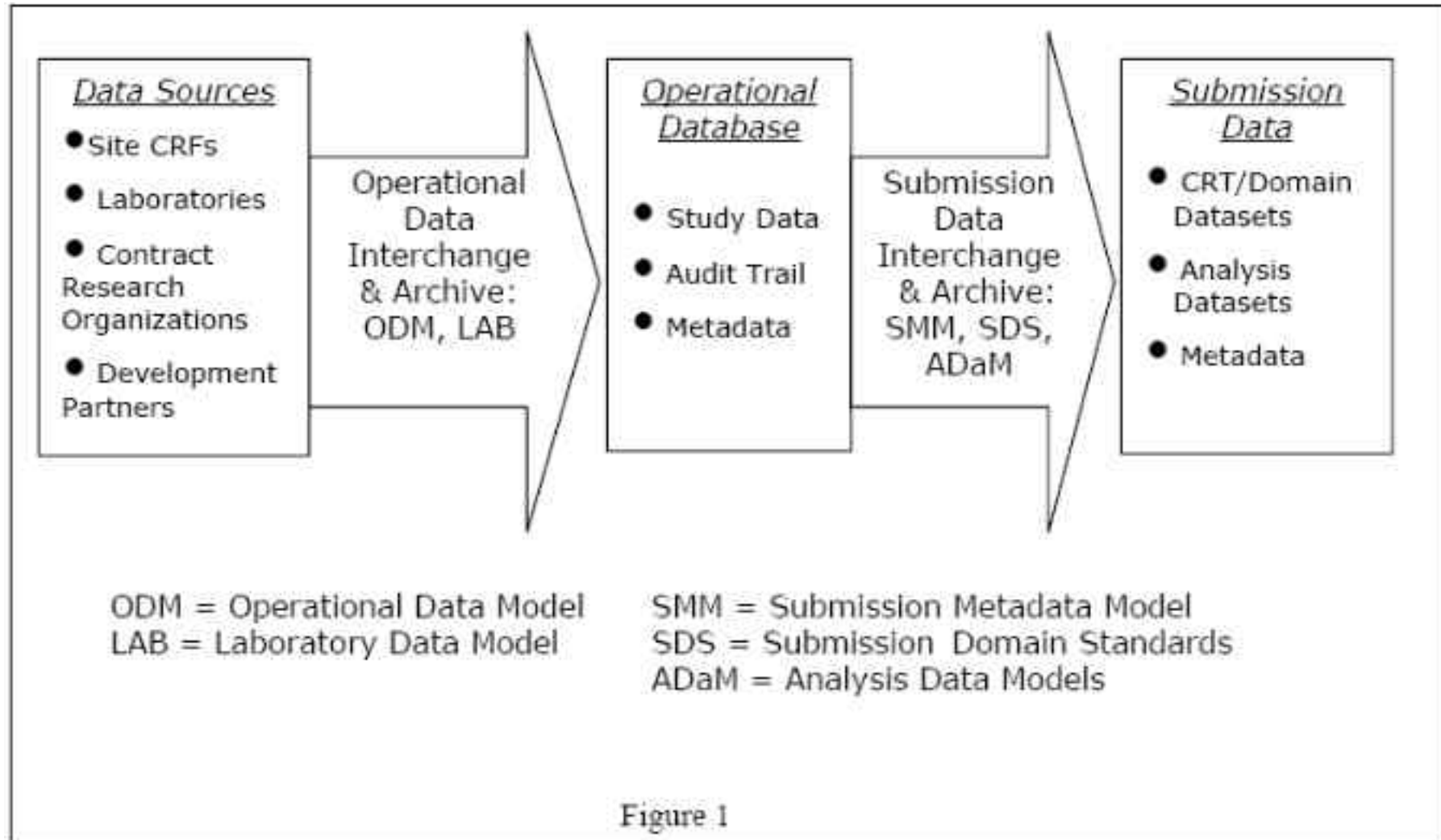
Notes:

- ◆ The use of the BSML 'seqref' attribute is to point to the sequence where this SNP occurs - value is the sequence id value.



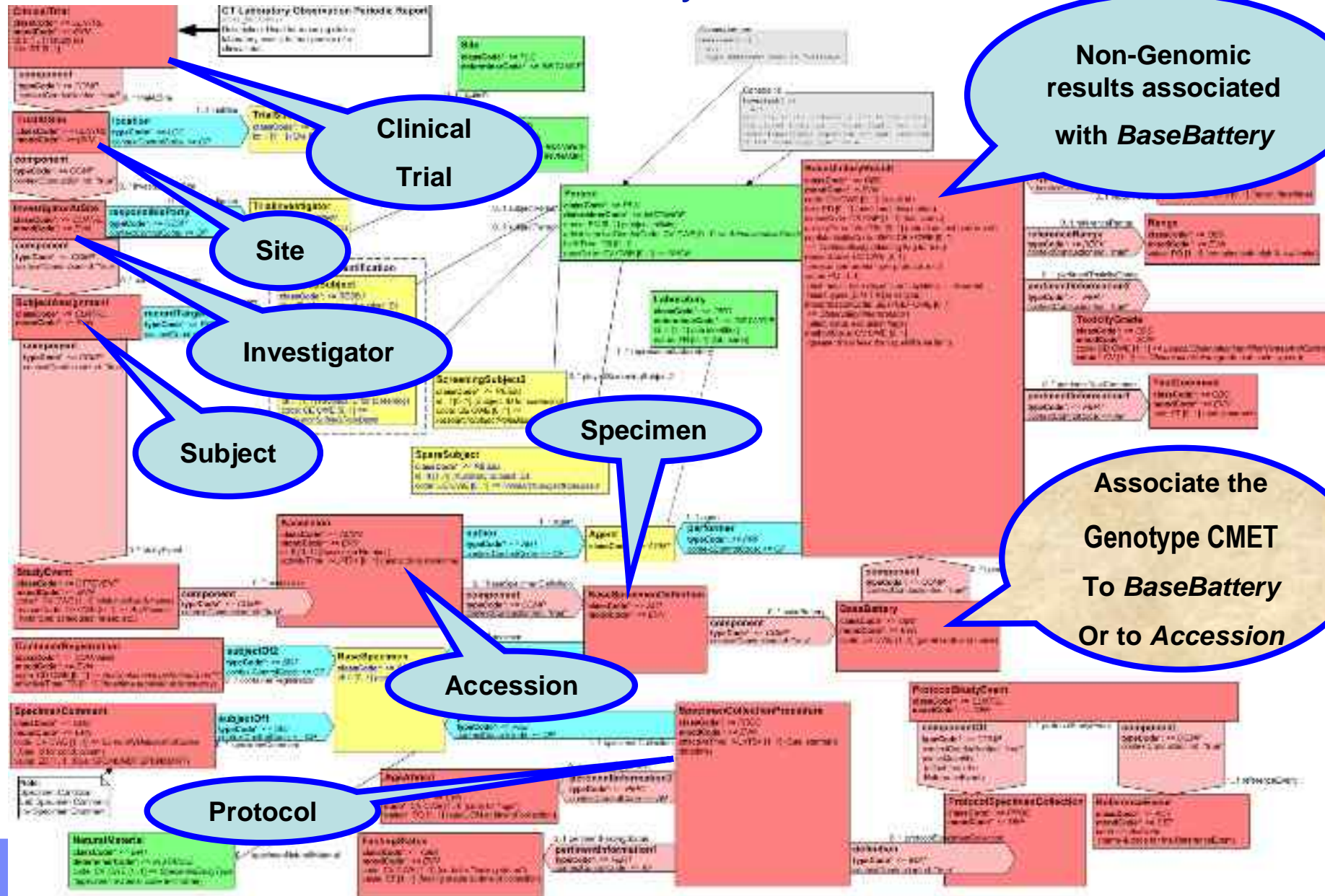
The CDISC Standardization Activities in Clinical Trials

Taken from the CDISC Web Site





The HL7 RCRIM CT Laboratory Model



Clinical Trial

Site

Investigator

Subject

Specimen

Accession

Protocol

Non-Genomic results associated with *BaseBattery*

Associate the Genotype CMET To *BaseBattery* Or to *Accession*



HL7 RCRIM-Clinical Genomics Joint Effort to address the need for information standards in FDA VGDS

- ◆ The Clinical Genomics SIG develops the Genotype Model
- ◆ The RCRIM TC develops Pharmacogenomics Message based on the CDISC Clinical Trials models
- ◆ The Pharmacogenomics Message utilizes the Genotype Model to convey genetic/genomic data
- ◆ The Pharmacogenomics Message will be proposed as the data standard in the FDA Guidance for VGDS – Voluntary Genomic Data Submission
- ◆ “The Agency has heard that pharmaceutical sponsors have been reluctant to embark on programs of pharmacogenomic testing during FDA-regulated phases of drug development because of uncertainties in how the data will be used by FDA in the drug application review process.”
(http://www.fda.gov/cder/guidance/6400fnl.htm#_Toc97697894)



Agenda / Key Points

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◆ Clinical Genomics & Clinical Trials Standards

- should implement the 'encapsulate & bubble-up' paradigm

◆ **The Final Frontier: EHR—Electronic Health Record**

- **personalized longitudinal and cross-institutional EHR**
- **personal genetic data should be part of the EHR**
- **inter/national Health Information Infrastructure is focused on EHR**
- **the inevitable sustainability model:
Independent Health Records Banks**



EHR Standards

ISO assessment...

“Previous attempts to develop a definition for the Electronic Health Record have **founded** due to the difficulty of encompassing all of the many and varied facets of the EHR in a single comprehensive definition.”



The HL7 EHR Functional Model DSTU

Direct Care	C1.0	Care Management
	C2.0	Clinical Decision Support
	C3.0	Operations Management and Communication
Supportive	S1.0	Clinical Support
	S2.0	Measurement, Analysis, Research, Reporting
	S3.0	Administrative and Financial
Information Infrastructure	I 1.0	EHR Security
	I 2.0	EHR Information and Records Management
	I 3.0	Unique identity, registry, and directory services
	I 4.0	Support for Health Informatics & Terminology Standards
	I 5.0	Interoperability
	I 6.0	Manage business rules
	I 7.0	Workflow



EHR Informational Models

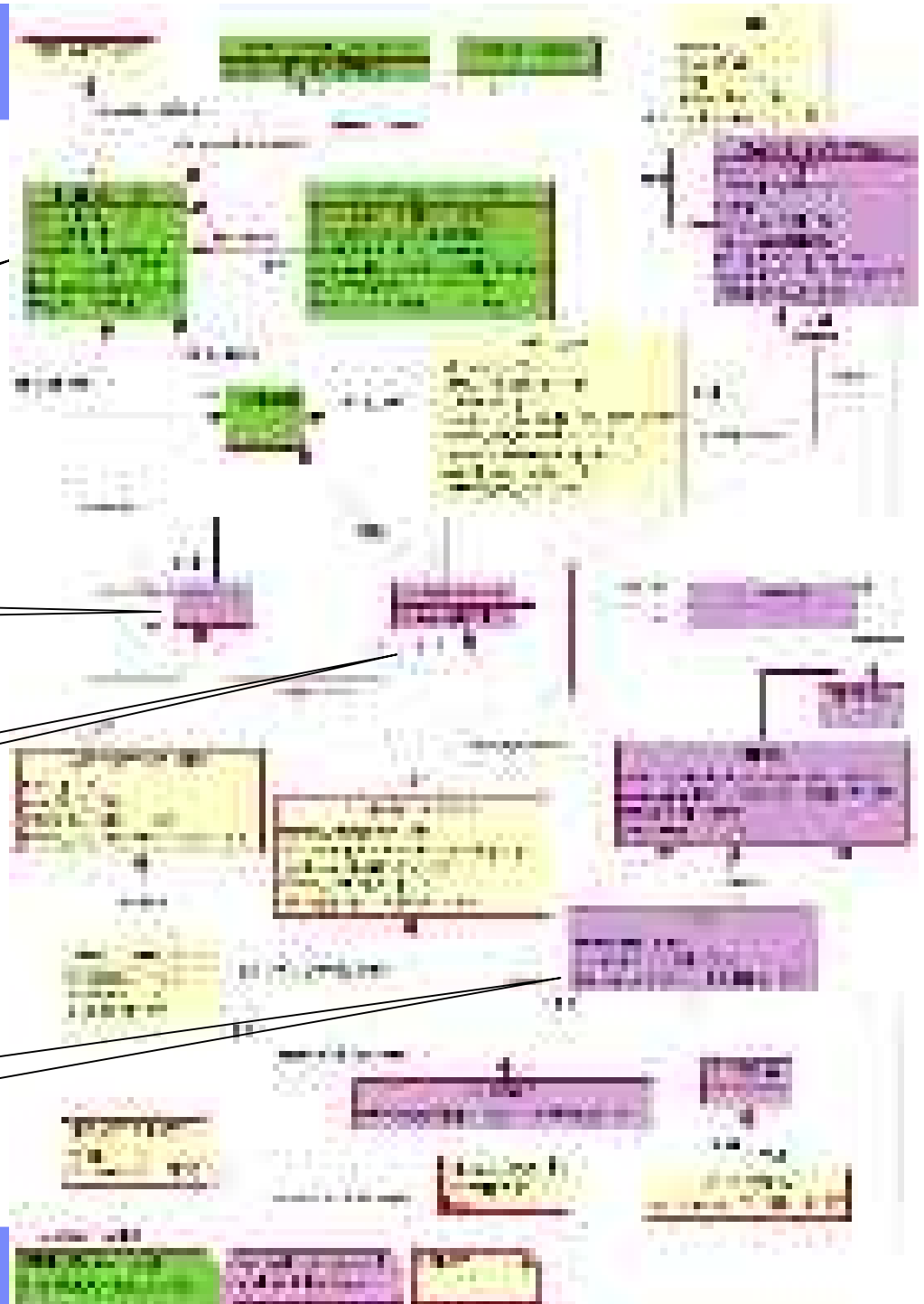
CEN TC251 EN 13606
EHR Model

EHR Extract

Folder

Composition

Entry/Item/Cluster





IHE (Integrating the Healthcare Enterprise) XDS New Profile

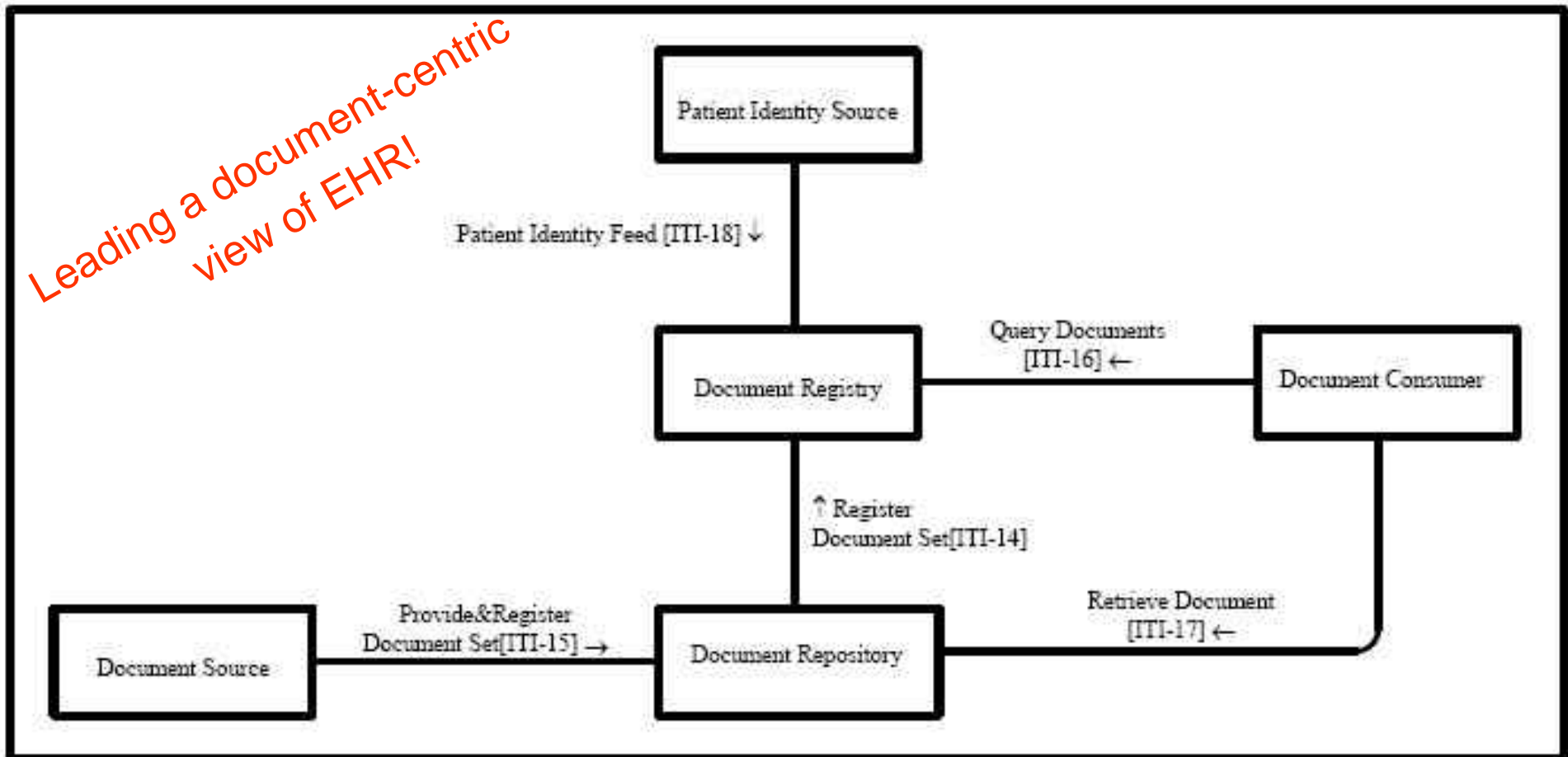
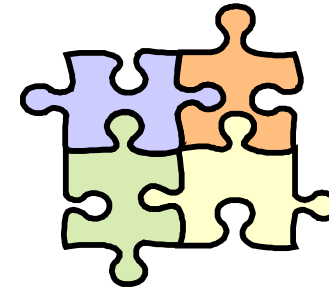


Figure 10.1-1 Cross-Enterprise Document Sharing Diagram



What's the Problem? (1)

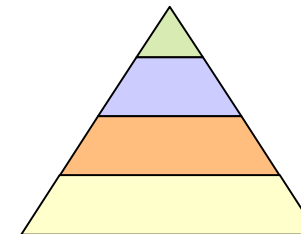
- ◆ So, we integrated all medical records...
...we even standardized & indexed them (!)...



- ◆ ...and the patient is now requesting care:
How does the current healthcare provider
make sense out of the pile of medical
records and have better medical reasoning?

- ◆ Those medical records could be numerous, using different standards, different codes, different units, could contain contradictory info., etc.

- ◆ Possible solution:
A lifetime electronic health record





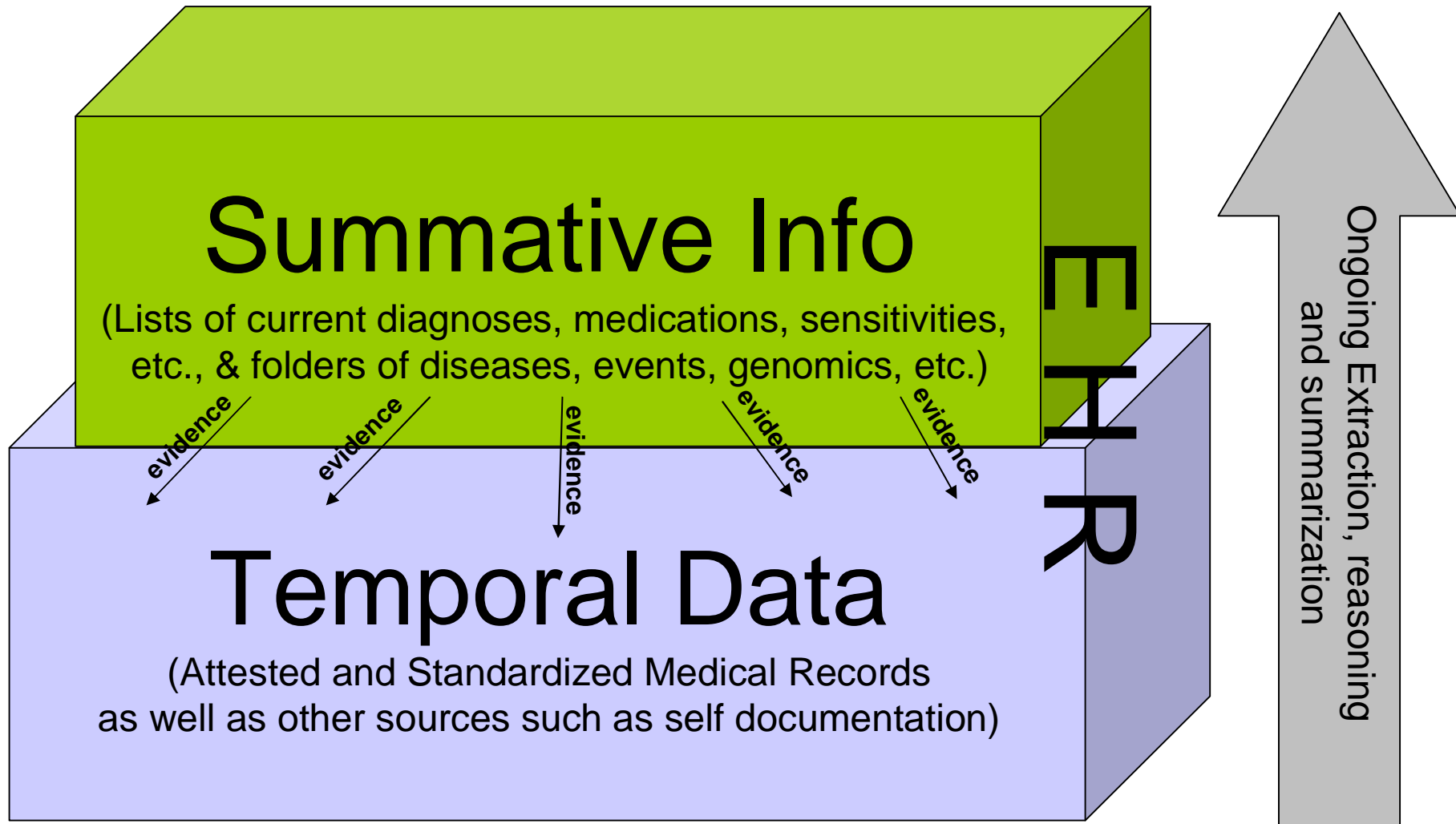
Main Features of a Lifetime EHR

- ◆ A **persistent** entity (not a query result!)
- ◆ Always **available** to **authorized** parties
- ◆ Continuously being **updated**
- ◆ **Embeds** the standardized medical records (preferably by value)
- ◆ Includes **folders** of topical & non-redundant information built on data from the standardized medical records & health records
- ◆ Folders are based on data from **standardized medical records**, captured as transactions into the EHR and extracted as **EHR Extracts**



The EHR Conceptual Structure

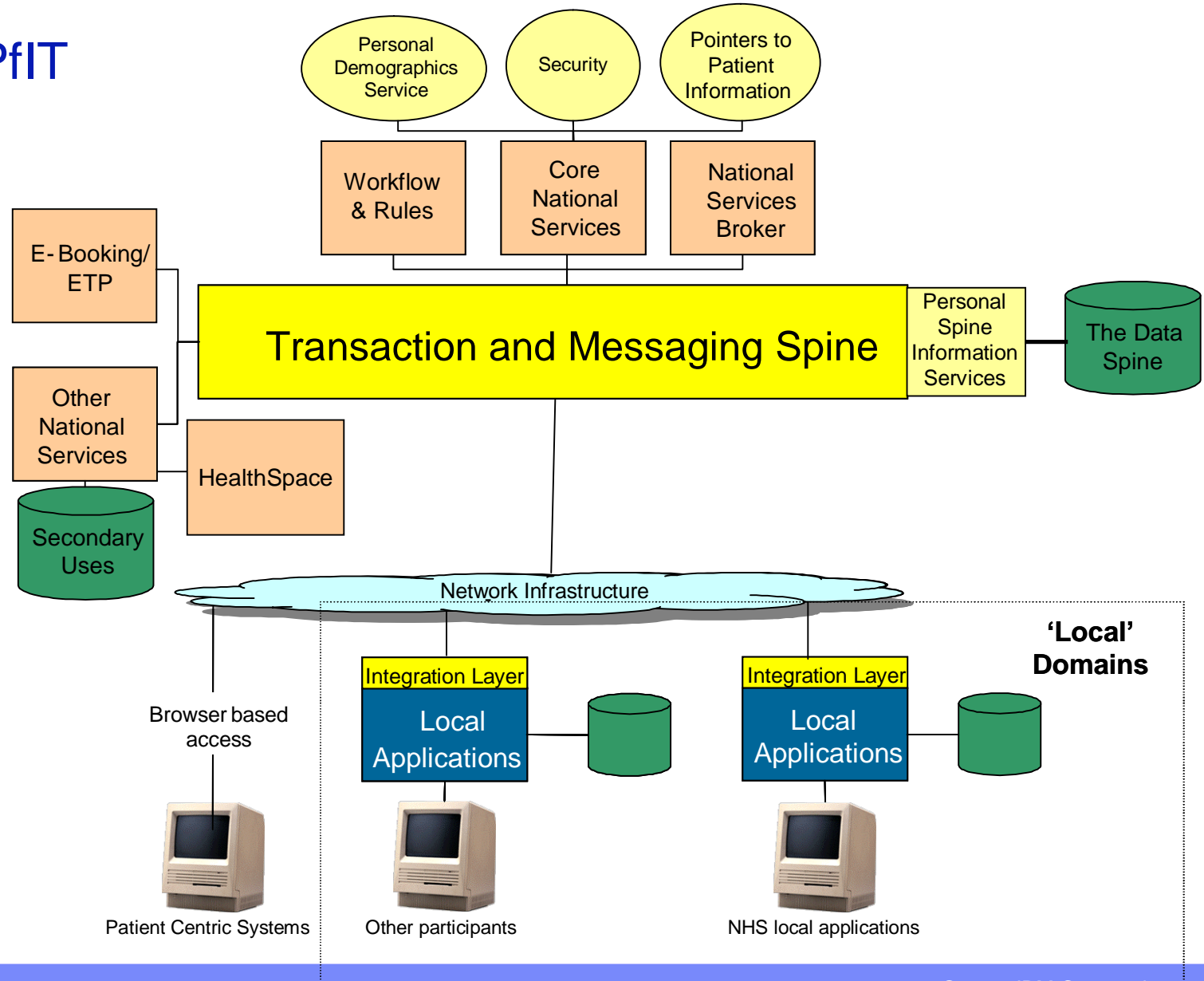
IBM Research is creating infrastructure for these processes.





UK NHS NPfIT

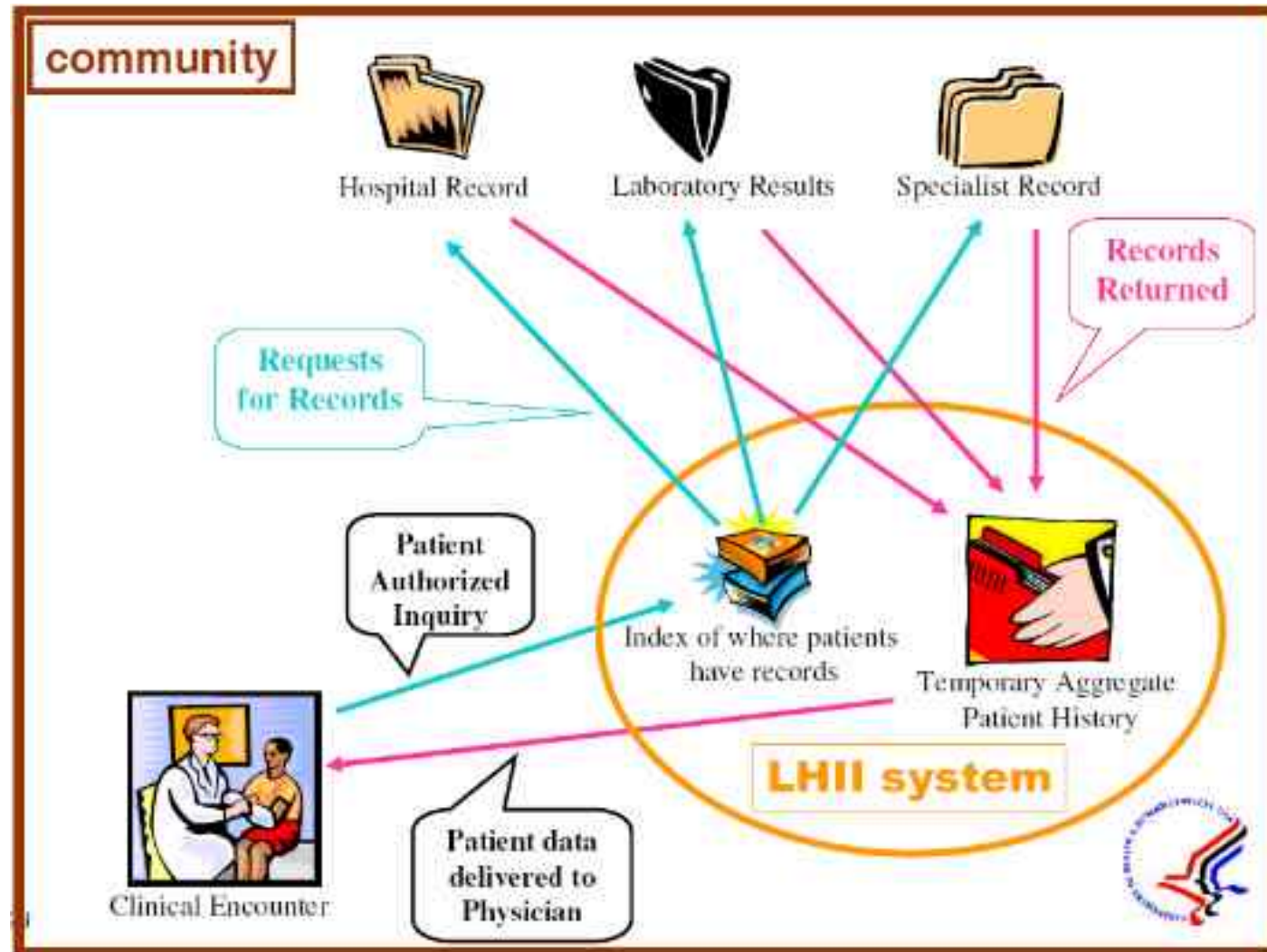
Simplified Conceptual Architecture





The USA NHII – The NHII 2004 Meeting

NOTE:
It's based on an **index** without meta-data, as opposed to the registry model!

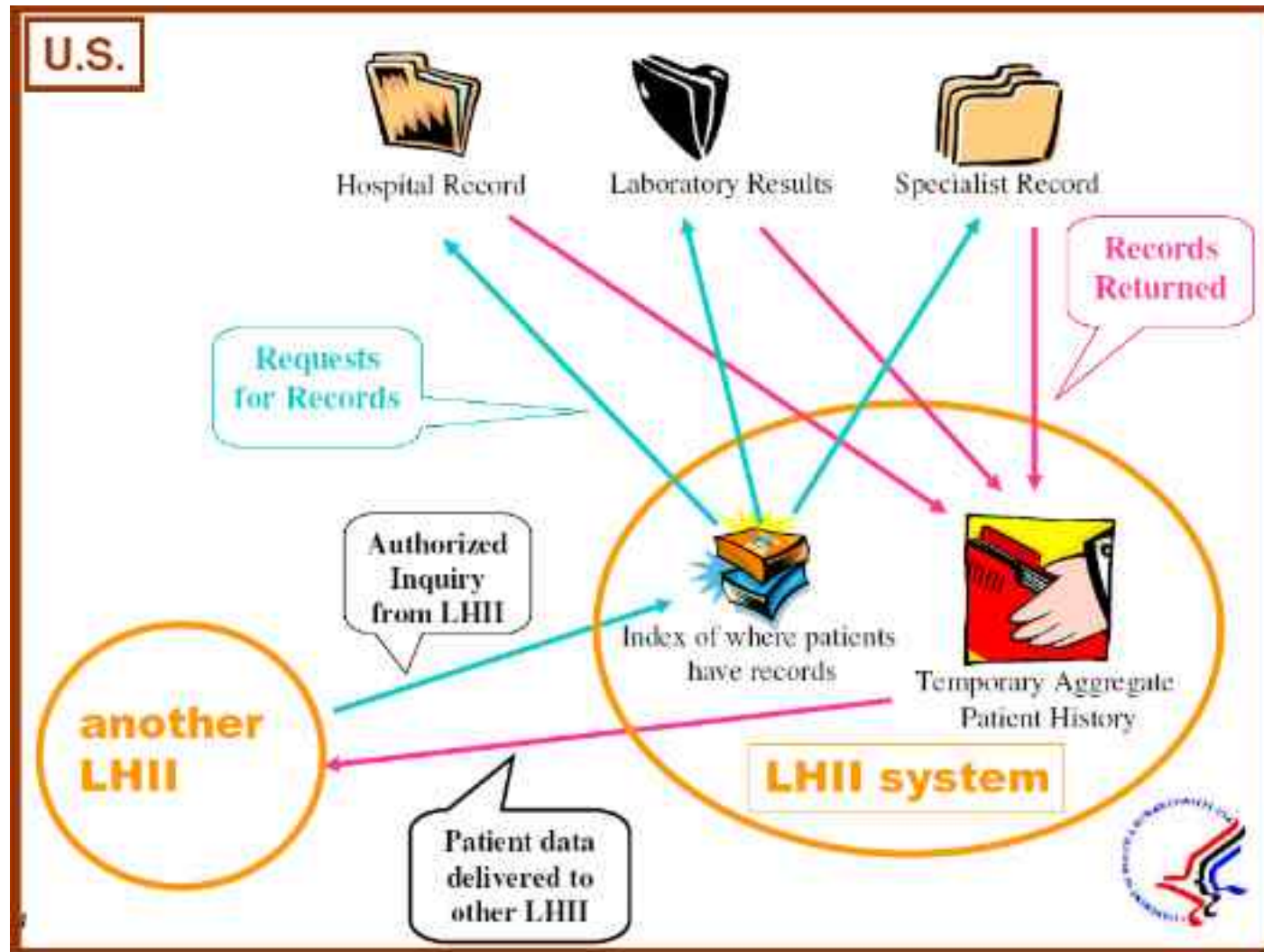


Taken from Dr. Yasnoff Presentation, NHII-2004



The USA NHII – The NHII 2004 Meeting

Key point:
Network of networks... not clear how it works and how do we uniquely identify a patient!



Taken from Dr. Yasnoff Presentation, NHII-2004



What's the Problem? (2)

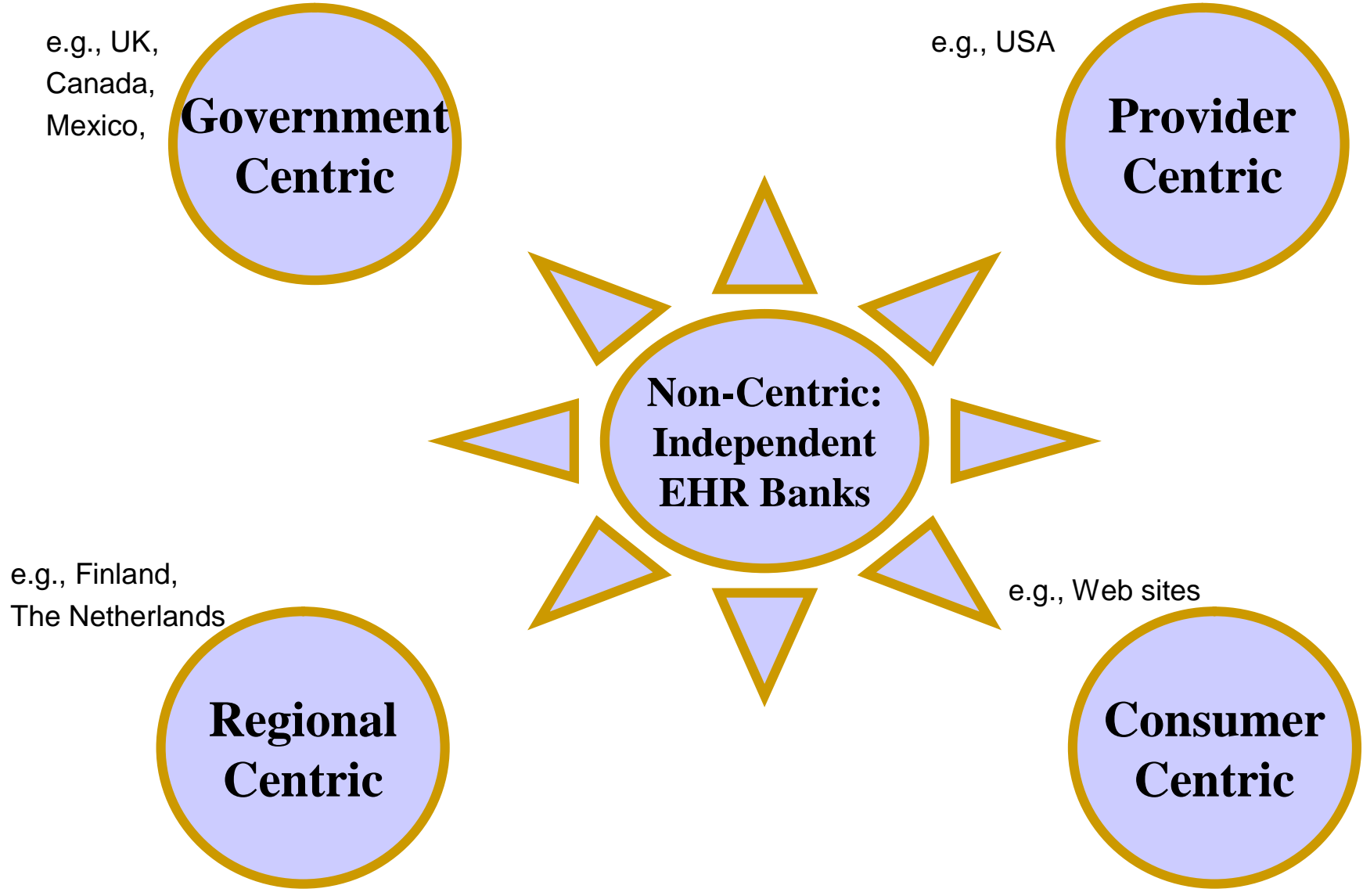
- ◆ Problem:
Who could possibly **sustain longitudinal EHRs throughout the lifetime** of its subjects?!

- ◆ Argument:
No single healthcare provider can or should sustain lifetime EHRs":
 - ◆ Involves specialization in archiving IT, not in health
 - ◆ Current situation occasionally leads to ethical conflicts

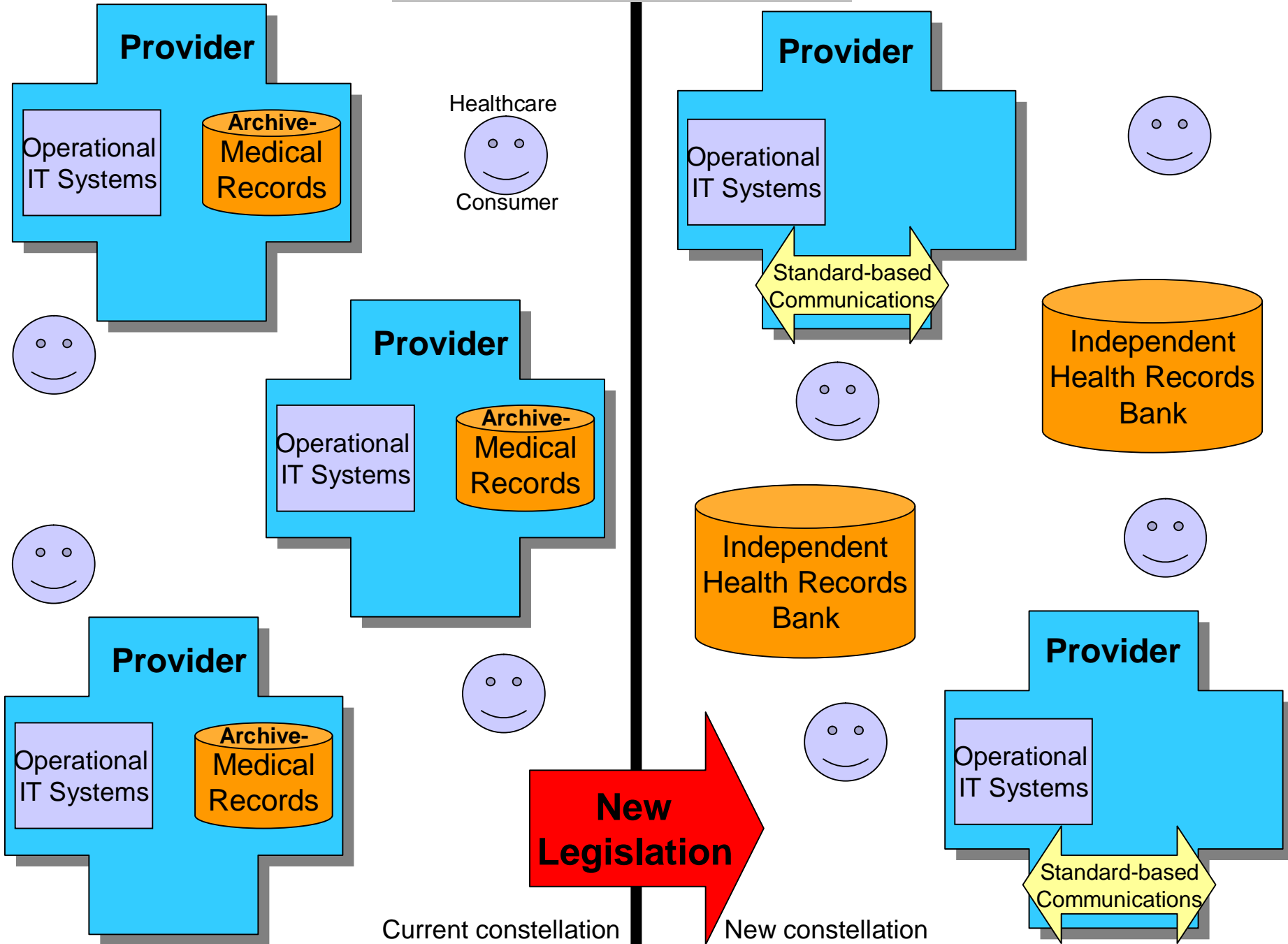
- ◆ Possible solution:
Multiple competing "Independent Health Records Banks", regulated by new legislation



Possible Models for EHR Sustainability



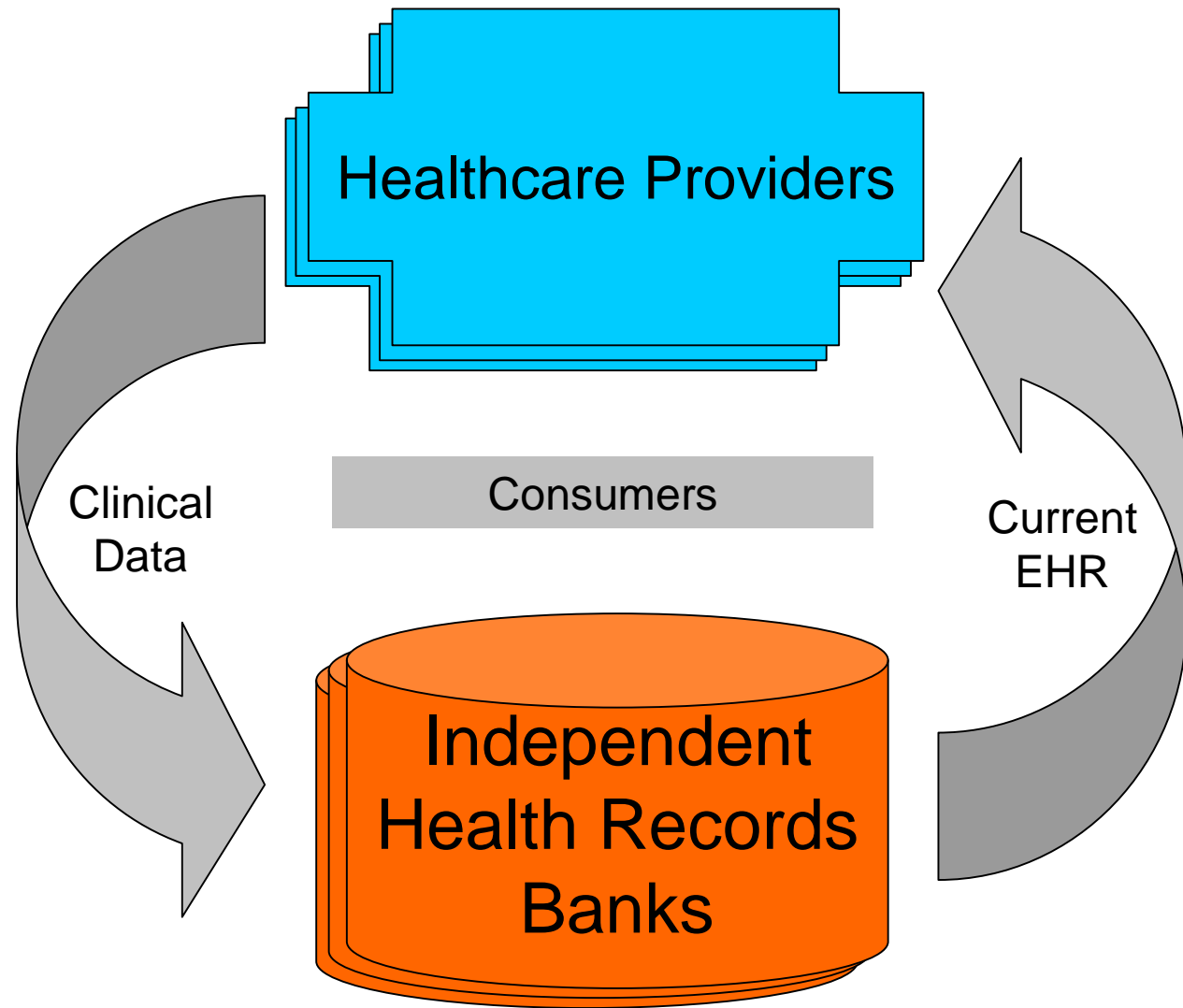
The Conceptual Transition





The IHRB Vision

- ◆ The medico-legal copy of a medical record solely resides in an IHRB
- ◆ IHRBs are Independent of healthcare providers, insurers and gov. agencies
- ◆ Multiple competing IHRBs, regulated by international law





The End

- ◆ Thanks for your attention!
- ◆ Questions?
- ◆ Comments: shabo@il.ibm.com

