Final Report for

Precision Medicine Informatics:
NIH - Creation of LOINC Equivalence Classes

Submitted to the

HHS Office of the Assistant Secretary for Planning and Evaluation

By the

National Center for Advancing Translational Sciences
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Background

A fundamental challenge to interoperable health information exchange is the copious idiosyncratic codes and names for identical concepts in separate electronic systems. The only way to overcome this barrier is to use common vocabulary standards that allow each system to understand the same clinical meaning.

Sending and receiving systems need a shared understanding of meaning for the data elements they exchange. Vocabulary standards that enable semantic interoperability are essential for enabling a learning health system and advancing the goals of precision medicine. Logical Observation Identifiers Names and Codes (LOINC©), developed by the Regenstrief Institute, Inc, is one of the essential vocabulary standards for efficient electronic processing and storage of clinical data that comes from many independent sources.

This proposal is significant because it addresses the significant challenge of efficient aggregation of laboratory data and other data from diverse health IT systems by creating a flexible, extensible, and computable mechanism for rolling up LOINC codes into relevant equivalence groups. Our approach will encourage widespread usage of this new resource by distributing it publicly at no cost under the existing LOINC release mechanism.

LOINC provides standardized codes and names for a wide range of clinical observations, from diastolic blood pressure to serum levels of hepatitis B surface antigen, from physical exam findings to the discharge summary. It provides codes for the observations recorded in clinical laboratory systems, electronic health record systems, research databases, and clinical flowsheets.

LOINC has been widely adopted around the world. At present, LOINC is used in more than 172 countries by many kinds of organizations, including large reference laboratories, healthcare organizations, insurance companies, regional health information networks, and national ministries of health. About 30 countries have adopted LOINC as a national standard. Within the United States, the Meaningful Use program requires LOINC in messages reporting laboratory test results, exchanging medical summaries, and sending data to cancer registries and public health agencies. Large scale research networks have also adopted LOINC. For example, the PCORnet Common Data Model leverages LOINC to enable interoperability.

Purpose

The goal of this proposal is to create a flexible, extensible, and computable mechanism for rolling up LOINC codes into clinically relevant equivalence groups that enable more efficient processing and aggregation of laboratory and other data from diverse health IT systems.

Project Summary

The potential value of integrated data from clinical research systems and clinical care systems requires connections that implement both standard interfaces and standard vocabularies. LOINC is a universal coding system for laboratory tests and other clinical observations. LOINC is used widely around the world to support electronic delivery of health data for clinical care, public health reporting, and in research networks like PCORnet.

Variations in mapping approach can create interoperability problems because the same clinical data can be assigned different LOINC codes by different institutions. Furthermore, across institutions and use cases, the specific aggregation rules needed for various approaches may vary significantly.

The goal of this project is to create a flexible, extensible, and computable mechanism for rolling up LOINC codes into clinically relevant equivalence groups. The specific aims of this project are to:
1) identify high priority content for representing in the new LOINC hierarchy;
2) develop a clinically-relevant roll-up hierarchy for LOINC terms;
3) disseminate the aggregation hierarchy within the main LOINC release distribution.

Overall, this project is expected to help overcome the barrier of laboratory and other data from diverse health IT systems being mapped to LOINC codes with different levels of granularity. By creating a flexible and computable mechanism for aggregating groups of "equivalent" LOINC codes this proposal will facilitate more effective use of LOINC in clinical flowsheets, data analytics, and quality management. Distributing this new resource through the existing LOINC publication mechanism will make it widely available at no cost worldwide and will encourage open feedback from the user community. Having such a rigorously developed, computable hierarchy of LOINC codes will accelerate the pace and achievement of clinical and translational research.

For implementation, the National Center for Advancing Translational Sciences (NCATS) at the NIH awarded an administrative supplement (3UL1TR001108-04S1) to the Indiana Clinical and Translational Sciences Institute (Indiana CTSI) on 09/23/2016. The Indiana CTSI then subcontracted the Regenstrief Institute to obtain the services of the LOINC effort.

The Major Accomplishments and Deliverables are summarized in the following section of this report.

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Background

The potential value of integrated data from clinical research systems and clinical care systems requires connections that implement both standard interfaces and standard vocabularies. Logical Observation Identifiers Names and Codes (LOINC©), developed by the Regenstrief Institute, Inc, is a universal coding system for laboratory tests and other clinical observations. LOINC is used widely around the world to support electronic delivery of health data for clinical care, public health reporting, and in research networks like PCORnet. Variations in mapping approach can create interoperability problems because the same clinical data can be assigned different LOINC codes by different institutions. Furthermore, across institutions and use cases, the specific aggregation rules needed for various approaches may vary significantly.

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Major Accomplishments

Under this project we created and published equivalence groups of LOINC terms as the LOINC Group File that is included in as an artifact in the official LOINC release. The artifact is described and made available on a special LOINC Groups landing page. It is also available from the main LOINC website as a standalone release artifact and included in the complete LOINC release download file. During this project we published iteratively-improved versions of the LOINC Group File within each regular, bi-annual LOINC release. Like all LOINC release artifacts, the LOINC Group File contains the data content, a detailed ReadMe file, and a ReleaseNotes file that highlights version to version changes.

The first version, LOINC Group File Alpha 1, was released on June 23, 2017 (included in LOINC release 2.61). This first release contained 12 Parent Groups and 2178 Groups that aggregate a total 6438 unique LOINC terms. After iterative feedback, review, and expansion, the next version, LOINC Group File Alpha 2,was released on December 15, 2017. This version included the revised format and the inclusion of ancillary data such as molecular weight. It contained 21 Parent Groups, 4,100+ equivalence groups, that aggregate more than 17,500 unique LOINC terms. The final version published under this award was released on June 15, 2018 (included in LOINC release 2.64) as LOINC Group File Beta 1. This latest version contained 36 parent groups, containing 5650 groups, that organize 24,075 unique LOINC terms. It included groups in several new areas, including radiology terms by region imaged, document ontology groups based on the setting, several groups based on a broader clinical concept, such as social determinants of health and physical activity. Inside the LOINC Group File are UsageNotes and Component-level molecular weights from the PubChem database for nearly 900 Groups.

To foster ongoing input from the LOINC community, we developed a [portal on the LOINC website](#) for users to recommend and submit groups. We have received substantial contributions of additional content that will be incorporated in subsequent LOINC releases, including additional groups of microbiology, drug testing, smoking, pregnancy, and pain terms.

In addition to defining and publishing the LOINC Group content in the standard release file format, we have made the latest LOINC Groups content available via an application programming interface (API) based on the [HL7 FHIR® standard specification](#). We deployed a new web server located at [fhir.loinc.org](#) that uses the [HAPI](#) open-source FHIR library in JAVA that makes all of the LOINC Groups available as FHIR ValueSet resources. Making the LOINC Groups available in this format provides dynamic, queryable, and machine readable content via a standardized interface.

Throughout the contract period we disseminated information about the newly created LOINC Groups to the LOINC user community (with over 60,000 users), the [Clinical Laboratory Improvement Advisory Committee (CLIAC)](#), and health information technology developers at the [FHIR DevDays](#) conference.

Deliverables

Through enhanced query methods and tools, iteratively review LOINC content

Throughout the contract period we developed and continued to improve techniques for reviewing LOINC content and building and maintaining LOINC Groups. This maintenance infrastructure uses software and rules that builds on and leverages the existing technology environment used to maintain the base LOINC terminology. In addition, we sought feedback from a broad user community and an expert advisory group to identify areas of LOINC content to prioritize development of new groups.

Through iterative review, each release of the LOINC Group File contained new content and new aggregation groups. The initial release contained aggregation groups focused primarily on laboratory LOINC content and a small set of clinical variables. The second release added groups in several domains, including reportable microbiology, radiology, and the LOINC Document Ontology. The third iteration of the LOINC Groups File incorporated feedback from various stakeholders and featured new groups aggregating quantitative exercise or activity terms, key social determinants of health, smoking status, radiology terms by region imaged, and clinical document terms by care setting. We also revised our approach for finding, validating, and storing molecular weight information for measured chemicals based on API calls to PubChem. Molecular weights are included in the release artifact so that users can equivalence between tests reported in molar and mass concentrations.

We also prepared additional groups of microbiology, drug testing, smoking, pregnancy, and pain terms that were not completed in time for inclusion in the latest release, but that we anticipate being published in a future version. We reviewed our linkages from LOINC Parts to RxNorm clinical drug concepts, added new mappings, and used that information to prepare additional drug testing groups.

Convene and receive feedback from expert advisory group

Throughout the period of performance we convened an expert advisory group that met quarterly. The Advisory Group provided input on new content, suggested ideas for future development, and reviewed the existing file structure. They were

provided early access to content under development and were given the first opportunity to comment. They also discussed and encouraged our development of a community portal for users to submit ideas for new groups and a FHIR-based API service that would allow dynamic access to the LOINC groups. They also gave input about its presentation and demonstration to the LOINC Committee and other stakeholders.

Promote and receive feedback from LOINC user community (ongoing)

We created multiple avenues for feedback from the user community on the LOINC Groups file. We created a topic/thread on the online LOINC user forum. Additionally, we send each person who downloads the file a brief survey to complete. With each LOINC release, a news post highlighting key additions and updates is published and sent out to the LOINC mailing list.

We highlighted the LOINC Groups content at the LOINC Laboratory Committee and Clinical Committee meetings, which occur four times each year, throughout the contract period. In addition, we presented to the Clinical Laboratory Improvement Advisory Committee (CLIAC), which provides scientific and technical advice to the Department of Health and Human Services, and to the health IT development community at the FHIR DevDays conference.

In addition, we have also published a community portal that allows users to share their own equivalence groups that they find useful and request that particular groups be added to the standard distribution.

Draft equivalence groupings including final formats for distribution

As described earlier, we have published three versions of equivalence groups the LOINC Group file as part of the normal LOINC release process. The latest version was released on June 15, 2018 and is available at https://loinc.org/groups. Over time we have incrementally improved the content and format of the release artifact based on feedback.

We have also launched pilot tools that make the equivalence groupings available dynamically from an application programming interface (API) based on the HL7 FHIR® standard. The LOINC Groups content from the latest release (version 2.64) are now available as FHIR Valueset resources from our server at fhir.loinc.org. Access to the server uses a person's main loinc.org credentials as does other release content. Creating a LOINC user account is free.

For example, to retrieve all of the items in the LOINC Group LG11363-5, an application can use the FHIR Valueset $expand operation and call:

```
GET https://fhir.loinc.org/ValueSet/LG11363-5/$expand
```

To test whether a particular LOINC term, such as the serum sodium term 2951-2, is in a given group, the application can use the $validate-code operation:

```
GET https://fhir.loinc.org/ValueSet/LG11363-5/$validate-code?
system=http://loinc.org&code=2951-2
```

Vet draft equivalence groupings with expert advisory group

Throughout the project, the Advisory Group has been engaged in review of the equivalence groupings through its quarterly meetings and offline review of the files. The Advisory Group has gotten early access to new groups that are under development, and provided feedback that helped refine them.

Publish equivalence groupings with LOINC releases

The LOINC Groups file has been published with three LOINC releases (June 2017, December 2017, and June 2018). News releases about each of these LOINC releases are available online:

1. LOINC version 2.61 released June 2017

2. LOINC version 2.63 released December 2017

3. LOINC version 2.64 released June 2018

Overall, during the period of performance, the standalone LOINC Group file has been downloaded more than 900 times and the complete LOINC release package (which contains the LOINC Group content as well as the other LOINC content) has been downloaded more than 8,300 times.

Additionally, with the LOINC release in June 2018 we have deployed a FHIR server with terminology services that makes the equivalence groups dynamically available as machine readable value sets of LOINC codes. This new services will greatly enhance the availability of the equivalence classes to the Health IT user community.

Publications and Presentations

As mentioned and reported previously, the LOINC Groups content was presented at each of the public LOINC Laboratory Committee and Clinical Committee meetings, which occur four times each year, throughout the contract period. In addition we made several presentations to other audiences.

Dr. Vreeman presented to the Clinical Laboratory Improvement Advisory Committee (CLIAC), an advisory committee to HHS, about improving lab data interoperability including use of the LOINC equivalence groups. Slides from this presentation are available online.

Dr. Vreeman presented at the FHIR DevDays Conference about the new API capabilities for accessing LOINC content, including LOINC groups. The audience of this sold-out conference is IT professionals in healthcare, whether new to FHIR or with previous experience, to learn about FHIR in a collaborative environment. HL7 FHIR DevDays offers a chance to work with the specification surrounded by others doing the same thing, side by side with experts to answer any questions. The full educational session slides and a detailed tutorial of exercises is available online.

We were also pleased that a systems demonstration abstract was accepted presentation at the AMIA 2018 Annual Symposium. This event is the premiere academic biomedical informatics conference. Session citation: Abhyankar S, Zabriskie M, Hook J, Briscoe T, Finnell JT, Vreeman DJ. *LOINC Groups: A novel tool for data aggregation.*

Conclusion

This project created a novel resource called LOINC Groups that provide a flexible, computable mechanism for rolling up LOINC terms to support data aggregation and retrieval. By publishing LOINC Groups in the main LOINC release, establishing an online community and API-based access, we hope to further support their use for many purposes.