Newborn Screening Health Information Exchange: Updated Guidance for Coding and HL7 Electronic Messaging

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Abstract

Newborn screening has high-stakes health implications and requires rapid and effective communication between many people and organizations. Multiple agencies worked together to create national guidance for reporting newborn screening results with HL7 messages that contain LOINC and SNOMED CT codes, report quantitative test results, and use standardized computer-readable UCUM units of measure. This guidance (a LOINC panel and an example annotated HL7 message) enables standard HL7 v2.5.1 laboratory messages to carry the information required for reporting newborn screening results. If the guidance is used nationally, regional and national registries can aggregate results from state programs to facilitate research and quality assurance. Using national standards for coding (that are already required for certified EHRs) enables implementation with fewer burdens on vendors, labs, hospitals and pediatric providers to customize systems for every change and implementation – a large group of users will be ready to receive data electronically from newborn screening laboratories. The results messaging guidance served as a foundation for developing the PHII HL7 implementation guides for newborn dried blood spot screening orders and results. NLM and HRSA have worked closely with several state newborn screening laboratories and programs that are implementing this guidance, whose feedback helped refine the LOINC panel. Excellent collaboration enabled us to rapidly develop codes for severe combined immunodeficiency (SCID) when it was added as a core condition to the Recommended Uniform Screening Panel of the Secretary's Advisory Committee on Heritable Disorders in Newborns and Children, and to develop a panel of codes for lysosomal storage disorders that several states have added to their screening protocol. We are now developing codes for short- and long-term follow up, beginning with the laboratory tests for confirmation and diagnosis of conditions targeted by newborn screening.

Introduction

Newborn screening (NBS) has high-stakes health implications and requires rapid and effective communication between many people and organizations. The importance of this public health program, combined with the growing adoption of electronic health records (EHRs) and electronic exchange of laboratory test results, created an opportunity to develop consensus-based standard vocabularies that would enable newborn screening health information exchange (HIE), as well as provide a foundation for establishing research and quality measures.[1] Our objective is to create and refine the resources that will help states adopt national coding and messaging standards, including HL7®, LOINC®, SNOMED CT©, and UCUM©, in order to exchange electronic NBS order and result messages.

Background

The push for EHR adoption and electronic transmission of lab results provided the motivation to develop standard guidance for electronic reporting of NBS results[2] using nationally-accepted vocabulary (LOINC, SNOMED CT, UCUM)[3] and electronic messaging (HL7) standards. LOINC (Logical Observation Identifiers Names and Codes) contains standard codes for identifying laboratory tests and other clinical measures,

and SNOMED CT (Systematized Nomenclature of Medicine--Clinical Terms) is an international terminology standard for systematically specifying symptoms and diagnoses. UCUM units of measure specify the units for a given test or measure in a standard, machine-readable format, and HL7 (Health Level 7) specifies the standards for electronic messaging.

Members of multiple agencies, NBS programs and laboratories worked together to create guidance for electronic reporting of newborn screening results.[4] This guidance includes a comprehensive LOINC panel and an example annotated HL7 message that the states can use as a template to develop their specifications for transmitting electronic NBS result messages. There are many benefits to standardizing. Even if different states develop unique specifications for the tests and variables that they use in that state, if they are using the same foundation of codes, the information that is common across programs will be interoperable. If the guidance is used nationally, regional and national registries can aggregate results from state programs to facilitate research and quality assurance. Using national standards for coding (that are already required for certified EHRs) enables implementation with fewer burdens on vendors, labs, hospitals and pediatric providers to customize systems for every change and implementation because they are already using the same terminology and codes.

Methods

NLM and HRSA worked closely with several state newborn screening laboratories and programs that are implementing this guidance, reviewed their early test messages, and refined the LOINC panel and HL7 messaging guidance based on their feedback. We gathered input from state NBS programs during an HIE workshop in November 2010. We also helped some of these programs map their local codes for newborn screening tests to LOINC analyte codes and for newborn screening conditions to LOINC answer (LA) and SNOMED CT codes, which gave us insight into some of their coding needs.

We formed a partnership with the Secretary's Advisory Committee on Heritable Disorders in Newborns and Children (SACHDNC) Laboratory Standards and Procedures Subcommittee to review and achieve consensus on requests for new variables and codes. When severe combined immunodeficiency (SCID) was added to the Recommended Uniform Screening Panel by the SACHDNC in May 2010, we developed new condition and analyte variables for this condition. In May 2011, the SACHDNC Laboratory Standards and Procedures Subcommittee suggested that NLM review and expand the answer list for 57713-0 "Clinical events that affect newborn screening interpretation." NLM reviewed the "clinical events" answer list with representatives from many newborn screening state labs and programs at the quality indicators workshop co-sponsored by APHL, HRSA, CDC, and Genetic Alliance in June 2011. We also worked closely with three states on the verge of sending orders and results messages and the APHL Newborn Screening and Genetics in Public Health Committee to examine this list, conducted an evidence-based literature search to develop a proposal for revising it,[5,6,7] and reached consensus for a revised set of LOINC codes and answer lists.

NLM and the Regenstrief Institute worked with Oregon's newborn screening program to develop new LOINC codes for analytes measured using the non-derivatized tandem mass spectrometry (MS/MS) test kit method. The methods for derivatized and non-derivatized MS/MS are similar and nearly all analytes and ratios are identical; however, there are a limited number of exceptions which we reviewed and for which we obtained new LOINC codes.

Several states have started pilot studies or implemented screening for five of the lysosomal storage disorders (LSDs): Fabry disease, Pompe disease, Gaucher disease, Niemann-Pick disease A/B, and Krabbe

disease. A workgroup of LSD experts analyzed variations in naming LSDs and the tests used for screening, as part of a larger evidence review and guideline development process on the diagnosis and management of the presymptomatic LSD patient. [8] Informed by this work, NLM and HRSA collaborated with the workgroup plus other LSD and NBS experts, selected standard names, assigned standard LOINC and SNOMED CT codes to LSD tests and conditions, and updated the example electronic HL7 message to illustrate how to use these codes to report NBS LSD results.

We also worked with the Public Health Informatics Institute (PHII) as part of the workgroup to develop HL7 implementation guides for newborn dried blood spot screening orders[9] and results[10], both of which were based on our result messaging guidance. While working on these implementation guides, the workgroup found several important variables for which there were no existing LOINC codes. We requested new LOINC codes and incorporated them into the PHII implementation guides as well as the HRSA/NLM guidance.

Lastly, we worked with several NBS programs and laboratories as well as experts in hemoglobinopathy screening to develop a new method for reporting NBS hemoglobinopathy results. This work is discussed in a separate paper in these proceedings.[11]

Table 1. New Codes for Conditions Detectable by NBS: SCID and LSDs

Condition Name (and Abbreviation)	SNOMED CT code	LOINC (Analyte) Name	LOINC Code
Severe Combined Immunodeficiency (SCID)	31323000	T-cell receptor excision circle [#/volume] in Dried blood spot by Probe & target amplification method	62320-7
Fabry disease (GLA)	16652001	Alpha galactosidase A [Enzymatic activity/volume] in Dried blood spot	55908-8
Gaucher disease (GBA)	190794006	Acid beta glucosidase [Enzymatic activity/volume] in Dried blood spot	55917-9
Krabbe disease (GALC)	192782005	Galactocerebrosidase [Enzymatic activity/volume] in Dried blood spot	62310-8
Niemann Pick disease A/B (ASM)	58459009	Acid sphingomyelinase [Enzymatic activity/volume] in Dried blood spot	62316-5
Pompe disease (GAA)	237968007	Acid alpha glucosidase [Enzymatic activity/volume] in Dried blood spot	55827-0

Results

We developed condition and analyte codes for SCID and 5 LSDs (see Table 1). The SCID panel (LOINC code 62333-0) includes codes for the quantitative TREC assay, test interpretation and comment/discussion. The LSD panel includes codes for overall LSD interpretation, conditions suspected, and comment/discussion, as well as subpanels for each of the five individual disorders.
We developed 5 new LOINC codes for analytes measured using the non-derivatized (MS/MS) method. For some of the quantitative newborn screening measures, we updated data types to NM/ST, and expanded guidance related to units of measure and reference ranges.

Based on suggestions made during the November 2010 NBS HIE meeting, we added new LOINC codes for Date of last blood product transfusion, Birth hospital facility information (ID, name, address, and phone number), Post-discharge provider information (ID and name) and Post-discharge practice information (ID, name, address, and phone number).

Based on work with Kentucky and input from the SACHDNC Lab Standards and Procedures Subcommittee, we expanded the answer lists for overall NBS interpretation, and reason for lab test. For "Newborn screening report – overall interpretation" (LOINC code 57130-7), we added codes for "Screening not done due to parental refusal," "One or more tests pending," and "Specimen unsatisfactory for at least one condition." In each of the condition-specific panels, in the answer list for

condition-specific interpretations, we also added answer codes for "One or more tests pending," and "Specimen unsatisfactory for at least one condition." For "Reason for lab test in Dried blood spot" (LOINC code 57721-3), we added a new answer for "No sample collected due to parental refusal," and defined each of the answers.

We split the answers in the original 57713-0 "Clinical events that affect newborn screening interpretation" into three separate LOINC codes: "Infant NICU Factors that Affect Newborn Screening Interpretation (Table 2)," "Maternal Factors that Affect Newborn Screening Interpretation" (Table 3) and "Feeding Types " (Table 4). Each question can have one or more answers based on the infant's history, and each of the 3 questions has an answer option "Other." If the "Other" answer is used, there are three more new LOINC codes of the Nar data type to provide details. Each of these three LOINC codes with answer lists also includes a definition/description explaining which newborn screening assays are affected by particular feeding types or infant NICU or maternal factors. For example, the definition for "Infant NICU Factors" (LOINC code 57713-0) provides the following guidance: "Steroid treatment can affect NBS results for TSH and 17-OHP. Iodine can affect NBS results for TSH and T4. Antibiotics can affect NBS results for C5."

Table 2. Answer list for LOINC code 57713-0 Infant NICU Factors that affect newborn screening interpretation

None	LA137-2
Infant in ICU at time of specimen collection	LA12419-0
Any blood product transfusion (including ECMO)	LA12417-4
Dopamine	LA16923-7
Topical iodine	LA16924-5
Parenteral steroid treatment	LA16925-2
Systemic antibiotics before newborn screening specimen	LA12420-8
Meconium ileus or other bowel obstruction	LA16927-8
Other	LA46-8
67703-9 Other infant NICU factors that affect newborn screening interpretation *(Use this term to give additional detail if you select answer "Other" LA46-8)*	

Table 3. Answer list for LOINC code 67706-2 Maternal Factors that affect newborn screening interpretation

None	LA137-2
HELLP syndrome	LA16928-6
Fatty liver of pregnancy	LA16929-4
Packed red blood cell (PRBC) transfusion	LA16930-2
Steroid treatment	LA16931-0
Thyroid treatment (including propylthiouracil (PTU), methimazole (Tapazole), or past treatment with radioactive iodine (I-131))	LA16932-8
TPN	LA12418-2
Other	LA46-8
67707-0 Other maternal factors that affect newborn screening interpretation from mother *(Use this term to give additional detail if you select answer "Other" LA46-8)*	

Table 4. Answer list for LOINC code 67704-7 Feeding Types

Breast milk	LA16914-6
Lactose formula	LA16915-3
Lactose free formula	LA14041-0
NPO	LA16917-9
TPN	LA12418-2
Carnitine	LA16918-7
MCT (medium-chain triglyceride) oil	LA16919-5
IV dextrose	LA16920-3
Other	LA46-8
Unknown	LA4489-6
67705-4 Other feeding types *(Use this term to give additional detail if you select answer "Other" LA46-8)*	

We provided guidance for transitioning from local codes to standard codes or, for systems that need to continue using local codes, for incorporating both into their HL7 messages. For example, the HL7 message can include both the standard LOINC code and name, and the local code and name, for the third field (observation ID) of the observation (OBX) segment (see figure 1). The fifth field of the OBX segment can carry both a standard SNOMED CT code and name, and a LOINC answer (LA) code and name or a local code and name (see figure 2) for the NBS condition name.

Figure 1. Example of LOINC (bold) and local (italic) codes and names in OBX-3

OBX|36|NM|**29573-3^Phenylalanine [Moles/volume] in Dried blood spot^LN^***1234^PhenylAlynine^L***||104.61|umol/L|99-135|N|||F

Figure 2. Example of SNOMED CT (bold) and LOINC answer (italic) codes and names in OBX-5

OBX|60|CE|57719-7^Conditions tested for in this newborn screening study [Identifier] in Dried blood spot^LN|52|**7573000^Classical phenylketonuria ^SCT^***LA12520-5^PKU^LN***|||N|||F

Discussion

To help facilitate adoption of the standards, NLM and HRSA made numerous updates and modifications to the national guidance for reporting newborn screening results based on feedback from many different NBS programs, laboratories, and other agencies. We added new variables and updated our guidance on how to transition from paper-based reporting or legacy systems to systems that comply with nationally accepted standards.

Creating LOINC variables for SCID was straightforward; however, developing codes for the LSDs was more challenging. Each lysosomal storage disorder can have multiple names based on researchers' names, related genes in which mutations occur, and affected enzymes. In addition, prior to this work, there was no consensus on naming conditions, enzymes, or tests, method for reporting screening results, or screening method. For example, the original LOINC code request for the affected enzyme in Gaucher disease was "glucocerebrosidase." Based on an investigation of the name variants used by different sources for this enzyme (see Table 5), the LOINC name ultimately selected for the newborn screening code was "Acid beta glucosidase," which is a computer-readable variant of the name used by ACMG and OMMBID. Instead of the Greek letter symbol β, we spell out "beta" to ensure that message recipients will properly display the name. OMMBID was the only source to give a rationale for preferring the enzyme name acid beta glucosidase in this context: *"The enzymatic defect in Gaucher disease was shown to be due to impaired glucosylceramide hydrolysis…Because glucosylceramide (glucocerebroside), glucosylsphingosine, and potentially other β-glucosides are natural substrates for this enzyme, the more general terms acid β-glucosidase or lysosomal β-glucosidase are preferred to glucocerebrosidase. Acid β-glucosidase (EC 3.2.1.45) will be used in this chapter."*[12]

Table 5. Name Variants for the Enzyme Affected in Gaucher Disease

Source	Enzyme Name
American College of Medical Genetics (ACMG) LSD Workgroup	acid β-glucosidase
Scriver's *Online Metabolic and Molecular Bases for Inherited Disease* (OMMBID)	Acid β-glucosidase
LOINC (14 terms existing Oct 30, 2010)	beta glucosidase
OMIM 606463	Glucosidase, beta, acid (GBA); "alternative titles" include: Acid beta-glucosidase, glucocerebrosidase, and glucosylceramidase)
E.C. 3.2.1.45	Glucosylceramidase is accepted name (12 "other names" include acid β-glucosidase and glucocerebrosidase)
UniProt P04062	Glucosylceramidase is recommended name (5 alternative names include Acid beta-glucosidase and Beta-glucocerebrosidase)

States that have legacy electronic systems or paper-based systems that use local codes can send both local and standard codes in their HL7 messages as a way to preserve backwards compatibility during the transition from legacy local coding systems to national standard codes.

Electronic messaging allows newborn screening laboratories and programs to send data to multiple recipients at the same time, including the birth hospital, post-discharge provider and practice, metabolic specialist, health information exchange, and state registry. Because some states may not want to send all quantitative results to all message recipients, they can utilize HL7 features such as normal/abnormal flags or filtering on specific LOINC codes to send specific results or types of results to selected categories of message recipients. We encourage NBS laboratories to consider reporting all quantitative results (and not just interpretations) and appropriate accompanying explanatory information to the NBS programs

so information is captured for comparison over time, and to consider sending at least the quantitative results when they are abnormal or equivocal to the birth institution and attending clinicians, particularly when fixed cutoffs are used. Only about 3% of NBS results are abnormal,[13] so the amount of quantitative data will not overwhelm clinicians. In addition, having quantitative data can sometimes help providers interpret the results and provide more information to the family until the infant sees the appropriate specialist or has follow-up testing done. In cases where dried bloodspot result ranges differ from the usual serum results familiar to primary care physicians, minimal educational information delivered with the results should assist them in result interpretation.

We assigned two data types – NM/ST – to each of the LOINC codes for quantitative newborn screening measures, so that states have the option of using either NM (numeric) or ST (string). NM is used for pure numeric results, and ST (string) can accommodate numbers that include other characters (e.g. >, <). While reviewing test messages from one state, we discovered that they were using Greek symbols (e.g., μ) as well as multiple varying strings for the same unit of measure (e.g., μ, u and m for micro). Receivers may not be able to process units with Greek symbols, and using different strings for the same unit can create confusion for receivers. Therefore, we advise using UCUM (the preferred standard to represent units of measure in electronic messages and electronic health records) to specify the unit of measure. The newborn screening LOINC panel now uses {Ratio} as the units of measure for results that are ratios, which strictly speaking do not have units of measure, to be consistent with other quantitative result segments. Another issue we found in the test messages was that the reference ranges were missing for many quantitative variables, and we highly recommend including the reference range for quantitative results to facilitate interpretation.

Because many states share a regional laboratory or use the same laboratory information systems (LIS) software, such as STARLIMS or Perkin Elmer Specimen Gate, there is an opportunity for states to share their methods with other programs. In addition, open source MIRTH software[14] and commercial BizTalk software can facilitate development of messaging by adapting existing functions to local needs through use of mapping tables, and implementation protocols could be shared between early implementers and other laboratories and programs.

In summary, standard codes and names will enable researchers, clinicians and public health surveillance efforts to exchange and aggregate NBS results from all of the states. This is critical for research, quality assurance and disaster preparedness. In addition, these data are essential for creating case definitions and providing effective follow-up care. As new conditions are added to the Recommended Uniform Screening Panel and NBS technology evolves, we will create or assign LOINC and SNOMED CT codes to conditions and analytes and will continue to review and update the HRSA/NLM guidance for sending electronic result messages.

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