**Report Section 1 for Variables that apply to the Overall Study.**

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Data Type** | **LOINC #**  **Note**  **Links** | **ROC** | **Observation display Name- draft version** | | **Card** | **OBX-4** | **OBX-5**  **Examples data** | **Comments** | |
|  |  |  |  |  | |  |  |  |  | |
|  |  | **81247-9** |  | | **Master HL7 genetic variant reporting panel** | 1..1 |  |  | Note all of the genomic data reported in this panel assume that nucleotide positions starts at 1, and focuses on the positive strand. This is the assumption embedded in HGVS, the public distribution of NCBI, Ensembl, COSMIC, and most other genomic databases. | |
|  |  | **81294-1** |  | | **Genetic form configuration panel** | 0..\* |  |  | This is the first one. Needed for controlling input into form. These are not LOINC codes that would be included in the HL7 message. | |
|  |  |  |  | | Configuration LOINC term from Ye | 0..1 | 1 |  |  | |
|  |  |  | O | | 2nd configuration term from Ye | 0..1 | 1 |  |  | |
| A | CWE | 81248-7 | O | | Default Transcript reference sequence coding system | 0..1 | 1 | NCBI-NM; | Answer list will include: a) Ensembl transcript identifiers with prefix =”ENST”,  b) NCBI’s RefSeq transcript RefSeq’s with prefix =”NM\_”,  c) Other T RefSeq coding system  If user pick this “other” choice he/she will have to identify the OID for this other coding system in subsequent questions | |
| B | CWE | 81249-5 | O | | Default Genomic reference sequence coding system | 0..1 | 1 | NCBI-NG-NC | Answer list will include  a) Ensembl genomic prefix =”ENSG”,  b) NCBI-NG-NC – which includes RefSeq g, prefix =”NG\_” or “NC\_”,  d)Other G RefSeq coding system  If user picks “other G RefSeq Coding system”, he/she will have to identify the OID for this other coding system in subsequent questions | |
| C | CWE | **82122-3** | O | | Genetic variant coding system | 0..1 | 1 |  | Identifies the public source that carries the code name and other attributes for the genetic variant.    An entry is needed but only for controlling form behavior. Message developers can assert the coding system of choice where applicable. Answer list choices for now will be ClinVar Variant ID, COSMIC (?? Should we provide an “other” with option to specify an OID to generalize the variant ID ) | |
| D | ST | 81295-8 | C | | OID For other T RefSeq coding system | 0..1 | 1 | #### #### ##### | If answer to LOINC 81248-7 Default transcript Reference coding system is “Other T RefSeq coding system” then ask for the OID for this other coding system. | |
| E | ST | 81296-6 | C | | OID For other G RefSeq coding system | 0..1 | 1 | ##### #### ##### | If answer to question 81249-5 is Other G RefSeq coding system – ask for the OID for this other coding system | |
|  |  | **81306-3** |  | | **Variables that apply to the overall study** | | | |  |
| A | TX | [53577-3](http://s.details.loinc.org/LOINC/53577-3.html) | O | Reason for study | | 0..\* | 1 | “Worried about family planning” | HL7 provides OBR-31 for recoding 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 it should be delivered in HL7 OBR-31.This is an ask-at-order-entry question. | |
| B | CWE | [51967-8](http://s.details.loinc.org/LOINC/51967-8.html) | O | Genetic disease(s) assessed | | 0..1 | 1 | 2971795010^Deficiency of isoibutyryl-coenzyme A dehydrogenase (disorder)^SCT | Identifies the disease (usually genetic) being assed. If entered as a code may use a variety of coding systems (SNOMED CT, ICD-9CM, ICD10, NCBIs genetic diseases list (more than 20,000 genetic diseases and their codes link to SNOMED codes when available.  For the example values shown in the OBX-5 column we show SNOMED –CT Codes (SCT) as coding system), but cause that is the direction we will go in the US. However, the L-forms demo of this draft specification shows the content from the NCBI MedGen | |
| C | CWE | 51963-7 | C | Medications assessed [ID] | | 0..\* | 1 | 50005^Fluoxitine ^RxN-ingrd~ 84701^Atorvastatin^RxN-ingrd~   45000^Naproxin^RxN-Ingrd~ 11289^Coumadine^RxN-ingrd | Applies only to pharmacogenomic studies. Carries the medications for which there is concern that genetic variation might influence the efficacy and/or the rate of metabolism. (These would typically be medications being considered for use, or being used by the patent). If this variable is empty or not used, the lab will provide the usual information they provide about common affected drugs. This content will usually be an ask-at-order-entry question Can enter multiple medication identifiers separated by repeat delimiters. Or send each in a separate OBX, but in that case OBX-4 must be different for each OB-4.We recommend 1.1, 1.2 ,1.3 etc. | |
| D | CWE | [36908-2](http://s.details.loinc.org/LOINC/36908-2.html) | C | Gene mutations tested for[NOM] | | 0..\* | 1 |  | Required if the study is a targeted (looking at specific known mutation) mutation analysis.  Multiple mutations can be entered in one OBX-5 if separated by repeat delimiters. Alternatively they can each be reported in a separate OBX. In that case OBX-4 should be different for each such OBX, We recommend 1.1, 1.2, 1.3, etc. ( This variable could also be an ask-at-order-entry question, through which the placer could specify the mutations of interest especially for known familial mutation analyses.. | |
| E | CNE | [48018-6](http://s.details.loinc.org/LOINC/48018-6.html) |  | Gene(s) assessed [ID] | | 0..\* | 1 | 21497^ACAD9^HGNC-symb | The code is the HGNC code for the gene, the print string (name) is the HGNC – symbol. 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 1.2, 1.2, 1.3 etc. for this variable.  HCNC focuses on Human genes (H stands for human) so the look up option in the NLM-form for this field assumes only Human genes. (May extend this to other species in the future). | |
|  |  |  |  | **Summary results** | |  |  |  |  | |
| B | CNE | [51968-6](http://s.details.loinc.org/LOINC/51968-6.html) | R | Genetic analysis overall interpretation | | 1..1 | 1 | 51968-6^Positive^LN | Provides a coarse overall interpretation of the report. More detailed interpretations are associated with the individual variants reported. | |
| C | FT;ED | 51969-4 | O | Full narrative report  *(e.g. PDF, Word Document that would look like current reports)* | | 0..1 | 1 | Need example | 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 media types. Follow HL7 V2 specifications for recording an encapsulated data type’s media type. | |
|  |  |  |  | **Technical details** | |  |  |  |  | |
| D | NR | 51959-5 | C | Ranges of DNA sequence examined | | 0..\* | 1 | 2000753^2234579 | Preferred if the method is sequencing study. The first value of the range defines the start location, the second value, the end location of the Sequence. We recognize that this information may be proprietary and is often not revealed. The variable may repeat if the range is discontinuous, In HL7 V2 each repeat requires a separate OBX, and the OBX-4 values wlll have to differ among such repeats. We recommend 1.1, 1.2 1.3 etc.  The locations are specified in terms of the associated Genomic reference sequence.- may repeat if the range is discontinuous | |
| E | TX | 81293-3 | C | Description of ranges of DNA sequences examined | | 0..1 | 1 | All coding regions and appropriate flanking regions | Genetic test reports only rarely include explicit numeric ranges because they are often proprietary. So reports tend to describe the regions in narrative. E.g. “all coding regions and appropriate flanking regions”. This variable is included to capture such descriptions. It is only relevant to sequencing studies. | |
| F | CWE | 62374-4 | C | Human reference sequence assembly [ID] | | 0..1 | 1 | GRCh37 | May or may not be needed depending on the Reference sequences to which the results are anchored. It is needed for when the References sequences are NCBI genomic sequences without the version number and for Ensembl genomic reference sequences. Not required or transcript reference sequences.  One slot is provided for the assembly and build in the overall report section. This assumes that laboratories do not reference more than one assembly and build per report. | |
| G | ST | 81303-0 | P | HGVS version [ID] | | 0..1 | 1 | 2.120831 | HGVS now gives new version numbers when its recommendations change based on the date of the change. So if the change date was e 2012-08-31. The version of the HGVS version would be specified as **2.120831**. | |
| H | CWE | 82115-7 | O | dbSNP version [ID] | |  | 1 | <need example> | Version changes are only made to correct errors. The version does not change the meaning of the dbSNP RS #, But may change the value of the location number in relation to the build. | |

**Report Section 2 for Variables that define a Simple Variant (could be more than one simple variant not related to each other).**

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| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Data Type** | **LOINC #** | **R**  **CO** | **Observation display Name- draft** | **card** | **OBX-4** | **OBX-5 Example values** | **Comments** |
|  | N/A | **81250-3** |  | **Simple genetic variant panel** | 0..\* |  | Does not carry values | **Repeats for each simple variant reported.**  This panel code does not carry values in its OBX-5 It defines the structure within the LOINC data base. It will not be included in the message since we are planning to use OBX-4 content to define the hierarchy rather than by nested OBRs |
| A | CWE | 81252-9 | C | Simple genetic variant [ID] | 0..1 | 2.1 | 30880^NM\_014049.4(ACAD9):c.1249C>T (p.Arg417Cys)^ClinVar-V | The code for the CWE is the ID specified for the variant in the source public data base, the name is that given by the public data base—usually a combination of attributes e.g. the RefSeq, gene, c.HGVS etc. If the variant has been registered in a public database, these attributes can be automatically pulled from the public database and loaded into into attribute specific LOINC terms (See those that follow this term in the panel) If it has not been registered, reporters can enter the details for each component in the OBX’s specified by the terms that follow . Either the simple variant or at least the three following terms must be included |
|  |  |  |  | **Separate observations for each of the components of the simple genetic variant name.** | | | | |
| B | CWE | [48018-6](http://s.details.loinc.org/LOINC/48018-6.html) | C | Gene studied [ID] | 0..1 | 2.1 | 21497^ACAD9^HGNC-symb | The code is the HGNC code for the gene, the print string (name) is the HGNC – symbol. The gene identifier is also carried in the transcript reference sequence data base; so the gene information tends to be redundant but is almost always stated seperately. |
| C | CWE | 51958-7 | C | Transcript Reference Sequence ID: | 0..1 | 2.1 | NM\_014049.4^^NCBI-NM | If At least one of the transcript or genomic reference sequence must be included. If the c.HGVS) is included, the transcript RefSeq must be included. |
| D | CWE | 48004-6 | C | DNA change c.HGVS | 0..1 | 2.1 | c.1249C>T^^c.HGVS | HGVS specification of the change at the DNA level relative to the transcript RefSeq |
| E | CWE | [48005-3](http://s.details.loinc.org/LOINC/48005-3.html) | C | Amino acid change p.HGVS: | 0..1 | 2.1 | p.Arg417Cys^^p.HGVS | 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 |
| F | CWE | 48019-4 | O | DNA change [type] | 0..1 | 2.1 | LA6690-7^Substitution^LN | Type of DNA variation reported |
| G | CWE | 48006-1 | O | Amino acid change [type] | 0..1 | 2.1 | LA6698-0^missense ^LN | Type of amino acid change reported |
|  |  |  |  | **Genomic specification** | | | |  |
| H | CWE | 48013-7 | C | Genomic Reference Sequence [ID}: | 0..1 | 2.1 | NG\_017064.1^^NCBI-NG-NC | Required if 69547-8, 81254-5 or 69551-0 is present- |
| I | ST | [69547-8](http://s.details.loinc.org/LOINC/69547-8.html) | C | Genomic Ref allele: | 0..1 | 2.1 | C | The DNA string in the reference sequence (ref Allele) with which the DNA in the test sample differs starting at the position given in 81254-5 Genome Allele location |
| J | NR | 81254-5 | C | Genomic Allele location: | 0..1 | 2.1 | 31731^31731 | 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 sequence where anything changed in the sample DNA being tested, and the end is the comparable last position. |
| K | ST | [69551-0](http://s.details.loinc.org/LOINC/69551-0.html) | C | Genomic Alt allele: | 0..1 | 2.1 | T | The DNA sequence in the test sample (ref allele) that is different from the DNA in the reference sequence (ref Allele) –  Note the content of 69547-8, 81254-5 and 69551-0could also be described in a g.HGVS expression as: g.31731C>T |
|  |  |  |  | **Other optional codes related to simple genetic variant** | | | |  |
| L | ID | 81255-2 | O | dbSNP ID: | 0..10..1 | 2.1 | rs[368949613](http://www.ncbi.nlm.nih.gov/snp/368949613)^^dbSNP | The “SNP” in NCBI’s dbSNP data base name, originally meant Single Nucleotide variants, but not defined to mean “Simple Nucleotide. Variants.  The code is the HGNC code for the gene, the print string (name) is the HGNC – symbol Variant”. Each DB SNP is given an ID with a prefix of “rs”. , The dbSNP data base defines the location and size of the variant, but does not distinguish among different patterns of the same size at the same location. So there would be one RS SNP codes for AAA and ACA at the same location, but AAAA at that location would get a different dbSNP code.  DbSNP has versions, but they don’t change the meaning of a dbSNP RS#s. Some Rs#s may have different locations with respect to the build depending on the version, but only when a change was made to correct an error. The actual meaning of the SNP RS code does not change |
| M | CWE | 81256-0 | C | COSMIC-simple variant | 0..1 | 2.1 |  | COSMIC- Catalogue of Somatic Mutations in Cancer is the preferred code for cancer mutations. COSMIC simple mutations data base carries records that include a Mutation and a specimen ID as well as mutation (HGVS) the organ, histology and other specifics for each submission. It stores simple mutations and structural mutations in different tables. And carries many records for each distinct mutation – one for each submission.  Their simple variant file has fields that correspond too many of the fields in ClinVar except that COSMIC uses Ensembl RefSeqs the single letter code for p.HGVS. This LOINC code carries simple Cosmic mutations. |
| N | CWE Allele | 81257-8 | O | CIGAR [Nom} | 0..1 | 2.1 |  | Used primarily for alignment in earlier stages of genetic study analysis. |
|  |  |  |  | **Other possible attributes** | | | |  | 1.1 |
| O | NM | 81258-6 | P | Allelic Frequency[NFR] | 0..1 | 2.1 | 0.47 | This variable, reports the fraction of all of the reads at this genomic location that were represented by the reported allele. For homozygotes it will be close to one, For heterozygotes it will be close to 0.5. It can be a smaller number when mosaics or multiple chromosome, or mixtures of tumor cells and normal cells are mixed |
| P | CWE | 48001-2 | O | Chromosome location of variant | 0..1 | 2.1 | 3q21 | These locations can be recorded as text or taken from a list of Cytogenetic chromosome locations as explained by NLM’s Genetic Home Reference (https://ghr.nlm.nih.gov/primer/howgeneswork/genelocation). This set includes all of those reported as locations in NCBI’s ClinVar and many more. (? As to whether we should support this as a table that others could download?) |
| Q | CNE | 69548-6 | O | Genetic variant assessment in Blood or Tissue by Molecular genetics method [Imp] | 0..1 | 2.1 | LA9633-4^present^LN | Genetic reporting is usually by exception. So for targeted mutation analyses, the lab lists the mutations they looked for and report the ones they it found. For sequencing studies, similarly, they report the genetic range studied and the variants found.  This variable permits a different style of reporting in which a set of examined variations or loci could be described individually as present absent (or no call). |
| Q | CNE | [48002-0](http://s.details.loinc.org/LOINC/48002-0.html) | O | Genomic source class [Type] |  | 2.1 | LA6683-2^Germline^LN | We associate this variable with the variant so that distinction about the kind of variant can be made when somatic and germline variants will be observed in one study and they have to be distinguished in the report. |
|  |  |  |  | **Allelic state and interpretive attributes** | | | |  |
| R | CNE | [53034-5](http://s.details.loinc.org/LOINC/53034-5.html) | C | Allelic state: | 0..1 | 2.1 | LA6706-1^Heterozygous^LN | This variable describes the relationship between the alleles found at the same locus on different chromosomes. It is not always discerned by the study |
| S | CNE | [53037-8](http://s.details.loinc.org/LOINC/53037-8.html) | O | **Genetic variation clinical significance** [Imp]: | 0..1 | 2.1 | LA6668-3^Pathogenic^LN | See answer list |
| T | CWE | 81259-4 | O | Probable associated phenotype [Nom]: | 0..1 | 2.1 | Acyl-CoA dehydrogenase family, member 9, deficiency of | The disorder with which this variant is associated. Allow same coding systems as for disease assessed , but this term may more often be recorded as narrative text to allow more qualifiers |
|  |  |  |  | **Other candidate variables** | | | |  |
|  |  | 82120-7 |  | Allelic Phase |  | 2.1 |  | Defines which variations are on the same or different chromosomes. Can accommodate trisomys and distinguishing whether the chromosome is maternal or paternal when such details can be inferred (e.g. when the parent’s genotype is also available. (This is a trial set of answers and will likely expand –or change.)  Answers 1, 2, 3, 4 ,, Maternal, Paternal |
|  | NM | 82121-5 |  | Allelic read depth |  | 2.1 | 208 | A whole number, usually less than 300 and more than 25-20. Different methods and purposes have different numbers of reads to be acceptable. |

**Report Section 3: Complex Variants (those with multiple alleles)** -- structure can repeat because there can be more than one complex variant within one study (e.g. two haplotypes).

Sources for example: <http://www.ncbi.nlm.nih.gov/clinvar/variation/16895/> <http://www.ncbi.nlm.nih.gov/gene/1565>

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|  | **Data Type** | **LOINC #** | **R**  **CO** | **Observation display Name- draft version** | **card** | **OBX-4** | **OBX-5 Example values** | **Comments** |
|  |  | **81251-1** |  | **Complex genetic variant – panel** | 0..\* |  |  | **(repeats for each complex variant)**  Carries information about multiple simple variants that together have a clinical implication-usually are associated with some information about phase (i.e. whether reported chromosomes are on same or different chromosome).  OBX-4 will increment by 1 for each repeated complex variant. |
|  |  |  |  | Information that  applies to the complex variant as a whole | | | |  |
| B | CWE | 81260-2 | C | Complex genetic variant [Identifier] | 0..1 | 3 | 16895^NM\_000106.5(CYP2D6):c.[886C>T;457G>C] – Haplotype^ClinVar | Following the pattern of simple variant, the code is the identifier from a public genetic data base and the name is a concatenation of the RefSeq, the gene symbol, the HGVS describing for the multiple variants, and the complex variant type |
| F | CWE | 81262-8 | C | Complex variant HGVS name | 0..1 | 3 | c.[1749A>G ; 2549delA]^^HGVS | Includes HVGS 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 or depending on other syntax – the phase is unknown. |
| G | CWE | 81263-6 | C | Complex variant type | 0..1 | 3 | LAXXXXX-X^Haplotype^LN | Answer list can include Haplotype, Complex heterozygote, and others (to be determined) |
| H | CWE | 81259-4 | O | Associated phenotype | 0..1 | 3 | 688395015^Debrisoquine adverse reaction (disorder)^SCT | Disorder with which this complex variant is associated (See same term in simple variant |
| I | CNE | [53037-8](http://s.details.loinc.org/LOINC/53037-8.html) | O | Clinical significance | 0..1 | 3 | LA6668-3^Pathogenic^LN | See same term in simple variant |
| J | CNE | [53034-5](http://s.details.loinc.org/LOINC/53034-5.html) | O | Allelic state | 0..1 | 3 | LA6706-1^Heterozygous^LN | See same term in simple variant- but applies to the whole complex variant |
|  |  |  |  | **Information that applies to the simple variants that make up the complex variant (one at a time)** | | | |  |
|  |  | **81250-3** |  | **Simple genetic variant panel** | 1..\* |  | Does not deliver data, and this code will not be included in the message if we use the OBX-4 instead of nested OBR’s to organize the hierarchy | **Same as stand-alone simple variant panel – This is the first simple variant within a complex variant and will repeat** |
| A | CWE | 48008-7 | R | Simple Variant: | 0..1 | 3.1 | 31934^NM\_000106.5(CYP2D6):c.886C>T (p.Arg296Cys)^ClinVar-V | See previous instance of same term |
|  |  |  |  | **Transcript specification** | | | |  |
| B | CWE | [48018-6](http://s.details.loinc.org/LOINC/48018-6.html) | C | Gene: | 0..1 | 3.1 | 2625^CYP2D6^HGNC-symbol | See previous instance of same term |
| C | CWE | 51958-7 | C | Transcript Reference Sequence ID (aka NM\_RefSeq): | 0..1 | 3.1 | NM\_000106.5^^RefSeq | See previous instance of same term |
| D | CWE | [41103-3](http://s.details.loinc.org/LOINC/41103-3.html) | C | DNA change: | 0..1 | 3.1 | c.886C>T^^c.HGVS | See previous instance of same term |
| E | CWE | [48005-3](http://s.details.loinc.org/LOINC/48005-3.html) | C | Amino acid change: | 0..1 | 3.1 | p.Arg296Cys^^p.HGVS | See previous instance of same term |
| F | CWE | 48019-4 | O | DNA sequence variation type | 0..1 | 3.1 | LA6690-7^Substitution^LN | See previous instance of same term |
| G | CWE | 48006-1 | O | Amino acid change type | 0..1 | 3.1 |  |  |
|  |  |  |  | **Genomic specification** | | | |  |
| H | CWE | 48013-7 | C | Genomic Reference Sequence: | 0..1 | 3.1 | NG\_008376.3^^RefSeqGene | See previous instance of same term |
| I | ST | [69547-8](http://s.details.loinc.org/LOINC/69547-8.html) | C | Genomic Reference (Ref) allele: | 0..1 | 3.1 | C | See previous instance of same term |
| J | NM | 81254-5 | C | Genomic Allele location: | 0..1 | 3.1 | 42127941 | See previous instance of same term |
| K | ST | [69551-0](http://s.details.loinc.org/LOINC/69551-0.html) | C | Genomic Alternate (Alt) allele: | 0..1 | 3.1 | T | See previous instance of same term |
|  |  |  |  | **Other optional codes related to simple variation** | | | |  |
| L | CWE | 48004-6 | O | dbSNP ID: | 0..1 | 3.1 | rs16947^^dbSNP |  |
| M | CWE | 81256-0 | C | COSMIC | 0..1 | 3.1 |  | See previous instance of same term |
| N | CWE | 81257-8 | O | CIGAR | 0..1 | 3.1 |  | See previous instance of same term |
|  |  |  |  | **Other possible attributes** | | | |  |
| O | NM | 81258-6 | P | Allelic Frequency NFR | 0..1 | 3.1 | 0.40045 | See previous instance of same term |
| P | CWE | 48001-2 | O | Cytogenetic Location (Synonym -Chromosome region) | 0..1 | 3.1 | 22q13.2 | See previous instance of same term |
|  |  | **81250-3** |  | **2nd Simple variant panel within complex variant. Same as stand-alone simple variant panel -- repeats for each Simple variant making up a complex variant** | | | | |
| A | CWE | 48008-7 |  | Simple variant: | 0..1 | 3.2 | 38485^NM\_000106.5(CYP2D6):c.1457G>C (p.Ser486Thr)^ClinVar | See previous instance of same term |
|  |  |  |  | **Transcript specification** | | | |  |
| C | CWE | 48019-4 | C | DNA sequence variation type | 0..1 | 3.2 | LA6690-7^Substitution^LN | See previous instance of same term |
| D | CWE | [48018-6](http://s.details.loinc.org/LOINC/48018-6.html) | C | Gene: | 0..1 | 3.2 | 2625^CYP2D6^HGNC-symb | See previous instance of same term |
| E | CWE | 51958-7 | C | Transcript Reference Sequence ID : | 0..1 | 3.2 | NM\_000106.5^^NCBI-NM | See previous instance of same term |
| F | CWE | [41103-3](http://s.details.loinc.org/LOINC/41103-3.html) | C | DNA change: | 0..1 | 3.2 | c.1457G>C^^c.HGVS | See previous instance of same term |
| G | CWE | [48005-3](http://s.details.loinc.org/LOINC/48005-3.html) | C | Amino acid change: | 0..1 | 3.2 |  | See previous instance of same term |
|  |  |  |  | **Genomic specification** | | | |  |
| H |  | 48013-7 | C | Genomic Reference Sequence: | 0..1 | 3.2 | NG\_008376.3^^NCBI-NG-NC | See previous instance of same term |
| I | ST | [69547-8](http://s.details.loinc.org/LOINC/69547-8.html) | C | Genomic Reference (Ref) allele: | 0..1 | 3.2 | G | See previous instance of same term |
| J | NM | 81254-5 | C | Genomic Allele location: | 0..1 | 3.2 | 42126611 | See previous instance of same term |
| K | ST | [69551-0](http://s.details.loinc.org/LOINC/69551-0.html) | C | Genomic Alternate (Alt) allele: | 0..1 | 3.2 | C | See previous instance of same term |
|  |  |  |  | **Other optional codes related to simple variation** | | | |  |
| L | CWE | 48004-6 | O | dbSNP: | 0..1 | 3.2 | rs[368949613](http://www.ncbi.nlm.nih.gov/snp/368949613)^^dbSNP | See previous instance of same term |
| M | CWE | 81256-0 | C | COSMIC | 0..1 | 3.2 |  | See previous instance of same term |
| N | CWE | 81257-8 | O | CIGAR | 0..1 | 3.2 |  | See previous instance of same term |
|  |  |  |  | **Other possible attributes** | | | |  |
| O | NM | 81258-6 | P | Allelic Frequency NFR | 0..1 | 3.2 | 0.59168 | See previous instance of same term |
| P | CWE | 48001-2 | O | Chromosome region | 0..1 | 3.2 | 22q13.2 | See previous instance of same term |
|  |  |  |  | **Allelic state and interpretive attributes** | | | |  |
| Q | CNE | [53034-5](http://s.details.loinc.org/LOINC/53034-5.html) | C | Allelic state: | 0..1 | 3.2 | LA6706-1^Heterozygous^LN | See previous instance of same term |
| R | CNE | [53037-8](http://s.details.loinc.org/LOINC/53037-8.html) | O | Clinical significance: | 0..1 | 3.2 | LA6668-3^Pathogenic^LN | See previous instance of same term |
| S | TX | 81259-4 |  | Associated phenotype: | 0...1 | 3.2 | 688395015^Debrisoquine adverse reaction (disorder)^SCT | See previous instance of same term |

**Report Section 4 – Structural Variations**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Data Type | LOINC # | RCO | Observation display Name- draft version | card | OBX-4 | OBX-5 Example values | Comments |
|  | N/A | **81297-4** |  | **Genomic structural variant panel** | 0..\* |  |  | **Repeats for each structural variant.**  This is the first.  Does not carry values – Defines the structure but would not be carried into the message if we organize via OBX-4 content rather than by nested OBX  Note some structural variants can be reported via strict ClinGen IDs and/or COSMIC IDs in the above sections |
| A | CWE | 81286-7 | P | Genomic structural variant | 0..1 | 4.1 | nsv995237^17p12(chr17:14184616-15581544)x1 | NC\_000017.11:g.(?\_14184616)\_(15581544\_?)del (GRCh38) |
|  | CWE | 82154-6 |  | Genomic structural variant name |  | 4.1 | GRCh38/hg38 17p12(chr17:14184616-15581544)x1 | Not sure what this is –Maye the HGVS- just keep as place holder |
|  | NM | 82155-3 |  | Genomic structural variant copy number |  | 4.1 | <need example> | The number of repeats of the large variant. |
| B | NR | 81287-5 | P | Genomic structural variant start-end: | 0..1 | 4.1 | 14184616^15581544 |  |
| C | NM | 81299-0 | C | Genomic structural variant reported arrCGH ratio: | 0..1 | 4.1 |  | Usually only applicable to ArrCGH and related studies.  Its value is a number (less than 1. |
| D | CWE | 48019-4 | P | DNA structural variation type : | 0..1 | 4.1 | LA6686-5^Deletion^LN | Base answer list taken from NCBI <http://www.ncbi.nlm.nih.gov/dbvar/content/overview/#ref22> |
| E |  | 82119-9 | O | COSMIC structural variant | 0..1 | 4.1 | <<need example>> | Codes taken from COSMIC structural variations |
| F | NM | 81300-6 | O | Structural variant length: | 0..1 | 4.1 | 1,396,929 | Don’t often see this detail in clinical reports |
| G | NR | 81301-4 | O | Structural variant outer start and end: | 0..1 | 4.1 | 13200589^15592000 | Don’t often see this content in routine clinical reports. |
| H | NR | 81302-2 | O | Structural variant inner start and end: | 0..1 | 4.1 | 14184616^15581544 | Don’t often see this content in routine clinical reports |
| I | CWE | 81290-9 | O | Structural variant HGVS: | 0..1 | 4.1 | NC\_000017.11:g.(?\_14184616)\_(15581544\_?)dup | HGVS |
| J | CWE | 81291-7 | C | Structural variant ISCN: | 0..1 | 4.1 | <<need example>> | Include if available |
| K | CWE | 81298-2 | P | Structural variant cytogenetic location: | 0..1 | 4.1 | 17p12 |  |
| L | CWE | 81304-8 | P | Structural variant method type | 0..1 | 4.1 | Sequencing | Answer list **still to be developed** candidates include:  a) oligonucleotide microarray analysis b)(ROMA) and Gfosmid paired-end mapping (PEM);  c)Oligo ArrCGH ;  d)the analysis of SNP genotyping data [[7]](http://www.ncbi.nlm.nih.gov/dbvar/content/overview/#ref7) [[12-13]](http://www.ncbi.nlm.nih.gov/dbvar/content/overview/#ref12) [[29-34]](http://www.ncbi.nlm.nih.gov/dbvar/content/overview/#ref29)   d) PEM using next-generation 454 sequencing [[27]](http://www.ncbi.nlm.nih.gov/dbvar/content/overview/#ref27) .  e)FISH;  f) ArrCGH;  g) MLFP;  h) next generation sequencing  i)CNV-seq,  (others to consider : FREEC, read Depth, CNVnator, SegSeq and event-wise testing (EWT)). NEED INPUT  PMID:23527109/PMCID: PMC3604020 |

**Report Section 5 supplemental content for pharmacogenomics studies – the detailed allelic content could be reported in Section 2 or 3 and this would be additional information/interpretation**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Data Type** | **LOINC #** | **R**  **CO** | **Observation display Name- draft version** | **Card.** | **OBX-4** | **OBX-5 Example values** | **Comments** |
|  |  | 82118-1 |  | **Pharmacogenomics results panel** |  |  |  | Will repeat for each gene tested |
|  |  |  |  | **Results for first gene in the study** |  |  |  |  |
| A | CNE | [48018-6](http://s.details.loinc.org/LOINC/48018-6.html) |  | Gene studied | 1..3 | 5.1 | 1559^CYP2C9^HGNC-Symbol~  23661^VKORC1^HGNC-Symbol | In some cases, such as in the example of CYP2C9 and VKORC1, the effect of variations in more than one gene can determine the effect on drug metabolism or efficacy, in which case the genes with the combined effect and be listed separated by repeat delimiters. |
| B | ST | 47998-0 |  | Genotype display name  Display name ( general) | 1..3 | 5.1 | \*2/\*5~\*A/\*A | In this context the corresponding alleles for one gene are shown separated by a slash e.g., \*1/\*2 as is the common usage. If the effect metabolism/efficacy effect is based on 2 genes the results for each gene are shown separate by repeat delimiter in the same order as the gene symbols are displayed in YYYYY |
| C | CWE | 53040-2 | C | Genetic variation’s effect on drug metabolism [Imp]interp | 0..1 | 5.1 | LA9657-3^Rapid metabolizer ^LN | For pharmacogenomics studies at least one of 53040-2 (effect on drug metabolism ) or 51961-1 (effect on drug efficacy ) must be included in the panel |
| D | CWE | 51961-1 | C | Genetic variation’s effect on drug efficacy interp | 0..1 | 5.1 | <not in this example> | For pharmacogenomics studies at least one of 53040-2 (effect on drug metabolism ) or 51961-1 (effect on drug efficacy ) must be included in the panel One of the two “effect on” terms must be included when the study is a pharmacogenomic study |
| E | - | 82117-3 | O | Medication usage implications panel | 0..\* | 5.1.1 | This term carries the LOINC terms needed, but would not be included in the message assuming we use the OBX-4 construct to organize the hierarchy | A way to present the guidance about specific drugs or drug classes. May repeat for as many drugs as relevant to the tested gene. The alternative is narrative or PDF of current guidance now being delivered. (see <<term 51969-4>> provided for that purposes . |
| F | CWE | New | R | Medication | 0..\* | 5.1.1 | 7258^Naproxen^RxN-ingred | Required when the medication usage panel is implemented .The coding system could be an RxNorm ingredient subset RxN-ingrd. |
| G | CWE | New | C | Medication usage suggestion [type] | 1..1 | 5.1.1 | ^Increase the dosage ^LN | There is little consistency in the answer lists used by different laboratories. S, Until there is a consensus this will have to be locally decided. We have suggested a draft starter set. At least one of the medication usage type or narrative should be included when the panel is implemented. |
| H | TX |  | C | Medication usage suggestion [narrative] | 0..1 | 5.1.1 | May need higher dosage than usual. | Used to deliver whatever specific content hat laboratories want to deliver. At least one of the medication usage type or narrative should be included when the panel is implemented |
| I | - | **82117-3** | O | Medication usage implications panel | 0..\* | 5.1.2 | This term carries the LOINC terms needed, but would not be included in the message assuming we use the OBX-4 construct to organize the hierarchy |  |
| J | CWE | New | R | Medication | 0..\* | 5.1.2 | 611247^Fluoxetine olanzapine^RxN-ingd |  |
| K | CWE | New | C | Medication usage suggestion [type] | 1..1 | 5.1.2 | ^Increase the dosage^LN |  |
| L | TX |  | C | Medication usage [narrative] | 0..1 | 5.1.2 | May need higher dosage than usual. |  |
|  |  |  |  | **Results for second gene in the study** | | | |  |
| A | CNE | [48018-6](http://s.details.loinc.org/LOINC/48018-6.html) |  | Gene studied | 1..3 | 5.2 | 1557^CYP2C19^HGNC-Symb | This names the gene(s) –usually CYP genes-- for which specific results are being reported usually one at a time. In some cases, such as in the example of CPY2C9 and VKORI, the effect of variations in more than one gene can determine the effect on drug metabolism or efficacy, in which case the genes with the combined effect and be listed separated by repeat delimiters |
|  | ST | 47998-0 |  | Genotype display name | 1..3 | 5.2 | \*1/\*1 | In this context the corresponding alleles for one gene are shown separated by a slash e.g., \*1/\*2 as is the common usage. If the effect metabolism/efficacy effect is based on 2 genes the results for each gene are shown separate by repeat delimiter in the same order as the gene symbols are displayed in the gene(s) studied observation |
|  | CWE | 53040-2 | C | Genetic variation’s effect on drug metabolism interp | 0..1 | 5.2 | LA25391-6^Normal metabolizer^LN | For pharmacogenomics studies at least one of 53040-2 (effect on drug metabolism ) or 51961-1 (effect on drug efficacy ) must be included in the panel |
|  | CWE | 51961-1 | C | Genetic variation’s effect on drug efficacy interp | 0..1 | 5.2 | Not applicable -- term would not be include in report | For pharmacogenomics studies at least one of 53040-2 (effect on drug metabolism ) or 51961-1 (effect on drug efficacy ) must be included in the panel One of the two “effect on” terms must be included when the study is a pharmacogenomic study |
|  | N/A | 82117-3 | O | Medication usage implications panel | 0..\* | 5.2.1 | This term carries the LOINC terms needed, but would not be included in the message assuming we use the OBX-4 construct to organize the hierarchy | A way to present the guidance about specific drugs or drug classes. May repeat for as many drugs as relevant to the tested gene. The alternative is narrative or PDF of current guidance now being delivered. (See <<new term 51969-4>> provided for that purposes. |
|  | CWE | New | R | Medication | 1..1 | 5.2.1 | 6754^Meperidine^RxN-ingd | Required when the medication usage panel is implemented. The coding system could be an RxNorm ingredient subset RxN-ingrd. If there is really a modest sized fixed list, would entertain that |
|  | CWE | New | C | Medication usage suggestion [type] | 0..1 | 5.2.1 | ^usual dosage^LN | There is little consistency in the answer lists used by different laboratories. S, Until there is a consensus this will have to be locally decided. We have suggested a draft starter set. At least one of the medication usage type or narrative should be included when the panel is implemented |
|  |  |  |  | **Results for third gene or gene pair studied** | | | |  |
|  | CNE | YYYYY |  | Gene studied | 1..3 | 5.3 | 2637^CPY3A4^HGNC-Symbol~1577^CYP3A5^HGNC-Symb | ? change name above from gene to gene studied  This names the gene(s) –usually CYP genes-- for which specific results are being reported usually one at a time. In some cases, such as in the example of CPY2C9 and VKORI, the changes in two genes may be reported as unit because they have a combined effect In this case the genes with the combined effect can be listed in one OBX separated by repeat delimiters |
|  | ST | 47998-0 |  | Genotype display name | 1..3 | 5.3 | \*1/\*1 | In this context the corresponding alleles for one gene are shown separated by a slash e.g., \*1/\*2 as is the common usage. If the effect metabolism/efficacy effect is based on 2 genes the results for each gene are shown separate by repeat delimiter in the same order as the gene symbols are displayed in the gene(s) studied observation |
|  | CWE | 53040-2 | C | Genetic variation’s effect on drug metabolism interp | 0..1 | 5.3 | LA25391-6^Rapid Metabolizer^LN | For pharmacogenomics studies at least one of 53040-2 (effect on drug metabolism ) or 51961-1 (effect on drug efficacy ) must be included in the panel |
|  | CWE | 51961-1 | C | Genetic Variation’s effect on drug efficacy interp | 0..1 | 5.3 | <not represented in this example> |  |

**Suggested answer list for structured variant type** -- from NCBI <http://www.ncbi.nlm.nih.gov/dbvar/content/overview/#ref22>

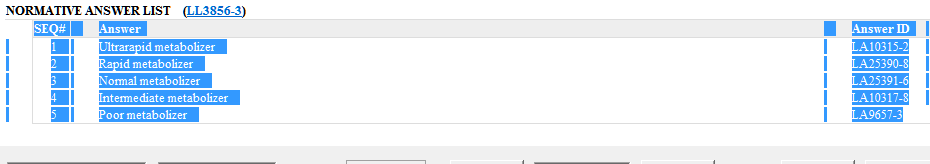
|  |  |  |
| --- | --- | --- |
| **Variant Call Type** | **Type abbreviation** | **Sequence Ontology ID** |
| copy number gain |  | SO:0001742  A sequence alteration whereby the copy number of a given region is greater than the reference sequence. |
| copy number loss |  | SO:0001743  A sequence alteration whereby the copy number of a given region is less than the reference sequence. |
| duplication | dup | SO:0001742 (copy number gain)  A sequence alteration whereby the copy number of a given region is greater than the reference sequence. |
| deletion | del | SO:0000159  The point at which one or more contiguous nucleotides were excised. |
| insertion |  | SO:0000667   The sequence of one or more nucleotides added between two adjacent nucleotides in the sequence. |
| mobile element insertion |  | SO:0001837   A kind of insertion where the inserted sequence is a mobile element. |
| novel sequence insertion |  | SO:0001838   An insertion the sequence of which cannot be mapped to the reference genome. |
| tandem duplication |  | SO:1000173   A duplication consisting of 2 identical adjacent regions. |
| inversion | inv | SO:1000036   A continuous nucleotide sequence is inverted in the same position. |
| intrachromosomal breakpoint |  | SO:0001874   A rearrangement breakpoint within the same chromosome. |
| interchromosomal breakpoint |  | SO:0001873   A rearrangement breakpoint between two different chromosomes. |
| translocation |  | SO:0000199   A region of nucleotide sequence that has translocated to a new position. |
| complex |  | SO:0001784   A structural sequence alteration or rearrangement encompassing one or more genome fragments. |
| sequence alteration |  | SO:0001059   A sequence\_alteration is a sequence\_feature whose extent is the deviation from another sequence. |

**Cc? add count of copy (copy number)**

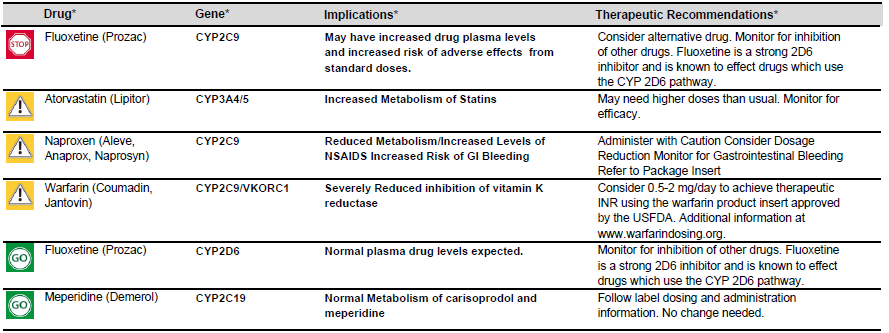
**Include start and end for the position of genomic variants**

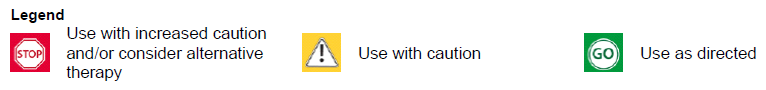
1. We only need the assembly and build for genomic coordinates – and there is more than one way to specify. Presume we would only have to specify the assembly and build once in the overall report section. That would make things simpler if so.
2. We presume there is no need for an explicit node (level) for genotype, because the whole report is the genotype and we have an overall report section where we could put any needed “genotype” information without adding another level.

The HGVS of the complex small variants really “says it all” and one could conceive of reports that did not carry the detailed information about each contained Allele. In that case, would not have a place for the amino acid level definition or the genomic specification or the allelic frequency. Just something to think about.



**Pharmacogenomics Report Example**





| **Variant Call Type** | **Sequence Ontology ID** | **Variant Region Type** |
| --- | --- | --- |
| **copy number gain** | **SO:0001742** A sequence alteration whereby the copy number of a given region is greater than the reference sequence. | **copy number variation** |
| **copy number loss** | **SO:0001743** A sequence alteration whereby the copy number of a given region is less than the reference sequence. | **copy number variation** |
| **duplication** | **SO:0001742** (copy number gain)  A sequence alteration whereby the copy number of a given region is greater than the reference sequence. | **copy number variation** |
| **deletion** | **SO:0000159** The point at which one or more contiguous nucleotides were excised. | **copy number variation** |
| **insertion** | **SO:0000667** The sequence of one or more nucleotides added between two adjacent nucleotides in the sequence. | **insertion** |
| **mobile element insertion** | **SO:0001837** A kind of insertion where the inserted sequence is a mobile element. | **mobile element insertion** |
| **novel sequence insertion** | **SO:0001838** An insertion the sequence of which cannot be mapped to the reference genome. | **novel sequence insertion** |
| **tandem duplication** | **SO:1000173**A duplication consisting of 2 identical adjacent regions. | **tandem duplication** |
| **inversion** | **SO:1000036** A continuous nucleotide sequence is inverted in the same position. | **inversion** |
| **intrachromosomal breakpoint** | **SO:0001874**A rearrangement breakpoint within the same chromosome. | **translocation or complex chromosomal mutation** |
| **interchromosomal breakpoint** | **SO:0001873**A rearrangement breakpoint between two different chromosomes. | **translocation or complex chromosomal mutation** |
| **translocation** | **SO:0000199** A region of nucleotide sequence that has translocated to a new position. | **translocation** |
| **complex** | **SO:0001784** A structural sequence alteration or rearrangement encompassing one or more genome fragments. | **complex** |
| **sequence alteration** | **SO:0001059** A sequence\_alteration is a sequence\_feature whose extent is the deviation from another sequence. | **sequence alteration** |

**Overview: Genomics LOINC panel names**

81247-9           HL7 genetic variant reporting panel

81250-3           Simple variant panel

81251-1           Complex variant panel

81294-1           Genetic form configuration controls

81297-4           Structural variant panel

82118-1           Pharmacogenomics result panel

82117-3           Medication usage implications panel

**Proposed short names (CWE.3) for new coding systems**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Name of source system** | **Coding system short name** | **Coding system long name** | **Coding system OID**  **(will fill in after we register in Hl7)** | **Comment** | **URL** |
| RxNorm Ingredients subset | RxN-ingrd |  |  |  |  |
| HGVS- Transcript syntax |  |  |  |  |  |
| HGVS- transcript syntax | c.HGVS |  |  |  |  |
| HGVS- Genomic syntax | g.HGVS |  |  |  |  |
| HGVS-Protein syntax | p.HGVS |  |  |  |  |
| NCBI-transcript reference sequences | NCBI-NM |  |  |  |  |
| NCBI genomic or chromosome reference sequence | NCBI-NG-NC |  |  |  |  |
| Ensembltranscript reference sequence | ENST |  |  |  |  |
| Ensemblgenomic reference sequence | ENSG |  |  |  |  |
| Ensemblproteinreference sequence | ENSP |  |  |  |  |
| DbSNP | dbSNP |  |  |  |  |
| Gene identifiers HGNC- with symbol defined as the print string ( CWE.2) in the coding system | HGNC-symb |  |  |  |  |
| SNOMED-CT | SCT |  |  |  |  |
| LOINC | LN |  |  |  |  |
| COSMIC –simple variants | COSM-Smpl |  |  |  |  |
| COSMIC-Structural variants | COSMIC-Strc |  |  |  |  |
| Clinvar variant ID coding system | ClinVar-V |  |  | Uses variant ID as the code (CWE-1) rather than the allele code –also available in each record |  |
| NCBI Medgen disease subset | NCBI-DS |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |