# bionano™

# Bionano VIA™ Software Version 7.0 Release Notes

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# Revision History

| REVISION | NOTES |
|---|---|
| A | Initial release. |

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# Bionano VIA<sup>TM</sup> Software

This document describes the v7.0 release of Bionano VIA software. In this document we will provide an overview of what is changing with this release so that you may better understand the impact of moving to this version. Should you have any questions please contact software-support@bionano.com

## Introduction

Variant Intelligence Applications (VIA) software is a complete and integrated solution for the visualization, interpretation and reporting of genomic variants from multiple technology types. The predecessor version of VIA 7.0 is $N_x$Clinical 6.2. By supporting multiple genome-wide data modalities, VIA provides the most comprehensive view of genomic variants of any interpretation, annotation, and reporting software tool available. As a platform-agnostic tertiary analysis solution, VIA stores and manages distinct types of genomic data from various platforms enabling the extraction of meaningful insights from standalone or combined analysis.

The software includes algorithms to detect copy number variants (CNV) from major microarray vendors, optical genome mapping (OGM), and next generation sequencing (NGS) methodologies as well as Absence of Heterozygosity (AOH), from data types that assess B-allele frequency. VIA also provides interpretation assistance to analyze CNVs, Loss of Heterozygosity (LOH) and Structural Variants (SV) from OGM data. As a centralized analysis solution spanning technologies and application areas, VIA provides an efficient environment to keep pace with advancements in technology while retaining access to historical platform data. By being adaptive to whichever technology is used to generate CNV, LOH, or SV genomic variants, VIA provides rich annotations for the co-analysis of sequence variants from NGS to provide a complete picture of genomic variation and reveal more answers for disease association.

## Supported Implementation Options

VIA is a scalable enterprise solution comprised of three components: the VIA Server, VIA Processing, and VIA Client applications. The server is the primary component of the system that manages the data in the repository. Installed adjacent to the Server is the Processing application that executes processing jobs for segmentation and annotation. The Client software is the User Interface (UI) utilized by all users to access sample data hosted in the VIA Server. There are three implementation options to deploy the VIA system; installation of the VIA Server and VIA Processing on the Bionano Access Server (BAS), local network server, or hosted in a cloud environment as illustrated below in **Figure 1**. In each implementation option, the VIA Client software is installed locally on each analyst's workstation with network access to the VIA Server. Further information on hardware requirements is available in the VIA System Requirements Guide.

- Option 1: VIA Server and VIA Processing are hosted on the BAS and is a common installation strategy for OGM users primarily interested in analyzing OGM data in VIA software.
- Option 2: VIA Server and VIA Processing are hosted on a local network and is a common installation strategy for NxClinical users primarily interested in array or NGS technology.
- Option 3: VIA Server and VIA Processing are hosted on a site-administered cloud environment and is a common installation strategy for users seeking production-scale analysis with VIA.
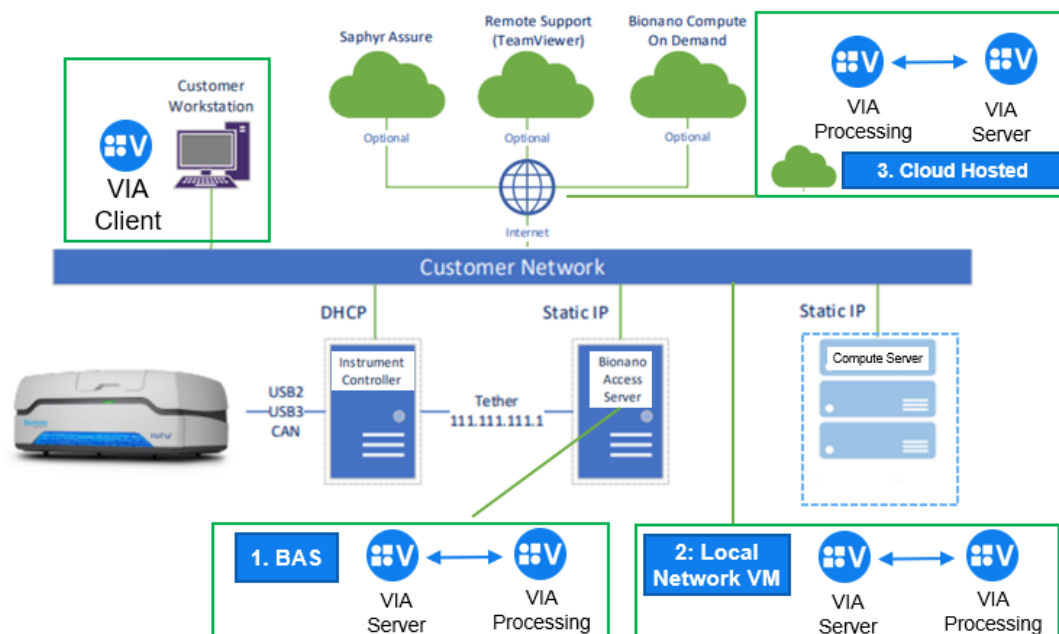
**Figure 1**. VIA Implementation Options Illustration

**Compatibility**

VIA 7.0 is compatible with Bionano Access™ 1.8, Bionano Solve® v3.8 pipeline running on either Saphyr® Compute, Bionano Compute servers or Bionano Compute On Demand v1.4. Please refer to the *VIA System Requirements* for hardware requirements to install the software on local network and client workstations.

# New Features in Version 7.0

**NOTE**: Some features are license-dependent so may not apply to your specific installation of VIA. E.g., CNV from NGS and Seq Var analysis capabilities are only available to those with a license that includes capabilities to process NGS data.

**Integration of OGM data**

1. Admin users are able to create and edit sample types that use OGM data in the **Admin** tab, these sample types load with default processing settings in the **Platforms** tab.
2. Admin users can set preferences for structural variant (SV) filters for OGM Sample Types.
3. A new **Admin** tab called "OGM BAM References" displays MultiScale references (.msr files) created by the MSR Builder with ogm.bam files from copy neutral samples.
4. A new Sample Class, "OGM Only," is available for importing OGM.BAM and OGM.VCF sample data.
5. Another new Sample Class, "OGM+NGS", is available for importing OGM.BAM, OGM.VCF and a small variant VCF for combined processing and analysis of OGM and NGS data.
6. OGM samples can be imported directly from Bionano Access and the usual VIA methods through "Data" or "Batch import".

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7. Uploading the OGM.BAM file using the Upload Sample Data window or Batch Import requires the OGM.BAM.BAI (bam index) file.
8. OGM variants are displayed in existing tracks, plots, karyograms, and variant details.
9. VIA displays segment values in the whole genome plot for OGM data. A new Circos plot is available for OGM samples. The Circos plot can display combination of SV events, CN events, Allelic events, and Seq Var events in a circular whole genome plot.
10. New installations of VIA will come pre-loaded with OGM sample types: AML hg38, MDS hg38 and Pan Heme hg38, which include configurations for conducting heme analysis workflow for OGM data types.
11. Human genomes NCBI Build 37, NCBI Build 38 and T2T CHM13v2.0 are included with the installation of VIA on the BAS.
12. Added support for CNV and AOH/LOH segmentation from OGM.BAM data with new OGMBamMultiScale data type for SNP FASST3 processing.
    a. Processing of OGM BAMs calculates "average coverage depth" and "average molecule length" and these are stored in the processing stats.
    b. VIA displays the event significance for OGM CNV events that were made during OGM BAM processing.
    c. Event Significance for CNVs from OGM BAM can be filtered in the filter pipeline, the default value of the cutoff is 10-5 (1e-5).
13. Added support for new event type, Structural Variants (SV).
    a. Added a filter pipeline for SV events. The filters in the pipeline include:
        i. VCF Filter Values, to filter SV events based on the PoorMoleculeSupport flag contained within the ogm.vcf file.
        ii. Classified Events filter
        iii. Panel Selection filter to apply gene or region panels.
        iv. Percent in OGM Control Database Filter.
        v. Event type filter to remove specific SV event types.
        vi. SV event-size filtering is enabled but does not apply to intrachr_fusion events.
        vii. SV Variant Allele Fraction filter.
    b. **Report** tab in sample review supports custom regions for SVs.
    c. **SV Event** label is completely displayed on the SV track when the event is at the start of the chromosome.
    d. Selecting an SV event in the **Event** table causes the track view focus to switch to the SV region selected.
    e. Support for SV events in Word report template.
    f. Included SV events in classification counts displayed on **Home** page.
    g. Implemented SV events into the variant filter panels. An **SV Event** icon is displayed in the **Filter** tab next to the other modalities, this icon can be toggled ON/OFF to display or remove SV variants.
    h. Users can view SV event associated data in the table including SV Quality, molecule Count, VCF Filter values, % in OGM Control DB, SV VAF, Zygosity and coordinates for Fusion Junctions 1 and 2 for specific variant types.
    i. VIA shows marked SV events in the table when the quick filter is active and notify user when marked events unexpectedly appear in the table.
    j. Users can export the table for OGM samples, the table export includes defined VCF filter settings. OGM molecules track show red/blue indels at detailed zoom.
14. Implemented **Variant Details** tab for SV Types with gene lists that vary depending on the SV type:

a. For Deletion, Duplication, and Insertion: genes overlapping the breakends + confidence interval and in the area between the two breakend regions are displayed.

b. For Intrachr Fusion, Interchr Translocation, Paired Inversion and Partial Inversion: genes overlapping the two breakend + confidence interval regions are displayed as well as a 50kb region surrounding each breakend.

c. For an Inverted duplication: genes overlapping the breakends + confidence interval + the area between the two breakend regions are displayed and 50kb surrounding the event.

d. Genes in the gene list of the **Variant Details** tab are highlighted depending on their location within the event (red/blue overlap with the break end 1 or 2, yellow overlap both break ends, non-highlighted genes are within the intervening region or in the regions surrounding the break ends). Highlighting colors are explained in the tooltip above the gene list.

e. For SV events with fusion junctions that are formed as compound events ( e.g., translocation), the gene or region content shows overlaps on each end of the fusion junction separated by a semicolon.

15. Display of OGM data is integrated across the software interface.

a. VIA shows region overlap content in the event table for SV events covering a particular genomic region.

b. Zygosity of SV events is shown in the table and **Variant Details** tab.

c. Support paired inversions in the OGM VCF where SVTYPE is INV. Maintain backward compatibility to display paired inversions when SVTYPE is BND.

d. ISCN nomenclature for OGM detected variants is displayed in the events table.

e. ISCN nomenclature for SVs and CNV generated by OGM is displayed with the prefix "ogm."

f. Hyperlinked cyto band labels are displayed in the SV track view, clicking on the hyperlink moves to the paired breakend.

g. Event Significance is updated and saved when CNV events from OGM BAM are added/edited in the UI.

h. Users can enter Variant interpretation and notes for all SV variants.

i. VIA Shows region overlap content in the event table for SV events covering a particular genomic region.

j. Classification of SV variants is included in the count of classified variants displayed at the bottom of the **Sample Review** screen and in the **Home** tab when the sample is displayed.

16. Established connection to Bionano Access

a. Users can launch **Access** view for a selected SV event or a specific region from **Single Sample Review** tab track, by right clicking on a SV event in the SV Events track Browse Region>Access and in addition Access circos plot can be launched from the **Home** tab.

b. The repository window displays Access server information.

c. VIA allows users to load structural variants form OGM VCF containing missing VAF values for structural variants.

d. VIA can import CNV and AOH events generated by Bionano Solve as an alternative to SNP FASST3 CNV data.

e. OGM data types supported for CNV include "OGM VCF," "OGM BAM Multiscale" and "OGM BAM Self-Reference" while SV data types are uploaded from "OGM VCF." The data type used is displayed in sample info under the SV Processing section.

17. Additional capabilities supporting the integration of OGM Data and SV Events

a. Track options OGM sample review "molecules track" and "OGM Coverage" are available track preferences to be added by Admin.

b. Display "Undefined" for an unrecognized SV event.

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c. Parameters"Break end Expansion Width" and "Fusion junction score" are added to the Sample Review Preferences for OGM Sample types.

d. The json export includes event significance for each copy number event from OGM BAM MSR samples.

e. VIA prevents re-processing of OGM samples when no changes have been made.

f. Default attributes for OGM samples: "Control Gender" sample attribute for OGM BAM MultiScale samples), "Assessment of stable regions of the genome" (this field is not editable), QC metrics (not editable).

g. For samples processed with OGM BAM as either Self-Reference or MSR, users can view the OGM label positions in the OGM molecules track.

## New Circos plot for visualization of genomic variants

A new tab **Circos Plot** is now available for the review of all variants and is key for analysis of OGM data.

1. **Circos Plot** is the first tab in the top panel (users may change this by saving preferred views)
2. **Circos Plot** displays sequence variants, CNVs, allelic events, and Structural Variants
3. Clicking on a chromosome in the Circos plot changes the view to the chromosome in the **Tracks** tab.
4. When hovering over a translocation line, a tool tip displaying the corresponding ISCN is shown.
5. Clicking on a translocation event on the Circos plot changes the view to the chromosome closest to where the user clicked and zooms to the translocation break end in the **Tracks** tab.
6. Sequence variants are shown as lollipop icons on the outside of the Circos plot.
7. The display size of CNV and sequence variants displayed in the Circos plot can be changed using the Ideogram event size selections in the track preferences.
8. The Circos plot can be exported as a JPEG/PNG file and can also be copied to the clipboard.
9. Selecting an SV event in the Circos plot displays the event in the **Tracks** view, highlights it in the table and scrolls the table to the event.

## Autoclassification of Structural Variants (SV)

Pre-classification of structural variants can be implemented via the **Decision Tree**

1. Structural variants are defined using the function SV_EVENT_KIND IS. The allowed values for this function are Insertion, Deletion, Inverted duplication, Tandem_duplication, Inversion, Inversion_breakpoint, Interchr_translocation and Intrachr_function
2. The **Decision Tree** text editor autocompletes the new SV keywords and SV functions.
3. Autocomplete in the **Decision Tree** editor is case insensitive.
4. The **EVENT_OVERLAP** function was extended to support structural variants. The function accepts a **Region** list and returns a value between 0 and 1 to determine SV overlap.
5. A new function named **FUSION_MATCH** was created to enable auto-classification of SV intra and inter-chromosomal fusions. This function requires a region list with paired entries. The two breakends of the SV fusion event are compared to the two entries in the region list and return as true ifs there is a match.
6. Implemented an optional argument to the EVENT_OVERLAP and FUSION_MATCH functions for padding or buffer around the SV event.. The padding region can be specified in the following ways:
   i. Base pair size with integers(e.g., 45000)
   ii. Base pair size with units Gb (gigabase), Kb (kilobase), or Mb (megabase) (e.g., 45 Kb)
   The specified base pair padding is applied to both ends of the SV event.

**New SNP-FASST3 Algorithm for Enhanced CNV & AOH Segmentation**

1. New FASST3 and SNP-FASST3 segmentation algorithms were implemented for all data types, including OGM data. The new algorithm provides additional processing parameters for detecting mosaic events. The SNP-FASST3 algorithm takes both BAF and Log R data together when possible, to make CN calls. Mosaic thresholds are hard-coded based on the % mosaic threshold provided by the user.
2. Mosaic thresholds are displayed in the **Sample Information** window and in the table export txt file.
3. SNP-FASST3 description and performance is provided in the *VIA Theory of Operations* document.
4. In **Processing settings**, the section previously called Mosaic Calling is now called **Mosaic Labeling** to prevent any confusion from the new mosaic calling features of FASST3 and SNP-FASST3 algorithms.
5. Users can specify different thresholds for CNVs and SNPs in the processing settings: "CN significance threshold" and "SNP significance threshold."
6. A GxA Cyto Array-specific gamma parameter was added to use in the aberrant cell fraction calculator and for GxA Cyto Array samples during SNP-FASST3 processing.
7. Remove Mosaic Events was added to the **Event Types** filter to allow removal of mosaic events.
8. Mosaic thresholds are implemented for sex chromosomes.
9. Addition of mosaic CN and SNP calling stringency value parameters to FASST3 calling algorithms in Processing settings.
    a. Mosaic CN significance offset (FASST3 and SNP-FASST3)
    b. Mosaic SNP significance offset (SNP-FASST3 only)

**Variant Interpretation panel and support for rich text reporting of Variant Interpretation**

The new **Variant Interpretation** panel in the **Variant Details** tab and the pop-out editor are rich text editors. Variant interpretation text can be edited using rich text formatting which can also be exported to the report.

1. Event interpretations are now saved in the database and can be edited with audit tracking like the **Notes** field. A new tab, **Interpretation**, is present in the **Variant Details** tab next to the **Notes** tab and a new column, **Variant Interpretation,** can be displayed in the **Results** table.
2. The **Variant Interpretation** field can be populated from the interpretation saved with an existing KB record. The KB record has a button **Add Interpretation** which adds the interpretation from the KB entry to this field in the **Event table/Variant Details** tab.
3. A pop-out **Variant Interpretation** window now appears when a user selects the **Interpretation** column.
4. Users can include variant interpretations to be exported to the report.
5. The variant interpretation editor saves and displays rich text with styling and formatting. The following rich text styles are supported for export to the report: bold, italics, underline, text color, background color.
6. Variant interpretation is rendered as plain text in the table.
7. Variant interpretation text is saved when clicking the **Done** button in the pop-out window.
8. Variant interpretation using rich text can be exported with styling and formatting (including text color and background color, paragraph formatting like bullet and number lists).
9. Variant interpretations contain timestamp for export.
10. Users can copy notes and interpretation from the **Variant Details** tab.

**Guideline Panel and Reporting of Guideline Specific Results and Whole Genome Results**

Admin may upload a list of variants that users can mark as "detected" or "not detected." This list can be used to generate reports that include results for a set of specific genetic regions/variants, for instance disease-relevant practice Guidelines.

1. When admin logs in and navigated to Admin> Sample Type, there is a new tab, **Guidelines**, where admins can load a Guidelines file. The **Guidelines** text file to load must contain a single column with "Guideline-based variants" as the header and each row with the name of a guideline-based variant.
2. The **Guideline** file is associated with the specific Sample Type. A sample type may only have one Guideline file associated with it.
3. A new tab is displayed below the **Panels** tab on the sample review table with the label "Guidelines". A list of guideline-based variants are displayed in the **Guidelines** tab. The guidelines panel is displayed in a sample that has been processed using a sample type that has a guidelines tab.
4. Users are able to select Detected or Not-Detected depending on their classification and review of the data.



**Figure 2**. Guidelines tab

5. VIA persists detected/not detected selections for the guideline-based variants in each sample.
6. Once users interact with the guidelines through a selection in the guidelines panel, admins are prevented from deleting the guideline associated with a sample type and prevented from uploading a new guideline list for the sample type.
7. Multiple Guideline-based variants can be selected at the same time using the inbuilt row selection functionality. Hold **control** key and click on the variant to select multiple variants one at a time or hold **Shift** key and click on the two variants to select all variants in between. Then click on mark selected guideline rows.
8. 
9. The rows in the **Guidelines** panel can be sorted in ascending/descending order.
10. An audit log is generated and persisted for the Detected/Not-detected selections in the **Guideline** tab



11. The audit log indicates user, time, guideline variant name and new state, to review the log click the **View audit log** button to view the audit log of the selections for all guideline variants in a new modal window.
12. The content of the **Guidelines** tab (detected/not-detected and the Guideline variant name) is exported into a table in the report when associated using the «T:Guideline Variants» tag.
13. A warning message is displayed when user attempts to generate a report but detected/not-detected selection of the guidelines is incomplete.
14. The sample info displays the name of the guidelines file associated with the sample.

15. The **Guidelines** tab in the admin displays a count of the total number of samples using the guidelines. This count is reset when a sample that had been using the guidelines is reset.
16. Tags in the report template are validated, for example this tag in the report `<<T:Whole Genome Results>>` indicates that a whole genome result table (table B) is to be exported in the report . The table in the report contains the following columns:
    a. Chromosome: chromosome name
    b. Finding: ISCN value
    c. Tier: Classification
17. The **Whole Genome Results** table will have merged chromosome cells when there is more than one region to report on for a single chromosome.

## Report Generation with Word Templates

1. Users can create templates in Word specifying valid tags (sample level and event level) in the templates that will be populated with event data from table results.
2. Sample level tags are based on the Sample Attributes for a specific Sample Type, Custom Sample Attributes are also allowed in the templates. Sample level tags are denoted by S: (Example → «S:SampleId»)
3. Event Level tags are based on event table column headers and denoted by E: (Example → «E:Chromosome Region»)
4. Templates can be uploaded to the sample type by an Admin user.
5. VIA validates the Sample level and Event level tags when the template is loaded.



**Figure 3**. Guidelines tab

6. VIA has the ability to generate a report using a Word template associated with the Sample Type. A new button next to the existing pdf report button displays the various Word templates associated with the sample type.
7. A default report name can be specified via a sample attribute "Word Template Report File Name." This name is automatically used as the filename when saving a report.

## Deriving and analyzing CNV data from Illumina Methylation Arrays

1. New data types ""Illumina Methylation FinalReport" and "Illumina Methylation IDAT" are available, samples can be loaded individually through the VIA client.
2. Enabled support for CNV calling from Illumina Methylation arrays using IDAT data types.

a. **Methylation References** tab allows addition of a methylation reference generated by the Methylation Reference Builder. Details about the reference include the total probe count.

## Parent of Origin Calculation Enhancements

1. Parent of Origin calculations are now made during sample loading rather than only when the **Parent of Origin** column is enabled in the table.
2. The **Parent of Origin** field is now populated in the **Variant Details** tab even if the **Parent of Origin** column Is not enabled in the table.
3. Warnings about parental/BAF verification are now shown in more instances. E.g., when the **Parent-of-Origin** column is added to the table or when switching a sample View from one where the column is not visible to one where the column is visible.
4. ISCN information is now updated whenever Parent-of-Origin calculation is performed so that inheritance info. is consistently displayed in the table column as well as **Variant Details** header.
5. When the "minimum similarity" preference value changes, the Parent-of-Origin is re-calculated.
6. Parent of origin calculations now compute and report parental likelihood ratio.
7. BAF Probes for Parent of Origin are colored based on Difference in Probe Probabilities.

## Admin Tab Updates

1. Admin users can now view an audit record for deleted samples, by navigating to the **Processing Usage** column, which will list a row with the sample that was deleted and associated information (user name, time, etc.).
2. Added a new privilege setting so that admins can add "Ability to edit and delete Variant Interpretations" to user accounts. Only users with this privilege are able to add and remove variant interpretations.
3. The **Admin** tab displays a new tab, **Methylation References**. The tab displays all Methylation References already loaded with name, created by, and date created. Generating a Word Report is the first option in **A**dmin panel.
4. Added a new tab for admins to upload guideline-based variants for a sample type to support reporting of Guideline Specific results.
5. "Sample Interpretation" and "References", are now default Sample Info attributes for all new Sample Types.
6. Improved the display of the header in the **Sample Attributes** page so that both headers are fully displayed.

## HRD feature improvements

1. The genomic scars ideogram can now be exported and copied to the clipboard.
2. Percent genomic LOH (%gLOH) is now calculated when genomic scar analysis is selected.
    a. The %gLOH calculation includes OH only events + CN loss events with and without supporting AOH event.
    b. %gLOH has been added to the sample info window and table export txt file

## Track Updates and Improvements

1. The track updates **Available Resource Downloads** window now has a **Track Updates Release Notes** link which opens the pdf listing track update changes.

2. **Track Updates** now only show available tracks for the genome builds that are installed in the system.
3. Users can now adjust the size of tracks when the **R**esize cursor is away from the plot and more towards the left of the panel.
4. In the **Track** view standardized color display of Indels (blue/red) so that these variants are represented using the same colors regardless of zoom level.
5. Event terminology options in probe track when creating new CN events has been updated with new Event names.
6. Use genebases_default.txt and genebases.txt to support default and custom links for the genes track.

## ISCN nomenclature

1. Addition of a new default attribute "ISCN" for all Sample Types. This will be added to existing Sample Types upon upgrading to version 7.0. This field can be filled using the new **Save** button in the **ISCN Nomenclature** window launched *via* the **ISCN** button in the table.
2. ISCN is displayed in the sample info window using larger size text for ease of viewing.
3. ISCN for PAR1 and PAR2 regions for male samples now contains both the X and Y chromosome coordinates.
4. The ISCN nomenclature includes genomic coordinates.
5. The **ISCN** column nomenclature no longer specifies "dn" for CNVs that are "Presumed *De Novo".*
6. Users can fill the value for the ISCN field using the **ISCN** button in the event table during sample review.

## Sequence Variants

1. Updated the decision tree nomenclature, so that SV applies to structural variants and sequence variants are now SEQVAR.
2. For sequence variants with gnomAD frequency data, the population frequency table shows two additional rows at the bottom displaying the number of samples tested for each variant in males and females.
3. For sequence variant events, the variant details notes panel is now placed below the variant details panel to accommodate a larger display of notes, interpretation, and audit log tab.
4. In the SeqVar filtering pipeline in the processing settings, there is now an option to retain variants labeled with Drug Response in ClinVar.
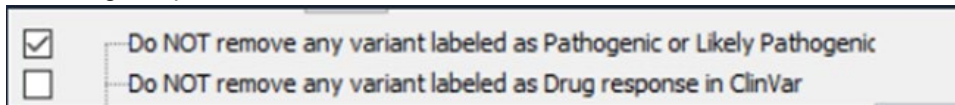


5. Added Mastermind logo to link out in the **Variant Details** tab for Sequence Variants.
6. The "Similar Previous Cases" filter stage in the Sequence Variants filter pipeline has been re-located further up under the Panel Selection filter stage.

## Results Table Updates

1. Checkboxes are now grayed out in the Table unless **Edit** mode is on.
2. Events that are marked via the checkbox column will always be displayed in the table regardless of any applied quick filters that would exclude the event. Now a message is displayed at the bottom of the table panel indicating "selected events are always displayed" when a quick filter is applied, and an event is displayed because it is checked off in the **Select** column.
3. New column called **Relevant Genes** has been added to the **Event** table. This can be populated with "Relevant Genes" from a KB record that contains Relevant Genes. Within the Relevant Genes section in

the KB record, clicking on the button **Add to Event Table** will add the relevant genes to this column in the **Event** table.

4. Improved performance when sorting SAP related columns in the sample review table.

5. Values entered by a user in the string filters at the top of the **Filter** panel can be saved as preferences. Next time the sample is opened using the same preferences, the saved string filter values are applied to the filter.
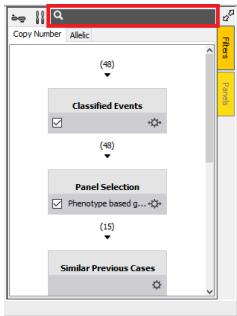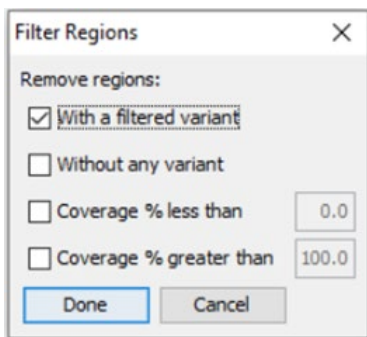


**Global Similarity Function**

1. For Oncology samples (Test Type = Oncology), the **Global Similarity** function can now be limited to comparing only specified profiles rather than all oncology profiles in the database.
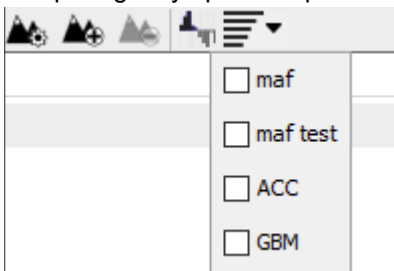


2. The Global Similarity function now displays a **Progress** bar. Change in the guides displayed via the **Help->User Guides** menu item with fewer guides displayed as the various guides have been consolidated.

3. Ability to filter gene panels based on event overlapping a gene/region in the selected panel. A filter icon on the bottom left of the **Panels** tab opens the **Filter Regions** pop up to display filtering options:



Multiple selections use the **AND** function for filtering so that the region must meet all selected criteria to be filtered out. The **Coverage** filter options are only present if the panel has coverage data.

4. Global Similarity preferences can now be saved with different Views through the **Save View Preferences** window.

## Command line Utilities Updates

1. A new java batch upload utility has been created; it uses the following parameters:
   **-server**, **-port**, **-user**, **-password**, **-descriptorFile**, **-overrideExisting**
2. Additional arguments are supported for command line processing:
   -server
   -port
   -log

## Home Page Updates and improvements

1. Users can now sort samples by "upload date" in the **Home** page. Samples are sorted regardless of the processing status.
2. Users can now specify font size from the new **Preferences** menu in the **Home** page (font size preferences can be independently set for the **Home** page and the tracks in sample review). Specified a default font size: 12 for **Home** page and 10 for tracks.
3. When the **Reference** attribute is displayed in the home page PMIDs are displayed as blue hyperlinks.
4. **Home** page querying is now case insensitive.
5. Changing a password now requires the user to enter existing password.
6. When a Sample Type is selected on **Home** page, list Processing types, Sample Attributes, and Workflow only for the selected sample type.

## Improvements to Sample Review Tabs

1. The chromosome ideogram on the left is now the full height of the **VIA Client** window, the chromosome number and the left/right navigation arrows are displayed on top of the ideogram.
2. Improved the zoom tool on the vertical ideogram, by changing the color and increasing the thickness.
3. Icons, images, and text updated in line with VIA rebranding including updates to the client's folder name for local cache, settings, and installers.
4. DGV pop-up window background is now yellow.
5. The **Previous Similar Cases Query** window did not display all available Sample Types. The space allocated to this has been increased and when the list is long, a scroll bar is used for navigation.
6. The region and gene link outs are presented in the same order as listed in the related files.
7. Persist quick filter setting with view preferences.

## VIA Error Messages and Warnings

1. Improved error message alerting about connection reset with display of "Client I/O error: Connection reset" rather than a more generic "Unexpected exception was thrown" error.
2. Improved error reporting during processing via Nirvana where an error is displayed immediately after it occurs during processing.
3. Improved error message is displayed in case of a failure to connect to the server on 8443 (secure port).
4. Introduced a warning message to display when users reset samples to inform users that the resetting action will delete all events as well as notes for the events. An option will now appear to confirm whether or not to proceed with resetting the sample.
5. Introduced a message to be displayed when user enters an invalid port number in login window.
6. A warning of incompatibility is generated when a user tries a 7.0 processing against a 6.2 server.

7. A message is displayed to inform users of the minimum version needed for the client to log onto a sever instance.
8. Improved the message displayed in case of failure to connect to the server on the secure port.

**Additional New Features and improvements:**

1. Changes to event terminology in sample review event table, table export, editing an event in a track, **Event Types** filter window, and the KB.

**Table 1**. Terminology changes

| Previous term | New term |
|---|---|
| CN Gain | Gain |
| High Copy Gain | Amplification |
| CN Loss | Loss |
| Homozygous Copy Loss | Homozygous Loss |
| Hemizygous Copy Loss | Hemizygous Loss |

**NOTE**: Terminology remains the same in the decision tree syntax (uses previous term).

2. Introduced compatibility with the T2T CHM13v2.0 human reference genome
3. The term "DGV Similarity" is now referred to as the "DGV Score" and the "DGV Similarity Comment" is now called "DGV Score Comment" in the table, preferences, **Report** tab, **Variant Details** tab, and table export.
4. Allow CRAM files to be processed for CNV from NGS.
5. Support for CRAM files in visualization of reads for CNV processing from NGS data.
6. Support for both compressed (e.g., hg19.fa.gz hg19.fa.gz.fai hg19.fa.gz.gzi) and uncompressed (e.g., hg19.fa hg19.fa.fai) CRAM reference genome files.
7. Updated the CRAM reference file cache path.
8. When a deleted event is restored, associated Notes, Variant interpretations, and the audit log are now also restored with the event.
9. Specification of URLs for gene-based link outs is segmented into those provided by Bionano and those that are user-specified.
10. Specification of URLs for gene-based link out is separated between test types Constitutional and Oncology. The files for user-specified gene URLs are located in the server as genebases.txt for Constitutional test type and genebasese_onc.txt for Oncology test type.
11. When adding or modifying an event that is either at the beginning or end of a chromosome, the **Snap to Probes** option now adjusts the boundary to the first or last probe in the chromosome rather than to the edge of the chromosome.
12. For CNV from BAM processing, BAF calculation is now performed using allele specific nucleotides for A and B alleles to ensure proper trio analysis based on BAF probes. The default SNP file in processing settings now uses an allele-specific file (SNP file for BAF parameter).
13. After an error occurs involving a VCF file, the VCF file is now released by the Processing component without having to shut down and restart the processing server.
14. Updated the copyright year to 2023.
15. Updated the order of report types in the sample type's reports tab so that the word report tab appears before the pdf report tab in the tab list.
16. The Similar Previous Cases query-to-event matching algorithm has been improved for sequence variants
17. VIA is set up to prevent using v7.0 client with v6.2 or below NxClinical server so that the most up-to-date server is used with an updated client.
18. Users can now easily add the Pubmed IDs stored in the KB for different variants into the Sample's Reference file.

# Bug Fixes in VIA Version 7.0

**NOTE**: Lists bugs that were present in previous version(s) and older builds of version 6.2 and are fixed in the current release of version 7.0.

1. Some BAF segment values were being reported as NaN if that segment was composed of even a single probe that had NaN as a value. Now NaN probes are ignored and the BAF segment value is comprised of the average value of the nonNaN probes.
2. Fixed issue where calls were being made on the Y chromosome for a female sample when using SNP Rank Segmentation algorithm.
3. The ability to revert the "Test Type" value to blank after it has already been processed using a specific test type has been removed.
4. Fixed an issue where attempting to delete a CN event that was overlapping an AOH event or attempting to delete both by selecting these events in the table would give an exception; now the events can be deleted without an exception.
5. The **Probes** track now displays a dashed line at the 0 baseline in logR scale like it is in CN scale.
6. Ability to submit a SeqVar event to the KB is now available by right clicking on the event in the SeqVar track.
7. Fixed an issue where deleted events did not persist when the sample was re-opened; now they remain deleted upon sample re-opening.
8. Fixed an issue where an error was thrown when attempting to export **Detailed Events** table from the **Home** page for more than 100 samples; now more than 100 samples can be exported.
9. Fixed an issue where opening a sample after creating a Sample Type in a build not previously used threw an exception upon clicking on an event.
10. Resolved a typo in the sample information window in the HRD scar section so that it now reads: "Telomeric Allelic Imbalance regions" instead of "Total Allelic Imbalance regions".
11. Resolved an issue where the icons on the karyotype change size, but the icons on the single chromosome ideogram on the left do not update until you click on a chromosome or scroll to another chromosome.
12. Resolved an issue where the changes in the rich text editor were not being saved when adding/editing a variant interpretation inline in the **Variant Details** tab if a new event in the table was selected.
13. Fixed a bug in the **Gene** column with multiple regions but no overlap can output a single semicolon, so that now:
    a. an event with no overlap with region should have empty value.
    b. If the right breakend has no overlaps, then the semicolon is to the right
    c. If the left breakend has no overlaps, then the semicolon is to the left.
14. Resolved a bug that caused an exception when clicking on the expand button when an interpretation was currently being edited in the variant details panel.
15. Resolved an issue which caused the **Progress Monitor** window to remain open when an exception occurs in the template report generation.
16. Fixed a bug that caused an exception when first clicking on an empty **Variant Detail** tab and then clicking away from it.
17. Resolved an issue that caused an exception and loss of a note when applying a filter that removed the note that was currently being edited.
18. Resolved an issue which caused Sample info event type counts to not update on samples that had processed on a prior version of VIA.

19. Fixed the display of the **Admin> Sample Attributes** tab so that now both column headers are displayed fully.
20. Updated the email address in the licRequest to [customer-services@Bionano.com](mailto:customer-services@Bionano.com).
21. Improved the error message displayed when login failed.
22. Resolved a bug that required clearing the cache to continue NxClinical/VIA work.
23. Fixed a bug that resulted in copy gain calls in observed in some normal male samples in the PAR region on chr. X.
24. Resolved a bug that stopped users from overwriting SV samples that were already processed.
25. Fixed bug that caused an error when reviewing CNVs in the chrX PAR region in samples with male gender.
26. Fixed bug that increased CPU usage and slowed down the client when using the string search filter.
27. Updated the UI to restrict the allowable array options for GxA-Cyto arrays so that GxA-Cyto is the only data type available in the drop down.
28. Fixed a bug that displayed the name of a Java object instead of the BAM file path currently in the database when using the Choose BAM File dialogue.
29. Fixed a bug that resulted in the loss of connection preferences after client update.
30. Resolved a bug that resulted in blank reports being generated when user failed to select events to report.
31. Fixed a bug where an empty Word doc report was generated if no events were selected when exporting a report. Now, an error message indicates that an event needs to be selected and a report is not generated.
32. Fixed bug where clicking on db in the link-outs list via right-click on an event in the CN Events track was not actually linking out to the site.
33. Fixed a bug that resulted in the program exiting abruptly when logging in without an internet connection.
34. Fixed bug where an exception was thrown when opening an SV Sample with Test Type = constitutional.
35. Resolved an issue which caused the Sample Info to be temporarily out of sync after edits.
36. Fixed bug which caused an error when a selected event in the **Sample Review** table is unselected when the filter is active.
37. Selecting the **Report** tab in sample review when SAP score related columns are visible does not generate an error. The rows in the **Report** tab display SV events without SAP score information.
38. There are no errors anymore when clicking on seqvar columns for a sample that has both seqvar and SV events.
39. Fixed bug that prevented loading Illumina final report and custom data types.
40. Fixed a bug that caused the filter details panel from clearing when Admin user selected a different event type tab in the **Admin>Sample type> Sample Review Preferences >** Filter.

## Known issues Version 7.0

1. For translocation structural variants the arrows displayed in the **Fusion Junction** columns may indicate incorrect direction. Similarly, the placement of the blue hyperlinked cytoband location of the fusion region on the SV track used to indicate orientation may be incorrect. Users should confirm the orientation of the fusion in Access.
2. Attempting to logout from the client multiple times if the server was shut down generates errors.
3. Attempting to resubmit a failed sample due to incompatible build succeeds when it should fail again due to incompatibility with the build.

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# Technical Assistance

For technical assistance, contact Bionano Genomics Technical Support.

You can retrieve documentation on Bionano products, SDS's, certificates of analysis, frequently asked questions, and other related documents from the Support website or by request through e-mail and telephone.

| TYPE | CONTACT |
|---|---|
| Email | support@bionano.com, software-support@bionano.com |
| Phone | Hours of Operation:<br>Monday through Friday, 9:00 a.m. to 5:00 p.m., PST<br>US: +1 (858) 888-7663 |
| Website | www.bionano.com/support |
| Address | Bionano Genomics, Inc.<br>9540 Towne Centre Drive, Suite 100<br>San Diego, CA 92121 |

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