

Supplementary Table 1: Current CStAG Membership and representation across the UK GLHs

Genomic Laboratory Hub (GLH)	Number of CStAG Representatives
Central and South GLH	1
East GLH	2
North West GLH	1
North Thames GLH	2
South East GLH	2
South West GLH	0
North East and Yorkshire GLH	2
N/A - Ireland (Dublin)	1

Supplementary Table 2: Full response breakdown for the 18 questions pertaining to laboratory workflows. To preserve anonymity, free-text comments are not provided.

Question	Options	Number of Responses	
1	Which of the following identifiers are present against a detected variant in the output of your NGS pipeline (VCF file and derived files)?	Hospital Trust ID NHS Number DOB Sample ID (not present in LIMs) Patient Name Patient Initials Run/NGS ID (not present in LIMs) Sex/Gender Run/NGS ID (that is also present in LIMs) Sample ID (that is also present in LIMs) Other	0 0 0 2 3 3 5 5 9 15 3
2	How are the QC'ed small variants (eg SNVs and indels) from your NGS pipeline outputs (VCF or VCF-derived file) CURRENTLY transferred to your LIMs?	Saved in separate location Attached as separate file Manual copy-and-paste Automatic and invisible (no action required from scientist) Manually typed out Predesigned 'push-button' transfer Other	2 1 4 0 8 2 0
3	For small variants: How many types/tiers of VCF-derived files do you generate?	>3 3 2 1 0	0 2 4 10 1
4	For small variants: How many types/tiers of VCF-derived files do you store?	>3 3 2 1 0	0 1 1 13 2
5	How are the QC'ed CNVs (eg exon-level deletion) from your pipeline outputs (from VCF, VCF-derived or MLPA workflow output) CURRENTLY transferred to your LIMs?	Saved in separate location Attached as separate file Manual copy-and-paste Automatic and invisible (no action required from scientist) Manually typed out Predesigned 'push-button' transfer Other	2 1 4 0 9 1 0
6	For CNVs: How many types/tiers of VCF-derived	>3	0

	files do you generate?	3 2 1 0	1 0 15 1
7	For CNVs: How many types/tiers of VCF-derived files do you store?	>3 3 2 1 0	0 1 0 14 2
8	What best describes the way CSG small variants are CURRENTLY stored on your LIMs?	In a single free text/unstructured field (which also includes additional clinical report wording) In a single free text/unstructured field (just contains variant name) As a single field of strict formal hgvs notation, ie: gene + transcript + genomic location + coding (c.) change + protein (p.) change As separate fields for gene/transcript/genomic location/coding (c.) change/protein (p.) change Stored outside of a LIMs system	5 5 2 4 1
9	What best describes the way CSG CNVs are CURRENTLY stored on your LIMs?	In a single free text/unstructured field (which also includes additional clinical report wording) In a single free text/unstructured field (just contains variant name) As a single field of strict formal hgvs notation, ie: gene + transcript + genomic location + coding (c.) change + protein (p.) change As separate fields for gene/transcript/genomic location/coding (c.) change/protein (p.) change Stored outside of a LIMs system	4 9 1 2 1
10	Which CSG variants are CURRENTLY stored in your LIMs?	All variants detected (rare and common) All rare variants detected (all class 3 and above, may also include rare class 1/2) All rare variants detected (all class 3 and above, no rare class 1/2) Most rare variants of relevance (all 4/5 and most interesting VUS) Only variants included in the clinical report No variants stored in the LIMs / No LIMs system	3 2 2 5 4 1
11	In the event of a variant re-classification (for example, up-classification of a previous cold class 3), how confidently/readily could you identify all patients in whom that variant had been identified (since inception of your current system)? (if not using a LIMs system for this process, please specify which system would instead be used to identify all patients)	5: extremely: all variants are stored in LIMs/current storage system in accurate structured format 4: very: all variants are stored in LIMs/current storage system but have been manually entered, so subject to typos 3: quite: cold class 3 variant likely not in LIMs/current storage system. Would require a comprehensive search of various historic bioinformatics systems/VCFs/derived files but these are stored so as to be easily searchable 2: not very: cold class 3 variant likely not in LIMs/current storage system. Would require a comprehensive search of various historic bioinformatics systems/VCFs/derived files which are stored in multiple locations 1: poorly: cold class 3 variant likely not in LIMs/current storage system. Would require a comprehensive search of various historic bioinformatics systems/VCFs/derived files which are not readily accessible	5 8 3 1 0
12	From what type of interface are the variants requiring interpretation viewed?	Within a bioinformatics processing system/dedicated in-house variant system In a spreadsheet (eg VCF, VCF-derived file.) Other (please specify)	8 5 4
13	Within the interface from which you view variants requiring interpretation, which description is most accurate?	Most/many of the relevant data sources have been pre-imported There are variant-specific hyperlinks to most/many of the relevant data sources. No/minimal annotations (eg only population frequencies). Accessing of relevant data sources (Alamut, CanVar-UK, ClinVar, literature) requires manual interrogation (variant name is typed/pasted in).	1 7 9

		Other	0
14	Following interpretation of a CSG variant, where do you store your updated detailed findings/pathogenicity classification (eg scoring on ACMG sub-elements)?	Dedicated in-house departmental variant datasystem	5
		Individual per-VARIANT files (excel, word, other document). Updated for recurrent viewings of variant.	5
		Individual per-VARIANT files (excel, word, other document). New file time a variant is encountered.	4
		Individual per-PATIENT EPISODE files (excel, word, other document) (may contain multiple variants)	4
		Commercial platform or software (eg Congenica, Alamut)	4
		LIMs (against specific patient)	3
		Individual per-GENE files (excel, word, other document).	1
		Individual per-DISEASE files (excel, word, other document).	1
		LIMs (against variant)	0
		Dedicated single departmental excel/spreadsheet	0
		Variant classifications are only documented on the patient report and not elsewhere stored	0
		Other (please specify)	0
15	How did you capture test context information in your laboratory patient-level datastorage system (LIMs) prior to the GMS test directory?	Clinical details/Phenotype information from test request or referral form	10
		Test/panel requested	15
		None	1
		Other (please specify)	1
16	How do you capture test context information in your laboratory patient-level datastorage system (LIMs) since the GMS test directory implemented?	Clinical details/Phenotype information from test request form or referral form	11
		Test/panel requested	14
		Test indication R number (since publication of the National Genomic Test Directory)	12
		None	0
		Other (please specify)	1
17	Following implementation of the GMS test directory, please estimate what % of CSG test requests now contain some clinical details/phenotype information (in addition to test requested/R number).	0-24%	0
		25-49%	2
		50-74%	8
		75-100%	6
18	When a single gene/small gene set is reported from a larger panel/exome, how is the gene set which is analysed captured in your LIMs?	Genes analysed are listed by name in LIMs against patient (free text entry eg list with commas)	4
		Name of subpanel(s) listed in LIMs against patient (structured entry)	4
		Genes analysed are listed by name in LIMs against patient (structured entry eg selected from a drop-down list, imported from a separate portal)	2
		Name of subpanel(s) listed in LIMs against patient (free text entry)	2
		Mixture of genes and subpanels (free text entry)	2
		Genes/panels analysed not documented in LIMs; requires reference to other files within NGS workflow	1
		Exported as a list from commercial platform and attached to LIMs record	1
		Other (please specify)	1