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

Association for Public Health Labs (APHL)
Newborn Screening and Genetic Testing Symposium
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Benefits of Standardizing NBS Data

• Rapid reporting and exchange
  ▫ Send results to multiple recipients at the same time

• Share data
  ▫ Follow-up
  ▫ Border states and Disaster preparedness

• Gather and re-use data
  ▫ Enable cross-referencing with other data sources (e.g. birth certificates, hearing screen results, immunization registries)

• Aggregate data for research and QA
Background

- Developing the HRSA/NLM guidance for sending electronic NBS result messages has been a collaborative effort with input from federal and state agencies and organizations
  - Guidance is based on nationally-accepted standards
    - LOINC® - for test results and card variables
    - SNOMED CT - for NBS conditions
    - UCUM© - units of measure for quantitative results
    - HL7 – for electronic messaging using above codes
  - Approved by the SACHDNC* Laboratory Standards and Procedures subcommittee
  - Initially released Sept 2009

* Secretary’s Advisory Committee on Heritable Disorders in Newborns and Children
What has to be standardized?

- **Messaging format**
  - (the “egg carton” container)
  - Standard messaging format to convey the content electronically
  - HL7

- **Content**
  - (the “eggs”)
  - Standard codes for test names, analytes, conditions screened and other categorical answers
  - LOINC and SNOMED CT
Refining the HRSA/NLM Guidance
Iterative Process

- Close gaps and achieve consensus
  - State Implementation
  - PHII HL7 implementation guides for NBS orders and results
  - SACHDNC Laboratory Standards and Procedures Subcommittee
  - APHL Newborn Screening and Genetics in Public Health Committee
New LOINC codes created for:

- Birth hospital facility, discharge provider/practice
  - ID, Name, address, phone number

- Test methods/analytes
  - Hemoglobin screening results
  - Underivatized MS/MS

- Card data – factors that affect NBS interpretation

- NBS report summary and NBS interpretation answers

- New conditions
Factors that Affect Newborn Screening Interpretation
Original clinical events → 3 new questions

Feedback from multiple NBS programs and SACHDNC Lab subcommittee that original Clinical events list was incomplete

Developed new codes for:
- Infant NICU factors that affect NBS
- Feeding types
- Maternal factors that affect NBS
57713-0 Infant NICU Factors that affect NBS – expanded list and new name

- None
- Infant in ICU at time of specimen collection
- Any blood product transfusion (including ECMO)***
  - Plus separate LOINC code for Date of last blood product transfusion
- Dopamine
- Topical iodine
- Parenteral steroid treatment
- Systemic antibiotics before newborn screening specimen***
- Meconium ileus or other bowel obstruction
- Other → Plus additional LOINC code to give details in free text

*** Answer was on the original Clinical events list
67704-7 Feeding Types – new code

- Breast milk
- Lactose formula
- Lactose free formula (including soy or hydrolyzed)***
- NPO
- TPN***
- Carnitine
- MCT (medium-chain triglyceride) oil
- IV dextrose
- Other → plus additional code to give details in free text
- Unknown

*** Answer was on the original Clinical events list
67706-2 Maternal Factors that affect NBS – new code

- None
- HELLP syndrome
- Fatty liver of pregnancy
- Packed red blood cell (PRBC) transfusion
- Steroid treatment
- Thyroid treatment (including propylthiouracil (PTU), methimazole (Tapazole), or past treatment with radioactive iodine (I-131))
- TPN
- Other \(\rightarrow\) plus additional code to give details in free text
NBS Interpretation and Report Summary
Overall NBS interpretation (LOINC code 57130-7)

- All screening is normal
- Screening is borderline for at least one condition
- Not normal requiring further filter paper testing for at least one condition
- Not normal requiring immediate non filter paper follow up for at least one condition
- Screening not done due to parental refusal ➔ NEW
- One or more tests pending ➔ NEW
- Specimen unsatisfactory for at least one condition ➔ NEW
Reason for lab test in Dried blood spot (LOINC code 57721-3)

• Streamlined list:
  1. Initial screen
  2. Subsequent screen - required by law
  3. Subsequent screen - required by protocol
  4. Subsequent screen – for clarification of initial results (not by law or protocol)
  5. Subsequent screen – reason unknown
  6. No sample collected due to parental refusal  ➔ NEW

• Defined each of the answers.
New Conditions: SCID and Lysosomal Storage Disorders
# 62333-0 Severe Combined Immunodeficiency (SCID) newborn screening panel

<table>
<thead>
<tr>
<th>LOINC Code</th>
<th>LOINC (Analyte) Name</th>
<th>Data Type</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>62321-5</td>
<td>Severe combined immunodeficiency newborn screen interpretation</td>
<td>CE</td>
<td></td>
</tr>
<tr>
<td>62322-3</td>
<td>Severe combined immunodeficiency newborn screen comment-discussion</td>
<td>TX</td>
<td></td>
</tr>
<tr>
<td>62320-7</td>
<td>T-cell receptor excision circle [#/volume] in Dried blood spot by Probe &amp; target amplification method</td>
<td>NM/ST</td>
<td>{copies}</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Condition Name (and Abbreviation)</th>
<th>SNOMED CT code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe Combined Immunodeficiency (SCID)</td>
<td>31323000</td>
</tr>
</tbody>
</table>
Lysosomal Storage Disorders (LSDs)

- Several states have started pilot studies or implemented screening for these lysosomal storage disorders: Fabry disease, Pompe disease, Gaucher disease, Krabbe disease, and Niemann-Pick disease A/B
- Genetic mutations cause specific enzyme deficiencies.
  - These enzymes are normally responsible for catalyzing breakdown of waste material in cells, so in people with LSDs, waste materials accumulate in the lysosomes.
  - Research and emerging therapies.
  - Early detection is vital.
Standardizing LSD NBS Reporting

• Challenges to standardizing:

  ▫ Each lysosomal storage disorder can have multiple names based on researchers' names, related genes, and affected enzymes.

  ▫ No consensus on naming conditions and tests, reporting screening results, or screening method.

  ▫ Special characters (Greek letters in enzyme names and units of measure) may not be computer-readable.
Standardizing LSD NBS Reporting

• Creating standards

  ▪ ACMG LSD expert workgroup* published guidelines for diagnostic confirmation and management of **presymptomatic** individuals with lysosomal storage disorders.

  ▪ HRSA and NLM developed a panel of standard NBS names and LOINC and SNOMED CT codes to use in HL7 messages for standardizing electronic reporting of LSD screening results.

*With funding from NIH NICHD. Part of the Newborn Screening Translational Research Network.
Pompe disease – condition name variants

• **Pompe disease** – after Dutch pathologist Dr Joannes Cassianus Pompe, who first recognized Pompe disease

• **Acid alpha glucosidase deficiency** – affected enzyme

• **Acid maltase deficiency** – affected enzyme (synonym)

• **Glycogen Storage Disease Type II** – glycogen is the material that accumulates in the lysosome as a result of the enzyme deficiency

• **GAA** – gene mutation that causes Pompe disease


## Name Variants for the Enzyme Affected by GBA gene mutation in Gaucher Disease

<table>
<thead>
<tr>
<th>Source</th>
<th>Enzyme Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>American College of Medical Genetics (ACMG) LSD Workgroup</td>
<td>acid β-glucosidase</td>
</tr>
<tr>
<td>Scriver’s Online Metabolic and Molecular Bases for Inherited Disease (OMMBID)</td>
<td>Acid β-glucosidase</td>
</tr>
<tr>
<td>LOINC (14 terms existing Oct 30, 2010)</td>
<td>Beta glucosidase</td>
</tr>
<tr>
<td>OMIM 606463</td>
<td>Glucosidase, beta, acid (GBA)</td>
</tr>
<tr>
<td></td>
<td>(alternative titles” include: Acid beta-glucosidase, glucocerebrosidase, and glucosylceramidase)</td>
</tr>
<tr>
<td>E.C. 3.2.1.45</td>
<td>Glucosylceramidase - accepted name</td>
</tr>
<tr>
<td></td>
<td>(12 “other names” include acid β-glucosidase and glucocerebrosidase)</td>
</tr>
<tr>
<td>UniProt P04062</td>
<td>Glucosylceramidase - recommended name</td>
</tr>
<tr>
<td></td>
<td>(5 alternative names include Acid beta-glucosidase and Beta-glucocerebrosidase)</td>
</tr>
</tbody>
</table>
LOINC Name Selected for Newborn Screening Assay to Detect Activity of the Enzyme Affected in Gaucher Disease:

**Acid beta glucosidase**

- Computer-readable version of “Acid β-glucosidase” -- the name from ACMG and Scriver’s Online Metabolic and Molecular Bases for Inherited Disease (OMMBID).
  - “beta” instead of Greek letter symbol “β” to ensure that electronic message recipients properly display the name.
- Scriver’s OMMBID rationale:
  - “The enzymatic defect in Gaucher disease was shown to be due to impaired glucosylerceramide hydrolysis ...Because glucosylerceramide (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.”

## 62311-6 Gaucher disease NBS panel

<table>
<thead>
<tr>
<th>LOINC Code</th>
<th>LOINC (Analyte) Name</th>
<th>Data Type</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>62312-4</td>
<td>Gaucher disease newborn screen interpretation</td>
<td>CE</td>
<td></td>
</tr>
<tr>
<td>62313-2</td>
<td>Gaucher disease newborn screen comment-discussion</td>
<td>TX</td>
<td></td>
</tr>
<tr>
<td>55917-9</td>
<td>Acid beta glucosidase [Enzymatic activity/volume] in Dried blood spot</td>
<td>NM/ST</td>
<td>umol/L/h</td>
</tr>
</tbody>
</table>
# New Codes for 5 LSDs Detectable by NBS

<table>
<thead>
<tr>
<th>Condition Name (and Abbreviation)</th>
<th>SNOMED CT code</th>
<th>LOINC Name for quantitative NBS analyte associated w/ each condition</th>
<th>LOINC Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fabry disease (GLA)</td>
<td>16652001</td>
<td>Alpha galactosidase A [Enzymatic activity/volume] in Dried blood spot</td>
<td>55908-8</td>
</tr>
<tr>
<td>Gaucher disease (GBA)</td>
<td>190794006</td>
<td>Acid beta glucosidase [Enzymatic activity/volume] in Dried blood spot</td>
<td>55917-9</td>
</tr>
<tr>
<td>Krabbe disease (GALC)</td>
<td>192782005</td>
<td>Galactocerebrosidase [Enzymatic activity/volume] in Dried blood spot</td>
<td>62310-8</td>
</tr>
<tr>
<td>Pompe disease (GAA)</td>
<td>237968007</td>
<td>Acid alpha glucosidase [Enzymatic activity/volume] in Dried blood spot</td>
<td>55827-0</td>
</tr>
<tr>
<td>Niemann Pick disease A/B (ASM)</td>
<td>58459009</td>
<td>Acid sphingomyelinase [Enzymatic activity/volume] in Dried blood spot</td>
<td>62316-5</td>
</tr>
</tbody>
</table>
Quantitative Measures
Quantitative Measures

- Assigned two data types to each of the LOINC codes for quantitative measures
  - NM (numeric) – for pure numeric results
  - ST (string) - to accommodate other characters (e.g. > <)
- The reference range for quantitative results to facilitate interpretation of the results
- UCUM standard for units of measure
  - Avoids Greek symbols (μ) that some systems can’t process.
  - Avoids multiple strings for the same unit (μ, u and m for micro), which may cause confusion.
  - {Ratio} for results that are ratios.
Reporting Quantitative Results

• NBS labs should consider reporting all quantitative results with accompanying explanatory information to NBS programs so data is captured for comparison over time

• Also consider sending the quantitative abnormal and equivocal results to the birth institution and attending clinicians, particularly when fixed cutoffs are used
  ▫ Only about 3%* of NBS results are abnormal
  ▫ Quantitative data can 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

*National Newborn Screening and Genetics Resource Center (NNSGRC).
http://genes-r-us.uthscsa.edu/
Customizing HL7 Messages

- Senders can filter on normal/abnormal flags or specific LOINC codes to send specific results or types of results to select categories of message recipients
- Recipients can use the same features to customize the level of detail seen by categories of users
Transitioning to Standard Codes
Transitioning to standard codes: Using both standard and local codes in HL7

- HL7 messages can carry two codes and names for each question/variable and answer
- States that have legacy systems that use local codes can send both local and standard codes
  - This preserves backwards compatibility during the transition from legacy local coding systems to national standard codes.
- OBX-3: Observation ID (e.g., lab test) can carry both:
  - Universal code (LOINC code) and name and Local code and name
- OBX-5: Observation Value (e.g., response when “question” in OBX-3 has a coded answer list) can carry any 2 code-name pairs:
  - SNOMED CT, LOINC answer (LA), or local
Example HL7 Message Segments
Example HL7 OBX (observation) segment: Quantitative screening result for Gaucher disease

```
OBX|3|NM|55917-9^Acid beta glucosidase
[Enzymatic activity/volume] in Dried blood spot^LN^4231^Glucocerebrosidase^L||
1.3|umol/L/h|>4.1|L||F
```

*Please note – for purposes of simplicity, the entire HL7 OBR/OBX structure is not shown. For more details, see http://newbornscreeningcodes.nlm.nih.gov/HL7
HL7 Message Panel for Gaucher NBS Results

OBX|1|CE|62312-4^Gaucher disease newborn screen interpretation^LN||LA12431-5^Not normal requiring immediate non-filter paper follow-up for at least one condition^LN|||A||F

OBX|2|TX|62313-2^Gaucher disease newborn screening comment-discussion^LN||Abnormal result indicates possible Gaucher Disease and immediate referral to a Metabolic Geneticist is indicated to confirm the diagnosis and begin treatment|||A||F

OBX|3|NM|55917-9^Acid beta glucosidase [Enzymatic activity/volume] in Dried blood spot^LN^4231^Glucocerebrosidase^L||1.3|umol/L/h|>4.1|L||F

*Please note – for purposes of simplicity, the entire HL7 OBR/OBX structure is not shown. For more details, see [http://newbornscreeningcodes.nlm.nih.gov/HL7](http://newbornscreeningcodes.nlm.nih.gov/HL7)*
HL7 Message Panel for Krabbe NBS Results

OBX|1|CE|62308-2^Krabbe disease newborn screen interpretation^LN||LA6626-1^Normal^LN|||N|||F

OBX|2|TX|62309-0^Krabbe disease newborn screening comment-discussion^LN||Any baby with clinical features suggestive of a metabolic disorder requires clinical and diagnostic follow-up regardless of whether the NBS result is normal or abnormal.|||N|||F

OBX|3|NM|62310-8^Galactocerebrosidase [Enzymatic activity/volume] in Dried blood spot^LN^4100^Galactosylceramidase^L||2.4|umol/L/h|>0.5|N|||F

*Please note – for purposes of simplicity, the entire HL7 OBR/OBX structure is not shown. For more details, see [http://newbornscreeningcodes.nlm.nih.gov/HL7](http://newbornscreeningcodes.nlm.nih.gov/HL7)
Dual observation ID codes and names, and HL7 abnormal flag

- OBX|107|CE|57719-7^Conditions tested for in this newborn screening study [Identifier] in Dried blood spot^LN|99|190794006^Gaucher’s disease^SCT^LA14039-4^GBA^LN|||A|||F

*Please note – for purposes of simplicity, the entire HL7 OBR/OBX structure is not shown. For more details, see [http://newbornscreeningcodes.nlm.nih.gov/HL7](http://newbornscreeningcodes.nlm.nih.gov/HL7)*
Next Steps

- CCHD
- MPS I and MPS II
- Follow Up
Conclusions

- Standardizing NBS results reporting across state programs is critical for information exchange, research, QA, and disaster preparedness.

- The HRSA/NLM guidance allows NBS labs and programs to send and store results in one common, coded format.

- As new conditions and tests are discovered and/or added to the SACHDNC recommendations, we will add new codes and update the guidance.

- If the NBS community requests other changes based on consensus within the community, we can easily update existing codes and templates.

- Many states are close to electronic reporting of NBS, and we hope others will soon follow their lead.
  - Join us for HIT Implementation Roundtable
    Wed 7:30am-8:15am (Spinnaker)
Acknowledgments

State programs and labs
- California
- Colorado*
- Illinois
- Indiana*
- Iowa
- Kentucky
- Massachusetts
- Minnesota
- Missouri
- New York*
- Oregon
- Pennsylvania
- Texas
- Utah*
- Virginia
- Washington

Federal and state agencies and organizations
- HRSA
- CDC
- NICHD
- NIH ORDR
- NNSGRC
- ACMG
- APHL
- PHII
- NBS lab system vendors
- Genetic Alliance
- ...and many more

*States funded by HRSA-09-242 – Effective Follow-up in Newborn Screening

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Thank you!

Any questions?


- LOINC NBS panel and annotated sample HL7 message for download
- Links to PHII HL7 Implementation Guides for Orders and Results
- Lists of conditions, associated analytes and their LOINC codes, as well as UCUM and SNOMED CT codes where appropriate
- XML download of coding content
- Updates page with RSS feed

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