

# **VariantStudio Software**

## **Release Notes**

**Version 2.2**

**June 18, 2014**

## Introduction

These Release Notes detail the key changes to software components for VariantStudio since the package containing 2.1.46.

Refer to the user guide for more details on how to operate VariantStudio:

[support.illumina.com/downloads/variantstudio\\_userguide\\_15040890.ilmn](http://support.illumina.com/downloads/variantstudio_userguide_15040890.ilmn)

The FAQs for the application can be found at this location:

[support.illumina.com/sequencing/sequencing\\_software/variantstudio/questions.ilmn](http://support.illumina.com/sequencing/sequencing_software/variantstudio/questions.ilmn)

The software package includes:

- Illumina VariantStudio v2.2.174

## I. Import

### NEW FEATURES:

- Modified import to exclude variants represented in a form other than SNVs and small indels in the VCFv.4.1 format (e.g. excludes lines displaying CNV events, missing CHR information, etc.).
- Added a warning dialog that is displayed if a user attempts to load more than 500,000 variants.
- Value from the DPI INFO field is used in the Read Depth column for insertion and deletion events reported from the Illumina Isaac Alignment and Variant Caller workflow.

### DEFECT REPAIRS:

- Fixed a known issue with filtering when handling hom ref positions in gVCF files. Filters now utilize allele matching where previously only used positional information.

### KNOWN ISSUES:

- If the sample import process is canceled during a multi-select import or a folder import, the samples that were successfully imported before cancellation may not immediately appear in the Variants table and the Current Sample menu. If so, then the recommendation is to save, close, and reopen the project. The samples should then be visible. Alternatively, the user may add or remove a sample to produce the same effect.
- When loading extremely large vcf.gz files, the import progress bar may not initially update.

## II. Annotation

### NEW FEATURES:

- An additional Custom Gene Annotation column has been added in the table of the Genes tab. This additional column has also been made available as a selectable Boolean logic (AND vs OR).

- Regulatory information for variants has been added in the Regulatory Element column. When Regulatory features are available for a variant, the Regulatory Element column is populated with a hypertext link to regulatory information in Ensembl for that genomic region. Regulatory annotations are included by default.

**DEFECT REPAIRS:**

- Fixed issue: now displays multiple COSMIC entries if they exist for a variant.
- Fixed issue: now displays multiple ClinVar entries if they exist for a variant.
- Fixed a known issue where some rsID entries that overlap the updated positions were missing from the September 2013 ClinVar release.

**KNOWN ISSUES:**

- For single nucleotide deletions, the annotation data for rsID, read depth, and sample coverage used with EVS comes from the following genomic position (variant position+1) as opposed to the variant position. Because everything is encoded in "VCF coordinates", the actual deletion takes place at the following base.
- A few rsIDs were inadvertently removed due to the way entries are matched that likely contain assembly artifacts. rsID entries overlapping genes with the phrase "CFL" contained in them are affected.
- The "Load Default Transcripts" feature does not allow the user to apply as default any transcript that is not in the pre-defined list of known gene-transcript sets built in to the software (those variants that show up in the table in the Load Default Transcripts window). If a user tries to change the default transcript to one that is not in this list by using the Import feature, the unknown transcript is ignored.

### III. Filtering

**NEW FEATURES:**

- The "Show only variants: Inside coding regions" option has been removed from the Variant section within the Filters pane.
- Several modifications were made to family-based filtering
  - Added an "Inherited From" category of "indeterminate" for child variants that
    - Are only hom-ref
    - Those variants that have alleles that cannot be accounted for in the parents because they are either no-calls in the parents or the parents are not supplied for the analysis
  - Analysis no longer requires at least one parent for family-based filtering. Analysis can now be run with one other sample, either a parent or a sibling. The (g)VCF files that are selected are used for the analysis
  - Variants that are no-called in one parent but otherwise consistent with the selected inheritance mode now pass the family-base filter.
  - Hemizygous variants now pass the dominant filter.

- Variants not associated with a gene (where Gene = "N/A") are now handled in Autosomal Recessive family-based filtering. Previously, all variants not associated with a gene were filtered out. Now, if they meet the criteria for a recessively inherited variant, these variants are passed through the Autosomal Recessive filter.
- Several modifications were made to the Advanced Filter
  - Only comparisons of columns of the same type (types include integer, string, float, etc.) are allowed
  - Added error checking when non-numeric values are set in "constant" field for read depth and alt read depth

**DEFECT REPAIRS:**

- Fixed a known issue with the auto-filter in the Default Transcript column in the table of the Default Transcript window (Annotation & Classification > Set Default Transcripts). Previously the Default Transcript column auto filter box threw an error when clicked. Now it does not.
- Fixed a known issue involving a double-quotation mark in the Advanced Filter editor. Previously exception thrown when string Right-hand side text box is just a double-quotation mark. Now the exception is not thrown and the user is allowed to keep typing after the double-quote.
- Fixed a known issue involving triallelic variants. Previously triallelic variants would pass through the filters when inappropriate.
- Fixed the filtering behavior when variants have multiple COSMIC/ClinVar records as follows:
  - Changed "where matches mutant allele" to return any variants where the allele B matches one or more of the COSMIC/ClinVar alleles.
  - Changed "where not matches mutant allele" to return any variants where the allele B does not match any of the COSMIC/ClinVar alleles match
- Fixed an issue in Advanced Filter where filtering by coordinate did not always return the correct result due to the float field not having enough precision.

**KNOWN ISSUES:**

- When Creating or Modifying an Advanced Filter through the text expression form of the filter, using the "!" character next to expressions enclosed in parentheses has the effect of negation, but this effect is not reflected in the graphical tree representation of the filter. Use the "not equals" operator in these situations. Using a "!" character outside of the square brackets, however, does not have the effect of negation, and when it is set in place, the character can only be cleared by using the Clear Filters button in the main Filters panel.
- The filter history shows the filter name for any saved filters. However, note that the name is displayed in the filter history only when an existing filter is reused. The saved name is not displayed in the "Filter Name" column when the filter is initially created and saved, only when it is reused.

## IV. Classification

### NEW FEATURES:

- None

### DEFECT REPAIRS:

- Fixed a known issue with the Classification Database. Previously, removing a Classification Category assigns those variants to the blank category, making them uneditable. Now these variants become unassigned but can be edited.
- Fixed a known issue with the Classification Database: Previously removing a variant from the database does not clear that variant's classification info in the Variants table. Now removing a variant Classification from the Classification Database also results in the removal of the Classification in the Variants Table.
- Fixed a known issue where if the last category in the Classification Categories list was removed, and then a new category is subsequently added, all variants from the old classification are assigned to the new classification automatically.

### KNOWN ISSUES:

- None

## V. Reporting

### NEW FEATURES:

- None

### DEFECT REPAIRS:

- Fixed an issue where the bin labels for the In-Del Variant Length histogram were off by one.
- Fixed an issue where the Filtered Variants pie charts for Genotype, Exonic, and Filtered/Unfiltered were returning incorrect proportions.

### KNOWN ISSUES:

- None

## VI. Outputs

### NEW FEATURES:

- Changed export filter history to TSV so that commas in string fields are handled properly
- Added ability to view exported filter history in Excel immediately after export

### DEFECT REPAIRS:

- None.

### KNOWN ISSUES:

- Some of the report-exporting processes are unable to be canceled. Specifically, you cannot cancel exporting Filtered Variants, All Transcripts for Variants, Filter History, Sample Report in PDF format, and Sample Report in RTF format. However, you can cancel the exporting process for the Genes table and the No-call Regions table. The impact here is that the exporting processes that cannot be canceled does not show a progress bar for the process.

## VII. Additional Features

### NEW FEATURES:

- Improved VCF load times when loading a subset of variants (e.g. exons +/-20bp, BED regions file, etc.)
- Saves currently selected sample in the project file so that one comes up initially when the project is reloaded
- Added option to save filtered variants when saving project in addition to saving all variants regardless of applied filters. Previously, when a Project is saved in VariantStudio, all variants of the samples within the Project are saved regardless of the filters currently applied to the samples. When reopening the Project, samples display all variants (i.e., state of previously applied filters is not stored). We have added an option where users can save the state of the filters applied when the Project was saved such that when reopening the Project, the filtered variants are displayed. When this option is applied, variants that had been filtered out are not saved in the Project and cannot be recovered.

### DEFECT REPAIRS:

- Changed behavior of Favorites to solve a previous issue. Removed the "Save As" button. Now "Save" acts as "Save As". Whenever the user changes a filter setting in the UI, the filter is compared against all of the favorites, and if it does not match any, then the favorite selected in the menu is set to blank. If it does match, then that filter is selected. This way, you are sure that whatever filters you have set in the UI match the currently displayed favorite filter.
- Fixed a known issue with a set of triallelic indels. Previously, when alternate alleles include both insertions and deletions, the type for the first allele is displayed for both alleles. Now the correct type is displayed for both alleles.
- Fixed an issue where memory consumption continues despite canceling VCF load.
- Fixed an issue where overlapping genes were not being displayed in Genes table.
- Fixed a known issue where in the Set Default Transcripts menu, clicking the column filtering text box for the Default Transcript column throws an error. Column filtering for the Default Transcript column is unavailable.
- Fixed an issue where the Disease column of the Genes table had data display issues when the table was manually sorted.

### KNOWN ISSUES:

- If the user zooms too far when zooming in or out of the Gene View, an error is thrown and the Gene View becomes disabled. Under normal usage, the zooming limits should not be reached. The loss of the Gene View has no impact on continued use of the rest of the application.
- Transcript column counts all transcripts present in the User Interface. Transcripts that are annotated as either upstream or downstream gene variants are counted in this count.
- The "Add Variants to Sample" import option does not limit importing additional variants from the sample multiple times. It is possible to import the same variants multiple times and have duplicate entries in the User Interface.
- If a workspace is overwritten, the existing \*.vbp file is deleted, but all other files in the subfolder remain.
- During application startup, if the user locks the screen or switches users, VariantStudio may throw an exception and close.
- The "Distance" column (hidden by default) sorts by the string value of the field, rather than as a number.
- When loading a VCF with " at the beginning or end of the Alt value, the variant is loaded as-is, with "Type" of "complex".