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		NA		[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 lite 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 in Lite 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), 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.
Table 1: Report Section 1 - Variables That Apply To The Overall Study								
A	Panel	81306-3	Variables that apply to the overall study	1	NA		[1..1]	
A.1	TX	53577-3	Reason for study	1	"Worried about family planning"	O	[0..1]	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 ideally, in a lab message it should be delivered in HL7 OBR-31.
A.2	CWE	51967-8	Genetic disease(s) assessed	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	Medications assessed	1.a	50005^Fluoxetine^RxT-Ingrd	C	[0..*]	Coding system: RxT-Ingrd Applies only to pharmacogenomics studies (See Table 4). 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	Medications assessed	1.b	84701^Atorvastatin^ RxT-Ingrd	C	[0..*]	See row A.3a for description for LOINC# 51963-7 Medications assessed.
A.3c	CWE	51963-7	Medications assessed	1.c	45000^Naproxen^RxT-Ingrd	C	[0..*]	See row A.3a for description for LOINC# 51963-7 Medications assessed.
A.3d	CWE	51963-7	Medications assessed	1.d	11289^Coumadin^RxT-Ingrd	C	[0..*]	See row A.3a for description for LOINC# 51963-7 Medications assessed.
A.4	CNE	48018-6	Gene(s) assessed [Nom]	1.a	21497^ACAD9^HGNC-Symb	C	[0..*]	Coding system choices: 1. HGNC-Symb 2. NCBI-gene code If the study includes more than one gene, they will be entered into separate OBX's but the content of OBX-4 will have to be unique for each such repeat. See Section 5.1 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).
A.5	CWE	36908-2	Gene mutations tested	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 5.1 for a specification of OBX-4 content.
A.6	NR	51959-5	Ranges 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 5.1 for a specification of OBX-4 content.

†The display text in these examples is bolded to make that portion easier to find.

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.8 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	Discrete variation analysis overall interpretation	1	LA6576^Posititive^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 mutation analysis (sequencing or targeted mutations) 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.
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	Full narrative report *(e.g. PDF, Word Document that would look like current reports)*	1	Example pending	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.
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 backward 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
Versions of Coding Systems								
A.12	CWE	62374-4	Human reference sequence assembly version [ID]	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 mutation name. We include only one slot for the assembly build in the overall report section, assuming that it 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
A.15	NM	83007-5	COSMIC version [Num]	1	78	O	[0..1]	As of September 2016, the latest COSMIC version numbers is 78. 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 of December 2016, but will soon add version numbers. This variable will accommodate that.

†The display text in these examples is bolded to make that portion easier to find.

Table 2: 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	NA		[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: 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: 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	C	[0..1]	Simple Variant coding systems: 1. clinVar-V 2. cosmic-Smpl Structural Variant coding systems: 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 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. 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.
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 Note: If 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 Transcript DNA change (cHGVS) is included, the transcript reference sequence must be included.
B.5	CWE	48004-6	Transcript DNA change (cHGVS)	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 (pHGVS)	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]	Single Variant Answer List : LL4033-8 Simple Variant types: 1. Wild Type LA9658-1 2. Deletion LA6692-3 3. Duplication LA6686-5 4. Insertion LA6687-3 5. Insertion/Deletion LA6688-1

†The display text in these examples is bolded to make that portion easier to find.

								6. Inversion LA6689-9 7. Substitution LA6690-7 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 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 (gHGVS)	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_?)	C	[0..1]	Coding system: HGVS.g If this is a structural variant, either the LOINC 81291-7 Variant ISCN or this term should be included with every structural variant report.
B.11	ST	69547-8	Genomic Ref allele	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 location.
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	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	48008-7	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. Not needed if the repeat includes an allele glossary – see Section 5.
B.15	ID	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 [Nom]	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 See details in row 1 "Cytogenetic (chromosome) location" in the Appendix Table A1 "Coding Systems".

†The display text in these examples is bolded to make that portion easier to find.

B.18	CNE	48002-0	Genomic source class [Type]	2a	LA6683-2^Germline^LN	R	[0..1]	Answer List: LL378-1 1. Germline LA6683-2 2. Somatic LA6684-0 3. Fetal Pending 4. Likely germline LA18194-3 5. Likely somatic LA18195-0 6. Likely fetal Pending 7. Unknown genomic origin LA18197-6 8. De novo LA26807-0 Reported when mutation analysis (sequencing or targeted mutations) 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.
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 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 variation clinical significance	2a	LA6668-3^Pathogenic^LN	O	[0..1]	Answer List: LL4034-6 1. Pathogenic LA6703-8 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 mutations (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 mutations 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. For an illustration of how this would work, see the examples in Section 6.
B.22	CWE	81259-4	Probable associated phenotype [Imp]	2a	C1970173^Acyl-CoA dehydrogenase family, member 9, deficiency of^ MedGen-Dis	O	[0..1]	Coding system choices: 1) SCT 2) MedGen-Dis 3) I10C 4) I9CDX 5) HPO 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 [Type]	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 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	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 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.

Table 2: 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 LOINC panel 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 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.

†The display text in these examples is bolded to make that portion easier to find.

Table 3: Report Section 3 for 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		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.
Information that applies to one complex variant as a whole								
C.1	CWE	81260-2	Complex genetic variant	3a	16895^NM_000106.5(CYP2D6):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.
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	Associated phenotype	3a	688395015^ Debrisoquine adverse reaction (disorder)^SCT	O	[0..1]	Coding system choices: 1) SCT 2) MedGen-Dis 3) I10C 4) I9CDX 5) HPO
C.5	CNE	53037-8	Genetic variation clinical significance [Imp]	3a	LA6668-3^ Pathogenic^LN	O	[0..1]	See the LOINC# 53037-8 in row B.22 for answer lists. 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 same term in simple variant- LOINC # 53034-5 in row B.25. 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	3a	LA26429-3^Inferred from population data^LN	O	[0..1]	See description in LOINC# 82309-6 in Row B.29.
Information that applies to the discrete variant(s) that make up the complex variant (one at a time)								
D		81250-3	Discrete genetic variant panel	3a.1a		NA	[0..*]	See Section 2 for the complete definitions. The full HGVS for the complex variant in row C may be sufficient fro many purposes in which case non 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 6 at 7.2.1 and 7.2.2.
D.1	CWE	81252-9	Discrete genetic variant	3a.1a	31934^NM_000106.5(CYP2D6):c.886C>T (p.Arg296Cys)^ CLINVAR	C	[1..1]	See the LOINC# 81252-9 in row B.1 description and answer list.
D.2	CWE	51958-7	Transcript RefSeq ID	3a.1a	NM_000106.5^ NM_000106.5^RefSeq-T	C	[0..1]	See the LOINC# 51958-7 in row B.6 for description and answer list.
D.3	CWE	41103-3	Transcript DNA change (c.HGVS)	3a.1a	c.886C>T^c.886C>T^ HGVS.c	C	[0..1]	See the LOINC# 41103-3 in row B.7 for description and answer lists.
D.4	CWE	48005-3	Amino acid change p.HGVS	3a.1a	p.Arg296Cys ^ p.Arg296Cys ^HGVS.p	C	[0..1]	See the LOINC# 48005-3 in row B.8 for description and answer list.
D.5	CWE	48019-4	DNA change type	3a.1a	LA6990-7^ Substitution^LN	O	[0..1]	See the LOINC# 48019-4 in row B.9 for description and answer lists.
D.6	CWE	48006-1	Amino acid change [type]	3a.1a	LA6698-0^Missense^LN	O	[0..1]	See the LOINC# 48006-1 in row B.10 for description and answer lists.

†The display text in these examples is bolded to make that portion easier to find.

Table 4: Report Section 4 for 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
E	N/A	82118-1	Pharmacogenomics results panel				0.*	Will repeat for each gene tested
Results for 1st gene of study								
E.1.a	CNE	48018-6	Gene(s) studied	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 mutations. 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.
E.2.a	ST	47998-0	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.
E.1.b	CNE	48018-6	Gene(s) studied	4a.b	23663^VKORC1^ HGNC-Symb		[1..*]	See row D.1.a for description for LOINC# 48018-6 Gene(s) studied.
E.2.b	ST	47998-0	Genotype display name	4a.b	*A/*A		[1..*]	See row D.2.a for description for LOINC# 47998-0 Genotype display name.
E.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).
E.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.
E.5	CWE	83009-1	Genetic variation's risk for hypersensitivity	4a	Pending	C	[0..1]	Answer list: LL2353-2 1. Low risk — LA19542-2 2. High risk — LA19541-4 Reports hypersensitivity that occurs with the drug specificity in row F.1 (LOINC 51963-7 Medication assessed), when some mutations, e.g. HLA alleles, are present. PMID: 17620823
Medication Panel								
F	-	82117-3	Medication usage implications panel	4a.1	This term identifies the set of LOINC terms that are part of the panel but not part of the 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 mayb e 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 Full narrative report in row A.11 is provided for that purpose).
F.1	CWE	51963-7	Medication assessed	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.
F.2	CWE	82116-5	Medication usage suggestion [type]	4a.1	LA26423-6^Increase dose^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 (82116-5) 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.
F.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.

†The display text in these examples is bolded to make that portion easier to find.

Table 5: 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
G		83011-7	Haplotype Definition Panel	5a			[0..*]	This panel defines the variables that are reported for each haplotype.
Haplotype Gene and Name								
G.1	CNE	48018-6	Gene(s) studied	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 mutations.
G.2	CWE	48008-7	Haplotype name	5a.a	*18	O	[0..*]	Usually used to report star alleles.
Defines the discrete variants that constitute the haplotype								
H		81250-3	Discrete genetic variant panel	5a.1a			[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 Section 2 for this purpose, and can repeat the panel for as many variations that define the haplotype.
H.1	ID	81255-2	dbSNP ID	5a.1a	1057910^ rs1057910	O	[0..1]	See LOINC# 81255-2 in row B.17 for description.
H.2	ST	69551-0	Genomic alt allele	5a.1a	C	C	[0..1]	See LOINC# 69551-0 in row B.15 for description.
I		81250-3	Discrete genetic variant panel	5a.2a			[1..*]	See LOINC# 81250-3 in row H for description.
I.1	ID	81255-2	dbSNP ID	5a.2a	72558193^ rs72558193^dbSNP	O	[0..1]	See LOINC# 81255-2 in row B.17 for description.
I.2	ST	69551-0	Genomic alt allele	5a.2a	C	C	[0..1]	See LOINC# 69551-0 in row B.15 for description.
J		81250-3	Discrete genetic variant panel	5a.3a			[1..*]	See LOINC# 81250-3 in row H for description.
J.1	ID	81255-2	dbSNP ID	5a.3a	1057911^ rs1057911^dbSNP	O	[0..1]	See LOINC# 81255-2 in row B.17 for description.
J.2	ST	69551-0	Genomic alt allele	5a.3a	T	C	[0..1]	See LOINC# 69551-0 in row B.15 for description.

†The display text in these examples is bolded to make that portion easier to find.