

CATS
(Cancer Genomic Test Standardized)
Format

Document for details

By Section of Genomic Data Management,
C-CAT

v1.0.1

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I. Introduction

I-1. Objectives

Currently, testing companies use different formats for data on gene alterations in cancer comprehensive genomic profiling tests. These differences make it difficult for a third party to annotate gene alterations with candidate drugs and clinical trials by the same software under one simple framework. In order to efficiently promote uniformity and homogeneity in the interpretation of cancer genomic test results, it is necessary to define a unified format for gene alteration data in cancer comprehensive genome profiling tests.

This document describes the CATS (cancer genomic test standardized) format, a standardized format for gene alteration data in cancer comprehensive genomic profiling tests. The data schema of the CATS format is defined by the JSON definition file "schema.json", of which the specifications are explained in this document.

Use of this format is as follows. A laboratory that performs cancer comprehensive genome profiling tests sends gene alteration data in the CATS format to a testing annotation organization such as C-CAT. The organization will annotate gene alteration data in the CATS format with candidate drugs and clinical trials, taking into account the clinical data of patients. This format only applies to gene alteration data, not to clinical data, because clinical data are stored in electronic medical records in hospitals and not likely to be accessible to testing companies.

I-2. Terms

- Testing annotation organization: An organization that receives gene alteration data in cancer comprehensive genome profiling tests from testing companies and clinical data from hospitals, and that uses the cancer knowledge base to annotate each gene alteration with candidate drugs and clinical trials. For example, C-CAT.
- Testing annotation document: A document that associates individual gene alterations in a cancer comprehensive genomic profiling test with candidate drugs and clinical trials per patient. An example is the C-CAT Findings document. In contrast to a testing annotation document, a testing report document is a report of test results issued by a testing company.
- Cancer knowledge base: A database that associates gene alterations in cancer with candidate drugs and clinical trials. Examples are C-CAT CKDB (cancer knowledge database) and OncoKB (Chakravarty et al, 2017, JCO Precision Oncology).

I-3. About the condition field

- Required: Required field when the JSON parent tag exists.
- Optional: Recommended field that may be associated with drug and clinical trial information in testing annotation documents, or that increases the accuracy of testing annotation documents according to testing reports issued by testing companies.

I-4. Format information

- Character code: UTF8
- Type: JSON
- Extension: json

II. Matters specific to C-CAT

II-1. Sending format of files

Gene alteration data in cancer comprehensive genomic profiling tests should be sent to C-CAT from the testing company in CATS (cancer genomic test standardized) format.

II-2. Scope of inputs

Quality-assured data on gene alterations (shortVariant, copyNumberAlteration, rearrangement, and otherBiomarker) are in the scope of inputs in CATS format. Please do not input alterations suspicious as false positives. You can choose whether or not to show alterations in C-CAT Findings by the tag ("reported") described below.

Please be sure to input data on gene alterations that are approved by the authority and be sure to output them in C-CAT Findings.

II-3. Requests

- Optional fields are fields recommended to input as many as possible. If you fill out more fields, information on more drugs or clinical trials may be added to C-CAT Findings, and the accuracy of C-CAT Findings based on laboratory's testing reports will be increased. In addition, more information linked to these fields may be added in future versions, even if such information does not appear in the current version of C-CAT Findings.
- Please try your best to input quality-assured data on all gene alterations (including those with the tag of "reported": false, as explained below) in CATS format. Otherwise, when the format or specifications of laboratory's testing reports is changed, C-CAT may make inquiries to the laboratory and possibly the production of C-CAT Findings may be delayed.

II-4. Notes

Detailed precautions specific to C-CAT are indicated by "*" in the Description below.

III. metaData tag

For metadata

Contains 4 keys: schemaVersion, referenceGenome, configOptions and comments.

Key	Condition	Data type	Description
metaData	required	object	Aggregation tag for metadata

III-1. schemaVersion key

Key	Condition	Data type	Description
schemaVersion	required	string regex: ^[0-9\\.]+\$	Schema version of this format

III-2. referenceGenome tag

For information on a reference genome sequence

Key	Condition	Data type	Description
referenceGenome	required	object	For information on a reference genome sequence

III-2-1. Tags within referenceGenome tag

Key	Condition	Data type	Description
name	required	string [choice]	Name of a reference genome sequence used in your test. Select a name from: <ul style="list-style-type: none">• "GRCh37"• "GRCh38" Please replace hg19 with "GRCh37" and hg38 with "GRCh38". * Please inform C-CAT beforehand if you use a different reference genome.
patch	required	string regex: ^p[0-9]+\$	The patch used in the reference genome sequence in the name tag, such as "p13" in "GRCh38.p13". null should be entered for a no-patch-applied reference genome sequence.
descriptions	optional	array (length: 0-N, string regex:	Description of the reference genome sequence in the name tag.

		^,+\$)	See the contents tag within the comments tag for usable languages and new lines.
--	--	--------	--

III-2-2. Example of referenceGenome tag

(Example)
<pre>"referenceGenome": { "name": "GRCh37", "patch": "p13", "descriptions": ["Homo sapiens (human) genome assembly GRCh37 (hg19) from Genome Reference Consortium."] }</pre>

III-3. configOptions tag

Tag that controls matching to cancer knowledge bases such as C-CAT CKDB, and whether or not to hide values measured in your test from testing annotation documents such as the C-CAT Findings document.

Key	Condition	Data type	Description
configOptions	optional	object	Aggregation tag that controls matching to cancer knowledge bases and listing in testing annotation documents

II-3-1. Tags within configOptions tag

Key	Condition	Data type	Description
typeLabelsInterpretedAsKbAmplification	optional	array (length: 1-4, string) [choice]	<p>The testing company's labels for gene alterations, which are interpreted as “amplification” (copy number amplification) in cancer knowledge bases. Choose from the following options.</p> <ul style="list-style-type: none"> • "copyNumberAlterationType: amplification" • "copyNumberAlterationType: gain" • "copyNumberAlterationType: duplication" • "rearrangementType: duplication" <p>(Default: "copyNumberAlterationType: amplification", "copyNumberAlterationType: gain", "copyNumberAlterationType: duplication")</p>

typeLabelsInterpretedAsKbLoss	optional	array (length: 1-3, string) [choice]	<p>The testing company's labels for gene alterations, which are interpreted as “loss” (copy number loss) in cancer knowledge bases.</p> <p>Choose from the following options.</p> <ul style="list-style-type: none"> • "copyNumberAlterationType: loss" • "copyNumberAlterationType: deletion" • "copyNumberAlterationType: homozygous deletion" • "rearrangementType: deletion" <p>(Default: "copyNumberAlterationType: loss", "copyNumberAlterationType: deletion", "copyNumberAlterationType: homozygous deletion")</p>
typeLabelsInterpretedAsKbGeneFusion	optional	array (length: 1-8, string) [choice]	<p>The testing company's labels for gene alterations, which are interpreted as “geneFusion” (gene fusion) in cancer knowledge bases.</p> <p>Choose from the following options.</p> <ul style="list-style-type: none"> • "rearrangementType: gene fusion" • "rearrangementType: frameshift gene fusion" • "rearrangementType: bidirectional gene fusion" • "rearrangementType: duplication" • "rearrangementType: deletion" • "rearrangementType: inversion" • "rearrangementType: truncation" • "rearrangementType: other" <p>(Default: "rearrangementType: gene fusion", "rearrangementType: frameshift gene fusion", "rearrangementType: bidirectional gene fusion")</p>
hideAlleleFrequency	optional	boolean	<p>Variant allele frequency values will not be shown in testing annotation documents when this is true.</p> <p>* Please input false or do not use the key itself for information approved by the authority.</p> <p>(Default: false)</p>
hideCnaValue	optional	boolean	Same for the values of copy number alterations.
hideMsiValue	optional	boolean	Same for the values of micro-satellite instability (MSI).
hideTmbValue	optional	boolean	Same for the values of tumor mutation burden (TMB).

hideLohValue	optional	boolean	Same for the values of Loss of Heterozygosity (LOH).
--------------	----------	---------	--

II-3-2. Example of configOptions tag

(Example)

```
"configOptions": {
  "hideTmbValue": true,
  "hideLohValue": true,
  "typeLabelsInterpretedAsKbAmplification": [
    "copyNumberAlterationType: amplification",
    "copyNumberAlterationType: gain",
    "copyNumberAlterationType: duplication"
  ],
  "typeLabelsInterpretedAsKbLoss": [
    "copyNumberAlterationType: loss",
    "copyNumberAlterationType: deletion",
    "rearrangementType: deletion"
  ],
  "typeLabelsInterpretedAsKbGeneFusion": [
    "rearrangementType: gene fusion",
    "rearrangementType: frameshift gene fusion",
    "rearrangementType: bidirectional gene fusion"
  ]
}
```

III-4. comments tag

You can make comments on gene alterations (variants), biomarkers (otherBiomarkers), and information on sequencing samples (sequencingSamples). This tag contains the tags of itemIds and contents.

Key	Condition	Data type	Description
comments	optional	array (length: 0-N, object)	Aggregation tag for comment information

II-4-1. Tags within comments tag

Key	Condition	Data type	Description
itemIds	required	array (length: 0-N, string regex: <code>^.+</code>)	The itemIds (multiple itemIds possible) of alterations (variants), biomarkers (otherBiomarkers), and information on sequencing samples (sequencingSamples).

			Possible to comment on a test overall if you set the length of this key to be zero. * This content will not be shown in C-CAT Findings, if itemId is specified.
contents	required	array (length: 1-N, string regex: ^.+ \$)	The content of the comment for itemId. The description can be in English or Japanese. Please use array elements if you make new lines, because we ignore line feed codes in this tag.

II-4-2. Example of comments tag

(Example)

```
"comments": [
```

```
{
```

```
  "itemIds": [],
```

Note: If the length of the itemIds array is zero, it represents a comment on this test overall.

```
  "contents": [
```

"Amplification of the FGFR1 gene is observed in 5 to 20% of squamous cell carcinomas, and it has been reported that FGFR1 is sensitive to FGFR inhibitors in vitro."

"FGFR2 and FGFR3 gene activating mutations and FGFR3 gene fusions have been reported one after another, and their frequency is low at around 3%, but therapeutic effects with FGFR inhibitors are expected."

Note: If you want to make new lines in testing annotation documents, sentences or phrases should be separated as elements of an array.

```
  ]
```

```
},
```

```
{
```

```
  "itemIds": [
```

```
    "variant-1"
```

Note: When describing a comment on a specific mutation, the itemId of the mutation should be written.

```
  ],
```

```
  "contents": [
```

```
    "TSC1 functions independently of TSC2 and mTORC1."
```

```
  ]
```

```
},
```

```
{
```

```
  "itemIds": [
```

```
    "variant-1",
```

```
    "variant-5"
```

Note: You can make comments on multiple mutations altogether if you list multiple itemIds.

```
  ],
```

```
  "contents": [
```

"Although CD4 T cell percentage in Tsc1^{-/-} mice was not strongly affected by Bim deficiency in vivo, TCR-mediated apoptosis of Tsc1^{-/-} Bcl2l11^{-/-} double knockout CD4 T cells was less pronounced compared with that of Tsc1^{-/-} cells. (Kai Yang et al.)"

]
}
]

IV. testInfo tag
Test information.

Key	Condition	Data type	Description
testInfo	required	object	Aggregation tag for test information

IV-1. Tags within testInfo tag

Key	Condition	Data type	Description
testId	required	string regex: ^..+\$	Any ID used by the testing company
testType	required	string [choice]	The combination of specimens used in the test. • "tumor-only": test using tumor samples only • "tumor and matched-normal": test using tumor and matched normal samples • "tumor-only (cell-free)": test using cell-free tumor samples only • "tumor (cell-free) and matched-normal": test using cell-free tumor samples and normal samples
softwareName	optional	string regex: ^..+\$	Name of gene analysis software
softwareVersion	optional	string regex: ^..+\$	Version of gene analysis software
panelName	required	string regex: ^..+\$	Name of your genomic profiling (gene panel) test. * Please inform C-CAT beforehand if you want to use a genomic test NOT approved to use under National Health Insurance.
panelVersion	required	string regex: ^..+\$	Version of your test

IV-2. Example of testInfo tag

<p>(Example)</p> <pre>"testInfo": { "testId": "12345678901231900001", "testType": "tumor and matched-normal", "softwareName": "variant caller A",</pre>

```
"softwareVersion": "ver.1.2",  
"panelName": "Multi-gene Panel A",  
"panelVersion": "ver.1.03-00"  
}
```

V. variants tag

Information on detected gene alterations. This tag contains shortVariants tag, copyNumberAlterations tag, and rearrangements tag.

Key	Condition	Data type	Description
variants	optional	object	Aggregation tag for information on alterations

V-1. shortVariants tag

Information on SNV (single nucleotide variation), insertion, deletion, delins (simultaneous insertion and deletion), indel (insertion and deletion), and MNV (multiple-nucleotide variant).

Key	Condition	Data type	Description
shortVariants	optional	array (length: 1-N, object)	Aggregation tag for information on single nucleotide variant (SNV), insertion (insertion), deletion (deletion), deletion and insertion (delins), insertion and deletion (indel), and multiple-nucleotide variant (MNV) of nucleotides

V-1-1. Tags within shortVariants tag

key	Condition	Data type	Description
itemId	required	string regex: ^\.+\$	An ID assigned to an alteration. It must be a unique string of characters within a single case.
chromosome	required	string regex: ^[a-zA-Z0-9_\-\-]+\$	Chromosome number
position	required	integer	Physical position in a chromosome. Please use the 1-based coordinate system.
referenceAllele	required	string regex: ^[ACGTN]+\$	Reference base. Deletion and insertion should be noted according to VCF v4.3 (For example, as stated on page 13 of VCF v4.3, when the reference sequence is atCga and

			the target sequence is at-ga, then denote it as "referenceAllele": "TC" and "alternateAllele": "T").
alternateAllele	required	string regex: ^[ACGTN*]+\$	Variant base. deletion and insertion should be noted in accordance with VCF v4.3 (see the example above). Multi-alleles – tri-alleles and more – should be listed as different elements in the shortVariants tag. In that case, indicate the itemIds and that the variants are multi-alleles in the comments tag.
alternateAlleleFrequency	required	number	Variant allele frequency (ranging from 0 to 1)
totalReadDepth	optional	integer	Total read depth (minimum value 1)
alternateAlleleReadDepth	optional	integer	Variant allele read depth (minimum value 1)
variantType	optional	string [choice]	Short variant type written in the report by the testing company. Select one from: <ul style="list-style-type: none"> • "SNV" • "insertion" • "deletion" • "delins" • "indel" • "MNV" * Please inform C-CAT beforehand if you use other types.
transcripts	required	array (length: 1-N, object)	Information on the representative transcript (One gene should have one representative transcript.)
transcriptId	required	string regex:	Transcription product ID (e.g., NM_000368.4).

		<u><code>^[^\s]+\$</code></u>	It is strongly recommended to include sub-numbers (underlined in red above) for accurate computation. If no transcriptId is present due to a mutation in an intergenic region, then you can describe "transcriptId": null.
transcriptDatabaseName	required	string [choice]	Database of the transcript ID. Select from the following two options. • "RefSeq" • "Ensembl" If the transcriptId is null, then you can describe "transcriptDatabaseName": null.
transcriptDatabaseVersion	optional	string regex: <code>^[^\s]+\$</code>	Version of the database. * If this is not described, the version C-CAT determines will be used.
geneSymbol	required	string regex: <u><code>^[^\s]+\$</code></u>	Name of the gene (gene symbol), as written in the report of the testing company. Enter "geneSymbol": null if a gene does not exist. Enter an associated gene such as "TERT promoter", if any.
strand	optional	string [choice]	Direction of transcription. If the orientation is the same as that of the reference genome sequence, it is "+"; if the orientation is opposite, it is "-". If the transcriptId is null, then you can describe "strand": null.
cdsChange	required	string regex: <code>^[^\s]+\$</code>	Enter changes at the DNA level, as written in the testing company's report.

			<p>Notation in HGVS is recommended.</p> <p>When an RNA is not transcribed as in an intergenic region, you can input null (in addition to the notation of non-coding regions such as n.*).</p>
aminoAcidsChange	required	<p>string regex: ^.*\$</p>	<p>Enter changes at the protein level, as written in the testing company's report.</p> <p>Notation in HGVS is recommended.</p> <p>If no change is observed in amino acids as in an untranslated region, you can input null.</p>
calculatedEffects	optional	<p>array (length: 0-N, string regex: ^.*\$)</p>	<p>Note the effects of alterations on transcripts, such as "splicing_variant", using Sequence Ontology terms.</p> <p>This field corresponds to "Effect (Sequence Ontology)" of the snpEff tool and VCF "Func.refGene" of the annovar tool. For annovar, this is explained at Output file 1 (refSeq gene annotation) on Gene-based Annotation in User Guide, whereby terms provided by annovar can be converted to Sequence Ontology terms.</p> <p>One term should be assigned to each element of an array.</p>
testMethod	required	<p>string [choice]</p>	<p>Derived from</p> <ul style="list-style-type: none"> • "DNA-seq": DNA sample • "RNA-seq": RNA sample
variantOrigin	optional	<p>string [choice]</p>	<p>Somatic or germline origin.</p> <p>* C-CAT uses a different cancer knowledge base, according to</p>

			<p>whether alterations are somatic or germline. If no input is provided, the knowledge base for somatic alterations is used.</p> <ul style="list-style-type: none"> • "somatic": derived from somatic cells • "germline": derived from germline cells • "likely somatic": typically in a tumor-only test, the alteration is likely to be somatic, and the knowledge base for somatic alterations is used. • "likely germline": typically in a tumor-only test, the alteration is likely to be germline, and the knowledge base for germline alterations is used.
reported	required	boolean	<p>Whether or not the alteration is reported in testing company's report or similar documents. When it is true, annotation is made based on the cancer knowledge base.</p>

V-1-2. Example of shortVariants tag

(Example1. for SNV)

```
{
  "itemId": "variant-1",
  Note: The itemId is a character string at the discretion of the testing company for the detected variant.
  "chromosome": "9",
  "position": 135781005,
  "referenceAllele": "C",
  "alternateAllele": "G",
  "alternateAlleleFrequency": 0.54,
  "alternateAlleleReadDepth": 108,
  "totalReadDepth": 200,
  "variantType": "SNV",
  "transcripts": [
    {
```

```

    "transcriptId": "NM_000368.4",
    "transcriptDatabaseName": "RefSeq",
    "transcriptDatabaseVersion": "Release 99",
    "geneSymbol": "TSC1",
    "cdsChange": "c.1960C>G",
    "aminoAcidsChange": "p.Q654E",
    "calculatedEffects": [
      "missense_variant"
    ]
  },
  "testMethod": "DNA-seq",
  "variantOrigin": "somatic",
  "reported": true
}

```

(Example2. for insertion)

```

{
  "itemId": "variant-4",
  "chromosome": "8",
  "position": 37553560,
  "referenceAllele": "A",
  "alternateAllele": "AAGCGGC",
  "Note: Describe \"referenceAllele\" and \"alternateAllele\" according to the rules of VCF v4.3.",
  "alternateAlleleFrequency": 0.4953,
  "alternateAlleleReadDepth": 368,
  "totalReadDepth": 743,
  "variantType": "insertion",
  "transcripts": [
    {
      "transcriptId": "NM_025069.2",
      "transcriptDatabaseName": "RefSeq",
      "transcriptDatabaseVersion": "Release 99",
      "geneSymbol": "ZNF703",
      "cdsChange": "c.63_64insAAGCGGC",
      "aminoAcidsChange": "G21_G22insSG"
    }
  ],
  "testMethod": "DNA-seq",
  "variantOrigin": "somatic",
  "reported": true
}

```

(Example3. for deletion)

```

{
  "itemId": "variant-2",
  "chromosome": "1",
  "position": 27097751,
  "referenceAllele": "TC",
  "alternateAllele": "T",

```

Note: Describe "referenceAllele" and "alternateAllele" according to the rules of VCF v4.3.

```
"alternateAlleleFrequency": 0.12,
"alternateAlleleReadDepth": 32,
"totalReadDepth": 266,
"variantType": "deletion",
"transcripts": {
  "transcriptId": "ENST00000324856.13",
  "transcriptDatabaseName": "Ensembl",
  "transcriptDatabaseVersion": "v99",
  "geneSymbol": "ARID1A",
  "cdsChange": "c.3340delC",
  "aminoAcidsChange": "p.P1115fs*46",
  "calculatedEffects": [
    "frameshift_variant"
  ]
},
"testMethod": "DNA-seq",
"variantOrigin": "somatic",
"reported": true
}
```

(Example4. for delins)

```
{
  "itemId": "variant-6",
  "chromosome": "1",
  "position": 26696982,
  "referenceAllele": "GC",
  "alternateAllele": "TT",
  "alternateAlleleFrequency": 0.25,
  "alternateAlleleReadDepth": 52,
  "totalReadDepth": 524,
  "variantType": "delins",
  "transcripts": {
    "transcriptId": "NM_007294.4",
    "transcriptDatabaseName": "RefSeq",
    "transcriptDatabaseVersion": "Release 99",
    "geneSymbol": "BRCA1",
    "cdsChange": "c.579_580delinsTT",
    "aminoAcidsChange": "p.E193_P194delinsDS"
  },
  "testMethod": "DNA-seq",
  "variantOrigin": "somatic",
  "reported": true
}
```

(Example5. for "TERT promoter")

```
{
  "itemId": "variant-5",
  "chromosome": "5",
  "position": 1295113,
```

```

"referenceAllele": "G",
"alternateAllele": "A",
"alternateAlleleFrequency": 0.163,
"alternateAlleleReadDepth": 15.9,
"totalReadDepth": 92,
"variantType": "SNV",
"transcripts": {
  "transcriptId": "ENST00000310581.9",
  "transcriptDatabaseName": "Ensembl",
  "transcriptDatabaseVersion": "Release 99",
  "geneSymbol": "TERT",
  "cdsChange": "n.1295113C>T",
  "aminoAcidsChange": null,
  "calculatedEffects": [
    "TF_binding_site_variant"
  ]
},
"testMethod": "DNA-seq",
"variantOrigin": "somatic",
"reported": true
}

```

V-2. copyNumberAlterations tag

For information on copy number alterations (CNAs).

Key	Condition	Data type	Description
copyNumberAlterations	optional	array (length: 1-N, object)	Aggregation tag for information on copy number alterations (CNAs)

IV-2-1. Tags within copyNumberAlterations tag

Key	Condition	Data type	Description
itemId	required	string regex: ^\.+\$	An ID assigned to an alteration. It must be a unique string of characters within a single case.
chromosome	required	string regex: ^[a-zA-Z0-9_\-\-]+\$	Chromosome number
startPosition	optional	integer	Physical starting position in a chromosome.

			Please use the 1-based coordinate system.
endPosition	optional	integer	Physical ending position in a chromosome. Please use the 1-based coordinate system.
copyNumberMetrics	optional	array (length: 0-N, object)	Measurements and units of the copy number alteration. Array of objects composed of two keys, value and unit. If there are two or more values in different units, register them as an array with the length of 2 or more.
value	required	number	Aberrated copy number measurement
unit	required	string [choice]	Unit for measured value. Select one from: <ul style="list-style-type: none"> • "absolute copy number": Absolute copy number • "fold-change": Ratio of (standardized) reading depth of tumor samples to normal samples • "log2 fold-change": log2 transformation of "fold-change" • "fraction-of-gene": fraction of a CNA region to the gene region of interest * Please consult C-CAT if you want to use other units.
copyNumberAlterationType	required	string [choice]	CNA type written in the report by the testing company. Select one from: <ul style="list-style-type: none"> • "amplification" • "gain" • "duplication" • "loss" • "deletion" • "homozygous deletion" • "neutral" * Please consult C-CAT if you want to use other types.

transcripts	required	array (length: 1-N, object)	See the description in the shortVariants tag.
transcriptId	optional	string regex: ^[^\\s]+\$	See the description in the shortVariants tag.
transcriptDatabaseName	optional	string [choice]	See the description in the shortVariants tag. If the transcriptId is entered, this key is recommended to input as well.
transcriptDatabaseVersion	optional	string regex: ^\\.+\$	See the description in the shortVariants tag.
geneSymbol	required	string regex: ^[^\\s]+\$	See the description in the shortVariants tag.
strand	optional	string [choice]	See the description in the shortVariants tag.
cdsChange	optional	string regex: ^\\.+\$	See the description in the shortVariants tag.
aminoAcidsChange	optional	string regex: ^\\.+\$	See the description in the shortVariants tag.
calculatedEffects	optional	array (length: 0-N, string regex: ^\\.+\$)	See the description in the shortVariants tag.
testMethod	required	string [choice]	See the description in the shortVariants tag.
variantOrigin	optional	string [choice]	See the description in the shortVariants tag.
reported	required	boolean	See the description in the shortVariants tag.

IV-2-2. Example of copyNumberAlterations tag

```
(Example)
{
  "itemId": "variant-9",
  "chromosome": "1",
```



```

"startPosition": 8921059,
"endPosition": 8939151,
"copyNumberMetrics": [
  {
    "value": 0.2309,
    "unit": "fold-change"
  },
  {
    "value": -2.1147,
    "unit": "log2 fold-change"
  }
],
"copyNumberAlterationType": "loss",
"transcripts": [
  {
    "transcriptDatabaseName": "RefSeq",
    "transcriptDatabaseVersion": "Release 99",
    "geneSymbol": "EN01"
  }
],
"testMethod": "DNA-seq",
"variantOrigin": "somatic",
"reported": false
}

```

V-3. rearrangements tag

For information on rearrangements such as fusions, duplications, large deletions, and inversions.

Key	Condition	Data type	Description
rearrangements	optional	array (length: 1-N, object)	Aggregation tag for information on rearrangements such as fusions, duplications, large deletions, and inversions

IV-3-1. Tags within rearrangements tag

Key	Condition	Data type	Description
itemId	required	string regex: ^.+ \$	An ID assigned to an alteration. It must be a unique string of characters within a single case.
breakends	required	array (length: 2, object)	Two breakends of the rearrangement
chromosome	required	string	Chromosome number

		regex: ^[a-zA-Z0-9_\\-]+\$	
startPosition	required	integer	Physical starting position in a chromosome. Please use the 1-based coordinate system.
endPosition	required	integer	Physical ending position in a chromosome. Please use the 1-based coordinate system.
matePieceLocation	optional	string [choice]	If the sequence of interest is bound to another sequence on the upstream (or downstream) of this sequence of interest along the reference genome sequence, it is input as "upstream" (or "downstream"). Regarding gene fusions and other rearrangements ("rearrangementType": "other"), it is strongly recommended to input this key for accurately identifying the genomic changes. See "VII-2. matePieceLocation" below for a detailed explanation.
transcripts	required	array (length: 1-N, object)	See the description in the shortVariants tag.
transcriptId	optional	string regex: ^[^\\s]+\$	See the description in the shortVariants tag.
transcriptDatabase Name	optional	string [choice]	See the description in the shortVariants tag. If the transcriptId is entered, this key is recommended to input as well.
transcriptDatabase Version	optional	string regex: ^\\.+\$	See the description in the shortVariants tag.

geneSymbol	required	string regex: ^[^\s]+\$	See the description in the shortVariants tag.
strand	optional	string [choice]	See the description in the shortVariants tag.
cdsChange	optional	string regex: ^.+	See the description in the shortVariants tag.
aminoAcidsChange	optional	string regex: ^.+	See the description in the shortVariants tag.
calculatedEffects	optional	array (length: 0-N, string regex: ^.+)	See the description in the shortVariants tag.
genePairs	optional	array (length: 0-N, string regex: ^.+\\-+)	<p>A transcriptionally ordered pair of gene names that straddle the break-ends in gene reconstruction. Connect the geneSymbols listed in transcripts with a "-" in the transcriptional direction. For example, for geneSymbols A and B, if A is upstream of transcription and B is downstream of transcription, it is represented as "A-B".</p> <p>* This directional information is taken into account in the cancer knowledge base search. In the absence of this tag, the pair of geneSymbols is treated as if there is no information on the transcriptional direction and the knowledge base is searched for the unordered pairs of gene names.</p> <p>* If this tag is omitted (and there is no mention in matePieceLocation), any pair of geneSymbols will be searched for unordered pairs of geneSymbols, but if you want to control the search in</p>

			detail, please describe it as ["A-B", "B-A", "C-B"].
insertedSequence	optional	string regex: ^[ACGTN]+\$	Sequence inserted between the two breakends of the genome sequence. If an inserted sequence does not exist, input null.
supportingReadCount	optional	integer	Number of support reads
alternateAlleleFrequency	optional	number	Variant allele frequency (ranging from 0 to 1)
expressionLevelMetrics	optional	array (length: 0-N, object)	Information on expression levels in RNA-seq
value	required	number	Value of an expression level
unit	required	string [choice]	Unit of an expression level. Select one from the following options: <ul style="list-style-type: none"> • "TPM" • "FPKM" • "FPM" • "RPKM" • "RPM" * Please consult C-CAT if you want to use other units.
rearrangementNames	optional	array (length: 0-N, string regex: ^\.+\$)	Individual rearrangement name given by the testing company. For example, "EML4-ALK fusion"
rearrangementType	required	string [choice]	Rearrangement type written in the report by the testing company. Select one from: <ul style="list-style-type: none"> • "gene fusion" • "frameshift gene fusion" • "bidirectional gene fusion" • "duplication" • "deletion" • "inversion" • "truncation" • "splice variant" • "other"

			* Please consult C-CAT if you want to use other types.
testMethod	required	string [choice]	See the description in the shortVariants tag.
variantOrigin	optional	string [choice]	See the description in the shortVariants tag.
reported	required	boolean	See the description in the shortVariants tag.

IV-3-2. Example of rearrangements tag

(example1. In case of existing genePairs)

```
{
  "itemId": "variant-13",
  "breakends": [
    {
      "chromosome": "2",
      "startPosition": 42510050,
      "endPosition": 42510050,
      "matePieceLocation": "downstream",
      "transcripts": [
        {
          "transcriptDatabaseName": "RefSeq",
          "transcriptDatabaseVersion": "Release 99",
          "geneSymbol": "EML4"
        }
      ]
    },
    {
      "chromosome": "2",
      "startPosition": 29445240,
      "endPosition": 29445240,
      "matePieceLocation": "upstream",
      "transcripts": [
        {
          "transcriptDatabaseName": "RefSeq",
          "transcriptDatabaseVersion": "Release 99",
          "geneSymbol": "ALK"
        }
      ]
    }
  ],
  "genePairs": [
    "EML4-ALK"
  ],
  "supportingReadCount": 30,
  "alternateAlleleFrequency": 0.07,
  "rearrangementType": "other",
}
```

```
"variantOrigin": "somatic",
"testMethod": "DNA-seq",
"reported": false
}
```

(example2. In case of existing insertedSequence)

```
{
  "itemId": "variant-14",
  "breakends": [
    {
      "chromosome": "14",
      "startPosition": 234567,
      "endPosition": 234567,
      "matePieceLocation": "downstream",
      "transcripts": [
        {
          "transcriptDatabaseName": "RefSeq",
          "transcriptDatabaseVersion": "Release 99",
          "geneSymbol": null
        }
      ]
    },
    {
      "chromosome": "2",
      "startPosition": 321672,
      "endPosition": 321672,
      "matePieceLocation": "upstream",
      "transcripts": [
        {
          "transcriptDatabaseName": "RefSeq",
          "transcriptDatabaseVersion": "Release 99",
          "geneSymbol": "LINC01865"
        }
      ]
    }
  ],
  "insertedSequence": "GTNNNNNCAT",
  "supportingReadCount": 30,
  "alternateAlleleFrequency": 0.07,
  "rearrangementType": "other",
  "variantOrigin": "somatic",
  "testMethod": "DNA-seq",
  "reported": false
}
```

VI. otherBiomarkers tag

For information on biomarkers other than alterations defined in the variants tag. Currently, Micro-Satellite Instability (MSI), Tumor Mutation Burden (TMB), and Loss Of Heterozygosity (LOH) can be noted.

Key	Condition	Data type	Description
otherBiomarkers	optional	array (length: 0-N, object)	Aggregation tag for information on biomarkers

VI-1. Tags within otherBiomarkers tag

Key	Condition	Data type	Description
itemId	required	string regex: ^.+ \$	An ID assigned to a biomarker. It must be a unique string of characters within a single case.
biomarkerType	required	string [choice]	Type of biomarkers. Select one from: <ul style="list-style-type: none"> • "TMB": Tumor Mutation Burden • "MSI": Micro-Satellite Instability • "LOH": Loss Of Heterozygosity * Inform C-CAT for other biomarkers.
biomarkerMetrics	optional	array (length: 0-N, object)	Inspection values and units
value	required	number	Measured value e.g.) 5.15
unit	required	string regex: ^.+ \$	Unit for the measured value. Units may vary depending on test types. e.g.) %
state	optional	string [choice]	Select the biomarker status from the following options. <ul style="list-style-type: none"> • "high" • "low" • "intermediate" • "stable" If the test was performed, but the results are not listed above, describe null. * Inform C-CAT for other options.

description	optional	array (length: 0-N, string regex: ^.+)\$)	Descriptions such as how to obtain the inspection value and the meaning of the inspection value. See the contents tag within the comments tag for usable languages and new lines.
biomarkerOrigin	optional	string [choice]	See the description in the shortVariants tag.
reported	required	boolean	See the description in the shortVariants tag.

VI-2. Example of otherBiomarkers tag

(Example)

```
"otherBiomarkers": [
{
  "itemId": "biomarker-1",
  "biomarkerType": "MSI",
  "biomarkerMetrics": [
    {
      "value": 5.15,
      "unit": "%"
    },
    {
      "value": 2,
      "unit": "MSIsensor score"
    }
  ],

```

Note: If one inspection item has values in multiple units, use array notation in the "biomarkerMetrics" tag.

```
  "state": "stable",
  "descriptions": [
    "MSI sensor score 10 points or more was MSI-H, 3 points or more and less than 10 points was indeterminate (MSI-I), and less than 3 points was microsatellite stable (MSS).",

```

```
    "https://www.gi-cancer.net/gi/ronbun/archives/201901-01.html"
  ],
  "reported": true
},
{

```

```
  "itemId": "biomarker-2",
  "biomarkerType": "TMB",
  "biomarkerMetrics": [
    {
      "value": 34.5680122,
      "unit": "Muts/Mb"
    }
  ],
  "state": "high",

```



```
    "reported": true
  },
  {
    "itemId": "biomarker-3",
    "biomarkerType": "LOH",
    "biomarkerMetrics": [
      {
        "value": 24.14,
        "unit": "%"
      }
    ],
    "state": "neutral",
    "reported": true
  }
]
```

VII. compositeBiomarkers tag

Information on composite markers (e.g., combinations of gene alterations, and fusions composed of three genes) that are represented by the combinations of elements in the shortVariants, copyNumberAlterations, and rearrangements tags.

Key	Condition	Data type	Description
compositeBiomarkers	optional	array (length: 0-N, object)	Aggregation tag for information on composite markers

VII-1.Tags within compositeBiomarkers tag

Key	Condition	Data type	Description
itemId	required	string regex: ^,+\$	An ID assigned to a composite marker. It must be a unique string of characters within a single case.
componentItemIds	required	array (length: 2-N, string regex: ^,+\$)	Array of component gene alterations (itemIds).
biomarkerNames	required	array (length: 1-N, string regex: ^,+\$)	The name of the composite marker, as listed in the testing company's report.
descriptions	optional	array (length: 0-N, string regex: ^,+\$)	Description on composite markers See the contents tag within the comments tag for usable languages and new lines.
reported	required	boolean	See the description in the shortVariants tag.

VII-2.Example of compositeBiomarkers tag

<p>(Example)</p> <pre>" compositeBiomarkers": [{ "itemId": "composite-1", "componentItemIds": ["variant-14", "variant-15"], </pre>

```
"biomarkerNames": [  
  "BRAF-NRG1-ALK fusion"  
],  
"descriptions": [  
  "Three genes are fused together to produce the fusion gene BRAF-NRG1-ALK."  
],  
"reported": true  
},  
]
```

VIII. sequencingSamples tag

For information on information on sequencing samples results in the NGS run.

Key	Condition	Data type	Description
sequencingSamples	optional	array (length: 1-N, object)	Aggregation tag for information on sequencing samples results

The maximum length of this array is 4, since the tumorOrNormal tag and the testMethod tag can each take two values “tumor” or “normal” and “dnaSeq” or “rnaSeq”, respectively.

VIII-1. Tags within sequencingSamples tag

Key	Condition	Data type	Description
itemId	required	string regex: ^.+\$\$	The ID of the item. It must be a unique string of characters within a single case.
tumorOrNormal	required	string [choice]	Whether the sequencing samples results are of tumor specimen or normal specimen. • "tumor" • "normal"
testMethod	required	string [choice]	Whether the sequencing samples results are derived from DNA or RNA samples. • "DNA-seq": DNA sample • "RNA-seq": RNA sample
duplicateReadsPercentage	optional	number	Percentage of duplicate reads in total reads
mappedReadsPercentage	optional	number	Percentage of mapped reads in total reads
meanReadDepth	optional	number	Mean read depth
medianReadDepth	optional	number	Median read depth
suspectedSampleStates	optional	array (length: 0-N, string) [choice]	The suspicious state of a DNA or RNA sample, such as "contaminated". • "contaminated": Possibility of contamination • "deaminated": Possibility of notable cytosine deamination in FFPE DNA • "fragmented": Possibility of notable (FFPE DNA) fragmentation.

			<ul style="list-style-type: none"> • "degraded": Possibility of notable (RNA) degradation
--	--	--	--

VIII-2. Example of sequencingSamples tag

(Example)

```
"sequencingSamples": [
  {
    "itemId": "sequence-1",
    "tumorOrNormal": "tumor",
    "testMethod": "DNA-seq",
    "duplicateReadsPercentage": 91.52,
    "mappedReadsPercentage": 87.31,
    "meanReadDepth": 247.8,
    "medianReadDepth": 238
  },
  {
    "itemId": "sequence-2",
    "tumorOrNormal": "tumor",
    "testMethod": "RNA-seq",
    "suspectedSampleStates": [
      "degraded"
    ]
  },
  {
    "itemId": "sequence-3",
    "tumorOrNormal": "normal",
    "testMethod": "DNA-seq"
  }
]
```

IX. Other notes
Precautions.

IX-1. itemId

The value of itemId must be unique within the file. The value can be any string.

IX-1-1. Example of itemId description

Examples of itemId values for each tag are as follows.

- For variants tag

"itemId": "variant-1"

"itemId": "variant-2"

"itemId": "variant-3"

- For otherBiomarkers tag

"itemId": "biomarker-1"

"itemId": "biomarker-2"

"itemId": "biomarker-3"

- For sequencingSamples tag

"itemId": "sequence-1"

"itemId": "sequence-2"

"itemId": "sequence-3"

- For compositeBiomarkers tag

"itemId": "composite-1"

"itemId": "composite-2"

"itemId": "composite-3"

IX-2. matePieceLocation

We will explain matePieceLocation in the breakends tag. We assume that “upstream” and “downstream” correspond to the direction of decreasing and increasing positional coordinates along a chromosome in a reference genome sequence, respectively.

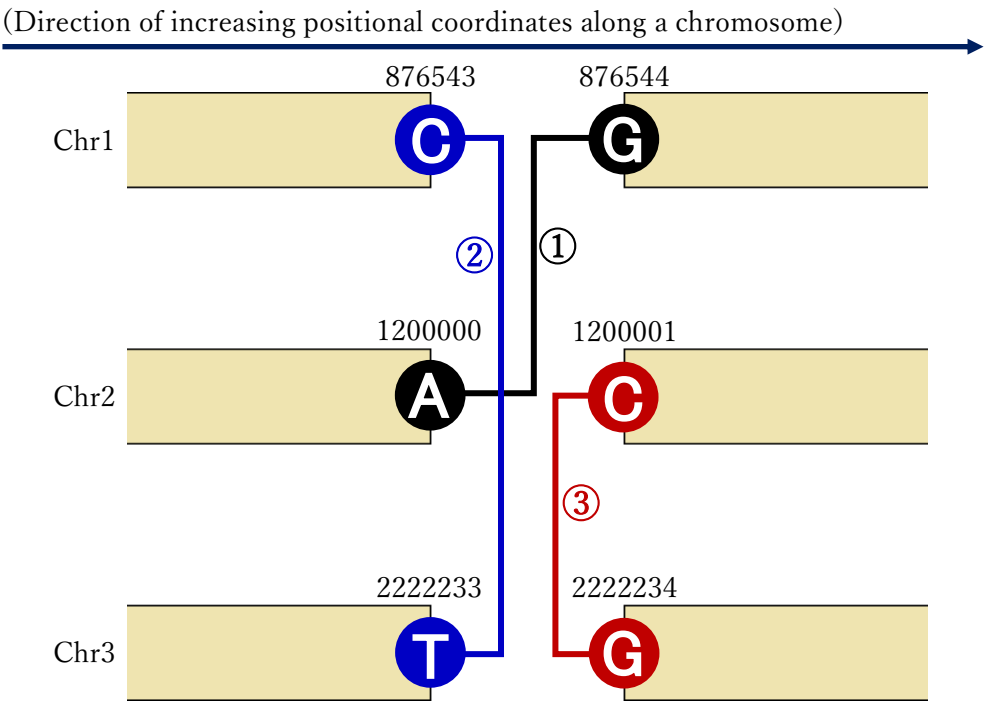
Note: These “upstream” and “downstream” are different from those of transcriptional direction.

VIII-2-1. Example of matePieceLocation description

We illustrate how to input matePieceLocation, also presenting representations in VCF format (v4.3). The examples below are modified from the figure in the following documents:

The Variant Call Format Specification VCF v4.3 and BCF v2.2
<https://samtools.github.io/hts-specs/VCFv4.3.pdf>

Example of rearrangements:



Description in VCF format:

The representations in VCF v4.3 for the figure above are as follows. The numbers in the leftmost column in the table below correspond to the numbers in the figure above.

	#CHROM	POS	ID	REF	ALT	QUAL	FILTER	INFO
①	1	876544	bnd_V	G]2:1200000]G	6	PASS	SVTYPE=BNĐ
2	2	1200000	bnd_U	A	A[1:876544[6	PASS	SVTYPE=BNĐ

②	1	876543	bnd_W	C	C]3:2222233]	6	PASS	SVTYPE=BNĐ
	3	2222233	bnd_Y	T	T]1:876543]	6	PASS	SVTYPE=BNĐ
③	2	1200001	bnd_X	C	[3:2222234[C	6	PASS	SVTYPE=BNĐ
	3	2222234	bnd_Z	G	[2:1200001[G	6	PASS	SVTYPE=BNĐ

Descriptions in the standardized format:

• Example①

For the chromosome 2 junction point, because the downstream sequence of the junction point is replaced with another sequence, the value of matePieceLocation is "downstream".

On the other hand, for the chromosome 1 junction point, because the upstream sequence of the junction point is replaced with another sequence, the value of matePieceLocation is "upstream".

(Example①)

```
"breakends": [
{
  "chromosome": "2",
  "startPosition": 1200000,
  "endPosition": 1200000,
  "matePieceLocation": "downstream"
},
{
  "chromosome": "1",
  "startPosition": 876654,
  "endPosition": 876654,
  "matePieceLocation": "upstream"
}
]
```

• Example②

For the chromosome 1 junction point, because the downstream sequence of the junction point is replaced with another sequence, the value of matePieceLocation is "downstream".

The same is true for chromosome 3; so, the value of matePieceLocation is "downstream".

(Example②)

```
"breakends": [
{
  "chromosome": "1",
  "startPosition": 876543,
  "endPosition": 876543,
  "matePieceLocation": "downstream"
},
{
  "chromosome": "3",
  "startPosition": 2222233,
```



```
"endPosition": 2222233,  
  "matePieceLocation": "downstream"  
}  
]
```

• Example③

For the chromosome 2 junction point, because the upstream sequence of the junction point is replaced with another sequence, the value of matePieceLocation is "upstream". The same is true for the chromosome 3 junction point; so, the value of matePieceLocation is "upstream".

```
(Example③)  
"breakends": [  
  {  
    "chromosome": "2",  
    "startPosition": 1200001,  
    "endPosition": 1200001,  
    "matePieceLocation": "upstream"  
  },  
  {  
    "chromosome": "3",  
    "startPosition": 2222234,  
    "endPosition": 2222234,  
    "matePieceLocation": "upstream"  
  }  
]
```

- X. For inquiries
C-CAT Help Desk
E-Mail: helpdesk_c-cat@ml.res.ncc.go.jp