V251_IG_LRI_R1_D4_2017MAY

HL7 Version 2.5.1 Implementation Guide: Lab Results Interface (LRI), Release 1, STU Release 3 – US Realm

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HL7 Standard for Trial Use Ballot

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Orders And Observations Work Group

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5 USE CASE – CLINICAL GENOMICS RESULTS REPORTING

This use case is supported by the LRI_CG_Component; see Section 6.3.13 LRI_CG_Component – ID: 2.16.840.1.113883.9.195.3.

Simple genomic studies are often reported in structured format as a simple categorical test with encoding. The studies typically include the variant name in the test name and report whether that variant is present or absent. An example is "`LOINC code 24475-6 "F2 gene c.20210G>A [Presence]...`".

However, the majority of complicated genetic test results are reported as purely narrative reports with no computer accessible coding. The goal of this component is to encourage and make it easier to add coded results to the purely narrative genomic reports. Structuring genetic reports defined by this IG would enable the delivery of data that could be used in decision support and medical record queries, and adoption could be relatively simple for the clinical laboratories that already use HL7 v2.x. It is not intended to satisfy all of the needs of all genomic studies.

5.1 Key Technical Decisions

The following items are specific to this use case.

5.1.1 SUPPORT FOR NUMERIC RANGE (NR) DATA TYPE

The Numeric Range (NR) HL7 data type is used to specify the lowest and highest values in a series of data. This component uses the NR data type for a number of variables in the specification (e.g. LOINC 51959-5 Ranges of DNA sequence examined; see Table 5-1, Row A.6), to specify the start and end location of the DNA sequence. Each repeat of an NR requires a separate OBX, and the OBX-4 values will have to differ among such repeats. See Section 5.4 OBX-4 (Observation Sub-ID) Dot Notation To Represent The Message Hierarchy for how to specify the OBX-4 values.

5.1.2 OBX-4 DOT NOTATION TO REPRESENT THE MESSAGE HIERARCHY

Please note that the OBX-4 notation used in the LRI_CG_Component uses the OG_02 data type flavor, which has changed since the 2013 Clinical Genomics Implementation Guide. See Section 9.2.5 for the CWE data type definition and Section 5.1.2 for more details on how to use the OBX-4 numbering in the CG component.

There are still questions as to whether the specification should use the 2013 OBR grouping version, so please be sure to comment on questions in Section 5.3 Model For V2 Genetics Reporting Message.

5.1.3 GUIDELINE FOR REPRESENTING CODED ELEMENTS

Value sets are comprised of a code and text (made of a print string) as defined in a code system. The following examples describe best practices for representing coded elements in Clinical Genomics reports.

5.1.3.1 HUGO GENE NOMENCLATURE COMMITTEE (HGNC)

This code system has a single code (e.g., "HGNC:1884") and two potential names: the symbol (e.g. "CFTR") and the full name (e.g., "cystic fibrosis transmembrane conductance regulator"). The gene coding system in this guide uses the symbol as the "name" in CWE.2 (Text), not the full name.

5.1.3.2 NON-STRUCTURED CODE SYSTEMS

While the HGNC has two possible names, some coding systems have no obvious name defined. The dbSNP database, which carries more than 150 million "rs" codes, is a case in point. This guide

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recommends the code be reported in CWE_05.1 (Identifier) and CWE_05.2 (Text) as demonstrated in the examples.

Some code systems do not have specific codes, but define a syntax for expressing a value, e.g., HGVS and ISCN. For the LRI_CG_Component, the guidance is to convey the syntax in CWE_05.2, consistent with guidance for reporting using code-only code systems.

5.1.4 CONVENTIONS FOR DIRECTION AND NUMBERING OF GENETIC SEQUENCES

All of the genomic data reported in this type of panel uses a coordinate system beginning with 1 and assumes the variants are reported from the positive strand and have an inclusive start-end. This is the assumption embedded in HGVS, the NCBI's public distributions, Ensembl, COSMIC, and most other genomic databases. This choice does not constrain receivers from converting to a different (e.g. 0 to start) coordinate system, it only specifies what goes in the message.

5.2 Scope

The following scope statements are in addition to those listed in Section 2.1 Scope.

5.2.1 IN-SCOPE

- Reporting one or more simple genetic variants – those with a contiguous set of changes in the tested sample compared to a reference sequence.
- Reporting structural and copy number variants – those with large changes in contiguous nucleotides, often including very large variants, tens of thousands to millions of nucleotides in length.
- Reporting pharmacogenomics studies, which look for simple or complex variants that affect the rate of metabolism, efficacy, or the risk of one or more drugs, and often include suggestions about possible change in dosing or the use of a different drug. These may or may not be linked to the very specific details reported about other types of variants covered in this guide.
- Reporting complex variants – those made up of multiple simple or structural variants, which together define or influence a phenotype. Haplotypes and Compound Heterozygotes (Hets) are examples. This guide provides variables for reporting information about the complex variant as a unit and for reporting full details about related simple and structural variants using the same variables as used for reporting unrelated simple and structural variants.
- Reporting germline and somatic variants.

The following are explicitly included in the guide to be unambiguous, even though they are already in scope by implication in this guide:

- Reporting partial or complete DNA sequencing, including whole genome and exome studies. Use the LOINC term, 81293-3 "Description of ranges of DNA sequences examined" to assert whether the study is a whole genome or whole exome study, and whether it is targeting only specific exons.
- Reporting mosaicism – Mosaics can be reported in ISCN syntax as the value of LOINC 81291-7 Variant ISCN (Table 5-1 Row A.11). The abbreviation for the mosaicism is in ISCN "mos" and a slash (/) is used to separate between karyotypes for each cell line in the mosaic, e.g.: mos 47,XXX[25]/46,XX[5] using ISCN syntax.
- Reporting mitochondrial DNA variation – Use NC_012920 as the genomic reference sequence for all mitochondrial variations. All of the mitochondrial genes are located in the RefSeq as though they had their own chromosome. Transcript reference sequences will each have their own NM_ RefSeq.

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5.2.2 OUT OF SCOPE

- Non-human genetic studies (Genetic studies with non-human subjects)
- Single variants that are reported as simple tests, e.g. LOINC 24475-6 F2 gene c.20210G>A [Presence].
- Gene/chromosome fusions (and trinucleotide repeats), and similar studies that are also reported as simple lab tests whose quantitative results may be the number of blood cells containing a specified anomaly, the ratio of a marker gene, or the number of trinucleotide repeats, and are accommodated by existing LOINC codes.
- Commercial Cell Free Prenatal studies and DNA based colon cancer screening tests, which at present, report conclusions and risk for various anomalies, but not raw genetic data.
- Reporting cytogenetic variants using legacy techniques such as conventional banding (e.g. G-banding), which are covered in the HL7 Version 2 Implementation Guide: Clinical Genomics; fully LOINC-Qualified Cytogenetics Model, Release 1 - US Realm, published in July 2014

5.3 Model For V2 Genetics Reporting Message

Figure 5-1. Object Model Of The Coded Clinical Genomics Results Message represents the clinical genetics report message showing all of the major LOINC panels that can make up a report and how they are related; this model does not show single observations that may repeat within a panel.

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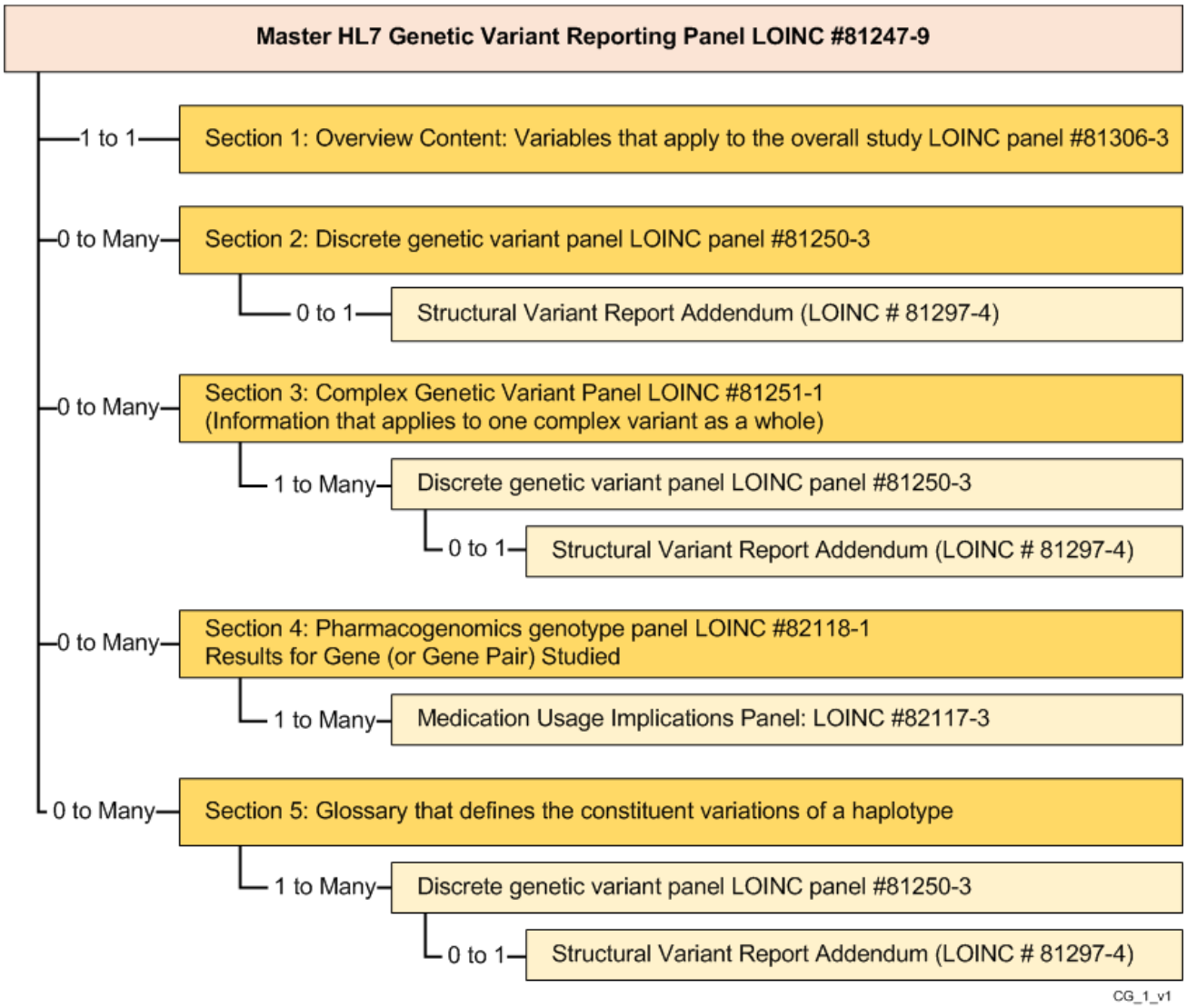

Figure 5-1. Object Model Of The Coded Clinical Genomics Results Message

5.4 OBX-4 (Observation Sub-ID) Dot Notation To Represent The Message Hierarchy

This LRI_CG_Component uses nested OBR-OBX relationships to represent the hierarchy of the message. The hierarchical panel structure in LOINC defines the message structure and the hierarchy is defined by a dot notation recorded in the OBX-4 (Observation Sub-ID) values of the message.

While the 2013 HL7 Clinical Genomics Implementation Guide for Clinical Genetics used nested OBR-OBX relationships to represent the structure of the message, the HL7 Clinical Genomics Work Group believes using dot notation (like a Dewey decimal) to represent nesting structure in OBX-4 is better. The message is still defined conceptually by a hierarchy of LOINC panels (as shown in the example/definition), but the LOINC panel codes are not included in the message at all, and the hierarchy is indicated by the dot notation in OBX-4 rather than as parent-child relationships between OBRs and OBXs. The message contains just one OBR, which carries the code for the order.

However, in the future, the CG component will choose a single method for specifying the OBX-4 before it becomes a normative standard.

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Balloters, please comment:

In light of the above, the OBX-4 content algorithm might be perceived as too complex and having a hierarchy that does not stand out. The alternative could be the return to the OBR nesting without ORCs (except as needed for the major order) as was present in the 2013 version. This could have the advantage of better alignment with the FHIR clinical genomics direction, which is naturally nested, and maps more directly to the LOINC paneled structure that defines it. Many have expressed a preference for the OBX-4 only approach, so, we would like explicit feedback especially those who have implemented the specification about how well the OBX-4 algorithm works, and whether we should reconsider the OBR nesting.

Please see Section 8.11.2 Grouping of Related OBX Segments for how other components in the LRI groups OBX segments and represents OBX-4 numbering.

5.4.1 ALGORITHM FOR DEFINING OBX-4 VALUES

The dot notation for all variables in a given section always begins with the parent section number. For the clinical genomics message, the section numbers are stable, and assigned by the report section topic, as seen in Table 5-1 through Table 5-6. Working top-down, the OBX-4 value for each question under that panel would begin with the section number. For example, if the message reports on a complex variant, the OBX-4 values for each question would begin with the number 3 to correspond to Section 5.6.3.3 Report Section 3 – Complex Variants. For all panels that can repeat, each question has a letter (without a dot) attached to the number, starting from "a". So because Report Section 3 can repeat, the questions in that panel would have OBX-4 values of 3a, (without a dot). If the panel that repeats is repeated a second time, then questions would be labeled 3b, and so on. If any individual question in this panel can repeat, then increment the OBX-4 values by the "dot-letter" starting with ".a", e.g. 3a.a, 3a.b, 3a.c, etc.

For a child panel nested inside of the parent panel, add a numbered level to the dot notation for each new child panel by incrementing by 1. Thus, all of the OBX-4s in the first panel at the first level in Section 3 would be valued with "3a", and its child panels would be "3a.1", "3a.2", etc. If the child panel itself can repeat, a letter (without a dot) is added to its section number, e.g. 3a.1a, 3a.1b, etc. If there is an individual question that repeats within the child panel, use the "dot-letter" notation, e.g. 3a.1a.a, 3a.1a.b, etc.

See HL7 V2 example messages in Section 5.9 Example Messages. The OBX-4 numbering following this algorithm is labeled in red colored font. For an example message that shows the full scope of the OBX-4 numbering, see the example report in Section 5.9.3.1 Example Of Pharmacogenomics Study Of 4 Genes With Guidance About Selected Drugs Nested In Results For Each Gene which illustrates repeated questions within repeated panels.

This description is written as pseudo-code below, in Section 5.4.2.

5.4.2 PSEUDO CODE FOR OBX-4 ALGORITHM

5.4.2.1 TERM DEFINITIONS

Containing Section: A section/panel that includes other sections/panels or questions.

Section Sequence Number (N): A sequence number starting from 1 used to differentiate unique sections on the same level of the structure.

Repeating Instance Letter (L): A letter starting from "a" to differentiate instances of a repeating section or question. If letter "z" is ever used, the next one would be "aa", and so on.

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Note: The form itself is NOT treated as a Containing Section.

5.4.2.2 RULES FOR CREATING THE DOT NOTATION

On a form, with or without multiple instances of repeating questions or sections, go through each questions/sections starting from top of the form to the bottom as follows:

1) Set a new **Section Sequence Number (N)** to 1. Within each **Containing Section**, a separate "N" starting with 1 is used.
2) If it is a non-repeating section:
   a) Its OBX-4 value is its **Containing Section's** OBX-4 value plus "." plus "N"; or just "N" if there is no **Containing Section**.
   b) For all questions and sections within this non-repeating section, repeat step (1) through (5)
   c) Increase "N" by 1.
3) If it is a repeating section:
   a) Its OBX-4 value is its Containing Section's OBX-4 value plus "." plus "N" plus "L"; or just "N" plus "L" if there is no Containing Section.
   b) For all questions and sections within this instance of the repeating section, repeat steps (1) through (5).
   c) Repeat steps (3.a.) and (3.b) until all the instances of the same repeating section are processed.
   d) Increase "N" by 1.
4) If it is a non-repeating question:
   a) Its OBX-4 value is its Containing Section's OBX-4 value or just an empty value if there is no Containing Section "N".
5) If it is a repeating question:
   a) Its OBX-4 value is its Containing Section's OBX-4 value plus "." plus "L"; or just "L" if there is no Containing Section.
6) Repeat step (5.a). until all repeating instances of the same question are processed.

5.5 Clinical Genomics Code Systems

Table 14-1. Clinical Genomics Coding Systems lists the 29 coding systems used by the LRI_CG_Component and defined in the HL7 Vocabulary Table 0396 – Coding Systems (https://www.hl7.org/Special/committees/vocab/table_0396/index.cfm.) The table carries one system per row, where each row includes information from the HL7 Vocabulary Table 0396, including their HL7 V2.x linkage names, coding long names, and OIDs. For each coding system, Table 14-1 also includes a description, and when available, a URL that provides an overview of the source table for that coding system, a URL that permits viewing/exploring the content of that table, and/or a URL for downloading that table.

The LOINC coding system is used to identify the observations in the message in OBX-3. UCUM is the units of measures for OBX-6. The remaining code systems provide codes for variables that use coding systems to report their values in OBX-5.

Table 14-1. Clinical Genomics Coding Systems includes only *external* coding systems, such as ICD-9-CM and SNOMED CT and NCBI/EBI genetic content. It does *not* include the short answer lists that are

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linked to specific LOINC terms in the LOINC database. The next set of tables (Table 5-1 through Table 5-6) provides the short answer lists associated with LOINC codes, which identify the LOINC observations used in this guide along with LOINC definitional content, such as the description, cardinality, and answer lists, etc.

For the LRI_CG_Component, the CWE_05.2 component is declared to have lengths of at least 500 characters to accommodate potentially long syntax codes (i.e. HGVS or ISCN). For details of the CWE_05 data type see Section 9.2.5.

5.5.1 USE OF OIDS FOR CODING SYSTEMS OUTSIDE OF THIS GUIDE

A method to report genomic identifiers for reference sequences and variants from *public* databases that are not listed in Table 14-1. Clinical Genomics Coding Systems, or "HL7 Vocabulary Table 0396 – Coding Systems" or in the HL7 OID registry, is described below.

The LRI_CG_Component uses the CWE_05 data type flavor as shown in Table 9-5. The code system ID would be communicated in CWE_05.1 (Identifier), and either CWE_05.3 (Name of Coding System) and/or CWE_05.14 (Coding System OID) must also be valued. Consider the recording of a transcript reference ID as the value of LOINC 51958-7, *Transcript reference sequence* (see Table 5-2, Row B.4 for an example). The ID for the reference sequence from that public source would be communicated in CWE_05.1 (Identifier) and the source OID in CWE_05.14 (Coding System OID). This same approach could be used for other genomic identifiers including genetic variation IDs, genomic reference sequence IDs, etc., that come from public sources not registered in HL7 Table 0396. Implementers are encouraged to request an HL7 OID and a coding system name for that source's genomic table from HL7 so that the identifiers for that source could be treated like all of the other coding systems used in this guide.

While this same OID mechanism could be used for identifying source tables for genomic identifiers from private databases, the submission of new variations and other genomic content to public registries such as NCBI or Ensembl is strongly encouraged, instead of, or in addition to, only keeping that data in a private database.

5.6 Structure of Clinical Genomics Messages

The set of closely related tables in the following Section 5.7 carry all of the LOINC codes (variables) that can be used in this component. They define the message structure and are organized in the form of an example "message". Each table describes one section of a clinical genomics report. This specification does not exemplify the content for each repeat of the potentially repeating panels, but instead, indicates that a given panel can repeat. The full V2 example messages in Section 5.9 do include many repeated panels based on real genomic reports.

Depending on the kind of analysis, clinical genomic reports will usually include observations from only a few of these sections. Almost all reports will carry some variables from Report Section 1, attributes that apply to the whole report. Typical variant analysis will carry content from Report Section 2. Pharmacogenomics reports typically carry only variables from Report Sections 1 and 4, but some pharmacogenomics labs want to be able to send the detailed genetic data that underlies their star allele results in the glossary specified in Report Section 5.

Note that the first column of each table has short alphanumeric row labels (e.g. A, A.1, A.2, etc.) to provide an easy way to reference specific content in this table. These labels have no meaning outside of this document, and have no role in HL7 messaging.

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5.6.1 EXAMPLE MESSAGE CONTENT AND LOINC USAGE RULES

To make it easier for readers to interpret the LOINC codes and how they are organized, each row in Table 5-1 through Table 5-5 corresponds to an OBX segment with example content for OBX-2, OBX-3.1, OBX-3.2, OBX-4 and OBX-5 appropriate to that row's LOINC code. For easy readability, these pseudo OBX's carry their values in table columns rather than as delimited text as one would see in a real message; see Section 5.9 for a series of example Coded Clinical Genomics Lite messages in standard delimited HL7 text.)

These tables also contain fields that carry information about the LOINC term itself: its optionality, its cardinality, narrative text that explains the term and how to use it, and for terms with coded answers, either its answer list or coding systems. Please note: the R/O/C and cardinality listed here are LOINC attributes that describe the "required-ness" of a LOINC term within a panel. They have no relationship to the field requirements in HL7, which are recorded separately in the tables, and indicate whether the term is required and how many repeats are permitted. For example, "optional with no upper bound" is displayed as "[0..*]". "Required but not permitted to repeat" is displayed as "[1..1]". So most of the information about a LOINC term is integrated into the same row that carries example data. More information about each coding system can be found in Section 14 Clinical Genomics Code Systems.

5.6.1.1 COMMENTS ON THE NUMBER OF LOINC CODES AND PANELS IN THIS GENETICS MESSAGE STRUCTURE

The Clinical Genomics component carries many variables (wherein the LOINC fields are equivalent to fields) to satisfy the interest of many kinds of reporting services and receivers. But most of these are optional and some represent alternative ways of saying the same thing. For example, the discrete variant ID is informationally equivalent to more than 10 of the variables that follow, because they are carried in the ClinVar, or some analogous public database, record that is identified in Row B.1. Indeed, the LHC-Form demo auto-populates these variables when specific ClinVar records are identified. These 10 components are included as separate observations so that reporters can fill this information in themselves when they are reporting a variation that is not registered in ClinVar, and to make it easier for receivers to access these individual components. Thus, the very large number of variables in the simple variant panel should not be off-putting. Much of what is currently reported could be reported by filling in one variable: LOINC 81252-9 (row B.1) using the coding system from ClinVar or COSMIC simple or structural variation codes. Further, the name of that variable includes the reference sequence, the gene symbol, the c.HGVS and the p.HGVS in one variable.

Ultimately, a laboratory professional should not have to use many of the LOINC codes to enrich their narrative report with a few important structured elements. So those interested in minimalist reports could report simple variants with one or two LOINC codes.

5.6.2 CONVENTIONS FOR NESTED AND REPEATING PANELS

Table 5-1 through Table 5-6 show the gist of a V2 clinical genomics message. The tables include groups of related rows that are defined by LOINC panels. The tables include these panels and their children to provide the hierarchy structure. However, these LOINC panel IDs are not included in the message as OBRs as they were in the 2013 HL7 Clinical Genomics Guide. Many of these panels are designed to repeat as many times as needed. Note that Table 5-1 through Table 5-6, with a few exceptions, do not include more than one instance of a repeating panel to save space. Instead, this version uses OBX-4 dot notation to define the hierarchy. In a real message, the LOINC terms from the panel that describe a discrete variation will repeat as many times as there are simple variations to report; the same applies to pharmacogenomics and complex variations. The pharmacogenomics part of the example table (Table 5-5) shows how a real message defined by this guide might look.

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The examples in Section 5.9 show repeats that might appear in real genomics reports.

5.6.3 OVERVIEW OF A CLINICAL GENETICS REPORT

Table 5-1 through Table 5-6 correspond to the five different sections of a V2 clinical genetics report, and together, they conceptually can represent one whole table and message. Within a given report section, the example content will represent a single consistent real world result. Across sections, they may not.

Report sections 1 and 2 (Table 5-1, Table 5-2) represent the Master HL7 Reporting Panel and the Discrete Variant Panel, which are comprised of a single panel each, and all of the rows within any such panel begin with the same letter (A or B, respectively, in this case). Although the HL7 message will not contain nested OBR sections, the illustrative tables include the LOINC panels to show the source panels and hierarchical relationship among groups of variables represented by the OBX-4 dot notation. Report sections 3 and 4 (Table 5-4, Table 5-5 represent the Complex and Pharmacogenomics variants, respectively, contain nested LOINC panels and the rows within these different panels begin with different letters i.e. “C” and “D” or “E” and “F”, for complex and pharmacogenomics variants respectively. Report section 5 (Table 5-6). Remember these lettered row labels are not codes and do not represent OBX-4 values – they are merely a convenient way to reference the tables for the discussions in this guide, not a formal part of the standard or the message.

5.6.3.1 REPORT SECTION 1 – VARIABLES THAT APPLY TO THE OVERALL STUDY

Table 5-1 carries the observations that would apply to the whole report. Some of these observations carry detailed technical content, such as the version number for the SNP codes in the report, the set of variants sought in targeted variant study, overall impression, and a copy of the whole report as delivered traditionally. The variable for reporting large deletion-duplications in ISCN syntax can include everything that has been observed as a single variable, so it is also part of the overall report section. Some content from this first section should be part of almost every clinical genetics report message. The other four sections are more specialized and only one or two of them are usually included in addition to the overall results in Report Section 1.

5.6.3.2 REPORT SECTION 2 – DISCRETE VARIANTS

Table 5-2 reports discrete variations. All of the variables in this section are part of one large panel, (LOINC 81250-3) – the discrete variant panel. This panel includes 31 variables, but most laboratories will use only four to six of them to designate a single variant. The rows for the discrete variant have labels beginning with “B”.

The “Discrete variant panel” now includes simple and structural variants because ClinVar includes both simple and structural variants, and because the both kinds of variants reflect a change in a single contiguous sequence, and share many attributes. The attributes that apply only to structural variants are part of a panel called the structural variant addenda (Table 5-3) for visual separation but in the HL7 V2 message, they are just part of the discrete variant panel.

Of note, in this section is LOINC 69548-6 Genetic variant assessment in row B.23. Most genetic reporting of negatives is by default. The front of the report describes what was tested for – either a list of discrete variants or regions of the genome that were sequenced and the results call out only the “abnormal” variations found. LOINC 69548-6 is the term that enables statements about all loci of interest whether normal or not, and carries “no call” as one of its answers. With this variable, reporters can specify whether each locus examined was “normal” or “abnormal”.

This report section also includes a variable for reporting the phase of each variant (Row B.28) and the kind of evidence used to decide the phase (Row B.29).

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5.6.3.3 REPORT SECTION 3 – COMPLEX VARIANTS

Table 5-4 reports complex variants, which are those for which many discrete (simple or structural) variants taken together have one effect or phenotype. The reason for this section is to provide a way to report something about a set of variants that together have a special meaning and to list the individual constituent variations nested below them. This section which reports the overall effect of the complex variant (whose row labels are C), thus also holds children panels (with row labels D) that make up the discrete variant panel constituents. The child panel can be used to specify details about the two or more constituent variants within the complex variant.

When the report recipients need only HGVS representation of the complex variant and no separate genetic details about each component simple variant, such child panels are not needed.

5.6.3.4 REPORT SECTION 4 – PHARMACOGENOMICS

Table 5-5 is dedicated to pharmacogenomics test reporting. It includes two nested panels. The first panel, whose row labels all begin with E, can repeat for each gene or gene pair with variants that would influence drug metabolism or efficacy. The second panel, nested inside of the first, whose row labels begin with F, provides guidance about adjustment for drugs whose actions (e.g. metabolism, efficacy, or risk) may be influenced by the variants reported in the parent panel. These latter nested panels repeat per drug, and provide guidance about the use of that drug given the pharmacogenomics variations reported above. In some cases the laboratory will only provide guidance about the drugs about which the ordering provider inquired, and in other cases, the laboratory reports this information about all common drugs.

Examples 5.9.3.1 and 5.9.3.3 show multiple genotypes and multiple drug guidance statements for each of them.

5.6.3.5 REPORT SECTION 5 – GLOSSARY THAT DEFINES THE CONSTITUENT VARIATIONS OF A HAPLOTYPE

Table 5-6 reports the constituent variants that define a haplotype, most commonly star alleles, which are used commonly in pharmacogenomic reports as shorthand to specify one or more specific variants in a gene that is known to impact drug metabolism or response. A star allele can identify either a single variant or a group of variants found in cis, and therefore it usually represents a haplotype. See Table 14-1 for more details.

However, the star nomenclature system is inadequately defined and inconsistently adopted. Therefore, although the system we are proposing supports the inclusion of pharmacogenomics star alleles as a legacy syntax, we strongly encourage messages that include star alleles to rigorously define those alleles in this section, which allows the reporting lab to specify the variants with their local definitions. This section mimics the way many laboratories present such information in hard copy reports—as an addenda at the end of a clinical report. Receivers can link the definitions up with the report via the gene allele names if desired. In general, we encourage messages to utilize a more discrete, unambiguous approach like the VCF-like approach found in Report Section 2, rows B.9-B.13, to describe all pharmacogenomics variants in the glossary. The HGVS nomenclature is more robust than star nomenclature, but its implementation is also somewhat inconsistent so it should be used in conjunction with a coordinate-based method (e.g., VCF).

The structure of the glossary consists of an upper level panel (with row labels H) that identifies the gene-star allele pair contains two variables, and is followed by discrete variant panels (with row labels I, J, K), one for each variant in the star allele. The whole structure would repeat for each star allele in the report.

Examples 5.9.3.2 and 5.9.3.4 show two examples of the glossary:

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1. CYP2C9 *18/*3 alleles where *18 is defined by 3 variants, and *3 by 1 variant
2. A glossary for two alleles on two different genes CYP2C9 *2/*5 alleles and VKORC1 *A/*A.

The first uses six LOINC codes per variant to describe the variations. The second example uses SNPs and Alt Alleles to specify the same variations. Reporters can choose any of the variables in the discrete variant panel to detail the constituent variables for a star allele.

Note that although we allow the inclusion of pharmacogenomics star alleles as a legacy syntax, we strongly encourage messages that include star alleles to rigorously define those alleles through this section, which allows the reporting lab to specify the variants with their local definitions.

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5.7 Clinical Genomics Report Structure Tables

5.7.1 CLINICAL GENOMICS REPORT SECTION 1 – MASTER HL7 REPORTING PANEL

TABLE 5-1 CLINICAL GENOMICS REPORT SECTION 1 – MASTER HL7 REPORTING PANEL								
	OBX-2	OBX3.1	OBX3.2	OBX-4	OBX-5	LOINC Panel/Definitional Terms		
Label	Type	LOINC	LOINC Name	Sub ID	Example values†	R/O/C	Cardinality	Term Description
	N/A	81247-9	Master HL7 genetic variant reporting panel		This term identifies the set of LOINC terms that are part of this panel but is not, itself, part of the HL7 message.		[1..1]	This panel term provides a handle within the LOINC database that holds together all of the terms and panels that are available for use in a V2 Clinical Genomics message. In the variables below, we list the answers for short answer lists or the choice of external coding systems when available. The kind of variations that is described uses skip logic, which is useful to the receiver to cue them to the right variables. Because this guide uses the OBX-4 to organize the hierarchy of "records" in the message (see details in Section 5.1.2), the LOINC codes for panels after the master panel will not appear as OBRs in the message as was the case in the 2013 HL7 clinical genomics message. All of the genomic data reported in this panel uses a coordinate system beginning with 1, assumes the variants are reported from the positive strand, and have an inclusive start-end.
Report Section 1 - Variables That Apply To The Overall Study								
A	Panel	81306-3	Variables that apply to the overall study	1	This term identifies the set of LOINC terms that are part of this panel but is not, itself, part of the HL7 message.		[1..1]	
A.1	TX	53577-3	Reason for study	1	**"Worried about family planning"**	O	[0..1]	HL7 provides OBR-31 for recording the reason for the study. The LOINC code is included in this panel for convenience of form definition, because it is often captured in a form with this variable. But ideally, in a lab message it should be delivered in HL7 OBR-31.

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TABLE 5-1 CLINICAL GENOMICS REPORT SECTION 1 – MASTER HL7 REPORTING PANEL								
	OBX-2	OBX3.1	OBX3.2	OBX-4	OBX-5	LOINC Panel/Definitional Terms		
Label	Type	LOINC	LOINC Name	Sub ID	Example values†	R/O/C	Cardinality	Term Description
A.2	CWE	51967-8	Genetic disease assessed [ID]	1.a	2971795010^**Deficiency of isobutyryl-coenzyme A dehydrogenase (disorder)**^SCT	C	[0..*]	**Coding systems:** 1. SCT (SNOMED-CT) 2. I9CDX 3. I10C 4. MedGen-Dis 5. HPO (Human Phenotype Ontology) Applies only to studies that target a disease. While this can be supplied by either the placer or the test performer, this question is typically answered by the placer. Any or all of the above coding systems could be used in the message. It will be up to the message generator to specify the coding system within the message. We encourage the use of SNOMED CT in this field because it is the preferred direction in the US, which is in the example values OBX-5 column. However, the LHC-forms demo of this draft specification shows the content from NCBI MedGen, because it is the most complete with respect to genetic diseases, and public. Further, MedGen includes mappings to SNOMED CT when available.
A.3a	CWE	51963-7	Medication assessed [ID]	1.a	50005^**Fluoxetine**^RxT-Ingrd	C	[0..*]	**Coding system: RxT-Ingrd** Applies only to pharmacogenomics studies (See Table 5-5). Carries the medications for which there is concern that genetic variation might influence the efficacy and/or the rate of metabolism. This content will usually be an Ask-at-Order-Entry (AOE) question. Repeats must be entered in separate OBX fields, as shown in the example where the OBX-4 must be different for each OBX segment (e.g. 1.a, 1.b, 1.c) – see Section 5.1 for an overview of OBX4 content.
A.3b	CWE	51963-7	Medication assessed [ID]	1.b	84701^**Atorvastatin**^ RxT-Ingrd	C	[0..*]	See row A.3a for the description of LOINC# 51963-7 Medication assessed [ID].

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TABLE 5-1 CLINICAL GENOMICS REPORT SECTION 1 – MASTER HL7 REPORTING PANEL								
	OBX-2	OBX3.1	OBX3.2	OBX-4	OBX-5	LOINC Panel/Definitional Terms		
Label	Type	LOINC	LOINC Name	Sub ID	Example values†	R/O/C	Cardinality	Term Description
A.3c	CWE	51963-7	Medication assessed [ID]	1.c	45000^**Naproxen**^RxT-Ingrd	C	[0..*]	See row A.3a for the description of LOINC# 51963-7 Medication assessed [ID].
A.3d	CWE	51963-7	Medication assessed [ID]	1.d	11289^**Coumadin**^RxT-Ingrd	C	[0..*]	See row A.3a for the description of LOINC# 51963-7 Medication assessed [ID].
A.4	CNE	48018-6	Gene studied [ID]	1.a	21497^**ACAD9**^HGNC-Symb	C	[0..*]	**Coding system choices:** 1. HGNC-Symb 2. NCBI-gene code This variable identifies the gene on which the variant is located. However, the gene identifier is also carried in the transcript reference sequence database, and is part of a full HGVS expression. The preferred coding system is HGNC-Symb but NCBI has created gene IDs that cover the genes that are not registered by HGNC, and the NCBI gene codes should be used in this case. If the study includes more than one gene, each gene will be entered into separate OBX's and the content of OBX-4 will have to be unique for each such repeat. See Section 5.4 for a specification of OBX-4 content. In this guide, we focus only on human genetics. (Will address extension to other species in the future).

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TABLE 5-1 CLINICAL GENOMICS REPORT SECTION 1 – MASTER HL7 REPORTING PANEL								
	OBX-2	OBX3.1	OBX3.2	OBX-4	OBX-5	LOINC Panel/Definitional Terms		
Label	Type	LOINC	LOINC Name	Sub ID	Example values†	R/O/C	Cardinality	Term Description
A.5	CWE	36908-2	Gene mutations tested for	1.a	7129^**NM_000492.3(CFTR):c.3846G>A (p.Trp1282Ter)**^ CLINVAR-V	C	[0..*]	The list of gene mutations tested for is required if the study is a targeted mutation analysis (i.e. either a study for known family mutations, or for a fixed set of mutations offered by the laboratory). Because laboratories will routinely report on only a subset of the mutations included in a gene chip, the identification of the gene chip alone is not enough. Instead, the gene chip information goes in 81293-3 "Description of ranges of DNA sequences examined" (row A.8). The whole list of the gene mutations testing for (usually a subset of the gene chip) should be listed here, each requiring its own separate OBX if more than one mutation is test for. Laboratories often report the mutations tests for as HGVS.p notation in narrative reports. However, the HGVS expression usually includes the gene symbol when applied as shown in the example. Multiple mutations need to be reported in a separate OBX. See Section 5.4 for a specification of OBX-4 content.
A.6	NR	51959-5	Range(s) of DNA sequence examined	1.a	**2000753^2234579**	C	[0..*]	Preferred if the method is a sequencing study. The first value of the numeric range defines the start location and the second value defines the end location of the Sequence. We recognize that this information may be proprietary and is often not revealed. The locations are specified to the associated Genomic reference sequence if the range is discontinuous where each distinct range is reported in a separate OBX, and the OBX-4 values will have to differ among such repeats. See Section 5.4 for a specification of OBX-4 content.

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TABLE 5-1 CLINICAL GENOMICS REPORT SECTION 1 – MASTER HL7 REPORTING PANEL								
	OBX-2	OBX3.1	OBX3.2	OBX-4	OBX-5	LOINC Panel/Definitional Terms		
Label	Type	LOINC	LOINC Name	Sub ID	Example values†	R/O/C	Cardinality	Term Description
A.7	TX	81293-3	Description of ranges of DNA sequences examined	1	**"All coding regions and appropriate flanking regions"**	C	[0..1]	Genetic test reports only rarely include explicit numeric ranges (as row A.6 could carry) because they are often proprietary. So reports tend to describe the regions in narrative (e.g. "all coding regions and appropriate flanking regions"). It is only relevant to sequencing studies. Either this code or LOINC 51959-5 Ranges of DNA sequence examined should be included when reporting structural variants. Whole genome studies should be identified first within either the string "Whole genome," whole exome studies with the string, "Whole exome," and individual exons, with the exon names in a list.
Summary Results								
A.8	CNE	51968-6	Genetic analysis overall interpretation	1	LA6576^**Positive**^LN^ 10828004^**Positive**^SCT	R	[0..1]	**Answer List: LL541-4** 1. Positive LA6576-8 2. Negative LA6577-6 3. Inconclusive LA9663-1 4. Failure LA9664-9 Reported when variant analysis (sequencing or targeted variantss) is done. Equivalent SCT codes are or will be available for LA codes in this guide. Provides a coarse overall interpretation of the results reported. More detailed interpretations are also associated with each distinct reported variant below. Note the example controls both the SNOMED code and the LOINC LA code.

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TABLE 5-1 CLINICAL GENOMICS REPORT SECTION 1 – MASTER HL7 REPORTING PANEL								
	OBX-2	OBX3.1	OBX3.2	OBX-4	OBX-5	LOINC Panel/Definitional Terms		
Label	Type	LOINC	LOINC Name	Sub ID	Example values†	R/O/C	Cardinality	Term Description
A.9	CWE	83006-7	Deletion-duplication overall interpretation	1	LA26803-9^**No deletion duplications detected in studied regions**^LN	C	[0..1]	**Answer List: LL4166-6** 1. No deletion or duplication detected in studied region LA26803-9 2. Deletion and/or duplication detected in studied region LA26804-7 3. Inconclusive LA9663-1 Only reported when deletion/duplication studies performed.
A.10	FT; ED	51969-4	Genetic analysis report	1	See Section 5.9 Example Messages for examples of genetic analysis report narratives.	O	[0..1]	This attribute can carry the full narrative report in two different data types, e.g. FT=Formatted text or as ED=encapsulated data which can accommodate Word DOCs, PDFs and other special MIME media types. In most cases these will be full reports with page headers and footers, similar or identical to the existing "paper" report. But this could be just narrative text to complement the other structured data delivered. If this content is not reported as the simple formatted text, follow HL7 V2 specifications for recording the media type and other attributes of an HL7 encapsulated data type.
A.11	CWE	81291-7	Variant ISCN	1	Example pending	C	[0..1]	**Coding System: ISCN** Like HGVS, ISCN is a syntax. It came out of cytopathology and its focus ranges from normal and abnormal chromosome numbers (e.g. XXX down to smallish copy number changes). It can fully describe mosaics: the abbreviation is "mos" and a slash (/) is used between karyotypes for each cell line, e.g.: mos 47,XXX[25]/46,XX[5]. Reference: An International System for Human Cytogenetic Nomenclature, J McGowan-Jordan, Simons A, M. Schmid (eds). S. Karger, Basel 2016

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TABLE 5-1 CLINICAL GENOMICS REPORT SECTION 1 – MASTER HL7 REPORTING PANEL								
	OBX-2	OBX3.1	OBX3.2	OBX-4	OBX-5	LOINC Panel/Definitional Terms		
Label	Type	LOINC	LOINC Name	Sub ID	Example values†	R/O/C	Cardinality	Term Description
Versions of Coding Systems								
A.12	CWE	62374-4	Human reference sequence assembly version	1	LA14029-5^ **GRCh37**^LN	C	[0..1]	**Answer List: LL1040-6** 1. NCBI35 LA14031-1 2. NCBI36 LA26805-4 3. GRCh37 LA14029-5 4. GRCh38 LA26806-2 May or may not be needed depending on the reference sequences to which the results are anchored. It is not needed for transcript reference sequences nor for NCBI genomic reference sequences when they include version numbers (the numbers after the dots). It is needed for genomic reference sequences if they lack the version number and for Ensembl genomic and chromosome reference sequences when the build is not part of the variant name. The overall report section includes only one slot for the assembly build, assuming that this term applies to all repeated variations.
A.13	ST	81303-0	HGVS version [ID]	1	15.11	O	[0..1]	HGVS (Human Genomic Variation Society) now includes new version numbers. As of November 2016, the most recent version number is 15.11. Reference: 2016 update. Hum. Mutat. 25: 37: 564-569. http://varnomen.hgvs.org/
A.14	NM	82115-7	dbSNP version [Num]	1	**137**	O	[0..1]	dbSNP version changes are only made to correct errors. The version # does not change the meaning of the dbSNP RS # per se, but may change the value of the location number in relation to the build. The current version number, as of April 2016 is 147. Details can be obtained from NCBI at http://www.ncbi.nlm.nih.gov/projects/SNP/buildhistory.cgi

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TABLE 5-1 CLINICAL GENOMICS REPORT SECTION 1 – MASTER HL7 REPORTING PANEL								
	OBX-2	OBX3.1	OBX3.2	OBX-4	OBX-5	LOINC Panel/Definitional Terms		
Label	Type	LOINC	LOINC Name	Sub ID	Example values†	R/O/C	Cardinality	Term Description
A.15	NM	83007-5	COSMIC version [ID]	1	**v82**	O	[0..1]	As of August 2017, the latest COSMIC version numbers is 82. More information can be found here: http://cancer.sanger.ac.uk/cosmic/download
A.16	NM	83008-3	ClinVar version [ID]	1	Pending	O	[0..1]	ClinVar does not include a version ID as April 2018, but will soon add version numbers. This variable will accommodate that.

5.7.2 CLINICAL GENOMICS REPORT SECTION 2 - VARIABLES THAT DEFINE A DISCRETE VARIANT

TABLE 5-2 CLINICAL GENOMICS REPORT SECTION 2 - VARIABLES THAT DEFINE A DISCRETE VARIANT								
	OBX-2	OBX3.1	OBX3.2	OBX-4	OBX-5	LOINC Panel/Definitional Terms		
Label	Type	LOINC	LOINC Name	Sub ID	Example values†	R/O/C	Cardinality	Term Description
B	N/A	81250-3	Discrete genetic variant panel	2a	This term identifies the set of LOINC terms that are part of this panel but is not, itself, part of the HL7 message.		[0..*]	Repeats for each discrete variant reported. A discrete variant is a contiguous set of changes in the tested sample compared to a reference sequence. It can be a simple or structural variant. This panel variable does not carry values in its OBX-5. It provides a handle for holding all of the LOINC terms needed to define a discrete variation. It is not included in the message because the guide uses the content of OBX-4 to define the hierarchy and grouping rather than nested OBRs and OBX's.
B.1	CWE	83005-9	Variant category	2a	LA26801^**Simple Variant^**LN		[0..1]	**Answer List: LL4165-8** 1. Simple Variant LA26801-3 2. Structural Variant LA26802-1 Not essential to the message, but can be used to distinguish the discrete variant as simple or structural.
B.2	CWE	81252-9	Discrete genetic variant	2a	Example of simple variant:	C	[0..1]	**Simple Variant coding systems:** 1. CLINVAR-V 2. COSMIC-Smpl **Structural Variant coding systems:**

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TABLE 5-2 CLINICAL GENOMICS REPORT SECTION 2 - VARIABLES THAT DEFINE A DISCRETE VARIANT								
	OBX-2	OBX3.1	OBX3.2	OBX-4	OBX-5	LOINC Panel/Definitional Terms		
Label	Type	LOINC	LOINC Name	Sub ID	Example values†	R/O/C	Cardinality	Term Description
					30880^**NM_014049.4(ACAD9):c.1249C>T (p.Arg417Cys)**^CLINVAR-V Example of structural variant: nsv995237^**17p12(chr17:14616-15581544)x1**^dbVar-GL 155448^**GRCh38/hg38 1q21.2-25.2(chr1:149854269-180267197)x3**^CLINVAR-V			3. dbVar-GL 4. dbVar-Som 5. COSMIC-Strct If the discrete genetic variant is fully specified with an ID in a coding system, none of the following fields are required because they can be retrieved from the reference database. However, for convenience of access, laboratories may include them. Message implementers will insert the appropriate coding system from the list above to indicate the coding system source. The code for the genetic variant would usually be the ID from the given database. The name (print text) is that given by the public database—usually a combination of attributes (e.g. the RefSeq, gene symbol, c.HGVS, or the HGVS expression for the variant etc.). If the variant has been registered in COSMIC or ClinVar, many of the following attributes under the Transcript specification and Genomic Specification subsections can be automatically pulled from the public database and loaded into separate LOINC terms (see those that follow this panel). Before a variable has been registered in a public allele registry, laboratories can enter these attributes in the OBXs specified by the terms that follow. NCBI is our primary source for the non-somatic structural variants because their files carry all of the European (EBI) structural variant as well as the US variants. Reporters could also code a structural variant with any HL7 OID structural variant identifiers.
Transcript Specification (Separate observations for each of the components of the Discrete genetic variant name)								
B.3	CWE	48018-6	Gene studied [ID]	2a	21497^**ACAD9**^HGNC-Symb	C	[0..1]	**Coding systems:** 1. HGNC-Symb 2. NCBI-gene code This variable identifies the gene on which the variant is located.

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TABLE 5-2 CLINICAL GENOMICS REPORT SECTION 2 - VARIABLES THAT DEFINE A DISCRETE VARIANT								
	OBX-2	OBX3.1	OBX3.2	OBX-4	OBX-5	LOINC Panel/Definitional Terms		
Label	Type	LOINC	LOINC Name	Sub ID	Example values†	R/O/C	Cardinality	Term Description
								See row A.4 for the full description of LOINC 48018-6 Gene studied [ID].
B.4	CWE	51958-7	Transcript reference sequence [ID]	2a	NM_014049.4^ **NM_014049.4**^ RefSeq-T	C	[0..1]	**Coding systems:** 1. RefSeq-T 2. Ensembl-T 3. LRG N.B: Most structural variants are based on genomic reference sequences, and the transcript reference sequences would not apply. At least one of the transcript or genomic reference sequence (rows B.4, B.9) must be included. If the LOINC 48004-6 DNA change c.HGVS (B.5) is included, the transcript reference sequence must be included.
B.5	CWE	48004-6	DNA change c.HGVS	2a	c.1249C>T^**c.1249C>T**^ HGVS.c	C	[0..1]	**Coding system: HGVS.c** HGVS specification of the change at the DNA level relative to the transcript RefSeq.
B.6	CWE	48005-3	Amino acid change p.HGVS	2a	p.Arg417Cys^ **p.Arg417Cys**^HGVS.p	C	[0..1]	**Coding system: HGVS.p** HGVS specification of the change at the amino acid (protein) level caused by the DNA change. If the change is in a non-coding region, this variable will not be reported. HGVS recommends that amino acid changes never be reported without also reporting the DNA change. There is no ambiguity about the amino acid change with transcript reference sequences, e.g. because they correspond to one and only one protein.
B.7	CWE	48019-4	DNA change [Type]	2a	LA6690-7^ **Substitution**^LN	O	[0..1]	**Discrete Variant Answer List: LL4033-8** **Simple Variant and Structural Variant types:** 1. Wild Type LA9658-1 2. Deletion LA6692-3 3. Duplication LA6686-5 4. Insertion LA6687-3 5. Insertion/Deletion LA6688-1 6. Inversion LA6689-9 7. Substitution LA6690-7

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TABLE 5-2 CLINICAL GENOMICS REPORT SECTION 2 - VARIABLES THAT DEFINE A DISCRETE VARIANT								
	OBX-2	OBX3.1	OBX3.2	OBX-4	OBX-5	LOINC Panel/Definitional Terms		
Label	Type	LOINC	LOINC Name	Sub ID	Example values†	R/O/C	Cardinality	Term Description
								Structural Variant Types only: 8. Copy number gain LA14033-7 9. Copy number loss LA14034-5 10. Mobile element insertion LA26324-6 11. Novel sequence insertion LA26325-3 12. Tandem duplication LA26326-1 13. Intrachromosomal breakpoint LA26327-9 14. Interchromosomal breakpoint LA26328-7 15. Translocation LA26331-1 16. Complex LA26330-3 17. Sequence alteration LA26329-5 Type of DNA variation reported. Taken from: 2013 HL7 V2 Clinical Genomics Implementation Guide. See also HGVS DNA variant descriptions. http://varnomen.hgvs.org/
B.8	CWE	48006-1	Amino acid change [Type]	2a	LA6698-0^**Missense**^LN	O	[0..1]	**Answer List: LL380-7** 1. Wild Type LA9658-1 2. Deletion LA6692-3 3. Duplication LA6686-5 4. Frameshift LA6694-9 5. Initiating Methionine LA6695-6 6. Insertion LA6687-3 7. Insertion and Deletion LA9659-9 8. Missense LA6698-0 9. Nonsense LA6699-8 10. Silent LA6700-4 11. Stop Codon Mutation LA6701-2 Type of amino acid change reported. Taken from http://www.hgvs.org/mutnomen/recs-prot.html.
Genomic specification (Separate observations for each of the components of the Discrete genetic variant name)								
B.9	CWE	48013-7	Genomic reference sequence [ID]	2a	NG_017064.1^ **NG_017064.1**^RefSeq-G	C	[0..1]	**Coding system choices:** 1) RefSeq-G 2) Ensembl-G

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TABLE 5-2 CLINICAL GENOMICS REPORT SECTION 2 - VARIABLES THAT DEFINE A DISCRETE VARIANT								
	OBX-2	OBX3.1	OBX3.2	OBX-4	OBX-5	LOINC Panel/Definitional Terms		
Label	Type	LOINC	LOINC Name	Sub ID	Example values†	R/O/C	Cardinality	Term Description
								If the genomic specification is given, then this and the following 3 terms must be presented: LOINC# 69547-8 (Row B.11), 81254-5 (Row B.12) and 69551 (Row B.13).
B.10	CWE	81290-9	Genomic DNA change g.HGVS	2a	Example for simple variant: NC_000003.11:g.128625063C>T^ **NC_000003.11:g.128625063C>T^** HGVS.g Example for structural variant: NC_000017.10:g.(?_14087933)_(15484858_?)del^ **NC_000017.10:g.(?_14087933)_(15484858_?)del^** HGVS.g	C	[0..1]	**Coding system: HGVS.g** If this is a structural variant, either the LOINC 81291-7 Variant ISCN (A.11) or this term should be included with every structural variant report.
B.11	ST	69547-8	Genomic ref allele [ID]	2a	**C**	C	[0..1]	The DNA string in the reference sequence (Ref Allele) with which the DNA string in the test sample differs, starting at the first position given in LOINC 81254-5's Genome Allele start-end (B.12).
B.12	NR	81254-5	Genomic allele start-end	2a	**31731^31731**	C	[0..1]	The beginning and end of the Ref Allele that was replaced by the Alt Allele. The beginning is counted as the first position in the genomic reference showing a contiguous set of base changes in the sample DNA being tested. The end is the comparable last position.
B.13	ST	69551-0	Genomic alt allele [ID]	2a	**T**	C	[0..1]	The DNA sequence in the test sample (Ref Allele) that is different from the DNA sequence in the reference sequence (Ref Allele) – Note the examples of LOINC#s 69547-8 (Row B.11), 81254-5 (Row B.12) and 69551 (Row B.13) – could also be described in a HGVS.g expression as: g.31731C>T in 48013-7 Genomic Reference Sequence ID (row B.9).
Other optional codes related to a Discrete genetic variant								
B.14	CWE	84414-2	Haplotype name	2a	*2	O	[0..1]	Reports the allele names to which the discrete variants belong. Most often used to report star alleles but might also be used to record HLA alleles.

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TABLE 5-2 CLINICAL GENOMICS REPORT SECTION 2 - VARIABLES THAT DEFINE A DISCRETE VARIANT								
	OBX-2	OBX3.1	OBX3.2	OBX-4	OBX-5	LOINC Panel/Definitional Terms		
Label	Type	LOINC	LOINC Name	Sub ID	Example values†	R/O/C	Cardinality	Term Description
								Not needed if the repeat includes an allele glossary – see Table 5-6 Clinical Genomics Report Section 5 – Glossary for Haplotype Definition
B.15	CWE	81255-2	dbSNP [ID]	2a	rs368949613^ **rs368949613**^dbSNP	O	[0..1]	**Coding system: dbSNP** More than 160 million dbSNP codes now exist (see https://lforms-service.nlm.nih.gov/apidoc/snps/v1/doc.html). Be aware that dbSNP codes cannot stand alone as a variant identifier -- it only identifies the position and the length of the variant, not the change. If you want to use dbSNP rs codes, you must also include the Genomic Alt allele (LOINC # 69551-0 in row B.13) in the message.
B.16	CWE	81257-8	CIGAR [ID]	2a	Pending	O	[0..1]	Used primarily for alignment in earlier stages of genetic study analysis. We have not seen usage in routine clinical reports.
Other possible attributes								
B.17	CWE	48001-2	Cytogenetic (chromosome) location	2a	3q21^**3q21**^Chrom-Loc	O	[0..1]	**Coding system: Chrom-Loc** Chromosome location (aka chromosome locus or cytogenetic location), is the standardized syntax for recording the position of genes and large variants. See details in row 1 “Cytogenetic (chromosome) location” in the Appendix Table 14-1. Clinical Genomics Coding Systems.
B.18	CNE	48002-0	Genomic source class [Type]	2a	LA6683-2^**Germline**^LN	R	[0..*]	**Answer List: LL378-1** 1. Germline LA6683-2 2. Somatic LA6684-0 3. Fetal LA10429-1 4. Likely germline LA18194-3 5. Likely somatic LA18195-0 6. Likely fetal LA18196-8 7. Unknown genomic origin LA18197-6 8. De novo LA26807-0

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TABLE 5-2 CLINICAL GENOMICS REPORT SECTION 2 - VARIABLES THAT DEFINE A DISCRETE VARIANT								
	OBX-2	OBX3.1	OBX3.2	OBX-4	OBX-5	LOINC Panel/Definitional Terms		
Label	Type	LOINC	LOINC Name	Sub ID	Example values†	R/O/C	Cardinality	Term Description
								The genomic class of the specimen being analyzed: Germline for inherited genome, somatic for cancer genome (e.g. DNA from tumor cells), and fetal for fetal genome. De novo is defined by NCBI to mean a novel variation present for the first time in one family member as a result of a variant in a germ cell of one of the parents, or a variant that arises in the fertilized egg itself during early embryogenesis. Reported when variant analysis (sequencing or targeted variants) is done. Equivalent SCT codes are or will be available for LA codes in this guide. The reported genomic source class is not always precise, and more detailed interpretations also associated with each distinct reported variant can be found below. It is strongly recommended to use the full list of Genomic Source Class values at the variant level; however, top level genomics source class (around the testing context) should only use the original three (somatic, germline or fetal) as it codifies the testing context (i.e. inherited genetic testing, tumor testing, or fetal testing) Note the example controls both the SNOMED code and the LOINC LA code. Taken from: NCBI Variation Glossay https://www.ncbi.nlm.nih.gov/variation/docs/glossary/ and the 2013 HL7 V2 Clinical Genomics Implementation Guide
B.19	CWE	81304-8	Variant analysis method [Type]	2a	LA26398-0^ **Sequencing**^LN	O	[0..*]	**Answer List: LL4048-6** 1. Sequencing LA26398-0 2. Oligo aCGH LA26399-8 3. SNP Array LA26400-4 4. BAC aCGH LA26401-2 5. Curated LA26402-0 6. Digital Array LA26403-8

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TABLE 5-2 CLINICAL GENOMICS REPORT SECTION 2 - VARIABLES THAT DEFINE A DISCRETE VARIANT								
	OBX-2	OBX3.1	OBX3.2	OBX-4	OBX-5	LOINC Panel/Definitional Terms		
Label	Type	LOINC	LOINC Name	Sub ID	Example values†	R/O/C	Cardinality	Term Description
								7. FISH LA26404-6 8. Gene Expression Array LA26405-3 9. Karyotyping LA26406-1 10. MAPH LA26407-9 11. MassSpec LA26408-7 12. Merging LA26808-8 13. Multiple Complete Digestion LA26414-5 14. MLPA LA26415-2 15. Optical Mapping LA26417-8 16. PCR LA26418-6 17. qPCR (Real-time PCR) LA26419-4 18. ROMA LA26420-2 19. Denaturing high pressure liquid chromatography (DHPLC) LA26809-6 20. DNA hybridization LA26810-4 21. Computational analysis LA26811-2 22. Single-stranded conformational polymorphism (SSCP) LA26812-0 23. Restriction Fragment Length Polymorphism (RFLP) LA26813-8 The variable is especially important for structural variants because the precision of the start and end position of this kind of variation is determined so strongly by the type of method. Taken from NCBI's dbVAR data submission template. 2015 review of the newest methods at: PMCID: PMC4479793 and, Kitts A, Phan L, Ward M, et al. The Database of Short Genetic Variation (dbSNP) 2013 Jun 30 [Updated 2014 Apr 3]. In: The NCBI Handbook [Internet]. 2nd edition. Bethesda (MD): National Center for Biotechnology Information (US); 2013-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK174586/
Interpretations								
B.20	CNE	53037-8	Genetic sequence	2a	LA6668-3^**Pathogenic**^LN	O	[0..1]	**Answer List: LL4034-6** 1. Pathogenic LA6703-8

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TABLE 5-2 CLINICAL GENOMICS REPORT SECTION 2 - VARIABLES THAT DEFINE A DISCRETE VARIANT								
	OBX-2	OBX3.1	OBX3.2	OBX-4	OBX-5	LOINC Panel/Definitional Terms		
Label	Type	LOINC	LOINC Name	Sub ID	Example values†	R/O/C	Cardinality	Term Description
			variation clinical significance [Imp]					2. Likely pathogenic LA6704-6 3. Uncertain significance LA6705-3 4. Likely benign LA6706-1 5. Benign LA6707-9 Answer list taken from PMID 25741868 (PMCID: PMC4544753).
B.21	CWE	69548-6	Genetic variant Assessment	2a	LA9633-4^**Present**^LN	O	[0..1]	**Answer List: LL1971-2** 1. Present LA9633-4 2. Absent LA9634-2 3. No call LA18198-4 4. Indeterminate LA11884-6 Most genetic reporting of negatives is by default, the specific variants (or DNA ranges) tested are reported and only the positives are reported explicitly. For those who want to report interpretations on a set of specified locations whether normal or not, LOINC # 69548-6 is the term that enables this style of reporting, and it includes in its answer list the “no call” option. Thus it permits every examined loci to be described individually as present, absent, (no call), or indeterminate. Of note, ‘No Call’ is different from ‘Absent’, because ‘No Call’ did not result in the determination of the marker’s presence or absence. This may be due to test failure or specimen specific context, rendering the test ineffective. If "No Call" implies that 1) the assay failed or 2) the region of the chromosome/gene containing the sequence variation being genotyped is deleted. For instance, if a portion of the PTEN gene is deleted, then all assays for variants within the deleted region would be ‘no call’ rather than describing the finding then as deleted, because the assays covering this region of interest may have simply failed.

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TABLE 5-2 CLINICAL GENOMICS REPORT SECTION 2 - VARIABLES THAT DEFINE A DISCRETE VARIANT								
	OBX-2	OBX3.1	OBX3.2	OBX-4	OBX-5	LOINC Panel/Definitional Terms		
Label	Type	LOINC	LOINC Name	Sub ID	Example values†	R/O/C	Cardinality	Term Description
B.22	CWE	81259-4	Probable Associated Phenotype	2a	C1970173^**Acyl-CoA dehydrogenase family, member 9, deficiency of**^ MedGen-Dis	O	[0..1]	**Coding systems:** 1. SCT (SNOMED-CT) 2. I9CDX 3. I10C 4. MedGen-Dis 5. HPO (Human Phenotype Ontology) The disorder with which this variant is associated. Allows same coding systems as for disease assessed. The message implementer inserts the approved coding system in CWE.3. See descriptions of the coding systems in Table A.1 of the Appendix.
Allelic State/Phase Information								
B.23	CNE	53034-5	Allelic state	2a	LA6706-1^ **Heterozygous**^LN	C	[0..1]	**Answer List: LL381-5** 1. Heteroplasmic LA6703-8 2. Homoplasmic LA6704-6 3. Homozygous LA6705-3 4. Heterozygous LA6706-1 5. Hemizygous LA6707-9 This variable describes the relationship between the alleles found at the same locus on different chromosomes. It is not always reported. Answer list taken from the 2013 HL7 V2 Clinical Genomics Implementation Guide.
B.24	NM	81258-6	Allelic Frequency [NFr]	2a	**0.47**	C	[0..1]	Reports the fraction of all of the reads at this genomic location that were represented by the given allele. For homozygotes it will be close to 1.0; for heterozygotes it will be close to 0.5. It can be a smaller number when there are mosaics or multiple chromosome, or mixtures of tumor cells and normal cells.
B.25	NM	82121-5	Allelic read depth	2a	**208**	O	[0..1]	Specifies the number of reads that identified the allele in question whether it consists of one or a small sequence of contiguous nucleotides. Different methods and

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TABLE 5-2 CLINICAL GENOMICS REPORT SECTION 2 - VARIABLES THAT DEFINE A DISCRETE VARIANT								
	OBX-2	OBX3.1	OBX3.2	OBX-4	OBX-5	LOINC Panel/Definitional Terms		
Label	Type	LOINC	LOINC Name	Sub ID	Example values†	R/O/C	Cardinality	Term Description
								purposes require different numbers of reads to be acceptable. Often >400, sometimes as few as 2-4.
B.26	CWE	82120-7	Allelic phase	2a	LA6112-2^**1st set of variants in cis relation to each other**^LN	O	[0..1]	**Answer List: LL4025-4** 1. 1st set of variants in cis relation to each other LA26814-6 2. 2nd set of variants in cis relation to each other LA26815-3 3. 3rd set of variants in cis relation to each other LA26816-1 4. 4th set of variants in cis relation to each other LA26817-9 5. 5th set of variants in cis relation to each other LA26818-7 6. Maternal LA26320-4 7. Paternal LA26321-2 8. Unknown LA4489-6 9. Other LA46-8 Defines which variations are in cis relationship (on the same chromosome) to one another. The first and second set could be in cis relation to one another and yet not be on the same chromosome. Can accommodate trisomies, mosaics, and other special cases, and distinguish whether the chromosome is maternal or paternal when such details can be inferred (e.g. when the parent's genotype is also available).
B.27	CWE	82309-6	Basis for allelic phase [Type]	2a	LA26429-3^**Inferred from population data**^LN	O	[0..1]	**Answer List: LL4050-2** 1. Directly measured LA26426-9 2. Family DNA LA26427-7 3. Family history LA26428-5 4. Inferred from population data LA26429-3

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TABLE 5-2 CLINICAL GENOMICS REPORT SECTION 2 - VARIABLES THAT DEFINE A DISCRETE VARIANT								
	OBX-2	OBX3.1	OBX3.2	OBX-4	OBX-5	LOINC Panel/Definitional Terms		
Label	Type	LOINC	LOINC Name	Sub ID	Example values†	R/O/C	Cardinality	Term Description
								If the allelic phase LOINC 82120-7 (row B.26) is included, this observation should also be included. This identifies the evidential basis on which the allelic phase and/or the allelic state was concluded.

5.7.3 CLINICAL GENOMICS STRUCTURAL VARIANT ADDENDA

TABLE 5-3 CLINICAL GENOMICS STRUCTURAL VARIANT ADDENDA								
	OBX-2	OBX3.1	OBX3.2	OBX-4	OBX-5	LOINC Panel/Definitional Terms		
Label	Type	LOINC	LOINC Name	Sub ID	Example values†	R/O/C	Cardinality	Term Description
	N/A	81297-4	Structural variant addendum panel		This term identifies the set of LOINC terms that are part of this panel but is not, itself, part of the HL7 message. Moreover, the terms of this panel is specific to structural variants, and will not be included in the message per se.		[1..1]	Provides variables that are unique to structural variants, most of which are not routinely included in clinical reports.
B.28	NM	82155-3	Genomic structural variant copy number	2a.1	**1**	O	[0..1]	The copy number of the large variant when applicable. In HGVS, this is the numeric value following the "X". It is a unit-less value. Note that a copy number of 1 implies a deletion. The copy number can usually be inferred from the HGVS or ISCN fields.
B.29	NM	81299-0	Genomic structural variant reported arrCGH [Ratio]	2a.1	**0.48**	C	[0..1]	Usually only applicable to ArrCGH and related studies. Its value can be more or less than 1, depending on if the variant is a deletion or duplication.
B.30	NM	81300-6	Structural variant [Length]	2a.1	**1396929**	O	[0..1]	This content is uncommon in today's clinical reports. (The units of measure are base pairs.) A field in dbVar.
B.31	NR	81301-4	Structural variant outer start and end	2a.1	**13200589^15592000**	O	[0..1]	This content taken with inner start-end provides a way to describe the uncertainty in the edge positions of

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TABLE 5-3 CLINICAL GENOMICS STRUCTURAL VARIANT ADDENDA								
	OBX-2	OBX3.1	OBX3.2	OBX-4	OBX-5	LOINC Panel/Definitional Terms		
Label	Type	LOINC	LOINC Name	Sub ID	Example values†	R/O/C	Cardinality	Term Description
								structured variation. These are available in NCBI's dbVar file, not commonly reported today.
B.32	NR	81302-2	Structural variant inner start and end	2a.1	**14184616^15581544**	O	[0..1]	This content is uncommon in today's clinical reports. A field in dbVar.

5.7.4 CLINICAL GENOMICS REPORT SECTION 3 – COMPLEX VARIANTS

TABLE 5-4 CLINICAL GENOMICS REPORT SECTION 3 – COMPLEX VARIANTS								
	OBX-2	OBX3.1	OBX3.2	OBX-4	OBX-5	LOINC Panel/Definitional Terms		
Label	Type	LOINC	LOINC Name	Sub ID	Example values†	R/O/C	Cardinality	Term Description
C		81251-1	Complex genetic variant panel	3a	This term identifies the set of LOINC terms that are part of this panel but is not, itself, part of the HL7 message.	NA	[0..*]	Repeats for each complex variant. The LOINC panel code defines the set of variables that may be included to describe a single complex variant, but the code itself is not included in the message. Complex variants are made up of two or more simple variants which together have phenotypic implications. In the OBX's that follow OBX-4 increments by 1 for each repeated complex variant. The example only presents one complex variant.
C.1	CWE	81260-2	Complex genetic variant [ID]	3a	16895^**NM_000106.5(CYP2D): c.[886C>T;457G>C] – Haplotype**^ CLINVAR-V	C	[0..1]	**Coding System: CLINVAR-V** Following the pattern of simple variant, the code is the identifier from a public genetic database and the name is a concatenation of the RefSeq, the gene symbol, the HGVS describing the multiple variants, and the complex variant type.
C.2	CWE	81262-8	Complex variant HGVS name	3a	c.[886C>T;457G>C]^ **c.[886C>T;457G>C]**^ HGVS.c	C	[0..1]	**Coding System: HGVS.c** Includes HGVS.c for the separate variants that make this complex variant. The square bracket surrounding multiple variants indicates they are together on one chromosome. When each simple variant is surrounded by square brackets that means they are on separate chromosomes. HGVS syntax can also assert that the phase is unknown.

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TABLE 5-4 CLINICAL GENOMICS REPORT SECTION 3 – COMPLEX VARIANTS								
	OBX-2	OBX3.1	OBX3.2	OBX-4	OBX-5	LOINC Panel/Definitional Terms		
Label	Type	LOINC	LOINC Name	Sub ID	Example values†	R/O/C	Cardinality	Term Description
C.3	CWE	81263-6	Complex variant type	3a	LA26218-0^ **Haplotype**^LN	O	[0..1]	**Answer List: LL3991-1** 1. Compound heterozygous LA26217-2 2. Double heterozygous LA26220-6 3. Haplotype LA26218-0 4. Hemizygous LA6707-9
C.4	CWE	81259-4	Probable Associated Phenotype	3a	688395015^ **Debrisoquine adverse reaction (disorder)**^SCT	O	[0..1]	**Coding systems:** 1. SCT (SNOMED-CT) 2. I9CDX 3. I10C 4. MedGen-Dis 5. HPO (Human Phenotype Ontology)
C.5	CNE	53037-8	Genetic sequence variation clinical significance [Imp]	3a	LA6668-3^ **Pathogenic**^LN	O	[0..1]	See row B.20 for the description of LOINC #53037-8 Genetic sequence variation clinical significance. This is the significance of the many simple variants in the first complex variant taken together.
C.6	CNE	53034-5	Allelic state	3a	LA6706-1^ **Heterozygous**^LN	O	[0..1]	See row B.23 for the description of LOINC # 53034-5 Allelic state. But this is the allelic state of the many simple variants taken together in the complex variant. (It will not apply to all complex variant types).
C.7	CWE	82309-6	Basis for allelic phase [Type]	3a	LA26429-3^**Inferred from population data**^LN	O	[0..1]	See row B.27 for the description of LOINC# 82309-6 Basis for allelic phase.
D		81250-3	Discrete genetic variant panel	3a.1a	This term identifies the set of LOINC terms that are part of this panel but is not, itself, part of the HL7 message.	NA	[0..*]	See Table 5-2 for the complete definitions of each variable. The full HGVS for the complex variant in row C may be sufficient for many purposes in which case none of these children panels will be included. This child panel repeats for as many discrete variables as contained in the complex variant. We show a few of the variable in this discrete variation panel in the follow rows, but not the whole panel or any of the panels describing other constituents of this complex variant to save space. Full V2 examples appear in Section 5.6.

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TABLE 5-4 CLINICAL GENOMICS REPORT SECTION 3 – COMPLEX VARIANTS								
	OBX-2	OBX3.1	OBX3.2	OBX-4	OBX-5	LOINC Panel/Definitional Terms		
Label	Type	LOINC	LOINC Name	Sub ID	Example values†	R/O/C	Cardinality	Term Description
D.1	CWE	81252-9	Discrete genetic variant	3a.1a	31934^**NM_000106.5(CYP2D6):c.886C>T (p.Arg296Cys)**^CLINVAR-A	C	[1..1]	See Table 5-2 for the complete definitions of each variable.
D.2	CWE	51958-7	Transcript RefSeq ID	3a.1a	NM_000106.5^**NM_000106.5**^RefSeq-T	C	[0..1]	See row B.4 for the description and answer list in LOINC# 51958-7 Transcript RefSeq ID.
D.3	CWE	48004-6	DNA change c.HGVS	3a.1a	c.886C>T^**c.886C>T**^ HGVS.c	C	[0..1]	See row B.5 for the description and answer list in LOINC# 41103-3 DNA change c.HGVS.
D.4	CWE	48005-3	Amino acid change p.HGVS	3a.1a	p.Arg296Cys ^ **p.Arg296Cys** ^HGVS.p	C	[0..1]	See row B.6 for the description and answer list in LOINC# 48005-3 Amino acid change p.HGVS.
D.5	CWE	48019-4	DNA change [Type]	3a.1a	LA6990-7^ **Substitution**^LN	O	[0..1]	See row B.7 for the description and answer list in LOINC# 48019-4 DNA change [Type].
D.6	CWE	48006-1	Amino acid change [Type]	3a.1a	LA6698-0^**Missense**^LN	O	[0..1]	See row B.8 for the description and answer list in LOINC# 48006-1 Amino acid change [type].
E		81250-3	Discrete genetic variant panel	3a.2a	This term identifies the set of LOINC terms that are part of this panel but is not, itself, part of the HL7 message.	NA	[0..*]	See Table 5-2 for the complete definitions of each variable.
E.1	CWE	81252-9	Discrete genetic variant	3a.2a	38486^**NM_000106.5(CYP2D6):c.1457G>C (p.Ser486Thr)**^CLINVAR-V	C	[1..1]	See LOINC# 81252-9 in row B.1 description and answer list.
E.2	CWE	51958-7	Transcript RefSeq ID	3a.2a	NM_000106.5^**NM_000106.5**^RefSeq-T	C	[0..1]	See row B.4 for the description and answer list in LOINC# 51958-7 Transcript RefSeq ID.
E.3	CWE	48004-6	DNA change c.HGVS	3a.2a	c.1457G>C^**c.1457G>C**^ HGVS.c	C	[0..1]	See row B.5 for the description and answer list in LOINC# 41103-3 DNA change c.HGVS.

Note that to save space, we did not put in the full details for the second discrete variant that comprises the complex variant. Please see Table 5-2 for the complete overview and definition of each variable under a discrete variant.

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5.7.5 CLINICAL GENOMICS REPORT SECTION 4 – PHARMACOGENOMICS STUDIES

TABLE 5-5 CLINICAL GENOMICS REPORT SECTION 4 – PHARMACOGENOMICS STUDIES								
	OBX-2	OBX3.1	OBX3.2	OBX-4	OBX-5	LOINC Panel/Definitional Terms		
Label	Type	LOINC	LOINC Name	Sub ID	Example values†	R/O/C	Cardinality	Term Description
F	N/A	82118-1	Pharmacogenomics results panel		This term identifies the set of LOINC terms that are part of this panel but is not, itself, part of the HL7 message.		[0.*]	Will repeat for each gene tested
Results for 1st gene of study								
F.1.a	CNE	48018-6	Gene studied [ID]	4a.a	2623^**CYP2C9**^ HGNC-Symb		[1..*]	**Coding system: HGNC-Symb** Identifies the gene or genes known to influence drug metabolism or efficacy being tested for relevant variants. In some cases, such as in the example of CYP2C9 and VKORC1, changes in more than one gene are required to cause the reported effect on a specific drug's metabolism or efficacy, but they will still be listed in separate OBX-5 fields.
F.2.a	ST	84413-4	Genotype display name	4a.a	***2/*5**		[1..*]	In this context, the corresponding alleles for each of the genes listed under gene(s) studied are also shown separated by a slash e.g., *1/*2 as is the common format. The genotype is almost always reported as a pair of star alleles in pharmacogenomics studies. If the metabolism/efficacy effect is based on 2 genes, the results for each gene are shown in separate OBXs and related to the gene via the same OBX-4 content. The implication variables e.g., 53040-2 the effect on metabolism, 51961-1 the effect on efficacy, or 83009-1 risk for hypersensitivity, specify the combined effect of the multiple alleles recorded in this panel. This content will be displayed using separate OBX-5 fields.
F.1.b	CNE	48018-6	Gene studied [ID]	4a.b	23663^**VKORC1**^ HGNC-Symb		[1..*]	See row F.1.a for description for LOINC# 48018-6 Gene studied [ID].
F.2.b	ST	84413-4	Genotype display name	4a.b	***A/*A**		[1..*]	See row F.2.a for description for LOINC# 84413-4 Genotype display name.

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TABLE 5-5 CLINICAL GENOMICS REPORT SECTION 4 – PHARMACOGENOMICS STUDIES								
	OBX-2	OBX3.1	OBX3.2	OBX-4	OBX-5	LOINC Panel/Definitional Terms		
Label	Type	LOINC	LOINC Name	Sub ID	Example values†	R/O/C	Cardinality	Term Description
F.3	CNE	53040-2	Genetic variation's effect on drug metabolism	4a	LA9657-3^**Rapid metabolizer**^LN	C	[0..1]	**Answer List: LL3856-3** 1. Ultrarapid metabolizer LA10315-2 2. Rapid metabolizer LA25390-8 3. Normal metabolizer LA25391-6 4. Intermediate metabolizer LA10317-8 5. Poor metabolizer LA9657-3 If this variable has repeats they should each be reported in a separate OBX-5 using the dot notation as 3.1a, 3.1.b, etc. For pharmacogenomics studies, one of, 53040-2 (effect on drug metabolism) and/or 51961-1 (effect on drug efficacy) must be included in the panel. Answer list comes from CPIC, a professional society (https://cpicpgx.org/wp-content/uploads/2016/01/CPIC_term_standardization_project_final_terms.pdf).
F.4	CWE	51961-1	Genetic variation's effect on drug efficacy	4a	NA	C	[0..1]	**Answer List: LL539-8** 1. Resistant LA6676-6 2. Responsive LA6677-4 3. Presumed resistant LA9660-7 4. Presumed responsive LA9661-5 5. Unknown significance LA6682-4 6. Benign LA6675-8 7. Presumed Benign LA6674-1 8. Presumed non-responsive LA9662-3 For pharmacogenomics studies, either 53040-2 (effect on drug metabolism) and/or 51961-1 (effect on drug efficacy) and or 83009-1 risk for hypersensitivity must be included in the panel. Answer list comes from the 2013 HL7 V2 Clinical Genomics Implementation Guide.

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TABLE 5-5 CLINICAL GENOMICS REPORT SECTION 4 – PHARMACOGENOMICS STUDIES								
	OBX-2	OBX3.1	OBX3.2	OBX-4	OBX-5	LOINC Panel/Definitional Terms		
Label	Type	LOINC	LOINC Name	Sub ID	Example values†	R/O/C	Cardinality	Term Description
F.5	CWE	83009-1	Genetic variation's effect on high-risk allele	4a	Pending	C	[0..1]	**Answer list: LL2353-2** 1. Low risk LA19542-2 2. High risk LA19541-4 Reports the risk that occurs with the drug specificity in row F.1 (LOINC 51963-7 Medication assessed [ID]), when some variants, e.g. HLA alleles, are present, or the variant RYR1 which causes malignant hyperthermia. PMID: 17620823
Medication Panel								
G	-	82117-3	Medication usage implications panel	4a.1	This term identifies the set of LOINC terms that are part of this panel but is not, itself, part of the HL7 message.	O	[0..*]	This panel provides guidance about drugs assessed in relation to variations observed in the above gene. It groups the set of variables that maybe reported per medication assessed, but is not itself included in the message. The set of variables that follow, or more extensive information can also be included as part of the results within the overall report PDF as it is commonly done now (See LOINC 51969-4 Genetic analysis report in row A.10 is provided for that purpose).
G.1	CWE	51963-7	Medication assessed [ID]	4a.1	11289^**Warfarin**^ RxT-Ingrd	R	[1..1]	**Coding system: RxT-Ingrd** This variable identifies the medication about which assessments will be made in the next two fields. Required if medication usage panel is employed.

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TABLE 5-5 CLINICAL GENOMICS REPORT SECTION 4 – PHARMACOGENOMICS STUDIES								
	OBX-2	OBX3.1	OBX3.2	OBX-4	OBX-5	LOINC Panel/Definitional Terms		
Label	Type	LOINC	LOINC Name	Sub ID	Example values†	R/O/C	Cardinality	Term Description
G.2	CWE	82116-5	Medication usage suggestion [Type]	4a.1	LA26421-0^ **Consider Alternative Medications not contraindicated or impacted by gene**^LN	C	[0..1]	**Answer List: LL4049-4** 1. Consider Alternative Medications not contraindicated or impacted by gene LA26421-0 2. Decrease Dose and titrate to response LA26422-8 3. Increase Dose and titrate to response if appropriate LA26423-6 4. Use with caution LA26424-4 5. Use standard dose LA26425-1 This variable (48005-3) or the following 83010-9 "Medication usage suggestion [narrative] should be included when any drug is named in Row E1.1. Answer list derived from example report with advice from CPIC expert.
G.3	TX	83010-9	Medication usage suggestion [Narrative]	4a.1	**May need higher dosage than usual.**	C	[0..1]	Used to deliver whatever specific content, in narrative, laboratories want to deliver. At least one of the medication usage type or narrative variables should be included when the panel is implemented.

5.7.6 CLINICAL GENOMICS REPORT SECTION 5 – GLOSSARY FOR HAPLOTYPE DEFINITION

TABLE 5-6 CLINICAL GENOMICS REPORT SECTION 5 – GLOSSARY FOR HAPLOTYPE DEFINITION								
	OBX-2	OBX3.1	OBX3.2	OBX-4	OBX-5	LOINC Panel/Definitional Terms		
Label	Type	LOINC	LOINC Name	Sub ID	Example values†	R/O/C	Cardinality	Term Description
H		83011-7	Haplotype definition panel	5a	This term identifies the set of LOINC terms that are part of this panel but is not, itself, part of the HL7 message.		[0..*]	This panel defines the variables that are reported for each haplotype.

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TABLE 5-6 CLINICAL GENOMICS REPORT SECTION 5 – GLOSSARY FOR HAPLOTYPE DEFINITION								
	OBX-2	OBX3.1	OBX3.2	OBX-4	OBX-5	LOINC Panel/Definitional Terms		
Label	Type	LOINC	LOINC Name	Sub ID	Example values†	R/O/C	Cardinality	Term Description
Haplotype Gene and Name								
H.1	CNE	48018-6	Gene studied [ID]	5a.a	2623^**CYP2C9**^ HGNC-Symb		[1..*]	**Coding system: HGNC-Symb** Identifies the genes known to influence drug metabolism or efficacy being tested for relevant variants.
H.2	CWE	84414-2	Haplotype name	5a.a	***18**	O	[0..*]	Usually used to report star alleles.
Defines the discrete variants that constitute the haplotype								
I		81250-3	Discrete genetic variant panel	5a.1a	This term identifies the set of LOINC terms that are part of this panel but is not, itself, part of the HL7 message.		[1..*]	This panel repeats for as many discrete variants as are constituents of the haplotype as defined by the reporting lab. The definition may vary across reporting laboratories. We show a very compact example using only SNP codes and alt allele to define the variations. But reporting laboratories can use any of the variables listed in Table 5-2 for this purpose, and can repeat the panel for as many variations that define the haplotype.
I.1	ID	81255-2	dbSNP ID	5a.1a	1057910^ **rs1057910** ^dbSNP	O	[0..1]	See row B.15 for the description of LOINC# 81255-2 dbSNP ID.
I.2	ST	69551-0	Genomic alt allele [ID]	5a.1a	**C**	C	[0..1]	See row B.13 for the description of LOINC# 69551-0 Genomic alt allele [ID].
J		81250-3	Discrete genetic variant panel	5a.2a	This term identifies the set of LOINC terms that are part of this panel but is not, itself, part of the HL7 message.		[1..*]	See row I for the description of LOINC# 81250-3 Discrete genetic variant panel.
J.1	ID	81255-2	dbSNP ID	5a.2a	72558193^ **rs72558193**^dbSNP	O	[0..1]	See row B.15 for the description of LOINC# 81255-2 dbSNP ID.
J.2	ST	69551-0	Genomic alt allele [ID]	5a.2a	**C**	C	[0..1]	See row B.13 for the description of LOINC# 69551-0 Genomic alt allele [ID].
K		81250-3	Discrete genetic variant panel	5a.3a	This term identifies the set of LOINC terms that are part of this panel but is not, itself, part of the HL7 message.		[1..*]	See row I for the description of LOINC# 81250-3 Discrete genetic variant panel.
K.1	ID	81255-2	dbSNP ID	5a.3a	1057911^ **rs1057911**^dbSNP	O	[0..1]	See row B.15 for the description of LOINC# 81255-2 dbSNP ID.

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TABLE 5-6 CLINICAL GENOMICS REPORT SECTION 5 – GLOSSARY FOR HAPLOTYPE DEFINITION								
	OBX-2	OBX3.1	OBX3.2	OBX-4	OBX-5	LOINC Panel/Definitional Terms		
Label	Type	LOINC	LOINC Name	Sub ID	Example values†	R/O/C	Cardinality	Term Description
K.2	ST	69551-0	Genomic alt allele [ID]	5a.3a	**T**	C	[0..1]	See row B.13 for the description of LOINC# 69551-0 Genomic alt allele [ID].

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5.8 Message Content Model As A Data Capture Form

To provide an easy overview of the content of the LRI_CG_Component, the Lister Hill National Center for Biomedical Communications (LHNCBC) at the U.S. National Library of Medicine has developed a web-based JavaScript tool called LHC-Forms[9], which generates input forms, based on definition files, for Web-based applications. LHC-Forms carries all of the observations that may be included in the Clinical Genomics component of the HL7 message. Users can access this model and generate HL7 messages through https://lhc-forms.lhc.nlm.nih.gov/81247-9, which contains LOINC codes and their answers, as well as links to the coded data sources in the Clinical Table Search Service, a web service software programs can use for querying clinical data tables like ICD-10-CM or ClinVar Alleles (found here: https://clin-table-search.lhc.nlm.nih.gov) for the look-up fields. Entering text into a field for a categorical observation in this form options (derived from the LOINC short answer lists or the coding system) appear as choices for auto-completion.

Figure 5-2, below, shows a screenshot of LHC-Forms, with the input fields filled for Discrete Variants. When a variation registered in ClinVar is chosen under the "Discrete genetic variant panel", as shown in the third field (LOINC 81252-9), many of its related fields are auto-populated from the ClinVar Clinical Search table in LHC forms. Users may also choose between NCBI and COSMIC identifiers for a few types of variables. In most cases, LHC-Forms assumes a default coding system for each variable, but V2 message implementers are free to insert the other coding systems associated with a given LOINC code as shown in Table 5-1 through Table 5-6 when they construct their messages directly.

Some of the coding systems are full enumerations and can be found in tables at their sources' web site (which are linked in Table 14-1. Clinical Genomics Coding Systems). These tables of enumerated codes are in some cases quite large (e.g. dbSNP's table carries 150 million rows). Others (e.g. UCUM, HGVS and ISCN) are defined by a syntax, and can't be fully enumerated though tables with common subsets of such codes may be available. Syntax validity checkers are available for UCUM (https://ucum.nlm.nih.gov/ucum-lhc/) and for HGVS (https://mutalyzer.nl).

Note that the LHC Clinical Table Search Service does not provide, or have readily accessible, tables for all potential coding systems in this guide. For example, the star alleles do not have a complete and consistent publically available table.

[9] Ye Wang Y, Lynch P, Kanduru A, Hook J, Mericle L, Ludet C, Vreeman DJ, Clement J. McDonald CJ. LHC-Forms and Related Widgets for Capturing and Tuning Health Data. AMIA Annu Symp Proc. 2016 (Accepted).

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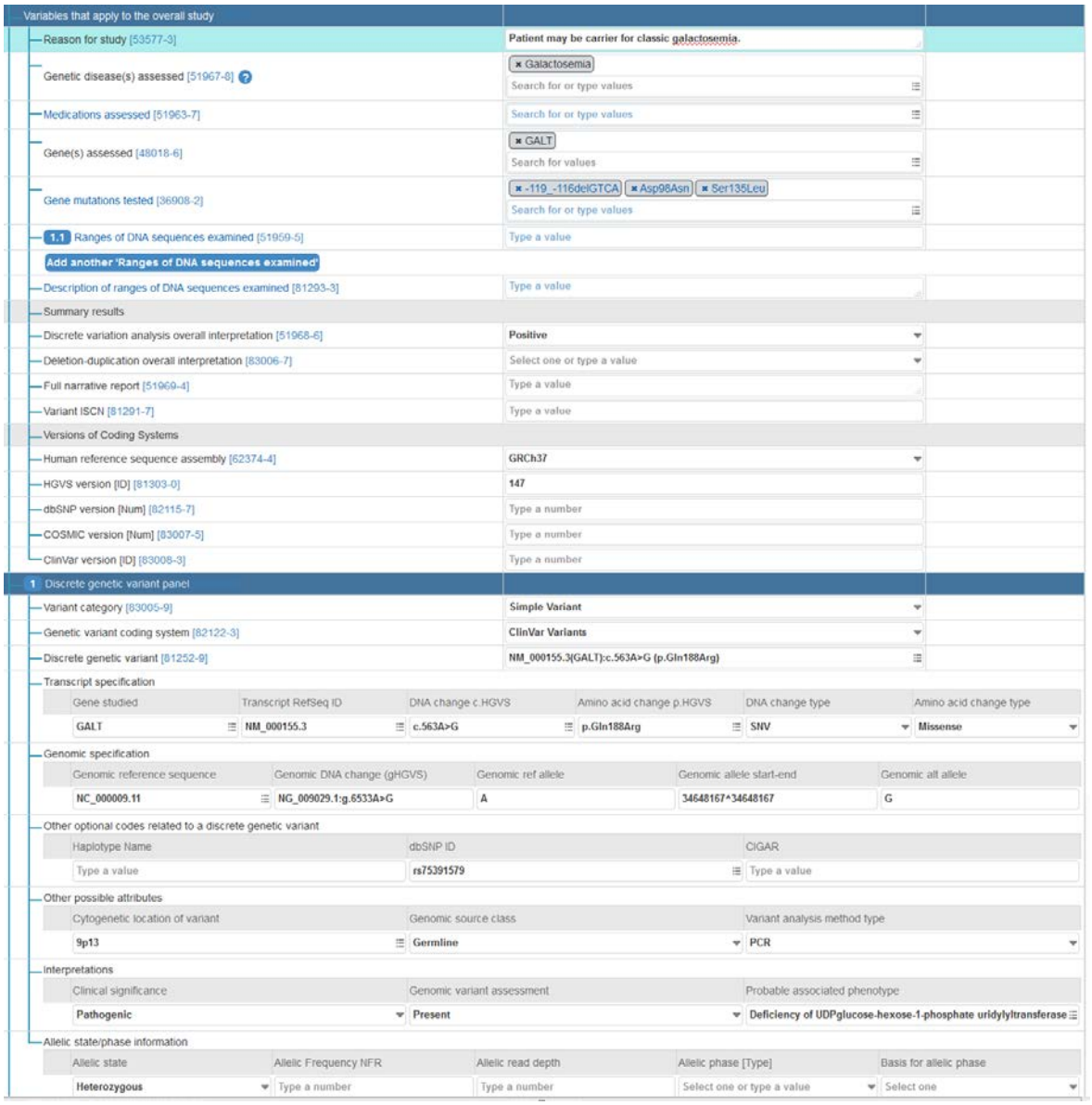

Figure 5-2. Screenshot Of LHC-Forms Widget For The LRI_CG_Component

The URL for the page that shows what you can do with these Clinical Table Search Services is available at: http://lhncbc.github.io/autocomplete-lhc/ and a developer's page is available at: https://lhncbc.github.io/autocomplete-lhc/docs.html**.**

The URLs for search service and for direct download of specific tables also appear in Table 14-1. Clinical Genomics Coding Systems). The URL for the UCUM validator developer's page is available at: https://github.com/lhncbc/ucum-lhc. The programs that deliver these autocomplete look-ups are available as open source as either JavaScript widgets or services from GitHub.

5.9 Example Messages

This section presents example V2 messages to illustrate the use of this specification for a variety of different genetic tests. These example messages are in a shortened form, leaving out the early segments like MSH and PID, which will not change across the examples, and have only populated the most important payload fields of the OBX segments, i.e., OBX-1 through OBX-6, to focus on the salient features of the examples.

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The example messages of the variants are in the order of the five sections of the clinical genetics report. Please note that there are multiple examples for each variant, with each example addressing the different ways to report the kind of variant. The example messages were taken from published and harmonized sample reports. Much thanks to the vendors who posted example reports with positive findings on the web.

Some example messages use laboratory tests that do not have LOINC codes, so they are labeled as "Sample Orderable Test" without a LOINC code number attached.

Note that in LOINC 81254-5 "Genomic allele start-end", when the variation is at a single locus, the start and end locations of the allele have the same value, e.g. "37070354^37070354" to show the locations are the same. The data type also allows the location to be reported as a single number, e.g. "37070354."

Also, for LOINC 69551-0 "Genomic alt allele," when the alt allele is absent, the message shows "-", as recommended by the Variant Call Format from IGSR: The International Genome Sample Resource.

Note that in a complex variant example, some alleles are submitted with a complex variant as one package, and such variants have not yet been assigned IDs. So in these cases, the LOINC 81252-9 "Simple Variant" field uses the allele ID rather than the variation ID as a temporary expedient. These variants will be assigned variant IDs by NCBI.

Note that on Clinvar, all variants are assigned variation IDs in the database. However, their website does not yet still all show variation IDs for the child variants in a complex variant

For all examples of discrete variant examples in this guide, the variation ID is used in the LOINC 81252-9 "Discrete Variant" field.

In the example messages, the text is selectively bolded to facilitate their reading. The bolded italic black text are to highlight the panel and subpanel subject headings, as well as explanatory comments within the message examples. The LOINC name and the example values are bolded in black text, and the OBX-4 numbering is bolded in red text. Note that real HL7 messages would not have bolded or italicized text.

5.9.1 DISCRETE GENETIC VARIANT EXAMPLE MESSAGES

5.9.1.1 FOUND DISCRETE VARIANT – MUTATION ANALYSIS OF ONE GENE BY SEQUENCING

The narrative text illustrates a sample report on Galactosemia Gene Analysis. The example shows that a heterozygous and known pathogenic variation was identified, indicating that the individual may be a carrier for galactosemia.

Note that the real tests will test for several gene variants. For brevity, this example lists only three of the gene variants tested, but actual reports would list every variant tested in a separate OBX field.

Example Gene Variant 1

```
OBR|1|Acme23469|Gen825750|42318-6^GALT gene targeted mutation
analysis^LN|R|201608030830|201608091650|

Variables that Apply to Overall Study: Report Section 1

OBX|1|TX|53577-3^Reason for study^LN|1|Patient may be carrier for
classic galactosemia.|

OBX|2|CWE|51967-8^Genetic disease(s) assessed^LN|1|
C0016952^Galactosemia^MedGen-Dis|
```


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OBX|3|CWE|51958-7^**Transcript reference sequence [Identifier]**^LN|**1|**
NM_000249^**NM_000249**^RefSeq-T|

OBX|4|CNE|48018-6^**Gene studied [ID]**^LN|**1.a|**4135^**GALT**^HGNC-Symb|

OBX|5|CWE|36908-2^**Gene mutations tested**^LN|**1.a|**-119_-116delGTCA^**-119_-116delGTCA**^HGVS.c|

OBX|6|CWE|36908-2^**Gene mutations tested**^LN|**1.b|**
Asp98Asn^**Asp98Asn**^HGVS.p|

OBX|7|CWE|36908-2^**Gene mutations tested**^LN|**1.c|**
Gln188Arg**^Gln188Arg**^HGVS.p |

OBX|8|CNE|51968-6^**Discrete variation analysis overall interpretation**^LN|**1|**LA6576-8^**Positive**^LN|

OBX|9|FT|51969-4^**Full narrative report**^LN|**1|Result Summary**-Positive \.br\\.br\ **Result** – The following heterozygous alteration was identified: Amino Acid change: p.Q188R (Gln188Arg). DNA change: c.563A>G (g.34648167), **Classification:** PATHOGENIC \.br\\.br\ **Interpretation -** Biochemical and molecular test results are in agreement. The observed GALT enzyme activity in red blood cells (12.2 nmol/h/mg Hb) and the presence of a single copy of p.Q188R suggest that this individual is a carrier of classic galactosemia. This individual should not be at risk for developing symptoms related to this disorder; however, he or she may be at risk for having offspring with galactosemia. If appropriate, enzymatic and molecular studies for this individual's reproductive partner are recommended to further clarify this risk. \.br\\.br\ **Method** - A multiplex PCR-based assay was used to test for the presence of the following mutations in the GALT gene.|

Technical details

OBX|10|CWE|62374-4^**Human reference sequence assembly**^LN|**1|**LA14029-5^**GRCh37**^LN|

OBX|11|NM|82115-7^**dbSNP version**^LN|**1|147|**

Attributes of Discrete Genetic Variants: Report Section 2

OBX|12|CNE|83005-9^**Variant Category**^LN|**2a|**LA26801-3^**Simple Variant**^LN|

OBX|13|CNE|81252-9^**Discrete genetic variant**^LN|**2a|**
3614^**NM_000155.3(GALT):c.563A>G(p.Gln188Arg)**^ClinVar-V|

Transcript Specification Variables

OBX|14|CWE|48018-6^**Gene studied**^LN|**2a|**3614^**GALT**^HGNC-Symb|

OBX|15|CWE|51958-7^**Transcript RefSeq ID**^LN|**2a|**
NM_000155.3^**NM_000155.3**^RefSeq-T|

OBX|16|CWE|41103-3^**Transcript DNA Change (cHGVS)**^LN|**2a|**
c.563A>G^**c.563A>G**^HGVS.c|

OBX|17|CWE|48005-3^**Amino acid change p.HGVS**^LN|**2a|**
p.Gln188Arg^**p.Gln188Arg**^HGVS.p|

OBX|18|CWE|48019-4^**DNA change type**^LN|**2a|**LA6690-7^**Substitution**^LN|

OBX|19|CWE|48006-1^**Amino Acid change type|2a|**LA6698-0^**Missense**^LN|

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```
Genomic specification (HGVS code and VCF-like representation)
OBX|20|CWE|48013-7^Genomic reference sequence^LN|2a|
NG_009029.1:g.6533A>G^NG_009029.1:g.6533A>G^RefSeq-G|
OBX|21|CWE|81290-9^Genomic DNA change(gHGVS)^LN|2a|
NC_000009.11:g.34648167A>G^NC_000009.11:g.34648167A>G^HGVS.g|
OBX|22|ST|69547-8^Genomic ref allele^LN|2a|A|
OBX|23|NR|81254-5^Genomic allele start-end^LN|2a|34648167^34648167|
OBX|24|ST|69551-0^Genomic alt allele^LN|2a|G|
Other variables
OBX|25|CNE|81255-2^dbSNP ID^LN|2a|rs75391579^rs75391579^dbSNP|
OBX|26|CWE|48001-2^Cytogenetic (chromosome) location^LN|2a|
9p13^9p13^Chrom-Loc|
OBX|27|CNE|48002-0^Genomic source class^LN|2a|LA6683-2^Germline^LN|
OBX|28|CNE|81304-8^Variant analysis method type^LN|2a|LA26418-
6^PCR^LN|
Interpretations
OBX|29|CNE|53037-8^Genetic variation clinical significance^LN|2a|
LA6668-3^Pathogenic^LN|
OBX|30|CNE|69548-6^Genetic variant assessment^LN|2a|LA9633-
4^Present^LN|
OBX|31|CWE|81259-4^Probable associated phenotype^LN|2a|
C0268151^Deficiency of UDPglucose-hexose-1-phosphate
uridylyltransferase^MedGen-Dis|
Allelic state/phase information
OBX|32|CNE|53034-5^Allelic state^LN|2a|LA6706-1^Heterozygous^LN|
```

5.9.1.2 FOUND DISCRETE – TARGETED MUTATIONS ANALYSIS THAT STUDIES MANY MUTATIONS (106)

The following example illustrates a sample report on Cystic Fibrosis Analysis. A heterozygous and known pathogenic variation was identified, which indicated the individual may be a carrier for cystic fibrosis.

Note that in LOINC 36908-2 “Gene mutations tested,” some reports will report variants as pure HGVS strings without the reference sequence and used the older amino acid representations as shown: deltaF508, delta I507, W1282X (TGG>TGA), 621+1G>T. This example replaces the pure HGVS strings with ClinVar variant IDs and also converts all of the amino acid one letter abbreviations to three letter abbreviations as required by today’s HGVS. For the variation, “W1282X (TGG>TGA),” the text reported an amino acid change to “X”, which represents a nonsense variant with the “X” signaling a terminate code. Currently, the three letter HGVS version uses a “*” or “Ter” in place of the “X” and this example uses a “Ter,” e.g. “Gly542Ter.”

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The example includes the full HGVS expression and ClinVar ID just to show how a full expression in the list of variants targeted would look and to illustrate the fact that different coding systems can be used for different elements in the list. The other variants listed depend on the "Transcript reference sequence [Identifier]" for their reference sequence, and are a mix of HGVS.c, HGVS.p and raw text, which is the exception referenced in the "Coding with Exception" data type. In the current laboratory standard, such raw text goes into CWE.9 – the "original text" field and is preceded by eight carets, "^^^^^^^^". Be aware that some in the V2 community believe it should go into CWE.2 – with nulls in CWE.1 and CWE.3. But because this is a laboratory message, the example uses the CWE.9 convention. A case in point is the variation,"the deletion of exons 2-3" is recorded as "^^^^^^^^the deletion of exons 2-3".

As per the guide, this example populates both CWE.1 and CWE.2 with the same string when the coding system does not have a name (print string) that is distinct from the code.

Note that the real tests will test for several gene variants. For brevity, this example lists only ten of the gene variants tested, but actual reports would list every variant tested in a separate OBX field.

Example Gene Variant 2

```
OBR|1|Acme23469|Gen825750|38404-0^CFTR gene targeted mutation
analysis in Blood or Tissue by Molecular genetics method
Narrative^LN|R|201608030830|201608091650|

Variables that Apply to Overall Study: Report Section 1

OBX|1|TX|53577-3^Reason for study^LN|1|Patient may be carrier for
cystic fibrosis|

OBX|2|CWE|51967-8^Genetic disease(s) assessed^LN|1|C0010674^Cystic
fibrosis^MedGen-Dis|

OBX|3|CWE|51958-7^Transcript reference sequence [Identifier]^LN|1|
NM_000492.3^NM_000492.3^RefSeq-T

OBX|4|CNE|48018-6^Gene studied^LN|1.a|1884^CFTR^HGNC-Symb|

OBX|5|CWE|36908-2^Gene mutations tested^LN|1.a|
7105^NM_000492.3(CFTR):c.1521_1523delCTT (p.Phe508delPhe)^ClinVar-V|

OBX|6|CWE|36908-2^Gene mutations tested^LN|1.b|
7106^NM_000492.3(CFTR):c.1519_1521delATC(p.Ile507del)^ClinVar-V|

OBX|7|CWE|36908-2^Gene mutations tested^LN|1.c|
7129^NM_000492.3(CFTR):c.3846G>A (p.Trp1282Ter)^ClinVar-V|

OBX|8|CWE|36908-2^Gene mutations tested^LN|1.d|
38799^NM_000492.3(CFTR):c.489+1G>T^ClinVar-V|

OBX|9|CWE|36908-2^Gene mutations tested^LN|1.e|
Gly542Ter^Gly542Ter^HGVS.p|

OBX|10|CWE|36908-2^Gene mutations tested^LN|1.f|
Arg117His^Arg117His^HGVS.p|

OBX|11|CWE|36908-2^Gene mutations tested^LN|1.g|
711+1G>T^711+1G>T^HGVS.c|

OBX|12|CWE|36908-2^Gene mutations tested^LN|1.h|
Asn1303Lys(C>A)^Asn1303Lys(C>A)^HGVS.p|
```


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OBX|13|CWE|36908-2^**Gene mutations tested**^LN|**1.i|**
Arg334Trp^**Arg334Trp**^HGVS.p|

OBX|14|CWE|36908-2^**Gene mutations tested**^LN|**1.j|**
Arg347Pro^**Arg347Pro**^HGVS.p|

OBX|15|CWE|36908-2^**Gene mutations tested**^LN|**1.k|**^^^^^^^^**the deletion of exons 2-3**|

OBX|16|CNE|51968-6^**Discrete variation analysis overall interpretation**^LN|**1**|LA6576-8^**Positive**^LN|

OBX|17|FT|51969-4^**Full narrative report**^LN|**1|Result Summary-**
Positive. \.br\\.br\ **Result-** The following heterozygous sequence change was identified. Amino Acid: p.F508del (Phe508del), DNA change: c.1521_1523delCTT (g.117199646_117199648), Classification: Pathogenic. \.br\\.br\ **Interpretation-** This result indicates that this individual is a carrier of cystic fibrosis (CF). This interpretation assumes that this individual is not clinically affected with CF. Since a mutation has been identified, genetic testing of at risk family members could be considered. If appropriate, genetic testing should be offered to this individual's reproductive partner to further clarify their risk of having a child with CF. \.br\\.br\ **Method-** A multiplex PCR based was used to detect 106 mutations, including the 23 mutations specified in the American College of Medical Genetics (ACMG) standards for population based carrier screening...Poly T determination and confirmatory testing of homozygous results are performed as reflex tests when appropriate.|

Technical details

OBX|18|CWE|62374-4^**Human reference sequence assembly**^LN|**1|**
LA14029-5^**GRCh37**^LN|

OBX|19|NM|82115-7^**dbSNP version**^LN|**1|147**|

Attributes of Discrete Genetic Variants: Report Section 2

OBX|20|CNE|83005-9^**Variant Category**^LN|**2a|**LA26801-3^**Simple Variant**^LN|

OBX|21|CNE|81252-9^**Discrete genetic variant**^LN|**2a|**
7105^**NM_000492.3(CFTR):c.1521_1523delCTT (p.Phe508delPhe)**^ClinVar-V|

Transcript Specification Variables

OBX|22|CWE|48018-6^**Gene studied**^LN|**2a|**1884^**CFTR**^HGNC-Symb|

OBX|23|CWE|51958-7^**Transcript RefSeq ID**^LN|**2a|**
NM_000492.3^**NM_000492.3**^RefSeq-T|

OBX|24|CWE|41103-3^**Transcript DNA Change (cHGVS)**^LN|**2a|**
c.1521_1523delCTT^**c.1521_1523delCTT**^HGVS.c|

OBX|25|CWE|48005-3^**Amino acid change p.HGVS**^LN|**2a|**
p.Phe508delPhe^**p.Phe508delPhe**^HGVS.p|

OBX|26|CWE|48019-4^**DNA change type**^LN|**2a|**LA6692-3l^**deletion**^LN|

Genomic specification (HGVS code and VCF-like representation)

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```
OBX|27|CWE|48013-7^Genomic reference sequence ID^LN|2a|
NG_016465.4:g.98809_98811delCTT^NG_016465.4:g.98809_98811delCTT^RefSeq-G|

OBX|28|CWE|81290-9^Genomic DNA change(gHGVS)^LN|2a|
NC_000007.13^NC_000007.13^HGVS.g|

OBX|29|ST|69547-8^Genomic ref allele^LN|2a|CTT|

OBX|30|NR|81254-5^Genomic allele start-end^LN|2a|
117199646^117199648|

OBX|31|ST|69551-0^Genomic alt allele^LN|2a|-|

Other variables

OBX|32|CNE|81255-2^dbSNP ID^LN|2a|rs113993960^rs113993960^dbSNP|

OBX|33|CWE|48001-2^Cytogenetic (chromosome) location^LN|2a|
7q31.2^7q31.2^Chrom-Loc|

OBX|34|CNE|48002-0^Genomic source class^LN|2a|LA6683-2^Germline^LN|

Interpretations

OBX|35|CNE|53037-8^Genetic variation Clinical significance^LN|2a|
LA6668-3^Pathogenic^LN|

OBX|36|CNE|69548-6^Genomic variant assessment^LN|2a|LA9633-
4^Present^LN|

OBX|37|CWE|81259-4^Probable associated phenotype^LN|2a|
C0010674^Cystic fibrosis^MedGen-Dis|

Allelic state/phase information

OBX|38|CNE|53034-5^Allelic state^LN|2a|LA6706-1^Heterozygous^LN|
```

5.9.1.3 SIMPLE VARIANT – MUTATION ANALYSIS WITH SEQUENCE PLUS DELETION-DUPLICATION STUDY

The following example illustrates a full gene analysis for MLH1 where a heterozygous and known pathogenic variation was identified, which results in a diagnosis of Lynch Syndrome.

Note that in this example, in LOINC 81252-9 “Simple variant”, the HGVS expression includes “Profs” which references Proline and a frameshift variation (this notation is found in the HGVS manual).

Example Gene Variant 3

```
OBR|1|Acme23469|Gen825750|Sample Orderable Test]^MLH1 gene
deletion+duplication and full mutation analysis in Blood or Tissue
by Molecular genetics method Narrative
^LN|R|201608030830|201608091650|

Variables that Apply to Overall Study: Report Section 1

OBX|1|TX|53577-3^Reason for study^LN|1|Patient may have Lynch
Syndrome|

OBX|2|CWE|51967-8^Genetic disease(s) assessed^LN|1|C0009405^Lynch
```


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syndrome^MedGen-Dis|

OBX|3|CWE|51958-7^**Transcript reference sequence [Identifier]**^LN|**1|**
NM_000249^**NM_000249**^RefSeq-T|

OBX|4|CNE|48018-6^**Gene studied**^LN|**1.a|**7127^**MLH1**^HGNC-Symb|

OBX|5|TX|81293-3^**Description of ranges of DNA sequences examined**^LN|**1|**Bi-directional sequence analysis was performed to test for the presence of a mutation in all coding regions and intron/exon boundaries of the MLH1 gene.|

OBX|6|CNE|51968-6^**Discrete variation analysis overall interpretation**^LN|**1|**LA6576-8^**Positive**^LN|

OBX|7|CWE|83006-7^**Deletion-duplication overall interpretation**^LN|**1|**LA26803-9^**No deletion duplications detected in studied regions**^LN|

OBX|8|FT|51969-4^**Full narrative report**^LN|**1|Result Summary-**
Positive \.br\\.br\ **Result-** The following heterozygous alteration was identified: Amino Acid change: p.R497PfsX6 (Arg497ProfsX6) DNA change: c.1489dupC (g.37070354) Classification: PATHOGENIC. \.br\\.br\ **Interpretation** - The c.1489dupC (p.R497PfsX6) alteration is a known pathogenic mutation. This result is consistent with a diagnosis of Lynch syndrome for this individual. \.br\\.br\ **Method –** Bi-directional sequence analysis was performed to test for the presence of a mutation in all coding regions and intron/exon boundaries of the MLH1 gene. Array comparative genomic hybridization (aCGH) was used to test for the presence of large deletions and duplications in this gene.|

Technical details

OBX|9|CWE|62374-4^**Human reference sequence assembly**^LN|**1**|LA14029-5^**GRCh37**^LN|

OBX|10|NM|82115-7^**dbSNP version**^LN|**1**|**147**|

Attributes of Discrete Genetic Variants: Report Section 2

OBX|11|CNE|83005-9^**Variant Category**^LN|**2a**|LA26801-3^**Simple Variant**^LN|

OBX|12|CNE|81252-9^**Discrete genetic variant**^LN|**2a**|
89753^**NM_000249.3(MLH1):c.1489dupC (p.Arg497Profs)**^ClinVar-V|

Transcript Specification Variables

OBX|13|CWE|48018-6^**Gene studied**^LN|**2a**|89753^**MLH1**^HGNC-Symb|

OBX|14|CWE|51958-7^**Transcript RefSeq ID**^LN|**2a**|
NM_000249.3^**NM_000249.3**^RefSeq-T|

OBX|15|CWE|41103-3^**Transcript DNA Change(cHGVS)**^LN|**2a**|
c.1489dupC^**c.1489dupC**^HGVS.c|

OBX|16|CWE|48005-3^**Amino acid change p.HGVS**^LN|**2a**|
p.Arg497Profs^**p.Arg497Profs**^HGVS.p|

OBX|17|CWE|48019-4^**DNA change type**^LN|**2a**|LA6686-5^**Duplication**^LN|

OBX|18|CWE|48006-1^**Amino acid change type**^LN|**2a**|

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```
LA6694-9^Frameshift^LN|

Genomic specification (HGVS code and VCF-like representation)

OBX|19|CWE|48013-7^Genomic reference sequence^LN|2a|
NG_007109.2:g.40514dupC^NG_007109.2:g.40514dupC^RefSeq-G|

OBX|20|CWE|81290-9^Genomic DNA change (gHGVS)^LN|2a|
NC_000003.11^NC_000003.11^HGVS.g|

OBX|21|ST|69547-8^Genomic ref allele^LN|2a|C|

OBX|22|NR|81254-5^Genomic allele start-end^LN|2a|
37070354^37070354|

OBX|23|ST|69551-0^Genomic alt allele^LN|2a|CC|

Other variables

OBX|24|CNE|81255-2^dbSNP ID^LN|2a|rs63751031^rs63751031^dbSNP|

OBX|25|CWE|48001-2^Cytogenetic (chromosome) location^LN|2a|
3p22.2^3p22.2^Chrom-Loc|

OBX|26|CNE|48002-0^Genomic source class^LN|2a|LA6683-
2^Germline^LN|

OBX|27|CWE|53037-8^Variant analysis method^LN|2a|LA26398-
0^Sequencing^LN|

Interpretations

OBX|28|CNE|53037-8^Genetic variation clinical significance^LN|2a|
LA6668-3^Pathogenic^LN|

OBX|29|CNE|69548-6^Genomic variant assessment^LN|2a|LA9633-
4^Present^LN|

OBX|30|CWE|81259-4^Probable associated phenotype^LN|2a|
C0009405^Lynch syndrome^MedGen-Dis|

Allelic state/phase information

OBX|31|CNE|53034-5^Allelic state^LN|2a|LA6706-1^Heterozygous^LN|
```

5.9.1.4 SIMPLE VARIANT – MULTI-GENE MUTATION ANALYSIS AND DUPLICATION-DELETION STUDY

The following example illustrates a sample report that tests for several genetic diseases associated with infantile epilepsy.

Note that this example message only reports three genetic diseases that are tested to save space but real messages would list all of them in separate OBX fields. Also, while real tests would test for several gene variants and list them in a separate OBX field, this example lists only five of the gene variants tested to save space.

Example Gene Variant 4

```
OBR|1|Acme23469|Gen825750|Sample Orderable Test^ Infantile
Epilepsy Panel – Multi Gene targeted analysis^LN|R|
201608030830|201608091650|
```


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Variables that Apply to Overall Study: Report Section 1

OBX|1|TX|53577-3^**Reason for study**^LN|**1**|Patient may have infantile epilepsy.|

OBX|2|CWE|51967-8^**Genetic disease(s) assessed**^LN|**1.a**|C0268126^**Adenylosuccinate lyase deficiency**^MedGen-Dis|

OBX|3|CWE|51967-8^**Genetic disease(s) assessed**^LN|**1.b**|C0162635^**Angelman syndrome**^MedGen-Dis|

OBX|4|CWE|51967-8^**Genetic disease(s) assessed**^LN|**1.c**|C2748910^**Atypical Rett syndrome**^MedGen-Dis|

OBX|5|CNE|48018-6^**Gene studied**^LN|**1.a**|291^**ADSL**^HGNC-Symb|

OBX|6|CNE|48018-6^**Gene studied**^LN|**1.b**|877^**ALDH7A1**^HGNC-Symb|

OBX|7|CNE|48018-6^**Gene studied**^LN|**1.c**|30881^**ALG13**^HGNC-Symb|

OBX|8|CNE|48018-6^**Gene studied**^LN|**1.d**|14561^**ARHGEF9**^HGNC-Symb|

OBX|9|CNE|48018-6^**Gene studied**^LN|**1.e**|18060^**ARX**^HGNC-Symb|

OBX|10|CNE|51968-6^**Discrete variation analysis overall interpretation**^LN|**1**|LA6576-8^**Positive**^LN|

OBX|11|CWE|83006-7^**Deletion-duplication overall interpretation**^LN|**1**|LA26803-9^**No deletion duplications detected in studied regions**^LN|

OBX|12|FT|51969-4^**Full narrative report**^LN|**1**|**Result**- Heterozygous for a single PNKP mutation; Heterozygous for a single PRRT2 mutation. No other reportable variants detected by sequencing and deletion/duplication analysis of the 75 genes included on this panel. \.br\\.br\ **Interpretation:** This individual is heterozygous for a novel disease-causing mutation in the PNKP gene. This gene is associated with an autosomal recessive disorder. A second mutation may exist that is undetectable by this test or this patient may incidentally be a heterozygous carrier of the PNKP mutation. The finding of a single mutation in PNKP is not sufficient to establish a diagnosis in this patient. This individual is heterozygous for a published missense variant in the PRRT2 gene. This gene is associated with autosomal dominant disorder. With the clinical and molecular information available at this time, the clinical significance of this variant is unknown. \.br\\.br\ **Method** – Using genomic DNA from the submitted specimen, the coding regions and splice junctions of 51 genes (all genes listed above except for CHRNA7 and MAGI2, since only large deletions have been reported in these genes) were sequenced with pair-end reads. Capillary sequencing was used to confirm all potentially pathogenic variants. Concurrent deletion/duplication testing was performed for the genes in the panel using exon-level oligo array CGH, except for FOXG1. Confirmation of copy number changes was performed by MLPA, qPCR, or repeat array CGH analysis. \.br\\.br\ **Additional Information** – The test also found likely benign variants in genes KANSL1 and PNKP.|

OBX|13|TX|81293-3^**Description of ranges of DNA sequences examined**^LN|**1**|The sequencing component of the test includes all

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```
genes listed above except for CHRNA7 and MAGI2, since only large
deletions have been reported in these genes.|

Technical details

OBX|14|CWE|62374-4^Human reference sequence assembly^LN|1|
LA14029-5^GRCh37^LN|

OBX|15|NM|82115-7^dbSNP version^LN|1|147|

Attributes of First Discrete Genetic Variants: Report Section 2

OBX|16|CNE|83005-9^Variant Category^LN|2a|LA26801-3^Simple
Variant^LN|

OBX|17|CNE|81252-9^Discrete genetic variant^LN|2a|No Variant
ID^NM_007254.3(PNKP):c.1315C>T(p.Arg439Ter)^ClinVar-V|

Transcript Specification Variables

OBX|18|CWE|48018-6^Gene studied^LN|2a|9154^PNKP^HGNC-Symb|

OBX|19|CWE|51958-7^Transcript RefSeq ID^LN|2a|
NM_007254.3^NM_007254.3^RefSeq-T|

OBX|20|CWE|41103-3^Transcript DNA Change (cHGVS)^LN|2a|
c.610C>T^c.1315C>T^HGVS.c|

OBX|21|CWE|48005-3^Amino acid change p.HGVS^LN|2a|
p.Arg204Ter^p.Arg439Ter^HGVS.p|

OBX|22|CWE|48019-4^DNA change type^LN|2a|LA6690-7^Substitution^LN|

OBX|23|CWE|48006-1^Amino acid change type^LN|2a|LA6699-
8^Nonsense^LN|

Genomic specification (HGVS code and VCF-like representation)

OBX|24|CWE|81290-9^Genomic DNA change (gHGVS)^LN|2a|
NC_000019.9^NC_000019.9^RefSeq-G|

OBX|25|ST|69547-8^Genomic ref allele^LN|2a|G|

OBX|26|NR|81254-5^Genomic allele start-end^LN|2a|
50367462^50367462|

OBX|27|ST|69551-0^Genomic alt allele^LN|2a|A|

Other variables

OBX|28|CNE|81255-2^dbSNP ID^LN|2a|rs796052850^rs796052850^dbSNP|

OBX|29|CWE|48001-2^Cytogenetic (chromosome) location^LN|2a|
19q13.33^19q13.33^Chrom-Loc|

OBX|30|CNE|48002-0^Genomic source class^LN|2a|LA6683-
2^Germline^LN|

Interpretations

OBX|31|CNE|53037-8^Genetic variation clinical significance^LN|2a|
LA6668-3^Pathogenic^LN|

OBX|32|CNE|69548-6^Genomic variant assessment^LN|2a|LA9633-
4^Present^LN|
```


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```
OBX|33|CWE|81259-4^Probable associated phenotype^LN|2a|
CN218420^Developmental delay AND/OR other significant
developmental or morphological phenotypes^MedGen-Dis|
```

Allelic state/phase information

```
OBX|34|CNE|53034-5^Allelic state^LN|2a|LA6706-1^Heterozygous^LN|
```

Attributes of Second Simple Genetic Variants: Report Section 2

```
OBX|35|CNE|83005-9^Variant Category^LN|2a|LA26801-3^Simple
Variant^LN|

OBX|36|CNE|81252-9^Discrete genetic variant^LN|2b|
130039^NM_145239.2(PRRT2):c.67G>A(p.Glu23Lys)^ClinVar-V|
```

Transcript Specification Variables

```
OBX|37|CWE|48018-6^Gene studied^LN|2b|30500^PRRT2^HGNC-Symb|

OBX|38|CWE|51958-7^Transcript RefSeq ID^LN|2b|
NM_145239.2^NM_145239.2^RefSeq-T|

OBX|39|CWE|41103-3^Transcript DNA Change (cHGVS)^LN|2b|
c.67G>A^c.67G>A^HGVS.c|

OBX|40|CWE|48005-3^Amino acid change p.HGVS^LN|2b|
p.Glu23Lys^p.Glu23Lys^HGVS.p|

OBX|41|CWE|48019-4^DNA change type^LN|2b|LA6690-7^Substitution^LN|
```

Genomic specification (HGVS code and VCF-like representation)

```
OBX|42|CWE|81290-9^Genomic DNA change (gHGVS)^LN|2b|
NC_000016.9^NC_000016.9^RefSeq-G|

OBX|43|ST|69547-8^Genomic ref allele^LN|2b|G|

OBX|44|NR|81254-5^Genomic allele location^LN|2b|29824442^29824442|

OBX|45|ST|69551-0^Genomic alt allele^LN|2b|A|
```

Other variables

```
OBX|46|CNE|81255-2^dbSNP ID^LN|2b|rs140383655^rs140383655^dbSNP|

OBX|47|CWE|48001-2^Cytogenetic (chromosome) location^LN|2b|
16p11.2^16p11.2^Chrom-Loc|

OBX|48|CNE|48002-0^Genomic source class^LN|2b|LA6683-
2^Germline^LN|
```

Interpretations

```
OBX|49|CNE|53037-8^Genetic variation clinical significance^LN|2b|
LA6671-7^Uncertain Significance^LN|

OBX|50|CNE|69548-6^Genomic variant assessment^LN|2b|LA9633-
4^Present^LN|

OBX|51|CWE|81259-4^Probable associated phenotype^LN|2b|
C1510586^Autism spectrum disorders^MedGen-Dis|
```

Allelic state/phase information

```
OBX|52|CNE|53034-5^Allelic state^LN|2b|LA6706-1^Heterozygous^LN|
```


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Attributes of Third Discrete Genetic Variants: Report Section 2

OBX|53|CNE|83005-9^**Variant Category**^LN|**2c**|LA26801-3^**Simple Variant**^LN|

OBX|54|CNE|81252-9^**Discrete genetic variant**^LN|**2c**|205776^**NM_001193466.1(KANSL1):c.727C>A(p.Gln243Lys)**^ClinVar-V|

Transcript Specification Variables

OBX|55|CWE|48018-6^**Gene studied**^LN|**2c**|24565^**KANSL1**^HGNC-Symb|

OBX|56|CWE|51958-7^**Transcript RefSeq ID**^LN|**2c**|NM_001193466.1^**NM_001193466.1**^RefSeq-T|

OBX|57|CWE|41103-3^**Transcript DNA Change(cHGVS)**^LN|**2c**|c.727C>A^**c.727C>A**^HGVS.c|

OBX|58|CWE|48005-3^**Amino acid change p.HGVS**^LN|**2c**|p.Gln243Lys^**p.Gln243Lys**^HGVS.p|

OBX|59|CWE|48019-4^**DNA change type**^LN|**2c**|LA6690-7^**Substitution**^LN|

OBX|60|CWE|48006-1^**Amino acid change type**^LN|**2c**|LA6698-0^**Missense**^LN|

Genomic specification (HGVS code and VCF-like representation)

OBX|61|CWE|81290-9^**Genomic DNA change (gHGVS)**^LN|**2c**|NC_000017.10^**NC_000017.10**^RefSeq-G|

OBX|62|ST|69547-8^**Genomic ref allele**^LN|**2c**|**G**|

OBX|63|NR|81254-5^**Genomic allele location**^LN|**2c**|**44248783^44248783**|

OBX|64|ST|69551-0^**Genomic alt allele**^LN|**2c**|**T**|

Other variables

OBX|65|CNE|81255-2^**dbSNP ID**^LN|**2c**|rs142096969^**rs142096969**^dbSNP|

OBX|66|CWE|48001-2^**Cytogenetic (chromosome) location**^LN|**2c**|17q21.31^**17q21.31**^Chrom-Loc|

OBX|67|CNE|48002-0^**Genomic source class**^LN|**2c**|LA6683-2^**Germline**^LN|

Interpretations

OBX|68|CNE|53037-8^**Genetic variation clinical significance**^LN|**2c**|LA6674-1^**Likely Benign**^LN|

OBX|69|CNE|69548-6^**Genomic variant assessment**^LN|**2c**|LA9633-4^**Present**^LN|

Allelic state/phase information

OBX|70|CNE|53034-5^**Allelic state**^LN|**2c**|LA6706-1^**Heterozygous**^LN|

Attributes of Fourth Discrete Genetic Variants: Report Section 2

OBX|71|CNE|83005-9^**Variant Category**^LN|**2d**|LA26801-3^**Simple Variant**^LN|

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```
OBX|72|CNE|81252-9^Discrete genetic variant^LN|2d|
159792^NM_007254.3(PNKP):c.188C>T(p.Ala63Val)^ClinVar-V|

Transcript Specification Variables

OBX|73|CWE|48018-6^Gene studied^LN|2d|9154^PNKP^HGNC-Symb|

OBX|74|CWE|51958-7^Transcript RefSeq ID^LN|2d|
NM_007254.3^NM_007254.3^RefSeq-T|

OBX|75|CWE|41103-3^Transcript DNA Change (cHGVS)^LN|2d|
c.188C>T^c.188C>T^HGVS.c|

OBX|76|CWE|48005-3^Amino acid change p.HGVS^LN|2d|
p.Ala63Val^p.Ala63Val^HGVS.p|

OBX|77|CWE|48019-4^DNA change type^LN|2d|LA6690-7^Substitution
^LN|

OBX|78|CWE|48006-1^Amino acid change type^LN|2d|LA6698-
0^Missense^LN|

Genomic specification (HGVS code and VCF-like representation)

OBX|79|CWE|81290-9^Genomic DNA change
(gHGVS)^LN|2d|NC_000019.9^NC_000019.9^RefSeq-G|

OBX|80|ST|69547-8^Genomic ref allele^LN|2d|G|

OBX|81|NR|81254-5^Genomic allele location^LN|2d|50369666^50369666|

OBX|82|ST|69551-0^Genomic alt allele^LN|2d|A|

Other variables

OBX|83|CNE|81255-2^dbSNP ID^LN|2d|rs3739173^rs3739173^dbSNP|

OBX|84|CWE|48001-2^Cytogenetic (chromosome)
location^LN|2d|19q13.33^19q13.33^Chrom-Loc|

OBX|85|CNE|48002-0^Genomic source class^LN|2d|LA6683-
2^Germline^LN|

Interpretations

OBX|86|CNE|53037-8^Genetic variation clinical significance^LN|2d|
LA6671-7^Uncertain Significance^LN|

OBX|87|CNE|69548-6^Genomic variant assessment^LN|2d|LA9633-
4^Present^LN|

OBX|88|CWE|81259-4^Probable associated phenotype^LN|2d|
C3150667^Early infantile epileptic encephalopathy 10^MedGen-Dis|

Allelic state/phase information

OBX|89|CNE|53034-5^Allelic state^LN|2d|LA6706-1^Heterozygous^LN|
```

5.9.1.5 STRUCTURAL VARIANT – WHOLE GENOME STUDY FOR DELETION DUPLICATION

This example report illustrates a whole genome study that found a structural variant that may contribute to a phenotype of intellectual disability. This report uses ISCN nomenclature to report the variant. Because this is a whole genome study, the build can be taken as the reference sequence.

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The field LOINC 82155-3 “Copy Number,” reports “3” because the specification requires a number even though real reports may report text, such as “partial trisomy.”

Example 5

```
OBR|1|Acme23469|Gen825750|62375-1^Cytogenomic SNP
Microarray^LN|R|201608030830|201608091650|

Variables that Apply to Overall Study: Report Section 1

OBX|1|TX|53577-3^Reason for study^LN|1|Patient has encephalopathy|

OBX|2|CWE|51967-8^Genetic disease(s) assessed^LN|1|
C1843367^Intellectual disability^MedGen-Dis|

OBX|3|TX|81293-3^Description of ranges of DNA sequences
examined^LN|1|Whole genome coverage, including subtelomeric and
pericentromeric regions. Affymetrix Cytogenetics platform contains
>2.1 million copy-number markers, including 750,000 single-
nucleotide polymorphism (SNP) probes to detect copy number changes
and LCSH.|

OBX|4|CWE|83006-7^Deletion-duplication overall
interpretation^LN|1| LA26804-7^Deletion and/or duplication
detected in studied region^LN|

OBX|5|FT|51969-4^Full narrative report^LN|1|Genetic Results: The
cytogenomic microarray analysis indicated that there was a gain
involving chromosome 16 (1.7 Mb duplicated) within 16p13.11,
suggesting partial trisomy for this region. This duplication has
been reported as a risk factor for neurocognitive disorders as it
appears to be enriched in children with intellectual disabilities,
but is also observed, at a lower frequency, in normal individuals.
\.br\\.br\ Method: CHROMOSOMAL MICROARRAY ANALYSIS (CMA).
\.br\\.br\ Methodology: This CMA was performed using Affymetrix(R)
Cytogenetics Whole-Genome 2.7M Array. The array offers a total of
2,141,868 markers across the entire genome, including 1,742,975
unique non-polymorphic markers, and 398,891 SNP markers.|

OBX|6|ST|81291-7^Structural variant ISCN^LN|1|arr
16p13.11(14,686,844x2,14776269-
16486370x3,16,494,405x2)(hg18)^ISCN|

Technical details

OBX|7|CWE|62374-4^Human reference sequence assembly^LN|1|LA26805-
4^NCBI36^LN|

Discrete genetic variants: Report Section 2

OBX|8|CNE|83005-9^Variant Category^LN|2a|LA26802-1^Structural
Variant^LN|

OBX|9|CWE|48019-4^DNA change type^LN|2a|LA6686-5^Duplication^LN|

OBX|10|CWE|48001-2^Cytogenetic chromosome location^LN|2a|
16p13.11^16p13.11^Chrom-Loc|

OBX|11|CWE|81304-8^Variant analysis method type^LN|2a|
LA26399-8^Oligo aCGH^LN|
```


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```
Structural variant addenda
OBX|12|ST|82155-3^Copy number^LN|2a|3|
```

5.9.1.6 STRUCTURAL VARIANT – EXAMPLE OF WHOLE GENOME STUDY FOR DELETION DUPLICATION

This example illustrates a sample report on a whole genome study that found a structural variant that may contribute to a phenotype of developmental delay, and uses ISCN nomenclature to report the variant.

Note that this is a whole genome study, so the build can be taken as the reference sequence.

Also, as of February 2017, the cytogenetics location table in the LHC Clinical Search Table (described in Section 14) does not include the description of adjacent chromosome locations, such as 4q35.1-q35.2, but they are in development.

As we understand, the source table for NCBI uses dashes to represent the adjacent locations, e.g. 4q35.1-q35.2. Some real reports do not use the dash to separate the locations, e.g. 4q35.1q35.2.

Example 6

```
OBR|1|Acme23469|Gen825750|Sample Orderable Test^SNP Microarray
Pediatric^LN|R|201608030830|201608091650|

Variables that Apply to Overall Study: Report Section 1

OBX|1|TX|53577-3^Reason for study^LN|1|Patient has developmental
delay.|

OBX|2|CWE|51967-8^Genetic disease(s) assessed^MedGen-
Dis|1|CN218420^Developmental delay AND/OR other significant
developmental or morphological phenotypes^MedGen-Dis|

OBX|3|TX|81293-3^Description of ranges of DNA sequences
examined^LN|1|SNP microarray analysis was performed using
Affymetric Cytoscan HD platform which uses over 743,000 SNP probes
and 1,953,000 NPCSN probes with a median spacing of 0.88 kb.|

OBX|4|CWE|83006-7^Deletion-duplication overall
interpretation^LN|1|LA26804-7^Deletion and/or duplication detected
in studied region^LN

OBX|5|FT|51969-4^Full narrative report^LN|1|Microarray Result- 6.0
MB Terminal Deletion of 4Q35.1 -> 4QTER; 8.5 MB Terminal
Duplication of XQ27.3 -> XQTER. \.br\\.br\ Interpretation- The
presence of both a significant terminal gain and significant
terminal loss in a different chromosome in the same analysis
suggests that the patient has inherited a single derivative
chromosome from a balanced translocation between the two
chromosomes. The whole genome chromosome SNP microarray copy
number analysis revealed a terminal 4q deletion [Flanking proximal
OMIM gene: MIR510] and a terminal gain of Xq [Flanking proximal
OMIM gene: IRF2] spanning the chromosomal segments listed below.
These intervals include numerous OMIM annotated genes that may
contribute to the patient phenotype...No other significant DNA
```


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```
copy number changes or copy neutral LOH were detected within our
present reporting criteria in the 2,695,000 region specific SNPs.|

OBX|6|ST|81291-7^Structural variant ISCN^LN|1.a|arr 4q35.1q35.2
(185, 135, 549-190, 957, 473)x1^ISCN|

OBX|7|ST|81291-7^Structural variant ISCN^LN|1.b|Xq27.3q28 (146,
734, 447-154, 943, 511)x3^ISCN|

Technical details

OBX|8|CWE|62374-4^Human reference sequence assembly^LN|1|LA14029-
5^GRCh37^LN|

Discrete Genetic Variants: Report Section 2

OBX|9|CNE|83005-9^Variant Category^LN|2a|LA26802-1^Structural
Variant^LN|

OBX|10|CWE|48001-2^Cytogenetic (chromosome) location^LN|2a|
4q35.1-q35.2^4q35.1-q35.2^Chrom-Loc|

OBX|11|CWE|48019-4^DNA change type^LN|2a|LA6692-3^Deletion^LN|

OBX|12|CWE|81304-8^Variant analysis method type^LN|2a|LA26400-
4^SNP Array^LN|

Structural variant addenda

OBX|13|ST|82155-3^Copy number^LN|2a|1|

Discrete Genetic Variants: Report Section 2

OBX|14|CNE|83005-9^Variant Category^LN|2a|LA26802-1^Structural
Variant^LN|

OBX|15|CWE|48001-2^Cytogenetic (chromosome) location^LN|2b|
Xq27.3-q28^Xq27.3-q28^Chrom-Loc|

OBX|16|CWE|48019-4^DNA change type^LN|2b|LA6686-5^Duplication^LN|

OBX|17|CWE|81304-8^Variant analysis method type^LN|2b|LA26400-
4^SNP Array^LN|

Structural variant addenda

OBX|18|ST|82155-3^Copy number^LN|2b|3|
```

5.9.1.7 STRUCTURAL VARIANT – EXAMPLE OF STRUCTURAL VARIANT REPORTED AS DBVAR CODE

This example illustrates a sample report on Tay-Sach's Disease, which found a structural variant that shows the patient is a carrier for Tay-Sach's disease. The structural variant is reported as a dbVar code, a NCBI (National Center for Biotechnology Information) database of genomics structural variations.

Example 7

```
OBR|1|Acme23469|Gen825750|76033-0^HEXA gene full mutation analysis
in Blood or Tissue by Sequencing Narrative
^LN|R|201608030830|201608091650|

Variables that Apply to Overall Study: Report Section 1
```


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OBX|1|TX|53577-3^**Reason for study**^LN|**1**|Patient may have Tay-Sach's Disease|

OBX|2|CWE|51967-8^**Genetic disease(s) assessed**^MedGen-Dis|**1**|C0039373^**Tay-Sachs disease**^MedGen-Dis|

OBX|3|CNE|48018-6^**Gene(s) assessed**^LN||**1.1**|4878^**HEXA**^HGNC-Symb|

OBX|4|TX|81293-3^**Description of ranges of DNA sequences examined**^LN|**1**|All coding regions and intron/exon boundaries of the HEXA gene.|

OBX|5|CWE|83006-7^**Deletion-duplication overall interpretation**^LN|**1**|LA26804-7^**Deletion and/or duplication detected in studied regions**^LN|

OBX|6|FT|51969-4^**Full narrative report**^LN|**1**|**Result Summary**- Positive. \.br\\.br\ **Result**- The following structural alteration was identified: DNA change: c.—2654_253+5128delinsG. Genome change: g.2644_10588del7945insG, Classification: PATHOGENIC. \.br\\.br\ **Interpretation** - The c.—2654_253+5128delinsG alteration is a known pathogenic mutation. This result indicates that this individual is a carrier of Tay Sachs disease (TSD). This assumes that this individual is not clinically affected with TSD. \.br\\.br\ **Method** - Bi-directional sequence analysis was performed to test for the presence of mutations in all coding regions and intron/exon boundaries of the HEXA gene.|

Technical details

OBX|7|CWE|62374-4^**Human reference sequence assembly**^LN|**1**|LA14029-5^**GRCh37**^LN|

Discrete Genetic Variants: Report Section 2

OBX|8|CNE|83005-9^**Variant Category**^LN|**2a**|LA26802-1^**Structural Variant**^LN|

OBX|9|CWE|81252-9^**Discrete genetic variant**^LN|**2a**|nsv513781^**15q23-q24(chr15)(72370592-72378536)x1**^dbVar-GL|

OBX|10|CWE|48019-4^**DNA change type**^LN|**2a**|LA9659-9^**Insertion/Deletion**^LN|

OBX|11|ST|**81290-8 Genomic DNA change (gHGVS)**^LN|**2a**|NG_009017.1:g.2644_10588del7945insG^**NG_009017.1:g.2644_10588del7945insG**^HGVS.g|

OBX|12|CWE|48001-2^**Cytogenetic chromosome location**^LN|**2a**|15q23q24^**15q23q24**^Chrom-Loc|

OBX|13|CWE|81304-8^**Variant analysis method type**^LN|**2a**|LA26402-0^**Curated**^LN|

Structural variant addenda

OBX|14|ST|81287-5^**Structural variant start-end**^LN|**2a**|**72370592^72378536**|

OBX|15|NM|81300-6^**Structural variant length**^LN|**2a**|**7945**|

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5.9.2 COMPLEX VARIANT EXAMPLE MESSAGES

5.9.2.1 COMPLEX VARIANT – EXAMPLE OF NON-PHARMACOGENOMIC COMPLEX VARIANT HAPLOTYPE

This is an example of a non-pharmacogenomics complex variant, which happens to be a haplotype.

This report illustrates a sample report for Gaucher's disease, where complex variant shows the patient is a carrier for the disease.

Example 8

```
OBR|1|Acme23469|Gen825750|46988-2^GBA gene mutations tested for in
Blood or Tissue by Molecular genetics method Nominal
^LN||R|201608030830|201608091650|

Variables that Apply to Overall Study: Report Section 1

OBX|1|TX|53577-3^Reason for study^LN|1|Patient may have Gaucher's
disease.|

OBX|2|CWE|51967-8^Genetic disease(s) assessed^MedGen-Dis|1|
C0017205^Gaucher disease^MedGen-Dis|

OBX|3|CWE|51958-7^Transcript reference sequence [Identifier]^LN|1|
NM_000157^ NM_000157^RefSeq-T|

OBX|4|TX|81293-3^Description of ranges of DNA sequences
examined^LN|1|Bi-directional sequence analysis was performed to
test for the presence of mutations in all coding regions and
intron/exon boundaries of the GBA gene.|

OBX|5|CNE|48018-6^Gene(s) assessed^LN|1|4177^GBA^HGNC-Symb|

OBX|6|CNE|51968-6^Discrete variation analysis overall
interpretation^LN|1|LA6576-8^Positive^LN|

OBX|7|FT|51969-4^Full narrative report^LN|1|Result Summary-
Positive \.br\\.br\ Result - The following haplotype heterozygous
alteration was identified: Amino Acid changes: p.Ala495Pro,
p.Val499=, p.Leu483Pro. DNA change: c.1483G>C (g.14481), c.1497G>C
(g.14495), c.1448T>C (g.14446), Classification: PATHOGENIC
\.br\\.br\ Interpretation - The haplotype 1483G>C (p.Ala495Pro),
c.1497G>C (p.Val499=), c.1448T>C (p.Leu483Pro) alteration is a
known pathogenic mutation. This result indicates that this
individual is a carrier of Gaucher disease. This assumes that this
individual is not clinically affected with Gaucher disease. While
the clinical presentation associated with Gaucher disease can be
variable, the p.Ala495Pro, p.Val499=, p.Leu483Pro haplotype
mutation is associated with Gaucher's disease, type 1, Acute
neuronopathic Gaucher's disease, Subacute neuronopathic Gaucher's
disease, and Gaucher disease, perinatal lethal. \.br\\.br\ Method
- Bi-directional sequence analysis was performed to test for the
the presence of mutations in all coding regions and intron/exon
boundaries of the GBA gene.

Technical details
```


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```
OBX|8|CWE|62374-4^Human reference sequence assembly^LN|1|
LA14029^GRCh37^LN|

OBX|9|NM|82115-7^dbSNP version^LN|1|147|

Complex Variant: Report Section 5

OBX|10|CWE|81260-2^Complex variant ID^LN|3a|
4297^NM_001005741.2(GBA):c.[1448T>C;1483G>C;1497G>C] -
Haplotype^ClinVar-V|

OBX|11|CNE|81263-6^Complex variant type^LN|3a|
LA26218-0^Haplotype^LN|

OBX|12|CWE|81259-4^Associated phenotype^LN|3a|C0017205^Gaucher
disease^MedGen-Dis|

OBX|13|CNE|53037-8^Genetic variation clinical significance^LN|3a|
LA6668-3^Pathogenic^LN|

OBX|14|CNE|53034-5^Allelic state^LN|3a|LA6706-1^Heterozygous^LN|

Attributes of First Discrete Variant within the complex variant

OBX|15|CNE|83005-9^Variant Category^LN|3a.1a|LA26801-3^Simple
Variant^LN|

OBX|16|CNE|81252-9^Discrete variant^LN|
3a.1a|93450^NM_001005741.2(GBA):c.1483G>C (p.Ala495Pro)^ClinVar-V|

Transcript Specification Variables

OBX|17|CWE|48018-6^Gene studied^LN|3a.1a|4177^GBA^HGNC-Symb|

OBX|18|CWE|51958-7^Transcript RefSeq ID^LN|3a.1a|
NM_001005741.2^NM_001005741.2^H|

OBX|19|CWE|41103-3^Transcript DNA Change (cHGVS)^LN|3a.1a|c.1483G
>C^c.1483G>C^HGVS.c|

OBX|20|CWE|48005-3^Amino acid change p.HGVS^LN|
3a.1a|p.Ala495Pro^p.Ala495Pro^HGVS.p|

OBX|21|CWE|48019-4^DNA change type^LN|3a.1a|
LA6690-7^Substitution^LN|

OBX|22|CWE|48006-1^Amino acid change type^LN|3a.1a|
LA6698-0^Missense^LN|

Genomic specification (HGVS code and VCF-like representation)

OBX|23|CWE|48013-7^Genomic reference sequence^LN|3a.1a|
NG_009783.1:g.14481G>C^NG_009783.1:g.14481G>C^RefSeq-G|

OBX|24|CWE|81290-9^Genomic DNA change (gHGVS)^LN|3a.1a|
NC_000001.10^NC_000001.10^HGVS.g|

OBX|25|ST|69547-8^Genomic ref allele^LN|3a.1a|C|

OBX|26|NR|81254-5^Genomic allele start-end^LN|3a.1a|
155205008^155205008|

OBX|27|ST|69551-0^Genomic alt allele^LN|3a.1a|G|

Other variables
```


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```
OBX|28|CNE|81255-2^dbSNP ID^LN|3a.1a|rs368060^rs368060^dbSNP|

OBX|29|CWE|48001-2^Cytogenetic (chromosome) location^LN|3a.1a|
1q22^1q22^Chrom-Loc|

OBX|30|CNE|48002-0^Genomic source class^LN|3a.1a|
LA6683-2^Germline^LN|

Interpretations

OBX|31|CNE|53037-8^Genetic variation clinical
significance^LN|3a.1a|LA6675-8^Benign^LN|

Allelic state/phase information

OBX|32|CWE|82120-7^Allelic phase [Type]^LN|3a.1a|LA6112-2^1st set
of variants in CIS relation to each other^LN|

OBX|33|CNE|82309-6^Basis for allelic phase^LN|3a.1a|
LA26426-9^Directly measured^LN|

Attributes of Second Discrete Genetic Variant within the complex
variant

OBX|34|CNE|83005-9^Variant Category^LN|3a.1b|LA26801-3^Simple
Variant^LN|

OBX|35|CNE|81252-9^Discrete genetic variant^LN|3a.1b|
93451^NM_001005741.2(GBA):c.1497G>C (p.Val499=)^ClinVar-V|

Transcript Specification Variables

OBX|36|CWE|48018-6^Gene studied^LN|3a.1b|4177^GBA^HGNC-Symb|

OBX|37|CWE|51958-7^Transcript RefSeq ID^LN|3a.1b|
NM_001005741.2^NM_001005741.2^RefSeq-T|

OBX|38|CWE|41103-3^Transcript DNA Change (cHGVS)^LN|3a.1b|
c.1497G>C^c.1497G>C^HGVS.c|

OBX|39|CWE|48005-3^Amino acid change p.HGVS^LN|3a.1b|
p.Val499=^p.Val499=^HGVS.p|

OBX|40|CWE|48019-4^DNA change type^LN|3a.1b|
LA6690-7^Substitution^LN|

Genomic specification (HGVS code and VCF-like representation)

OBX|41|CWE|48013-7^Genomic reference sequence^LN|3a.1b|
NG_009783.1:g.14495G>C^NG_009783.1:g.14495G>C^RefSeq-G

OBX|42|CWE|81290-9^Genomic DNA change (gHGVS)^LN|3a.1b|
NC_000001.10^NC_000001.10^RefSeq-G|

OBX|43|ST|69547-8^Genomic ref allele^LN|3a.1b|C|

OBX|44|NR|81254-5^Genomic allele start-
end^LN|3a.1b|155204994^155204994|

OBX|45|ST|69551-0^Genomic alt allele^LN|3a.1b|G|

Other variables

OBX|46|CNE|81255-2^dbSNP ID^LN|3a.1b|rs1135675^rs1135675^dbSNP|
```


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```
OBX|47|CWE|48001-2^Cytogenetic (chromosome) location^LN|3a.1b|
1q22^1q22^Chrom-Loc|

OBX|48|CNE|48002-0^Genomic source class^LN|3a.1b|
LA6683-2^Germline^LN|

Interpretations

OBX|49|CNE|53037-8^Genetic variation clinical
significance^LN|3a.1b|LA6675-8^Benign^LN|

Allelic state/phase information

OBX|50|CWE|82120-7^Allelic phase [Type]^LN|3a.1b|LA6112-2^1st set
of variants in CIS relation to each other^LN

OBX|51|CNE|82309-6^Basis for allelic phase^LN|3a.1b|
LA26426-9^Directly measured^LN|

Attributes of Third Discrete Genetic Variant within the complex
variant

OBX|52|CNE|83005-9^Variant Category^LN|3a.1c|LA26801-3^Simple
Variant^LN|

OBX|53|CNE|81252-9^Discrete genetic variant^LN|3a.1c|
4288^NM_000157.3(GBA):c.1448T>C (p.Leu483Pro)^ClinVar-V|

Transcript Specification Variables

OBX|54|CWE|48018-6^Gene studied^LN|3a.1c|4177^GBA^HGNC-Symb|

OBX|55|CWE|51958-7^Transcript RefSeq ID^LN|3a.1c|
NM_000157.3^NM_000157.3^RefSeq-T|

OBX|56|CWE|41103-3^Transcript DNA Change (cHGVS)^LN|3a.1c|
c.1448T>C^c.1448T>C^HGVS.c|

OBX|57|CWE|48005-3^Amino acid change p.HGVS^LN|3a.1c|
p.Leu483Pro^p.Leu483Pro^HGVS.p|

OBX|58|CWE|48019-4^DNA change type^LN|3a.1c|
LA6690-7^Substitution^LN|

OBX|59|CWE|48006-1^Amino acid change type^LN|3a.1c|
LA6698-0^Missense^LN|

Genomic specification (HGVS code and VCF-like representation)

OBX|60|CWE|48013-7^Genomic reference sequence^LN|3a.1c|
NG_009783.1:g.14496T>C^NG_009783.1:g.14496T>C^RefSeq-G|

OBX|61|CWE|81290-9^Genomic DNA change (gHGVS)^LN|3a.1c|
NC_000001.10^NC_000001.10^RefSeq-G|

OBX|62|ST|69547-8^Genomic ref allele^LN|3a.1c|A|

OBX|63|NR|81254-5^Genomic allele location^LN|3a.1c|
155205043^155205043|

OBX|64|ST|69551-0^Genomic alt allele^LN|3a.1c|G|

Other variables

OBX|65|CNE|81255-2^dbSNP ID^LN|3a.1c|rs421016^rs421016^dbSNP|
```


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```
OBX|66|CWE|48001-2^Cytogenetic (chromosome) location^LN|3a.1c|
1q22^1q22^Chrom-Loc|

OBX|67|CNE|48002-0^Genomic source class^LN|3a.1c|
LA6683-2^Germline^LN|

Interpretations

OBX|68|CNE|53037-8^Genetic variation clinical
significance^LN|3a.1c|LA6668-3^Pathogenic^LN|

OBX|69|CWE|81259-4^Probable associated
phenotype^LN|3a.1c|C0017205^Gaucher disease^MedGen-Dis|

Allelic state/phase information

OBX|70|CWE|82120-7^Allelic phase [Type]^LN|3a.1c|LA6112-2^1st set
of variants in CIS relation to each other^LN

OBX|71|CNE|82309-6^Basis for allelic phase^LN|3a.1c|LA26426-
9^Directly measured^LN|
```

5.9.2.2 COMPLEX VARIANT, EXAMPLE OF PHARMACOGENOMICS STUDY THAT DETAILS RESULTS FOR EACH ALLELE

This example illustrates a pharmacogenomics report on a complex variant, which happens to be a haplotype. Note that this example uses the allele ID in the LOINC 81252-9 “Simple Variant” field for the simple variants inside the complex variant instead of the variant ID, because some alleles are submitted with a complex variant as one package and do not have variant IDs.

Example 9

```
OBR|1|Acme23469|Gen825750|47403-1^CYP2D6 gene targeted mutation
analysis in Blood or Tissue by Molecular genetics method
Narrative^LN|R|201608030830|201608091650|

Variables that Apply to Overall Study: Report Section 1

OBX|1|TX|53577-3^Reason for study^LN|1|Patient drug not
responding|

OBX|2|CWE|51958-7^Transcript reference sequence [Identifier]^LN|1|
NM_000106.5^NM_000106.5^RefSeq-T|

OBX|3|CNE|48018-6^Gene(s) assessed^LN|1|2625^CYP2D6^HGNC-Symb|

OBX|4|CWE|36908-2^Gene mutations tested^LN|1|
16895^[NM_000106.5(CYP2D6):c.886C>T(p.Arg296Cys)][NM_000106.5(CYP2
D6):c.1457G>C (p.Ser486Thr)]^ClinVar-V|

OBX|5|CNE|51968-6^Discrete variation analysis overall
interpretation^LN|1|LA6576-8^Positive^LN|

Technical details

OBX|6|CWE|62374-4^Human reference sequence assembly^LN|1|
LA14029-6^GRCh37^LN|

OBX|7|NM|82115-7^dbSNP version^LN|1|147|

Complex Variant: Report Section 5
```


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```
OBX|8|CWE|81260-2^Complex variant^LN|3a|
16895^NM_000106.5(CYP2D6):c.[886C>T;457G>C]- Haplotype^ClinVar-V|

OBX|9|ST|81262-8^Complex variant HGVS name^LN|3a|
c.[886C>T;457G>C]^c.[886C>T;457G>C]^HGVS.c|

OBX|10|CNE|81263-6^Complex variant type^LN|3a|
LA26218-0^Haplotype^LN|

OBX|11|CWE|81259-4^Associated phenotype^LN|3a|
C1837157^Debrisoquine, ultrarapid metabolism of^MedGen-Dis|

OBX|12|CNE|53034-5^Allelic state^LN|3a|LA6706-1^Heterozygous^LN|

Attributes of First Simple Variant within the complex variant

OBX|13|CNE|83005-9^Variant Category^LN|3a.1a|LA26801-3^Simple
Variant^LN|

OBX|14|CNE|81252-9^Simple variant^LN|3a.1a|
31934^NM_000106.5(CYP2D6):c.886C>T(p.Arg296Cys)^ClinVar-V|

Transcript Specification Variables

OBX|15|CWE|48018-6^Gene studied^LN|3a.1a|2625^CYP2D6^HGNC-Symb|

OBX|16|CWE|51958-7^Transcript RefSeq ID^LN|3a.1a|
NM_000106.5^NM_000106.5^RefSeq-T|

OBX|17|CWE|41103-3^Transcript DNA Change (cHGVS)^LN|3a.1a|
c.886C>T^c.886C>T^HGVS.c|

OBX|18|CWE|48005-3^Amino acid change p.HGVS^LN|3a.1a|
p.Arg296Cys^p.Arg296Cys^HGVS.p|

OBX|19|CWE|48019-4^DNA change type^LN|3a.1a|
LA6690-7^Substitution^LN|

OBX|20|CWE|48006-1^Amino acid change type^LN|3a.1a|
LA6698-0^Missense^LN|

Genomic specification (HGVS code and VCF-like representation)

OBX|21|CWE|48013-7^Genomic reference sequence^LN|3a.1a|
NG_032843.1:g.5578C>T^NG_032843.1:g.5578C>T^RefSeq-G|

OBX|22|CWE|81290-9^Genomic DNA change (gHGVS)^LN|3a.1a|
NC_000022.10^NC_000022.10^HGVS.g|

OBX|23|ST|69547-8^Genomic ref allele^LN|3a.1a|A|

OBX|24|NR|81254-5^Genomic allele start-end^LN|3a.1a|
42523943^42523943|

OBX|25|ST|69551-0^Genomic alt allele^LN|3a.1a|A|

Other variables

OBX|26|CNE|81255-2^dbSNP ID^LN|3a.1a|rs16947^rs16947^dbSNP|

OBX|27|CWE|48001-2^Cytogenetic (chromosome) location^LN|3a.1a|
22q13.2^22q13.2^Chrom-Loc|

OBX|28|CNE|48002-0^Genomic source class^LN|3a.1a|
LA6683-2^Germline^LN|
```


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Interpretations

OBX|29|CNE|69548-6^**Genomic variant assessment**^LN|**3a.1a**|
LA9633-4^**Present**^LN|

Attributes of Second Discrete Genetic Variant

OBX|30|CNE|83005-9^**Variant Category**^LN|**3a.1b**|
LA26801-3^**Simple Variant**^LN|

OBX|31|CNE|81252-9^**Discrete genetic variant**^LN|**3a.1b**|
38485^**NM_000106.5(CYP2D6):c.1457G>C(p.Ser486Thr)**^ClinVar-V|

Transcript Specification Variables

OBX|32|CWE|48018-6^**Gene studied**^LN|**3a.1b**|38485^**CYP2D6**^HGNC-Symb|

OBX|33|CWE|51958-7^**Transcript RefSeq ID**^LN|**3a.1b**|
NM_000106.5^**NM_000106.5**^RefSeq-T|

OBX|34|CWE|41103-3^**Transcript DNA Change (cHGVS)**^LN|**3a.1b**|
c.1457G>C^**c.1457G>C**^HGVS.c|

OBX|35|CWE|48005-3^**Amino acid change p.HGVS**^LN|**3a.1b**|
p.Ser486Thr^**p.Ser486Thr**^HGVS.p|

OBX|36|CWE|48019-4^**DNA change type**^LN|**3a.1b**|
LA6690-7^**Substitution**^LN|

OBX|37|CWE|48006-1^**Amino acid change type**^LN|**3a.1b**|
LA6698-0^**Missense**^LN|

Genomic specification (HGVS code and VCF-like representation)

OBX|38|CWE|48013-7^**Genomic reference sequence**^LN|**3a.1b**|
NG_008376.3:g.8381G>C^**NG_008376.3:g.8381G>C**^RefSeq-G|

OBX|39|CWE|81290-9^**Genomic DNA change (gHGVS)**^LN|**3a.1b**|
NC_000022.10**^NC_000022.10**^HGVS.g|

OBX|40|ST|69547-8^**Genomic ref allele**^LN|**3a.1b**|**G**|

OBX|41|NR|81254-5^**Genomic allele start-end**^LN|**3a.1b**|
42522613^42522613|

OBX|42|ST|69551-0^**Genomic alt allele**^LN|**3a.1b**|**G**|

Other variables

OBX|43|CNE|81255-2^**dbSNP ID**^LN|**3a.1b**|rs1135840^**rs1135840**^dbSNP|

OBX|44|CWE|48001-2^**Cytogenetic (chromosome) location**^LN|**3a.1b**|
22q13.2^**22q13.2**^Chrom-Loc|

OBX|45|CNE|48002-0^**Genomic source class**^LN|**3a.1b**|
LA6683-2^**Germline**^LN|

Interpretations

OBX|46|CNE|69548-6^**Genomic variant assessment**^LN|**3a.1b**|
LA9633-4^**Present**^LN|

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5.9.3 PHARMACOGENOMICS EXAMPLE MESSAGE

5.9.3.1 EXAMPLE OF PHARMACOGENOMICS STUDY OF 4 GENES WITH GUIDANCE ABOUT SELECTED DRUGS NESTED IN RESULTS FOR EACH GENE

This is an example of a pharmacogenomics report, showing a report that tests for several drug responses.

Example 10

```
OBR|1|Acme23469|Gen825750|Sample Orderable Test^Multiple CYP genes
& VKORC1 gene Pharmacogenomic Analysis^LN|R|
201608030830|201608091650|

Variables that Apply to Overall Study: Report Section 1

OBX|1|TX|53577-3^Reason for study^LN|1|Patient not responding to
drug.|

OBX|2|CWE|51963-7^Medications assessed^RxT-Ingrd|1.a|
4493^Fluoxetine^RxT-Ingrd|

OBX|3|CWE|51963-7^Medications assessed^RxT-Ingrd|1.b|
83367^atorvastatin^RxT-Ingrd|

OBX|4|CWE|51963-7^Medications assessed^RxT-Ingrd|1.c|
7258^Naproxen^RxT-Ingrd|

OBX|5|CWE|51963-7^Medications assessed^RxT-Ingrd|1.d|
11289^Warfarin^RxT-Ingrd|

OBX|6|CWE|51963-7^Medications assessed^RxT-Ingrd|1.e|
6754^Meperidine^RxT-Ingrd|

OBX|7|CNE|48018-6^Gene(s) assessed^LN|1.a|2623^CYP2C9^HGNC-Symb|

OBX|8|CNE|48018-6^Gene(s) assessed^LN|1.b|2637^CYP3A4^HGNC-Symb|

OBX|9|CNE|48018-6^Gene(s) assessed^LN|1.c|2638^CYP3A5^HGNC-Symb|

OBX|10|CNE|48018-6^Gene(s) assessed^LN|1.d|23663^VKORC1^HGNC-Symb|

OBX|11|CNE|48018-6^Gene(s) assessed^LN|1.e|2625^CYP2D6^HGNC-Symb|

OBX|12|CNE|48018-6^Gene(s) assessed^LN|1.f|2621^CYP2C19^HGNC-Symb|

OBX|13|FT|51969-4^Full narrative report^LN|1|Results - Genes
CYP2C9, CYP2C9/VKORC1, and CYP3A4/CYP3A5 have abnormal drug
responses. CYP2C9 is a Poor Metabolizer for Fluoxetine and
Naproxen; CYP2C9/VKORC1 is a Poor Metabolizer with High
Sensitivity for Warfarin; CYP3A4/CYP3A5 is an Increased
Metabolizer for Atorvastatin. Genes CYP2C19 and CYP2D6 have normal
responses. \.br\\.br\ Method - Genomic DNA was extracted from the
submitted specimen and amplified by the polymerase chain reaction
(PCR) using consensus oligonucleotide primers specific for the
following genes: CYP2C9, VKORC1, CYP3A4, CYP3A5, Factor II, Factor
V Leiden, and MTHFR; assay may also include CYP2C19 and/or CYP2D6.
Clinically relevant genetic variants were detected after
amplification using the Luminex 100/200 Instrument|

Pharmacogenomics: Report Section 4
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Results for first gene in the study

OBX|14|CWE|48018-6^**Gene(s) studied**^LN|**4a.a**|2623^**CYP2C9**^HGNC-Symb|

OBX|15|CWE|48018-6^**Gene(s) studied**^LN|**4a.b**|23663^**VKORC1**^HGNC-Symb|

OBX|16|ST|47998-0^**Genotype display name**^LN|**4a.a**|***2/*5**|

OBX|17|ST|47998-0^**Genotype display name**^LN|**4a.b**|***A/*A**|

OBX|18|CWE|53040-2^**Genetic variation's effect on drug metabolism interp**^LN|**4a**|LA9657-3^**Poor metabolizer**^LN|

Medication usage implications panel

OBX|19|CWE|51963-7^**Medication assessed**^LN|**4a.1a**|
11289^**Warfarin**^RxT-Ingrd|

OBX|20|CWE|82116-5^**Medication usage suggestion [type]**^LN|**4a.1a**|
LA26425-1^**Use Caution**^LN|

OBX|21|TX|83010-9^**Medication usage suggestion [narrative]**^LN|**4a.1a**|Consider 0.5-2 mg/day to achieve therapeutic INR using the warfarin product insert approved by the USFDA.|

Results for second gene in the study

OBX|22|CWE|48018-6^**Gene(s) studied**^LN|**4b**|2623^**CYP2C9**^HGNC-Symb|

OBX|23|ST|47998-0^**Genotype display name**^LN|**4b**|***2/*5**|

OBX|24|CWE|53040-2^**Genetic variation's effect on drug metabolism interp**^LN|**4b**|LA9657-3^**Poor metabolizer**^LN|

Medication usage implications panel

OBX|25|CWE|51963-7^**Medication assessed**^LN|**4b.1a**|
4493^**Fluoxetine**^RxT-Ingrd|

OBX|26|CWE|82116-5^**Medication usage suggestion [type]**^LN|**4b.1a**|
LA26421-0^**Consider Alternative Medication**^LN|

OBX|27|TX|83010-9^**Medication usage suggestion [narrative]**^LN|**4b.1a**|Monitor for inhibition of other drugs. Fluoxetine is a strong 2D6 inhibitor and is known to effect drugs which use the CYP 2D6 pathway.|

Medication usage implications panel

OBX|28|CWE|51963-7^**Medication assessed**^LN|**4b.1b**|7258^**Naproxen**^RxT-Ingrd|

OBX|29|CWE|82116-5^**Medication usage suggestion [type]**^LN|**4b.1b**|
LA26424-4^**Use Caution**^LN|

OBX|30|TX|83010-9^**Medication usage suggestion [narrative]**^LN|**4b.1b**|Consider Dosage reduction. Monitor for Gastrointestinal Bleeding.|

Results for third gene in the study

OBX|31|CWE|48018-6^**Gene(s) studied**^LN|**4c.a**|2637^**CYP3A4**^HGNC-Symb|

OBX|32|CWE|48018-6^**Gene(s) studied**^LN|**4c.b**|2638^**CYP3A5**^HGNC-Symb|

OBX|33|ST|47998-0^**Genotype display name**^LN|**4c.a**|***1/*1**|

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```
OBX|34|ST|47998-0^Genotype display name^LN|4c.b|*1/*1|

OBX|35|CWE|53040-2^Genetic variation's effect on drug metabolism
interp^LN|4.3|LA25390-8^Rapid metabolizer^LN|

Medication usage implications panel

OBX|36|CWE|51963-7^Medication assessed^LN|
4c.1a|83367^atorvastatin^RxT-Ingrd|

OBX|37|CWE|82116-5^Medication usage suggestion [type]^LN|4c.1a|
LA26423-6^Increase Dose^LN|

OBX|38|TX|83010-9 ^Medication usage suggestion
[narrative]^LN|4c.1a|Monitor for efficacy.|

Results for fourth gene in the study

OBX|38|CWE|48018-6^Gene(s) studied^LN|4d|2625^CYP2D6^HGNC-Symb|

OBX|40|ST|47998-0^Genotype display name^LN|4d|*1/*1|

OBX|41|CWE|53040-2^Genetic variation's effect on drug metabolism
interp^LN|4d|LA25391-6^Normal metabolizer^LN|

Medication usage implications panel

OBX|42|CWE|51963-7^Medication assessed^LN|4d.1a|
4493^Fluoxetine^RxT-Ingrd|

OBX|43|CWE|82116-5^Medication usage suggestion [type]^LN|4d.1a|
LA26425-1^Normal Response Expected^LN|

OBX|44|TX|83010-9^Medication usage suggestion
[narrative]^LN|4d.1a|Monitor for inhibition of other drugs.
Fluoxetine is a strong 2D6 inhibitor and is known to effect drugs
which use the CYP 2D6 pathway.|

Results for fifth gene in the study

OBX|45|CWE|48018-6^Gene(s) studied^LN|4e|2621^CYP2C19^HGNC-Symb|

OBX|46|ST|47998-0^Genotype display name^LN|4e|*1/*1|

OBX|47|CWE|53040-2^Genetic variation's effect on drug metabolism
interp^LN|4e|LA25391-6^Normal metabolizer^LN|

Medication usage implications panel

OBX|48|CWE|51963-7^Medication assessed^LN|4e.1a|
6754^Meperidine^RxT-Ingrd|

OBX|49|CWE|82116-5^Medication usage suggestion
[type]^LN|4e.1a|LA26425-1^Normal Response Expected^LN|

OBX|50|TX|83010-9^Medication usage suggestion
[narrative]^LN|4e.1a|Follow label dosing and administration
information. No change needed.|
```

5.9.3.2 GLOSSARY FOR REPORTING HAPLOTYPES

This glossary would give the genetic details to the star alleles that the above example pharmacogenomics report tests for.

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Example 11

```
Haplotype Definition Panel
OBX|1|CWE|48018-6^Gene(s) Studied^LN|5a|2623^CYP2C9^HGNC-Symb|
OBX|2|CWE|48008-7^Allele Name^LN|5a|^^^^^^^^*2|
Attributes of First Genetic Discrete Variant
OBX|3|CNE|81255-2^dbSNP ID^LN|5a.1a|8409^rs1799853^dbSNP|
OBX|4|ST|69551-0^Genomic alt allele^LN|5a.1a|T|
Haplotype Definition Panel
OBX|5|CWE|48018-6^Gene(s) Studied^LN|5b|2623^CYP2C9^HGNC-Symb|
OBX|6|CWE|48008-7^Allele Name^LN|5b|^^^^^^^^*5|
Attributes of Second Discrete Genetic Variant
OBX|7|CNE|81255-2^dbSNP ID^LN|5b.1a|227774^rs28371686^dbSNP|
OBX|8|ST|69551-0^Genomic alt allele^LN|5b.1a|G|
Haplotype Definition Panel
OBX|9|CWE|48018-6^Gene(s) Studied^LN|5c|23663^VKORC1^HGNC-Symb|
OBX|10|CWE|48008-7^Allele Name^LN|5c|^^^^^^^^*A|
Attributes of First Genetic Discrete Variant
OBX|11|CNE|81255-2^dbSNP ID^LN|5c.1a|2211^rs9923231^dbSNP|
OBX|12|ST|69551-0^Genomic alt allele^LN|5c.1a|T|
Haplotype Definition Panel
OBX|13|CWE|48018-6^Gene(s) Studied^LN|5d|2637^CYP3A4^HGNC-Symb|
OBX|14|CWE|48008-7^Allele Name^LN|5d|*1B|
Attributes of First Discrete Genetic Variant
OBX|15|CNE|81255-2^dbSNP ID^LN|5d.1a|31955^rs2740574^dbSNP|
OBX|16|ST|69551-0^Genomic alt allele^LN|5d.1a|T|
Haplotype Definition Panel
OBX|17|CWE|48018-6^Gene(s) Studied^LN|5e|2638^CYP3A5^HGNC-Symb|
OBX|18|CWE|48008-7^Allele Name^LN|5e|^^^^^^^^*1D|
Attributes of First Discrete Genetic Variant
OBX|19|CNE|81255-2^dbSNP ID^LN|5e.1a|15524^rs15524^dbSNP|
OBX|20|ST|69551-0^Genomic alt allele^LN|5e.1a|T|
```

5.9.3.3 PHARMACOGENOMICS EXAMPLE

This example illustrates a pharmacogenomics report testing for Thiopurine S-Methyltransferase (TPMT) deficiency.

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Example 12

```
OBR|1|Acme23469|Gen825750|80738-8^TPMT gene targeted mutation
analysis ^LN|R|201608030830|201608091650|

Variables that Apply to Overall Study: Report Section 1

OBX|1|TX|53577-3^Reason for study^LN|1|Patient not responding to
drug.|

OBX|2|CWE|51963-7^Medications assessed^RxT-Ingrd|1.a|
103^Mercaptopurine^RxT-Ingrd|

OBX|3|CWE|51963-7^Medications assessed^RxT-Ingrd|1.b|
1256^Azathriopine^RxT-Ingrd|

OBX|4|CWE|51963-7^Medications assessed^RxT-Ingrd|1.c|
10485^Thioguanine^RxT-Ingrd|

OBX|6|CNE|48018-6^Gene(s) assessed^LN|1|12014^TPMT^HGNC-Symb|

OBX|7|FT|51969-4^Full narrative report^LN|1|Results - This
individual most likely has intermediate TPMT activity. Individuals
with intermediate TPMT activity can be treated with thiopurine
drugs with fewer side effects by reducing the initial dose.
Subsequent dose adjustments should be based on the degree of
myelosuppression and according to published guidelines. \.br\\.br\
Method - Direct analysis of the following TPMT (Genbank #
NM_000367.2, build hg19) alleles is performed by a polymerase
chain reaction (PCR)-based 5'-nuclease assay using fluorescently
labeled detection probes: *2 (c.238G>C), *3A (c.460G>A and
c.719A>G), *3B (c.460G>A), *3C (c.719A>G,) *4 (c.626-1G>A), *5
(c.146T>C), *8 (c.644G>A), and *12 (c.374C>T)|

Pharmacogenomics: Report Section 4

Results for first gene in the study

OBX|8|CNE|48018-6^Gene(s) assessed^LN|4a|12014^TPMT^HGNC-Symb|

OBX|9|CNE|47998-0^Genotype display name^LN|4a|^^^^^^^^*1/*3A|

OBX|10|CWE|53040-2^Genetic variation's effect on drug metabolism
interp^LN|4a|LA10317-8^Intermediate metaboliser^LN|

Medication usage implications panel

OBX|11|CWE|51963-7^Medications assessed^RxT-Ingrd|4a.1a|
103^Mercaptopurine^RxT-Ingrd|

OBX|12|CWE|82116-5^Medication usage suggestion [type]^LN|4a.1a|
LA26422-8^Decrease dose and titrate to response^LN|

OBX|13|TX|83010-9^Medication usage suggestion
[narrative]^LN|4a.1a|Start at 30-70% of the normal starting dose -
Adjust dose based on myelosuppression and disease-specific
guidelines - Allow 2-4 weeks to reach steady state after each dose
adjustment - Eventually, up to 65% of patients with intermediate
TPMT function may tolerate full doses of mercaptopurine.|

Medication usage implications panel
```


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```
OBX|14|CWE|51963-7^Medications assessed^RxT-Ingrd|4a.1b|
1256^Azathriopine^RxT-Ingrd|

OBX|15|CWE|82116-5^Medication usage suggestion [type]^LN|4a.1b|
LA26422-8^Decrease dose and titrate to response^LN|

OBX|16|TX|83010-9^Medication usage suggestion
[narrative]^LN|4a.1b|Consider starting at 30-70% of target dose if
"full doses" are to be used – Titrate doses based on tolerance –
Allow 2-4 weeks to reach steady state after each dose adjustment.|

Medication usage implications panel

OBX|17|CWE|51963-7^Medications assessed^RxT-Ingrd|4a.1c|
10485^Thioguanine^RxT-Ingrd|

OBX|18|CWE|82116-5^Medication usage suggestion [type]^LN|4a.1c|
LA26422-8^Decrease dose and titrate to response^LN|

OBX|19|TX|83010-9^Medication usage suggestion
[narrative]^LN|4a.1c|Start at 30-50% of the normal starting dose –
Adjust dose based on myelosuppression and disease-specific
guidelines – Allow 2-4 weeks to reach steady state after each dose
adjustment – Eventually, up to 65% of patients with intermediate
TPMT function may tolerate full doses of thioguanine.|
```

5.9.3.4 GLOSSARY FOR REPORTING HAPLOTYPES

This glossary would give the genetic details to the star alleles that the above example pharmacogenomics report tests for.

Example 13

```
Haplotype Definition Panel

OBX|1|CWE|48018-6^Gene(s) Studied^LN|5b|12014^TPMT^HGNC-Symb|

OBX|2|CWE|48008-7^Allele Name^LN|5b|^^^^^^^^*3a|

Attributes of First Genetic Discrete Variant

OBX|3|CNE|81255-2^dbSNP ID^LN|5b.1a|1800460^rs1800460^dbSNP|

OBX|4|ST|69551-0^Genomic alt allele^LN|5a.1a|A|

Attributes of Second Genetic Discrete Variant

OBX|5|CNE|81255-2^dbSNP ID^LN|5b.1b|1142345^rs1142345^dbSNP|

OBX|6|ST|69551-0^Genomic alt allele^LN|5b.1b|G|
```


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14 CLINICAL GENOMICS CODE SYSTEMS

Information on code systems with name, HL70396 Code, OID, Source Information Links, and description.

TABLE 14-1. CLINICAL GENOMICS CODING SYSTEMS		
Coding System name	HL70396 Code	HL7 OID
Cytogenetic (chromosome) location	**Chrom-Loc**	**2.16.840.1.113883.6.335**
	Source Organization: National Center for Biotechnology Information (NCBI) Source Table Information: https://www.ncbi.nlm.nih.gov/genome/tools/gdp/help Source Table Download: ftp://ftp.ncbi.nlm.nih.gov/pub/gdp Place to explore table: https://clin-table-search.lhc.nlm.nih.gov/apidoc/cytogenetic_locs/v3/doc.html	
	Chromosome location (AKA chromosome locus or cytogenetic location), is the standardized syntax for recording the position of genes and large mutations. It consists of three parts: the Chromosome number (e.g. 1-22, X, Y), an indicator of which arm – either "p" for the short or "q" for the long, and then generally a series of numbers separated by dots that indicate the region and any applicable band, sub-band, and sub-sub-band of the locus (e.g. 2p16.3). There are other conventions for reporting ranges and locations at the ends of the chromosomes. The table of these chromosome locations was loaded with all of the locations found in NCBI's ClinVar variation tables. It will expand as additional sources become available. This does not include all finely grained chromosome locations that exist. Users can add to it as needed.	
ClinVar Variant ID	**CLINVAR-V**	**2.16.840.1.113883.6.319**
	Source organization: National Center for Biotechnology Information (NCBI) Source table information: https://www.ncbi.nlm.nih.gov/clinvar/ Source table download: ftp://ftp.ncbi.nlm.nih.gov/pub/clinvar/tab_delimited/ Place to explore table: https://clin-table-search.lhc.nlm.nih.gov/apidoc/variants/v3/doc.html	
	ClinVar processes submissions reporting variants found in patient samples, assertions made regarding their clinical significance, information about the submitter, and other supporting data. The alleles described in submissions are mapped to reference sequences, and reported according to the HGVS standard. ClinVar includes simple and complex variants composed of multiple small variants. However, it now also includes large structural variants, which have a known clinical implication. So now simple, complex and many structural variants can all be found in ClinVar. The ClinVar records have a field for Allele ID and for Variant ID. All simple variants have an Allele ID. At present, all complex and most simple variants also have a Variant ID, and by the end of 2016, all simple variants will also have a variant ID. We focus mostly on the variant ID in this guide. This coding system uses the variant ID as the code and the variant name from NCBI's "variant_summary.txt.gz" file as the code's print string. The "variant_summary.txt.gz" file caries more than 20 useful fields, including the separate components of the variant name, the cytogenetic location, the genomic reference, etc. So based on the Variant ID, you can use ClinVar to find most you would ever want to know about the variant. In the LHC Clinical Table Search Service and LHC-Forms, we have indexed many of these attributes to assist users and applications that need to find the ID for a particular variant.	
COSMIC –Simple variants	**COSMIC-Smpl**	**2.16.840.1.113883.6.320**
	Source organization: Wellcome Trust Sanger Institute Source table information: http://grch37-cancer.sanger.ac.uk/cosmic Source table download: http://grch37-cancer.sanger.ac.uk/cosmic/files?data=/files/grch37/cosmic/v81/CosmicMutantExport.tsv.gz Place to Explore Table: https://clin-table-search.lhc.nlm.nih.gov/apidoc/cosmic/v3/doc.html Copyright: Wellcome Trust Sanger Institute: http://cancer.sanger.ac.uk/cosmic/license	

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TABLE 14-1. CLINICAL GENOMICS CODING SYSTEMS		
Coding System name	HL70396 Code	HL7 OID
	This table includes only simple somatic (cancer) variants, one per unique variant ID. The code is the COSMIC variant ID, and the name is constructed from Ensembl transcript reference sequences and p.HGVS that use the single letter codes for amino acids. It carries fields analogous to most of the key fields in ClinVar, but its reference sequences are Ensembl transcript reference sequences with prefixes of ENST; it specifies amino acid changes with the older HGVS single letter codes and it carries examples of primary cancers and primary tissues - fields that are not in ClinVar. COSMIC's source table includes multiple records per variant - one per submission. The COSMIC- Simple Variants table that we have extracted from the original file includes only one record per unique variant – a total of more than 3 million records. These contents are copyright COSMIC (http://cancer.sanger.ac.uk/cosmic/license). LHC has produced a look up table for these records, and for users to look up particular variant IDs, both with permission from COSMIC. However, interested parties must contact COSMIC directly for permission to download these records.	
COSMIC-Structural variants	**COSMIC-Strc**	**2.16.840.1.113883.6.321**
	Source organization: Wellcome Trust Sanger Institute Source table information: http://grch37-cancer.sanger.ac.uk/cosmic Source table download: http://grch37-cancer.sanger.ac.uk/cosmic/files?data=/files/grch37/cosmic/v81/CosmicStructExport.tsv.gz Place to Explore Table: https://clin-table-search.lhc.nlm.nih.gov/apidoc/cosmic_struct/v3/doc.html Copyright: Wellcome Trust Sanger Institute: http://cancer.sanger.ac.uk/cosmic/license	
	COSMIC also has files containing structural variants. These are divided into two tables, one containing structural variants and one containing copy number variants. In contrast, NCBI does not separate structural variants this way. The table for this coding system derives from COSMIC's structural variation tables. The identifiers for these are pure numbers with no prefix, and each record includes information about the variant type, the histological classification of the sample, and the primary tissue/cancer from which the sample originated. Like COSMIC simple variants, these also use Ensembl reference sequences, but uses the genomic reference sequences instead of the transcript ones (those whose codes begin with ENSG). These contents are copyright COSMIC (http://cancer.sanger.ac.uk/cosmic/license). LHC has produced a look up table for these records, also sub-setted to include only unique variants, for users to look up particular variant IDs with permission from COSMIC. However, interested parties must contact COSMIC directly for permission to download these records.	
dbSNP	**dbSNP**	**2.16.840.1.113883.6.284**
	Source organization: National Center for Biotechnology Information (NCBI) Source table information: http://www.ncbi.nlm.nih.gov/books/NBK21088/ Source table download: ftp://ftp.ncbi.nih.gov/snp/organisms/human_9606_b146_GRCh37p13/ASN1_flat/ Place to Explore Table: https://clin-table-search.lhc.nlm.nih.gov/apidoc/snps/v3/doc.html	
	The Short Genetic Variations database (dbSNP) is a public-domain archive maintained by NCBI for a broad collection of short genetic polymorphisms. The SNP ID is unique for each position and length of DNA change. For example, a change of 3 nucleotides will have a different SNP ID than a change of 4 nucleotides at the same locus, but the code will be the same for all changes at the same locus and with the same length. So to specify a variation, the alt allele and the SNP code must be included.	
dbVar- Germline	**dbVar-GL**	**2.16.840.1.113883.6.322**
	Source organization: National Center for Biotechnology Information (NCBI)	

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TABLE 14-1. CLINICAL GENOMICS CODING SYSTEMS		
Coding System name	HL70396 Code	HL7 OID
	Source table information: https://www.ncbi.nlm.nih.gov/dbvar/content/overview/ Source: ftp://ftp.ncbi.nlm.nih.gov/pub/dbVar/data/Homo_sapiens/ Place to Explore Table: https://clin-table-search.lhc.nlm.nih.gov/apidoc/dbvar/v3/doc.html	
	dbVar is NCBI's database of genomic structural variations (including copy number variants) that are larger than 50 contiguous base pairs. It is the complement of dbSNP, which identifies variants occurring in 50 or fewer contiguous base pairs. dbVar contains insertions, deletions, duplications, inversions, multi-nucleotide substitutions, mobile element insertions, translocations, and complex chromosomal rearrangements. dbVar carries structured Germline and Somatic variants in separate files. Accordingly, we have divided the coding system for dbVar the same way. This coding system represents the Germline dbVar variants. Its record ID may begin with one of four prefixes: nsv, nssv, esv and essv. These are accession prefixes for variant regions (nsv) and variant calls (or instances, nssv), respectively. Typically, one or more variant instances (nssv – variant calls based directly on experimental evidence) are merged into one variant region (nsv – a pair of start-stop coordinates reflecting the submitters' assertion of the region of the genome that is affected by the variant instances). The "n" preceding sv or indicates that the variants were submitted to NCBI (dbVar). The prefix, "e" for esv and essv represent variant entities (corresponding to NCBI's nsv and nssv) that were submitted to EBI (DGVa). The relation between variant call, and variant region, instances is many to one. The LHC lookup table for dbVar germline variants includes both variant instances (essv or nssv) and the variant region records (nsv, esv). Users can sub-select by searching on the appropriate prefix.	
dbVar- Somatic	**dbVar-Som**	**2.16.840.1.113883.6.323**
	Source organization: National Center for Biotechnology Information (NCBI) Source table information: http://www.ncbi.nlm.nih.gov/dbvar/content/overview/ Source table download: ftp://ftp.ncbi.nlm.nih.gov/pub/dbVar/data/ Place to Explore Table: Pending	
	dbVar is NCBI's database of genomic structural variations (including copy number variants) that are larger than 50 contiguous base pairs. It is the complement of dbSNP, which only contains variants occurring in 50 or fewer contiguous base pairs. It contains insertions, deletions, duplications, inversions, multi-nucleotide substitutions, mobile element insertions, translocations, and complex chromosomal rearrangements. Germline and Somatic variants are presented in separate files. Accordingly, we have divided the coding system within dbVar the same way. This coding system represents the Somatic (mostly cancer) variants in dbVar. As is true for the Germline portion of dbVar, the record IDs for the somatic dbVar's have prefixes of nsv, nssv, esv or essv with the leading "e" and "n" having the corresponding meaning as described above for germline or structural variant. We also include both the variant calls and variant region records in the LHC dbVar somatic variant file.	
Ensembl genomic reference sequence	**Ensembl-G**	**2.16.840.1.113883.6.324**
	Source organization: European Bioinformatics Institute (EBI) Source table information: http://useast.ensembl.org/info/genome/genebuild/genome_annotation.html Source table download: http://useast.ensembl.org/info/data/ftp/index.html Place to Explore Table: Pending	
	Set of Ensembl gene reference sequences whose identifiers have a prefix of "ENSG." It only includes genomic sequences associated with genes and uses the whole build plus the chromosome number to identify chromosome reference sequences, rather than a separate set of reference sequence identifier as NCBI does. LHC has not yet produced a convenient look up table for these files, but they are available from the URL cited above.	

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TABLE 14-1. CLINICAL GENOMICS CODING SYSTEMS		
Coding System name	HL70396 Code	HL7 OID
Ensembl protein reference sequence	**Ensembl-P**	**2.16.840.1.113883.6.325**
	Source organization: European Bioinformatics Institute (EBI) Source table information: http://useast.ensembl.org/info/genome/genebuild/genome_annotation.html Source table download: http://useast.ensembl.org/info/data/ftp/index.html Place to Explore Table: Pending	
	Set of Ensembl protein reference sequences. Their identifiers are distinguished by the prefix of "ENSP," and correspond to NCBI's "NP_" reference sequence identifiers. LHC has not yet produced a convenient look up table for these files, but they are available from the URL cited above.	
Ensembl transcript reference sequence	**Ensembl-T**	**2.16.840.1.113883.6.326**
	Source organization: European Bioinformatics Institute (EBI) Source table information: http://useast.ensembl.org/info/genome/genebuild/genome_annotation.html Source table download: http://useast.ensembl.org/info/data/ftp/index.html Place to Explore Table: Pending	
	Set of reference sequences for transcripts of coding regions. Their identifiers all have a prefix of "ENST." There are parallels for most (if not all) of what is in Ensembl within NCBI and most of the content is shared. "ENST" parallels NCBI's "NM_" identifiers. In general, Ensembl takes its reference sequences directly from the genomic build. NCBI may adjust its reference sequences by replacing known "variants" with sequences that better reflect the population "normal". LHC has not yet produced a convenient look up table for these files, but they are available from the URL cited above.	
HGNC-Symbol	**HGNC-Symb**	**2.16.840.1.113883.6.336**
	Source organization: HUGO Gene Nomenclature Committee (HGNC) Source table information: http://www.genenames.org/ Source table download: ftp://ftp.ebi.ac.uk/pub/databases/genenames/new/tsv/hgnc_complete_set.txt Place to Explore Table: https://clin-table-search.lhc.nlm.nih.gov/apidoc/genes/v3/doc.html	
	The HGNC gene table carries the gene ID, gene symbol and full gene name. The GENE ID is specific to the species. The gene symbol and name is shared by all species with the same gene. The HGNC-Symb table carries only human genes. The code for this coding system is the HGNC gene code, the "name" or print string is the HGNC gene symbol. More than 28,000 human gene symbols and names have been assigned so far, including almost all of the protein coding genes. But close to 10,000 non-protein coding “genes” do not yet have HGNC names. NCBI creates what might be thought of as interim codes but includes many more genes. The codes from NCBI and from HGNC are pure numbers and can’t be distinguished by their format. The gene codes we propose in this guide and use in our examples and in the LHC form that inputs gene information are all HGNC codes. If the study includes more than one gene, they can all be entered in one OBX, separated by the repeat delimiter. Alternatively they can be entered into separate OBX’s but the content of OBX-4 will have to be unique for each such repeat. We recommend n.1, n.2, n.3 etc. for such repeated variables in the report section which reports gene symbols (See Table 2).	
HGVS-Genomic syntax	**HGVS.g**	**2.16.840.1.113883.6.327**
	Source organization: Human Genome Variation Society (HGVS) Source table information: http://varnomen.hgvs.org/bg-material/refseq/#DNAg HGVS validator: https://mutalyzer.nl/	

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TABLE 14-1. CLINICAL GENOMICS CODING SYSTEMS		
Coding System name	HL70396 Code	HL7 OID
	HGVS syntax that describes the variations (mutations) at the genome level (the DNA before it is spliced to remove introns). The genomic syntax statements which can describe simple or structural variants are distinguished by a leading "g."	
HGVS-Transcript syntax	**HGVS.c**	**2.16.840.1.113883.6.328**
	Source organization: Human Genome Variation Society (HGVS) Source table information: http://varnomen.hgvs.org/bg-material/refseq/#DNAc HGVS validator: https://mutalyzer.nl/	
	HGVS syntax that describes variations (mutations) at the transcript (messenger RNA) level. The transcript syntax statements, which can describe simple and complex variants, are distinguished by a leading "c."	
HGVS-Protein syntax	**HGVS.p**	**2.16.840.1.113883.6.329**
	Source organization: Human Genome Variation Society (HGVS) Source table information: http://varnomen.hgvs.org/bg-material/refseq/#proteinp HGVS validator: https://mutalyzer.nl/	
	HGVS syntax that specifies the variations (mutations) at the amino acid level, which are induced by underlying DNA variants. The protein change statements are distinguished by a leading "p." HGVS.p representations will not exist for variants that occur outside of coding regions.	
HLA Nomenclature	**HLA-Allele**	**2.16.840.1.113883.6.341**
	Source Organization: Immuno Polymorphism Database (IPD) Source Table Information: https://www.ebi.ac.uk/ipd/imgt/hla/ Source Table Download: ftp://ftp.ebi.ac.uk/pub/databases/imgt/mhc/hla/	
	Human leukocyte antigen (HLA) complex contains more than 220 genes that encode for the proteins of the immune system. HLA alleles are most commonly used for histocompatibility testing for stem cell and solid organ transplantation. The WHO Nomenclature Committee for Factors of the HLA System is responsible for a common nomenclature of HLA alleles, allele sequences, and quality control, to communicate histocompatibility typing information to match donors and recipients. An HLA allele is defined as any set of variations found on a sequence of DNA comprising a HLA gene. So, if there are five variations found in this one gene sequence, this set is defined as one allele (vs. the definition of an allele being the variation found between the test specimen and the reference along a contiguous stretch of DNA). In the case of HLA, the contiguous stretch of DNA represents the entire gene, and the variations do not need to be contiguous within the gene sequence. Each HLA allele name has a unique name consisting of the gene name followed by up to four fields, each containing at least two digits, separated by colons. There are also optional suffixes added to indicate expression status. For the full specification, please go to this website: http://hla.alleles.org/nomenclature/naming.html . HLA nomenclature can also be used to represent sets of alleles that share sequence identity in the Antigen Recognition Site (ARS). G-groups are alleles that have identical DNA sequences in the ARS, while P-groups are alleles that have identical protein sequences in the ARS. These are described, respectively, in http://hla.alleles.org/alleles/g_groups.html and http://hla.alleles.org/alleles/p_groups.html.	
HPO	**HPO**	**2.16.840.1.113883.6.339**
	Source organization: Human Phenotype Ontology Consortium Source table information: http://human-phenotype-ontology.github.io/about.html Source table download: http://human-phenotype-ontology.github.io/downloads.html Place to Explore Table: Pending License: Sebastian Köhler, Sandra C Doelken, Christopher J. Mungall, Sebastian Bauer, Helen V. Firth, et al.	

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TABLE 14-1. CLINICAL GENOMICS CODING SYSTEMS		
Coding System name	HL70396 Code	HL7 OID
	The Human Phenotype Ontology project: linking molecular biology and disease through phenotype data Nucl. Acids Res. (1 January 2014) 42 (D1): D966-D974 doi:10.1093/nar/gkt1026	
	The Human Phenotype Ontology (HPO) aims to provide a standardized vocabulary of phenotypic abnormalities encountered in human disease. Each term in the HPO describes a phenotypic abnormality, such as atrial septal defect.	
ICD-10-CM	**I10C**	**2.16.840.1.113883.6.90**
	Source organization: National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention (CDC) Source table information: https://www.cdc.gov/nchs/icd/icd10cm.htm Source table download: https://www.cdc.gov/nchs/icd/icd10cm.htm# FY 2017 release of ICD-10-CM Place to Explore Table: https://clin-table-search.lhc.nlm.nih.gov/apidoc/icd10cm/v3/doc.html Copyright: World Health Organization, http://www.who.int/classifications/icd/en/	
	The International Classification of Diseases (ICD) is the classification used to code and classify mortality data from death certificates. The International Classification of Diseases, Clinical Modification (ICD-10-CM) is used to code and classify morbidity data from the inpatient and outpatient records, physician offices, and most National Center for Health Statistics (NCHS) surveys. The ICD-10-CM is used to code and classify mortality data from death certificates, having replaced ICD-9 for this purpose as of January 1, 1999. ICD-10-CM is the replacement for ICD-9-CM, volumes 1 and 2, effective October 1, 2015, but of course, decades of ICD-9 data recorded before 2015 will be in medical record systems for a long time. The codes are an alphanumeric string. The name is a diagnosis, symptom or other clinical concepts. Some of these codes can be related in a shallow hierarchy. ICD-10-CM codes are 7 digits: digit 1 is alpha; digit 2 is numeric; digits 3–7 are alpha or numeric; and a decimal/dot is placed after the third character. ICD-10-CM includes extensive Combination Codes to better capture complexity. NCHS, which is part of the U.S. Centers for Disease Control and Prevention (CDC), serves as the World Health Organization (WHO) Collaborating Center for the Family of International Classifications for North America and in this capacity is responsible for coordination of all official disease classification activities in the United States relating to the ICD and its use, interpretation, and periodic revision.	
ICD-9-CM	**I9CDX**	**2.16.840.1.113883.6.103**
	Source organization: National Center for Health Statistics (NCHS) Source table information: https://www.cdc.gov/nchs/icd/icd9.htm Source table download: http://www.cdc.gov/nchs/icd/icd9cm.htm; https://www.cms.gov/medicare/coding/ICD9providerdiagnosticcodes/codes.html Place to Explore Table: https://clin-table-search.lhc.nlm.nih.gov/apidoc/icd9cm_dx/v3/doc.html Copyright: World Health Organization, http://www.who.int/classifications/icd/en/	
	The International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9- CM) is a subset of ICD-9. ICD-9-CM is the official system of assigning codes to diagnoses and procedures associated with hospital utilization in the United States. The ICD-9 was used to code and classify mortality data from death certificates until 1999, when use of ICD-10 for mortality coding started. Most ICD-9-CM codes are purely numeric consisting of 3 digits followed by a dot and one or more digits. A select subset start with the letter E or V followed by a number. ICD-9-CM codes are 3-5 digits. This subset of ICD-9 carries only diagnostic codes (the surgical and other procedure codes are excluded).	

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TABLE 14-1. CLINICAL GENOMICS CODING SYSTEMS		
Coding System name	HL70396 Code	HL7 OID
International System for Human Cytogenetic Nomenclature (ISCN)	**ISCN**	**2.16.840.1.113883.6.299**
	Source organization: The International System for Human Cytogenetic Nomenclature (ISCN) Source table information: https://www.karger.com/Article/FullText/353118 ISCN (2016): An International System for Human Cytogenetic Nomenclature, J McGowan-Jordan, Simons A, M. Schmid (eds). S. Karger, Basel 2016	
	Like HGVS, The International System for Human Cytogenetic Nomenclature (ISCN) is a syntax. It came out of cytopathology and deals with reporting karyotypes down to the chromosome fusions and many types of small copy number variants. However, cytogenetics is out of the scope in this guide. We use ISCN syntax to report large deletion-duplications in structural variants, as well we include other variants that have been observed.	
Logical Observation Identifier Names and Codes	**LN**	**2.16.840.1.113883.6.1**
	Source organization: Regenstrief Institute Source table information: http://loinc.org/background Source table download: http://loinc.org/downloads Place to Explore Table: https://clin-table-search.lhc.nlm.nih.gov/apidoc/loinc/v3/doc.html Copyright: Regenstrief Institute, http://loinc.org/terms-of-use	
	Logical Observation Identifiers Names and Codes (LOINC®) provides a set of universal codes and names for identifying laboratory and other clinical observations. One of the main goals of LOINC is to facilitate the exchange and pooling of results for clinical care, outcomes management, and research. LOINC was initiated by Regenstrief Institute research scientists who continue to develop it with the collaboration of the LOINC Committee.	
Locus Reference Genomic (LRG)	**LRG-RefSeq**	**2.16.840.1.113883.6.337**
	Source organization: Locus Reference Genomic (LRG) Source table information: http://www.lrg-sequence.org/about Source table download: http://www.lrg-sequence.org/downloads Place to Explore Table: Pending	
	LRG is a manually curated record that contains stable, and thus un-versioned, reference sequences designed specifically for reporting sequence variants with clinical implications. It provides a genomic DNA sequence representation of a single gene that is idealized, has a permanent ID (with no versioning), and core content that never changes. Their database includes maps to NCBI, Ensembl and UCSC reference sequences. It contained sequences for a total of 1073 genes as of April 2016, with identifiers of the form: "LRG_####", where #### can be from 1 to N, and N is the last gene processed. See PMIDs: 24285302, 20398331, and 20428090 for more information.	
NCBI MedGen disease subset	**MedGen-Dis**	**2.16.840.1.113883.6.333**
	Source organization: National Center for Biotechnology Information (NCBI) Source table information: https://www.ncbi.nlm.nih.gov/medgen/ Source table download: ftp://ftp.ncbi.nlm.nih.gov/pub/medgen/ Place to Explore Table: https://clin-table-search.lhc.nlm.nih.gov/apidoc/disease_names/v3/doc.html	
	MedGen-disease is a subset of disease concepts (about 20,000 as of January 2016) taken from the NCBI's MedGen table. It includes most known genetic and clinical diseases. It drew its content from the NIH Genetic Testing Registry (GTR®), UMLS, HPO, OMIM, Orphanet, ClinVar and other sources, and is probably the most complete compendium of genetic diseases, though it also includes most	

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TABLE 14-1. CLINICAL GENOMICS CODING SYSTEMS		
Coding System name	HL70396 Code	HL7 OID
	common clinical diseases. It uses UMLS IDs when they exist and its own ID when not, and links to SNOMED CT and other disease identifiers. The MedGen database includes the inheritance and clinical features of each disease, as well as the map location of underlying genetic basis.	
NCBI- gene code	**NCBI-gene code**	**2.16.840.1.113883.6.340**
	Source organization: National Center for Biotechnology Information (NCBI) Source table information: https://www.ncbi.nlm.nih.gov/gene Source table download: ftp://ftp.ncbi.nih.gov/gene/ Place to Explore Table: https://clin-table-search.lhc.nlm.nih.gov/apidoc/ncbi_genes/v3/doc.html	
	When applicable, this variable identifies the gene on which the variant is located. The gene identifier is also carried in the transcript reference sequence database, and is part of a full HGVS expression. Not all genes have HGNC names and codes so NCBI has created gene IDs that cover the genes that are not registered by HGNC.	
NCBI -genomic and chromosome reference sequences	**RefSeq-G**	**2.16.840.1.113883.6.330**
	Source organization: National Center for Biotechnology Information (NCBI), U.S. National Library of Medicine (NLM) Source table information: https://www.ncbi.nlm.nih.gov/refseq/ Source table download: ftp://ftp.ncbi.nlm.nih.gov/genomes/Homo_sapiens/ARCHIVE/BUILD.37.3/GFF/ Place to Explore Table: https://clin-table-search.lhc.nlm.nih.gov/apidoc/refseqs/v3/doc.html	
	Subset of NCBI Human RefSeqs with prefix of NC_ or NG_. Those prefixed with "NC_" represent the whole genomic RefSeq for individual chromosomes. Those prefixed with "NG_" represent genes with all of their introns and flanking regions and other larger or smaller genomic sequences. These are available separately in the NCBI source data file, which includes all human RefSeqs (including those with prefix of NR_ or XM_): ftp://ftp.ncbi.nlm.nih.gov/genomes/Homo_sapiens	
NCBI -protein reference sequence	**RefSeq-P**	**2.16.840.1.113883.6.331**
	Source organization: National Center for Biotechnology Information (NCBI) Source table information: https://www.ncbi.nlm.nih.gov/refseq/ Source table download: ftp://ftp.ncbi.nlm.nih.gov/genomes/Homo_sapiens/ARCHIVE/BUILD.37.3/GFF/ Place to Explore Table: https://clin-table-search.lhc.nlm.nih.gov/apidoc/refseqs/v3/doc.html	
	Subset of NCBI RefSeqs that represent reference sequences for proteins. Not routinely included in reports because Amino acid changes can be computed directly from DNA changes based on transcript reference sequence. However some fields are interested only in the protein sequence change, and proteins can be sequenced independently of DNA sequencing. We will explore the creation of coding systems for other protein reference identifiers such as UniProtKB accession numbers (http://www.uniprot.org/help/uniprotkb).	
NCBI-transcript reference sequences (RefSeq)	**RefSeq-T**	**2.16.840.1.113883.6.332**
	Source organization: National Center for Biotechnology Information (NCBI) Source table information: https://www.ncbi.nlm.nih.gov/refseq/ Source table download: ftp://ftp.ncbi.nlm.nih.gov/genomes/Homo_sapiens/ARCHIVE/BUILD.37.3/GFF/ Place to Explore Table: https://clin-table-search.lhc.nlm.nih.gov/apidoc/refseqs/v3/doc.html	
	Subset of NLM RefSeq records with prefix of "NM_" are reference sequences that represent messenger RNA.	

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TABLE 14-1. CLINICAL GENOMICS CODING SYSTEMS		
Coding System name	HL70396 Code	HL7 OID
RxTerms- Ingredients Subset	**RxT-Ingrd**	**2.16.840.1.113883.6.334**
	Source organization: National Center for Biotechnology Information (NCBI) Source table information: https://wwwcf.nlm.nih.gov/umlslicense/rxtermApp/rxTerm.cfm Source table download: https://wwwcf.nlm.nih.gov/umlslicense/rxtermApp/rxTermCondition.cfm Place to Explore Table: https://clin-table-search.lhc.nlm.nih.gov/apidoc/drug_ingredients/v3/doc.html	
	RxT-Ingrd is a specialization of the RxNorm database that includes the ingredients in RxTerms (derived from RxNorm) except allergens (used for allergy testing), combination ingredients, and inactive ingredients. The subset is designed for identifying drugs that might be the focus of pharmacogenetic testing.	
SNOMED-CT	**SCT**	**2.16.840.1.113883.6.96**
	Source organization: International Health Terminology Standards Development Organisation Source table information: http://www.snomed.org/snomed-ct Source table download: https://www.nlm.nih.gov/healthit/snomedct/us_edition.html (requires free UMLS License) Place to Explore Table: Not implemented in the LHC public site, but registered users (with free UMLS license) can browse SNOMED CT via: https://www.nlm.nih.gov/research/umls/Snomed/snomed_browsers.html Copyright: International Health Terminology Standards Development Organisation, http://www.snomed.org/snomed-ct/get-snomed-ct	
	SNOMED CT is a concept-based, scientifically validated terminology that provides a unique and permanent concept identifier that can be included in multiple HL7 data types, including CD and CE. If the concept is found to be ambiguous or the meaning changes, the concept is inactivated but still retained and the identifier is never reused. It is required by Meaningful Use for many purposes. SNOMED CT's concepts are interrelated hierarchically and use description logic. SNOMED CT code development is in process for the answer lists in this guide, and in the meantime only LOINC answer codes are available.	
Star Alleles (Pharmacogenomic)	**Star-Allele**	**2.16.840.1.113883.6.342**
	Source Organization: The Human Cytochrome P450 (CYP) Allele Nomenclature Database Source Table Information: http://www.cypalleles.ki.se/	
	The star allele nomenclature is commonly used in pharmacogenomics as shorthand to specify one or more specific variants in a gene that is known to impact drug metabolism or response. A star allele can identify either a single variant or a group of variants found in cis, and therefore it usually represents a haplotype. A star allele name is composed of the gene symbol and an allele number, separated by an asterisk, e.g. TPMT*2. By convention, the *1 allele represents the allele that contains the "reference" sequence, although that is not true in all cases. Closely related alleles may be assigned a common number and be differentiated by a unique letter that specifies the suballele (e.g., TPMT*3A, TPMT*3B). Pharmacogenomics tests commonly report patient phenotypes as diplotypes, i.e. *1/*3A. The star nomenclature system is inadequately defined and inconsistently adopted. Therefore, although the system we are proposing supports the inclusion of pharmacogenomics star alleles as a legacy syntax, we strongly encourage messages that include star alleles to rigorously define those alleles in Report Section 5, Glossary for Haplotype Definition, which allows the reporting lab to specify the variants with their local definitions.	
Unified Code for Units of Measure (UCUM)	**UCUM**	**2.16.840.1.113883.6.8**
	Source organization: Regenstrief Institute HL7 Long Name: Unified Code for Units of Measure Source table information: http://unitsofmeasure.org/trac Source table download (common UCUM units in clinical care): https://loinc.org/usage/units	

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TABLE 14-1. CLINICAL GENOMICS CODING SYSTEMS		
Coding System name	HL70396 Code	HL7 OID
	UCUM validator and converter: http://lhncbc.github.io/ucum-lhc/	
	Unified Code for Units of Measure (UCUM) is a syntax for defining units of measure including both metric and conventional units. It comes with tables and software for validating and converting values expressed in one unit of measure to a different but commensurate unit of measure. Its purpose is to facilitate unambiguous electronic communication of quantities together with their units. UCUM codes are intended for computer use. In HL7 V2, traditional unit strings can be included along with UCUM as needed. UCUM defines a syntax; so, like HGVS, there is no numeric code attached and no table with a complete enumeration. However, NLM and Regenstrief Institute developed a table of common UCUM units used in clinical care, available at: https://loinc.org/usage/units. Lister Hill Center at NLM has also developed a JavaScript program to convert and validate UCUM units, available at: https://github.com/lhncbc/ucum-lhc.	

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