RELEASE NOTES

iontorrent

Genexus™ Software 6.6

Release Notes

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Contents

Contents	1
Revision History	
Release Notes Overview	
Oncomine™ Myeloid Assay GX v2 ADF 4.3.2	3
Issues fixed in Oncomine™ Myeloid Assay GX v2 ADF 4.3.2	3
Install Genexus™ Software 6.6.2.1	3
Issues fixed in Genexus™ Software 6.6.2.1 patch	4
Updates for Genexus™ Software 6.6.0.3	
Genexus™ Software 6.6.0.3 and PQ verification	5
Install Genexus™ Software 6.6.0.3	
Version information	
Log4j versions	
log4j and logback packages included in Genexus™ Software 6.6	5
log4j and logback packages included in Genexus™ Software 6.6.0.3	
Updates for Genexus™ Software 6.6.0.1	6
Install Genexus™ Software 6.6.0.1	6
GX 6.6 Key Enhancements	
Support integration of the Ion Torrent™ Genexus™ Purification Instrument	7
Performance improvements	7
Dashboard	
Enhancements to custom variant reports	7
Positive control	
Multiple electronic signatures for variant reports	
Enhancements to Results screens	
Enhancements to data backup	7
Enable LIMS sample attribute and vocabulary mapping	8
Variant classifications are shown in VCF files	8
New TNA custom assay creation	8
Improvements to sample management	8
Encryption of sample information	
Updates to edit a sample after a run is complete	8
Improvements to sign in	
Enable custom RNA Exon Tile assay baselines and sequencing variants baselines	8
Enable import from AmpliSeq.com	
Enable reanalysis	
GRCh38 Support	
User experience improvements	
New BAM to Result workflow	
Extraction and control kit barcodes	9
Enable support of Genexus to Genexus sample and BAM file transfer	
Update Genexus™ Software to 6.6	
Format a USB drive for a software update	10
Download and install software with a USB drive (administrator)	10
Issues fixed in Genexus™ Software 6.6	11
Known issues in Genexus™ Software 6.6 and 6.6.2.1	
View the correct orientation of transcripts that are transcribed from the reverse strand	
Enable IGV	
System Requirements	22



Package and version information	22
Software packages versions in 6.6	22

Revision History

Revision	Date	Description
F.0	4 April 2023	Updated for the release of Oncomine Myeloid Assay GX v2 ADF 4.3.2. The following issues are fixed in the 4.3.2 ADF. • 23586. For the Oncomine™ Myeloid v2 - GX5 - DNA and Fusions - w4.2.2 assay, Purification QC was not included by default. • 23818. Gene symbol correction for C11orf88.
E.0	3 June 2022	Updated for Genexus™ Software release notes for Genexus™ Software 6.6.2.1 The following issues are fixed in Genexus™ Software 6.6.2.1 28040. Security vulnerability. 24649. Unresponsive system after data backup. 26086. Raw data storage and deletion. 25465. Display of average base coverage depth results. 26088. Operator role permissions. 1399. Salt bridges. 1425. Alert shown when not necessary. 1435. Missing PCR lid failure alert. 1421. Motor configuration issue on the sequencer. The following known issues were added. 30178. Plugins that are run after a run is complete cannot be run while backup is in process. 29229. Symantec™ antivirus software. 28945. Import single runs from another Genexus™ Integrated Sequencer. 29228. Edit default report template. 29089. Manager role. 28490. Import custom baselines. 25307. Manual signature title. 20701. Downloads of sequencing results from the Oncomine™ TCR Beta-LR Assay GX assay. 25474. Potential pool imbalance when selecting UDG option for AmpliSeq DNA and AmpliSeq DNA&RNA Assays. 29239. Manual and automated backups. 29239. Manual and automated backups. 29905, 30233, and 30234 Generate and download variant reports.
D.0	11 February 2022	Updated with issue 23068. If you create a custom panel for the Oncomine™ BRCA Assay GX, exon numbering remains set by the system-installed panel for the assay.
C.0	27 January 2022	 Updated for Genexus™ Software 6.6.0.1 and 6.6.0.3. Updated with the following issues. 23545. NTC QC results for Sample to Result runs are only visible for samples that are included in the purification batch with the NTC. 23057. When you view the exon tile fusion imbalance charts for a sample, then select a different sample, the charts are not updated for the new sample that is selected. 21541. When you view the exon tile fusion imbalance charts for a sample, then select a different sample, the charts are not updated for the new sample that is selected. 17803. Run reports for runs that are started on or completed on 26–31 December display the incorrect year. 23586. For the Oncomine™ Myeloid v2 - GX5 - DNA and Fusions - v4.2.2 assay, Purification QC is not included by default. 17738. An "Instrument Must be Serviced" alert appears even if the instrument does not need to be serviced.
B.0	3 December 2021	Updated with the following issues. • 22895. More than one gene annotation can be listed as Not Assayed even if one of the annotated genes is present in the panel.

		 22883. In some cases, the coverage graph is not shown for the selected gene. 23074. The Oncomine Extended (5.14) filter chain launched in Genexus™ Software 6.2.1 was updated in Genexus™ Software 6.6. 23399. The option to create a custom filter chain to filter variant results by allele frequency does not appear to be available. 23081. An error message is shown for some DNA + RNA assays when you prepare a library batch with more than 24 samples.
A.0	26 October 2021	New release notes for Ion Torrent Genexus™ Software 6.6.

Release Notes Overview

This document outlines features in Oncomine™ Myeloid GX v2 ADF- w4.3.2, major features in Ion Torrent™ Genexus™ Software 6.6, issues fixed in Genexus™ Software 6.6.2.1 and Genexus™ Software 6.6.0.3, and known issues to be fixed in subsequent releases.

Oncomine™ Myeloid Assay GX v2 ADF 4.3.2

The Oncomine™ Myeloid Assay GX v2 provides comprehensive genomic profiling of myeloid malignancies with analyses of SNPs and Indels in 45 genes, and an RNA fusion panel that is capable of detecting over 800 unique fusions. The updated Assay Definition File version 4.3.2 includes the following improvements:

- Assay performance improvements—workflow parameters for library preparation are optimized to enhance amplicon uniformity and increase assay robustness and reproducibility.
- Variant calling
 - o Ion Torrent™ Variant Caller (TVC) v5.16 module was updated to v5.20. The version number is visible in the header of the VCF file.
 - Improved sequence variant baseline and optimized parameters to detect key variants in ASXL1, RUNX1, and NPM1.
- Fusions—updated fusion reference files that enable identification of additional fusion isoforms.
- Genexus™ Purification Instrument—buffy coat sample type was added for use when running in integrated mode.

Issues fixed in Oncomine™ Myeloid Assay GX v2 ADF 4.3.2

Issue number	Issue Summary	Impact
23586	For the Oncomine™ Myeloid v2 - GX5 - DNA and Fusions - w4.2.2 assay, Purification QC was not included by default.	This issue is fixed in Oncomine™ Myeloid GX v2 ADF- w4.3.2.
23818	Gene symbol correction for C11orf88.	This issue is fixed in Oncomine™ Myeloid GX v2 ADF- w4.3.2.

Version information

Release Date	15 June 2022
Release Version	6.6.2.1

Install Genexus™ Software 6.6.2.1

- 1. In the Settings / Software Updates screen, click Software Updates in the upper right corner.
- 2. In the row for the **Torrent Suite** package with the **Available Version** as **6.6.2.1**, in the **Actions** column, click **Download**.
 - After the download is complete, the **Download** link changes to an **Install** link.
- 3. Click **Install**, then click **Yes** to confirm the installation.

Issues fixed in Genexus™ Software 6.6.2.1 patch

Issue	Issue Summary	Impact
number	· ·	·
28040	A critical security vulnerability was detected in the following third-party libraries. • Spring framework versions 5.3.17 and earlier • Spring Boot versions 2.5.11 and earlier • Apache HTTP server version 2.4.52 and earlier Genexus™ system software uses these third-party libraries and used versions that were impacted with these vulnerabilities.	The security vulnerability is fixed as part of the 6.6.2.1 patch release by upgrading Spring Framework version to 5.3.18, Spring Boot version to 2.5.12 and Apache HTTP server version to 2.4.53 which are included in the software. This issue is fixed in Genexus™ Software 6.6.2.1.
24649	Based on the backup settings, the sequencer backs up runs and saves data from the runs in the backup directory which was at times consuming excess memory and processing causing the system to become unresponsive.	This issue is fixed in Genexus™ Software 6.6.2.1.
26086	Disk space was used to store sequencing raw data that should have been deleted in the Genexus™ Sequencer for runs with a status of Analysis Complete.	This issue is fixed in Genexus™ Software 6.6.2.1.
25465	QC values were shown incorrectly as N/A in the QC tab even though the analysis generated values for the QC.	This issue is fixed in Genexus™ Software 6.6.2.1.
26088	In Genexus™ Software 6.6, users who were assigned the role of Operator were not able to view plugin results or the pileup view in Sample Results.	This issue is fixed in Genexus™ Software 6.6.2.1.
1399	On some instruments, after a run completes, leftover fluid may leak out from the chip clamp and dry, forming a "salt bridge" that leads to electrical noise during signal detection for follow on runs.	This issue is fixed in the Genexus™ Software 6.6.2.1. To prevent potential leaks from occurring after any run, the chip remains clamped in the sequencing position until a new initialization or run is started. You will be prompted to remove the chip before you load the instrument deck for a new run.
1425	The annual maintenance alert "The instrument needs to be serviced" was shown on the instrument every 4 weeks.	This issue is fixed in the Genexus™ Software 6.6.2.1.
1435	The instrument software did not show an error when the PCR lid failed to close and the instrument continued the run. This issue occurred after the instrument was serviced and a connection was loose. A loose connection can cause poor thermal uniformity during library amplification which biases amplicon coverage of the sample.	This issue is fixed in Genexus™ Software 6.6.2.1. If the PCR lid fails to clamp an error message is shown that the PCR lid is not behaving as expected. If you see this error message, please contact your Field Service representative to schedule a repair.
1421	On rare occasions the coupler shuttle on the instrument failed to clamp at the pipette loading position. The error shown on the instrument was "Coupler Shuttle failed to Engage-hi". This error occurred because motor default configurations were being overwritten when the coupler shuttle was moved by the instrument.	This issue is fixed in Genexus™ Software 6.6.2.1.

Updates for Genexus™ Software 6.6.0.3

Genexus[™] Software 6.6.0.3 is a security patch for the vulnerability in the Apache log4j library. Apache reports that the security vulnerability can allow an attacker to execute code and remotely take over a system through the log message parameters. Genexus[™] Software 6.6.0.3 is an upgrade to the log4j and logback versions to remove the security vulnerability. Genexus[™] Software 6.6.0.3 does not include any changes to the analysis pipeline or system software.

Genexus™ Software 6.6.0.3 and PQ verification

Due to design of the software, if a performance qualification (PQ) run has been completed on a Genexus™ Integrated Sequencer running 6.6.0, after an update to 6.6.0.3 the PQ status changes to **Not verified**. Although the software version and the PQ status have changed , there is no impact on instrument performance. To revert the PQ status to **Verified** and document a planned deviation, contact a Field Service Engineer.

Install Genexus™ Software 6.6.0.3

- 1. In the Settings / Software Updates screen, click Software Updates in the upper right corner.
- In the row for the Torrent Suite package with the Available Version as 6.6.0.3, in the Actions column, click Download.
 - After the download is complete, the **Download** link changes to an **Install** link.
- 3. Click **Install**, then click **Yes** to confirm the installation.

Version information

Release Date	28 January 2022
Release Version	6.6.0.3

Log4j versions

The security vulnerability affects log4j versions 2.0 through 2.15.0 and logback used by Genexus™ Software 6.6. The log4j versions used by Genexus™ Software 6.6 are not listed in the EULA's Appendix of third-party copyright notices and licenses. In the interim, please note as follows:

log4j and logback packages included in Genexus™ Software 6.6

Your continued use of Genexus™ Software 6.6 will be deemed to constitute your acceptance of the terms and conditions of all the third-party licenses that are listed below.

Package	Version	License	
log4j	1.2.17	APACHE LICENSE, VERSION 2.0	
log4j	1.2.15	APACHE LICENSE, VERSION 2.0	
log4j	2.13.3	APACHE LICENSE, VERSION 2.0	
Logback-core	1.2.3	Eclipse Public License - v 1.0, GNU Lesser General Public License 2.1	
Logback-classic	1.2.3	Eclipse Public License - v 1.0, GNU Lesser General Public License 2.1	

log4j and logback packages included in Genexus™ Software 6.6.0.3

Your use and installation of Genexus™ Software 6.6.0.3 will be deemed to constitute your acceptance of the terms and conditions of all the third-party licenses that are listed below. The log4j versions used by Genexus™ Software 6.6.0.3 are not listed in the EULA's Appendix of third-party copyright notices and licenses. The log4j version information that is not listed in the EULA is a known issue that will be fixed in an upcoming release of the software.

Package	Version	License	
log4j	1.2.17	APACHE LICENSE, VERSION 2.0	
log4j	1.2.15	APACHE LICENSE, VERSION 2.0	
log4j	2.17.0	APACHE LICENSE, VERSION 2.0	
Logback-core	1.2.9	Eclipse Public License - v 1.0, GNU Lesser General Public License 2.1	
Logback-classic	1.2.9	Eclipse Public License - v 1.0, GNU Lesser General Public License 2.1	

Updates for Genexus™ Software 6.6.0.1

Install Genexus™ Software 6.6.0.1 to have access to the latest version of the software help. The help content embedded in the software is not the latest version and does not completely align with the Genexus™ Software 6.6 User Guide (Pub. No. MAN0024953). Genexus™ Software 6.6.0.1 does not include any changes to the analysis pipeline or system software.

Install Genexus™ Software 6.6.0.1

- 1. In the Settings / Software Updates screen, click Software Updates in the upper right corner.
- 2. In the row for the **Torrent Suite** package, with the **Available Version** of 6.6.0.3, in the **Actions** column, click **Download.**
 - After the download is complete, the **Download** link changes to an **Install** link.
- 3. Click **Install**, then click **Yes** to confirm the installation.

GX 6.6 Key Enhancements

Support integration of the Ion Torrent™ Genexus™ Purification Instrument

The Ion Torrent™ Genexus™ System is the first turnkey next-generation sequencing (NGS) solution that automates the sample-to-report workflow and delivers results in a single day. Genexus™ Software 6.6 can be used to plan the Sample to Result run with the integrated Genexus™ Purification Instrument and Genexus™ Integrated Sequencer. The software tracks samples from purification through sequencing to post-run sample reports.

Performance improvements

Genexus™ Software 6.6 provides a faster import of files.

Dashboard

The dashboard is the home screen for the software. In the software dashboard, you can view details, such as the QC status, for the five most recent runs, the status of the instruments that are integrated with the software, and instrument alarms, if any.

Enhancements to custom variant reports

With custom variant report enhancements, you can now perform the following functions.

- Create custom report templates. In the template, you can customize sample details, variant sections, custom text, images, electronic signatures, and manual signature sections.
- Add descriptions, titles, and footnotes to each section of the template.
- Add custom text and images to the template that you can edit when you generate the report.
- Associate up to 3 default templates for an application category. When default templates are associated
 with an application category, a variant report is generated at the end of the run.
- Select the report language.
- Include images shown in the results screens in reports.

Positive control

You can include a positive control for Sample to Result runs.

Multiple electronic signatures for variant reports

Multiple users can electronically sign variant reports. The electronic signatures appear in the PDF report. In addition, multiple signature levels can be enabled in the software. One signature level can be designated to lock the report to prevent further changes. The first user who signs the report can modify the report template selection and modify the report. Subsequent users can only sign the report and add comments. Reports can be amended until 30 days after a run is complete.

You can also now send notifications to other users in Genexus™ Software. For example, you can notify another user when you have signed a variant report.

Enhancements to Results screens

- The **Key Variants** matrix provides a color-coded visual representation of the variant results. Each tile in the **Key Variants** matrix represents one variant and indicates whether a variant is detected or not.
- **Amplicon coverage graphs** provide a high-level overview of coverage to help you determine whether the sequencing reads across a gene are uniform and sufficient.
- Variant tracks are shown with the pileup view in Genexus™ Software. The pileup is a figure generated in the software that shows each BAM track represented by a single bar, with the sequence variation or variations denoted in each track. The BAM tracks are aligned against a reference track. The variant pileup can be used to identify potential variants.
- The variant results shown in the **Key Findings** are organized into the following categories: Key Variants Detected, Other Variants Detected, None Detected, and Not Assayed.

Enhancements to data backup

You can now automatically back up older run data, results files, and signed reports to local or cloud storage and set a schedule to automatically delete backed up runs after a specified amount of time.

Enable LIMS sample attribute and vocabulary mapping

You can now map the names of sample attributes that are used by external LIMS software to the names of the sample attributes recognized by Genexus[™] Software 6.6. The mapped sample attributes are associated with one or more application categories. LIMS attribute mapping allows you to seamlessly import a file, in XLS, CSV, or TSV format, that you have exported from external LIMS software to add samples in the software.

You can also now map alternate vocabulary values for sample attributes that are not recognized in the software.

Variant classifications are shown in VCF files

Custom classifications, such as benign or likely pathogenic, that you create and assign to variants, are now included in VCF files that you can download.

New TNA custom assay creation

You can now create custom assays for total nucleic acid (TNA) to detect and annotate DNA and fusion variants from cell free nucleic acid.

Improvements to sample management

You can now copy and edit multiple samples at once. You can also add sample tags to one or more samples or sample results. Sample tags can be used to group and track samples in the software. The tags that you create can be nested. You can easily find samples when you search or filter the samples or sample results according to a sample tag. Sample tags are also supported in the LIMS API.

Encryption of sample information

Sample information is now stored in an encrypted format in the software for increased security.

Updates to edit a sample after a run is complete

In Genexus™ Software 6.6, after a run is complete, a manager- or administrator-level user can edit a sample for 30 days. You must reanalyze the sample to generate results and a new variant report for the sample.

Improvements to sign in

You must now select and answer security questions the first time you sign in. The security questions are used to validate identity when the password is reset.

Enable custom RNA Exon Tile assay baselines and sequencing variants baselines

You can now generate panel specific custom RNA Exon Tile assay baselines and sequencing variant baselines. You can also export, import, and obsolete the custom baselines.

Enable import from AmpliSeq.com

Manager- and administrator-level users can now directly import custom or fixed panel files into Genexus™ Software from Ion AmpliSeq™ Designer.

Enable reanalysis

If a sequencing run fails to meet one or more QC parameters defined by the assay, you can adjust the assay parameters and reanalyze a sample or a run. Reanalysis of runs per assay can start from the alignment, basecalling, or signal processing steps. A sample can be reanalyzed starting only from the alignment step. For both runs and samples, the files needed for the stage of reanalysis that you select must be present in the software.

GRCh38 Support

Genexus™ Software 6.6 now includes the GRCh38 reference genome file as a preset to use in assays.

User experience improvements

• You can now search, filter, and sort the information that is shown in the software screens from each column header in the tables. This allows you to search and filter the information with multiple filter

- options enabled sequentially. This applies to the information shown in the samples, assays, run plans, and results screens.
- Actions that are available for an item in a table, such as copy or edit a sample in the **Manage Samples** screen, are now shown when you place the pointer over a row.
- System notifications are now shown with an alert and notifications button in the menu bar.

New BAM to Result workflow

You can now create samples from BAM files, then plan BAM to Result runs to analyze the BAM samples.

Extraction and control kit barcodes

You can track samples with the extraction kit barcode associated with the sample when you plan a Nucleic Acid to Result run. In addition, you can track control kits with the control kit barcode when you plan a Nucleic Acid to Result run. The barcodes are shown in the software screens and in the variant report PDF file.

Enable support of Genexus to Genexus sample and BAM file transfer

You can now upload BAM files to another Genexus[™] Software server and enable analysis in the target server to start immediately after the files are transferred. You can enable the file transfer when you plan a run or you can upload result files after a run is complete.

Update Genexus™ Software to 6.6

Format a USB drive for a software update

Pre-requisites:

- An Ubuntu Linux desktop machine with disk utility software.
- A USB drive with a capacity of 60 GB or more.
- 1. Insert the USB drive into the Ubuntu Linux machine.
- 2. With Ubuntu running, open the disk utility by navigating to **System Administration ➤ Disk Utility.**
- 3. Select the USB Flash Drive (SMI USB DISK) under **Peripheral Devices from Storage** Devices by clicking on it. Highlight the volumes (New Volume FAT >60 GB), click **Unmount Volume**, then click **Delete Partition**. Click **Delete** to confirm.
- 4. Select the free USB volume, then click Create Partition.
- 5. Deselect the **Take ownership of file system** check box.
- 6. Select **ext3** from the **Type** dropdown menu, then select the entire size of the partition. Name the partition *usbinstall*.
 - Note: The partition name must be completely lowercase.
- 7. Click Mount.
- 8. The mount point of the USB drive is /media/usbinstall.

Download and install software with a USB drive (administrator)

Pre-requisites:

- Format a USB drive for the software update. See Format a USB drive for a software update.
- Access or create a Thermo Fisher Connect account.
- 1. Sign in to the Thermo Fisher App Store on Connect at apps.thermofisher.com.
- 2. On the left side of the App Store screen, click the **AppConnect** button.
- 3. On the right side of the screen, under Resource Libraries, click Ion Torrent™ Genexus™.
- 4. Click Software Update.
- 5. In the Ion Torrent™ Genexus™ Software table, in the row for version 6.6, click the **Download** button.
- 6. Copy the downloaded package (.zip) to the /media/usbinstall folder in the USB drive.
- 7. After completion, unmount the USB drive, then insert the drive into one of the USB ports at the back of the Genexus™ Integrated Sequencer.
- 8. In the menu bar of the Genexus™ Software, click (Settings) ▶ Software Updates, then click Software Updates in the upper right corner.
- 9. Select USB.
- 10. Click **Install**. When the confirmation window appears, click **Yes** to confirm that you want to install the update.
- 11. Click **Installed Software** to verify the installation when installation is complete.

Issues fixed in Genexus™ Software 6.6

Issue number	Description		
11298	The session time-out on the Genexus™ Integrated Sequencer touchscreen does not work after you abort a run or after the post-run clean stage. This issue is fixed in Genexus™ Software 6.6.		
11310	Analysis for any assay that uses a non-hg19 reference genome fails. This issue is fixed in Genexus™ Software 6.6.		
12378	Sporadic failure while importing an assay. This issue is fixed in Genexus™ Software 6.6.		
13190	For some assays, when you create a library batch that does not include a no template control (NTC), then edit the library batch to include a NTC, unique barcodes are not assigned. This issue is fixed in Genexus™ Software 6.6.		
13192	The Download files menu fails to open intermittently. This issue is fixed in Genexus™ Software 6.6.		
13199	An incorrect start time is displayed for reanalyzed runs and assays. This issue is fixed in Genexus™ Software 6.6.		
13213	An incorrect message displayed when a new user is prompted to change the password. This issue is fixed in Genexus™ Software 6.6.		
13223	The Forgot password user link in the sign in screen forces you to set a new password twice. This issue is fixed in Genexus™ Software 6.6.		
13233	Users may experience a frozen popup window when adding a new user from Settings ▶ User Management . This issue is fixed in Genexus [™] Software 6.6.		
13234	For a multi-assay run, when the Customer Support Archive (CSA) plugin finishes execution for one of the assays, the status of the CSA plugin for the other assays also erroneously gets updated to a status of Completed . This issue is fixed in Genexus [™] Software 6.6.		
13238	The minimum cellularity threshold for a given assay should prevent only samples with a cellularity lower than the threshold from being added to a run plan. However, samples with passing criteria are also not added to a run plan. This issue is fixed in Genexus™ Software 6.6.		
13362	For an imported assay, the chip type value is NA in the audit record. This issue is fixed in Genexus™ Software 6.6.		
13593	Spearman's correlation coefficient is calculated incorrectly when performing a pairwise sample comparison in the Oncomine™ TCR Beta-LR GX assay. This issue is fixed in Genexus™ Software 6.6.		
15753	When you copy the Oncomine™ Myeloid Assay GX (using the Manage Assays Copy workflow) to modify system-installed assay settings, the PCR denature temperature parameter from the system-installed assay is not passed to the copied assay. This issue is fixed in Genexus™ Software 6.6.		

Known issues in Genexus™ Software 6.6 and 6.6.2.1

lssue number	Issue Summary	Impact and Mitigation ¹
30178	If you click Run Plugin for a sample result while data backup is in progress, the 1.wells files, the basecaller output, and the coverageAnalysis plugin source files for the sample result are deleted. If this issue occurs, the Loading Density image and histograms are not shown in the Assay Metrics and Run Report screens and values are absent for some QC metrics. Note: The affected run report data are available in the Run Report PDF.	This issue occurs if you click Run Plugin to re-run any plugin while data backup is in progress. After this issue occurs, all later runs are affected. Affected results include coverageAnalysis and molecularCoverageAnalysis plugin results and QC metrics. Mitigation: Do not run re-run any plugin after a run is complete while data backup is in progress or if there is another analysis in process. Contact an FBS or FSE if you observe that the Loading Density image and histograms are not shown in the Run Report screen or values are absent for some QC metrics.
29229	Updated definition files in Symantec™ antivirus software block the analysis process in Genexus™ Software .	This recent issue occurs if you have updated the Symantec™ definition files. Antivirus software definition files are updated frequently, sometimes daily. Definition file updates for antivirus software can bring additional settings or updates to the system which can affect Genexus™ Software.
		 Mitigation: Do not use Symantec™ antivirus software with Genexus™ Software. We have tested Genexus™ Software with the following antivirus software products and found them compatible as antivirus solutions: Bitdefender GravityZone™ Business Security with definition files updated on 6 May 2022. Kaspersky™ Endpoint Security for Linux with definition files updated on 5 May 2022. ESET NOD32 with definition files updated on 12 May 2022.
28945	If sequencing run results are imported to another Genexus™ Integrated Sequencer, a signed report that is locked for electronic signatures is shown as a draft report on the system with the imported results. The draft PDF report shows the electronic signature details for the sign-off.	Only runs with signed reports that are imported from one system to another are affected. Mitigation: You can optionally sign off the report after the report is imported or view the existing report with the sign off information.
29228	If there are three report templates marked as Default for an assay or application category, you cannot edit the report template.	This issue occurs only when there are three default report templates for the assay or application category. Mitigation: Remove the Default selection during editing, then set the report template back to default. Click Assays► Manage Presets► Report Templates, then in the row of the report template, click Undo Default or Set as Default.
29089	Users assigned to accounts with the Manager Role are unable to access Audit records for the Services screen and Sample Attribute mapping.	This issue affects only users accounts that are assigned Manager Role permissions. Mitigation: Sign in as an Administrator-user to view all audit records.

Issue number	Issue Summary	Impact and Mitigation ¹
28490	Custom baselines (CNV baselines, sequence variant baselines, exon tile assay baseline) created on one Genexus™ system cannot be imported to another Genexus™ system in ZIP format.	This issue affects the import of custom baselines from one Genexus™ system to another Genexus™ system. Mitigation: Create CNV and sequence variant baselines, then import the baseline files in H5 (CNV) or BED (SVB) format. Import exon tile assay baselines in TXT format.
25307	The manual signature title of a report is not displayed correctly when the default report template is used.	This issue affects only the manual signature titles when a default report template is used. Mitigation: For reports with a manual signature, use a report template that is not set as default to view the correct title for the manual signature in the report.
20701	Downloads of sequencing results from the Oncomine™ TCR Beta-LR Assay GX assay that include unmapped BAM and FASTQ files do not show a dialog box that shows the download has started and is successful.	This issue affects only files available to download for results from the Oncomine™ TCR Beta-LR Assay GX assay. Mitigation: When you download the files, do not exit from the software. Files are available after approximately five minutes.
25474	The Uracil DNA Glycosylase (UDG) Treat DNA setting is used to clean up deaminated Cytosine bases from degraded samples. If you enable the UDG Treat DNA parameter in an assay, you may observe read imbalance in the Barcodes with Reads Reported table. Read imbalance can occur because the on-instrument dilution of input sample nucleic acid is impacted by this setting.	This issue affects assays for DNA or DNA and Fusions if you enable the UDG Treat DNA parameter in the Library Prep & Templating section of the Parameters step in assay creation or when you copy, then edit an assay. The issue can result in over dilution of nucleic acid prior to library prep for AmpliSeq, and over dilution of the second pool in AmpliSeq and AmpliSeq HD two pool assays, leading to pool imbalance in the final reads. Mitigation: If possible, do not enable the UDG Treat DNA parameter for AmpliSeq HD assays with two or more pools and for AmpliSeq assays. Manually dilute the DNA sample if UDG treatment is necessary. Contact an FAS for help.
29239	If manual and automated backups occur at the same time, the intermediate files may be deleted without a successful backup.	When you use the Backup and Restore option, do not use the Start Now backup option if you want to back up intermediate files.
29905	If you enable Generate Report when you plan a run, you cannot download variant reports when you click(More Options) ➤ Download Files and select the Reports checkbox in the Download Files dialog box.	This issue affects only variant reports that are selected for download as part of the Reports list in the Download Files dialog box. Mitigation: Click Lab Reports in the Download Files dialog box to download variant reports.
30233	If you enable Generate Report when you plan a run, the report that is generated is always in English regardless of the language that is associated with the report template.	This issue affects report templates for non-English languages that are selected for generation when you plan a run. Mitigation: To create reports in languages other than English, do not enable the Generate Report option when you plan a run. Instead, use the Reports tab to generate reports after the run is complete.

Issue	Issue Summary	Impact and Mitigation ¹
number 30234	If you enable Generate Report when	This issue affects only the language information that is shown. The report is generated in English.
	you plan a run, the language is not shown in the pane for the report in the Reports tab.	
28908	For some results, the ClinVar track is not shown in the Integrative Genomics	This is an intermittent issue that affects only some results with ClinVar annotations.
	Viewer (IGV) view that is generated with the JNLP files that are downloaded from Genexus™ Software.	Mitigation: Use the pileup view in Genexus™ Software.
21372	The software update from version 6.2 to 6.6 fails when you try to install the software directly from the App Store.	This issue occurs for all software updates to version 6.6 from the App Store. Mitigation: Download and install Genexus™ Software 6.6 with a USB drive. For more information, see Update Genexus™ Software to 6.6.
20875	For samples with a disease category of cancer that were created in Genexus™ Software 6.2, you cannot plan a run or generate a report unless you first edit the application category of the samples.	This issue affects samples created in Genexus™ Software 6.2. Disease category was a sample attribute in version 6.2, but in version 6.6, the correlated attribute is application category. (Cancer is not an available option in version 6.6.)
		Mitigation: For samples with a disease category of cancer created in Genexus™ Software 6.2, edit the application category before you plan a run or generate a report with the samples in Genexus™ Software 6.6. Alternatively, you can copy samples that you created in version 6.2, edit the application category for version 6.6, then plan a run with the new samples.
20720	If you have added all available columns to the list of samples in the Samples / Manage Samples screen and then try to filter the list of samples with the Tags	This rare issue occurs only when you select all available columns in the Columns dropdown list and do not save the column preferences, then use the filter tool in the Tags column.
	column, an error message is shown.	Mitigation: Before you use the Tags column to filter the list of samples, save any new column preferences or ensure that at least one available column is unselected.
21585	When you edit multiple samples at once and change the cellularity or necrosis value for one sample, the new value is	This issue occurs only when you change the cellularity or necrosis value of a sample when you have selected multiple samples to edit together.
	applied to all samples in the Edit Sample screen.	 Mitigation: Only change the cellularity or necrosis of a single sample at a time. 1. In the Manage Samples screen, place the pointer over the row of a sample that you want to edit, click Edit. 2. Change the cellularity or necrosis value of the single sample.
21293	If you create a custom sample attribute with an attribute name that contains a full stop or period (.), the entries for that sample attribute are not shown in the Manage Samples table.	This issue affects only custom sample attributes with a period in the name of the attribute. Mitigation: • View the entry for a custom sample attribute for a single sample. (Click Samples► Manage Samples, then click a sample name.) • When you create a custom sample attribute, do not include a period in the name of the attribute.

Issue	Issue Summary	Impact and Mitigation ¹
number 20696	In any column header, when you click	This issue applies to all searches in the filter dialog
20090	Filter, enter any information in the	boxes in all screens.
	search field, then click Enter , all options that are listed in the filter dialog box are selected.	Mitigation: In the filter dialog boxes, do not click Enter except to select all options.
16405	If you have completed a run with Genexus™ Software 6.2, then upgrade to Genexus™ Software 6.6, the run	This issue affects results generated in version 6.2, then viewed in the version 6.6 software.
	report is not available to download.	Mitigation: Although you cannot download a PDF file of the run report, you can view the information that is shown in the run report when you view the Assay Metrics for each assay in the run.
21487	BAM to Result runs are not compatible with assays that are created or installed in previous versions of the software.	This issue affects all system-installed or custom assays from Genexus™ Software 6.2.1 or earlier.
21985	If you perform a run with a sample, then perform a second run with the same	This issue affects all samples that are included in at least two completed run plans.
	sample, you cannot edit the sample information if needed after the second run.	Mitigation: Ensure that all sample information is correct before you assign a sample to a second run plan. To preserve the option to edit a sample for 30 days after a run is complete, copy a sample that has been included in a completed run, then assign the new, copied sample to a run plan.
20742	If you enable the option to upload immune repertoire BAM files to another	This issue affects only immune repertoire assays when you plan a run.
	Genexus Software server when you plan a run, the option to perform an analysis in the target software automatically after run completion is not available.	Mitigation: After the sample data is transferred to the target server, plan a BAM to Result run with the transferred samples.
23545	NTC QC results for Sample to Result runs are only visible for samples that are included in the purification batch	This issue affects Sample to Result runs for some system-installed or custom assays that include more than one purification batch.
	with the NTC.	Mitigation: In the Run Summary, in the Batch ID column, view the purification batch of samples and the NTC. To view NTC QC results, view the QC tab for a sample that was included in the purification batch with the NTC.
21485	If you try to compare immune repertoire results from BAM samples that have been uploaded from another Genexus™ Software server, no comparison results are shown.	This issue affects only the comparison of immune repertoire results from BAM samples that have been uploaded from another Genexus™ Software server.
12692	Missing variant label and legend chart customization options for charts generated when you compare samples.	This is a chart customization issue that does not affect sequencing results.
22549	In the Key Findings tab, in the Coverage Graph for genes that are	This issue affects all genes transcribed from the reverse strand.
	transcribed from the reverse strand, the order of the exons is shown incorrectly when you place the pointer over the	Mitigation: Ignore the exon numbers that are shown in the transcript track.
	transcript track. Exons are always	For instructions to view the transcript and get the correct exon numbers for coverage metrics, see View
	numbered left to right, ignoring directionality of the gene.	the correct orientation of transcripts that are transcribed from the reverse strand.

Issue	Issue Summary	Impact and Mitigation ¹
22895	In the Key Findings tab, in the Key Variants matrix, variants with more than one gene annotation can be listed as Not Assayed even if one of the annotated genes is present in the panel. Affected variants are shown in the Key Variants matrix only when the Not Assayed checkbox is selected and appear at the end of the matrix in a white tile instead of a blue tile. Example: U2AF1L5 COSM166866 AA Change: p.? Allele Frequency: 0.066	This issue can affect variants with more than one gene annotation; for example, U2AF1L5/U2AF1. Identify if a variant is affected by this issue. 1. For any gene tile that is shown only when the Not Assayed checkbox is selected, click the Variant ID to open the Variants tab. 2. Scroll up to view the variant in the Variants table. 3. In Variants table, in the Gene column, if the variant is listed with ** to indicate that more than one gene is detected, click the Annotations tab. 4. Scroll to the Gene row to view the multiple annotations for the gene. Mitigation: When you view the Key Variants matrix, ensure that you select the Not Assayed checkbox, if available, to review variants that are not assayed.
22883	If you select a gene that is not shown by default in the Coverage Graphs , in some cases, the coverage graph is not shown for the gene that you select.	This issue affects some genes that are not shown by default in the Coverage Graph. Even if the graph is labeled correctly with the selected gene, the coverage information is not updated correctly. Mitigation: Ignore the Coverage Graph that appears when you first select a gene from the Show Coverage for Gene dropdown list. Refresh the browser window to view the correct Coverage Graph for the gene.
23074	The Oncomine Extended (5.14) filter chain launched in Genexus™ Software 6.2.1 was updated in Genexus™ Software 6.6. The improvements, which are part of Oncomine Extended (5.16) filter chain, are also included in the Oncomine Extended (5.14) filter chain in Genexus™ Software 6.6. This update can result in rare differences to Filtered Variants in Genexus™ Software 6.6 when compared to results viewed with the Oncomine Extended (5.14) filter chain in Genexus™ Software 6.2.1.	This rare issue affects results that are viewed when the Oncomine Extended (5.14) filter chain is applied and compared to results in Genexus™ Software 6.2.1. This rare issue could affect the following Filtered Variants. • Likely somatic de novo splice variants that are not hotspot splice variants or ClinVar pathogenic variants are filtered in. (Hotspot splice site variants and ClinVar pathogenic variants are not affected by this issue.)
21778	For some assays, when you view all of the variants in the Variants table, you can add the P-Value column to the table twice.	This issue occurs only for some assays when you view all variants in the Variants table. The data in the duplicated columns are the same. Mitigation: You can ignore or remove the duplicated P-Value column in the Variants table with the Columns dropdown list. Alternatively, you can view the SNVs/Indels or CNVs tables. A single P-Value column is available in the SNVs/Indels and CNVs tables.
23399	The option to create a custom filter chain to filter variant results by allele frequency does not appear to be available (Assays ➤ Manage Presets ➤ Filter Chains ➤ Add New ➤ Choose Filter).	This issue affects custom filter chains created to filter variant results by allele frequency. Mitigation: Select the Allele Fraction filter to create a custom filter chain to filter variant results by Allele Frequency.

Issue	Issue Summary	Impact and Mitigation ¹
21930	If you create a custom filter chain for a variant classification, then try to apply	This issue affects all custom filter chains that include a Variant Classification filter.
	the custom filter chain to a result, a "Data not available" message appears.	 Mitigation: Find and filter user classifications in the following ways. In the Variants tables, in the User Classification column header, use the filter and search tool to limit the variant classifications that are shown. Download the Filtered Variants VCF file to view and search for variant classifications.
17425	In rare instances, the order of the reads shown in the BAM track is not consistent each time you view the BAM track in the Gene Browser .	This issue occurs only when the total read count exceeds the maximum read count threshold that is set for optimal browser performance. When the threshold is exceeded, the Gene Browser shows a specified number of randomly sampled alignments configured by downsampling parameters. The coverage track is not affected by this issue.
		Mitigation: You can adjust the downsample reads parameter and view the full BAM track with the Broad Institute Integrative Genomics Viewer (IGV). For more information, see "View variants with IGV" in the software help system.
21794	In the Gene Browser , in some instances, the target region is represented with a black color instead of green.	This issue occurs only for some variants. There is no impact to the data, except for the color change in the image.
13478	When you click any of the links for the Exome Aggregation Consortium (ExAC) browser in the Annotations tab shown below the Variants table, the following message is shown: "The ExAC browser is no longer available. ExAC data is available in the gnomAD browser or can be downloaded from gs://gnomad-public/legacy. View this page in the gnomAD browser. You will be automatically redirected in 24 seconds. "	This issue occurs when you click any of the links for the ExAC browser. Mitigation: Click the updated gnomAD browser link or wait to be redirected.
23068	If you create a custom panel for the Oncomine™ BRCA Assay GX, exon numbering remains set by the systeminstalled panel for the assay. As a result, when you use a custom panel that is based on a reference sequence version that is different from the systeminstalled panel, exon numbering for BRCA1 is not correct when you visualize exon and whole gene CNVs.	This rare issue affects the visualization of BRCA1 for the Oncomine™ BRCA Assay GX if you use a custom panel with a version of the reference sequence that is different from the system-installed panel for the assay. The system-installed version of the reference sequence is NM_007294.4.

Issue	Issue Summary	Impact and Mitigation ¹
23057	When you view the exon tile fusion imbalance charts for a sample, then select a different sample, the charts are not updated for the new sample that is selected.	This issue affects the charts that are shown for the RNA exon tile fusion imbalance results for the Oncomine™ Precision Assay GX. Mitigation: 1. Leave the Results section. For example, click Dashboard. 2. Click Results ➤ Sample Results, then click the sample name for the RNA exon tile fusion imbalance charts that you want to view. 3. Click the Variants tab, then click Fusions. 4. Click Visualization ➤ RNA Exon Tile Fusion Imbalance.
21541	If you import a custom exon tile assay baseline file in an unsupported file format, you are not notified that the import failed. The unsupported file appears in the Exon Tile Assay baselines list after import. However, analysis fails if the custom assay baseline is used in a run plan.	This issue occurs only if you attempt to import a custom exon tile assay baseline file in an unsupported file format. Mitigation: Ensure that custom exon tile assay baselines that you import are in a supported file format.
21320	If the name of a variant report template includes a special character of @,*,#, or \$, you cannot view or download variant reports generated with the template.	This issue affects any variant report with @,*,#, or \$ in the name of the variant report template. Mitigation: Create a new variant report template without @,*,#, or \$ in the name, then generate a new report.
17803	The dates for runs that are started on or completed on 26–31 December display the incorrect year. The date that is shown is one year later than the actual date. For example, for a run started and completed on 2021-12-30, the started on and completed on date is incorrectly shown as 2022-12-30.	This issue affects all runs that are started on or completed on 26–31 December. The incorrect date is shown in the Variant Report PDF (if Sequencing Run Details are included in the report template), in the Run Report PDF, in the Sample Summary file (the info.csv file), in the Run Report tab, and in the Run Summary tab.
21508	If you have installed Ion Torrent™ Oncomine™ Reporter software and you generate an Oncomine™ Reporter Report in text format, the following error message is displayed: "Failed to load PDF document."	This issue affects only Oncomine™ Reporter Reports in text format. Mitigation: To view an Oncomine™ Reporter Reports in text format, download the report, then view the report in a compatible text file viewer.
23081	When you try to prepare a library batch with more than 24 samples, an error message is shown for some DNA + RNA assays.	This issue affects some system installed and custom DNA + RNA assays when you select more than 24 samples during library batch preparation. Mitigation: Create an XLS or XLSX file that contains the library batch information from a template file provided in the Import Library Batch screen, then import the library batch file.
20579	For runs that use an assay that has been enabled for resequencing, the log files for the resequencing portion of the run are located in a separate folder called "Reseq".	This issue affects all runs that include resequencing.

Issue number	Issue Summary	Impact and Mitigation ¹
22005	When you try to download a BAM result file that is larger than 2 GB, the file that is downloaded is 0 KB and does not contain any data.	This issue affects all BAM files larger than 2 GB that you attempt to download in the software or from the web services API. Mitigation: For help with the following procedure, contact a Field Bioinformatics Specialist (FBS). Pre-requisite: Administrator-level user with a configured Secure Shell (SSH) key 1. Use a command-line interface to view the BAM results files in the folder /results/analysis/output/reports/. 2. In the folder of files that is returned, search by sample name to find the BAM file of interest. Contact an FBS for help if the result was reanalyzed and multiple subfolders are listed. 3. Copy BAM files from the server to the computer with SSH. The file location on the server is: //results/analysis/output/reports/[Sample specific]
20738	Downloading multiple Customer Support Archive (CSA) files simultaneously fails.	LIMS folder]. This issue occurs when you try to download a CSA file while another CSA file is downloading. This issue occurs in the Run Results, Sample Results, and Verification Results screens. Mitigation: You must wait for a CSA file to download successfully before you can download another CSA file.
16765	Results generated by the coverageAnalysis plugin for RNA samples with an application category of oncology are not informative.	This issue occurs only when you view the coverageAnalysis plugin results in the Plugins tab for an oncology RNA sample. Mitigation: For oncology RNA samples, you can ignore the coverageAnalysis plugin results shown in the Plugins tab.
21486	If you upload a DNA & RNA sample result from one Genexus™ Software server to another and the name of the sample is more than 50 characters long, two samples are created on the target server. One sample is for DNA (with a sample type of DNA & RNA) and another is for RNA (with a sample type of RNA).	This issue affects only samples that have a name that is more than 50 characters long. Mitigation: When you create a sample, limit the name to less than 50 characters. For each sample that you want to upload to anther Genexus™ Software server, edit the sample name so that the name is less than 50 characters. If two samples are created on the target server, select both samples when you plan a BAM to Result run.
16763	If you import run results from another Genexus™ Software server that has a different version of a plugin used in the run; you cannot see the plugin results in the Plugins tab when you view the results on the target server.	This issue affects results that are imported in a Genexus™ Software server that has a different version than the source Genexus™ Software server. Mitigation: Run the plugins again in the target server (from a sample result, click the More Options button▶Run Plugin).

Issue number	Issue Summary	Impact and Mitigation ¹
21357	In the Manage Assays screen, when you select DNA and Fusions, DNA, Fusions to refine the assay list with the filter tool in the Research Application header, no records are shown even if records are available.	This issue affects only the filter selection of DNA and Fusions, DNA, Fusions in the Research Application column. Mitigation: First enter the term DNA and Fusions, DNA, Fusions in the search field, then select the DNA and Fusions, DNA, Fusions checkbox to refine the list.
21807	When you create some custom assays or copy and edit some assays, you can enable, edit, and view Microsatellite Instability (MSI) parameters in the Parameters step of assay creation even though the MSI parameters are not applied in the analysis.	This issue affects some custom assays. Mitigation: Ignore MSI parameter settings in custom assays when results do not show MSI metrics.
21712	When you try to sort by name the list of copy number baselines, sequence variant baselines, or exon tile assay	This issue occurs only when you try to sort the list of copy number baselines, sequence variant baselines, or exon tile assay baselines by name.
	baselines, the following error message appears: "We are unable to complete the requested action due to a system error."	Mitigation: You can sort the lists of baselines when you click any other column header. You can also scroll to the bottom of the screen, and if applicable, view other pages of each baseline, to view the baselines at the end of the list.
21086	When you click Settings ▶ Backup & Restore ▶ Start Now , system backup	This issue occurs when you start an unscheduled system backup.
	starts immediately without a confirmation dialog box.	Mitigation: Ensure that you intend to start a system backup before you click Settings ➤ Backup & Restore ➤ Start Now.
794	If a USB update for the purification instrument fails, you are not notified.	When you attempt to update the purification instrument software from a USB, the message "Install Completed; Please Reboot Now" appears regardless of whether the software update is successful.
		Tap Instrument Settings ► About to view the software version and confirm that the software update is complete.
13222	Deck loading instructions jump between sections before completion of each section.	This issue can result in a suboptimal user experience while the deck is set up. It does not, however, cause any misplacement of deck consumables.
1316	If the error message "Lane clog check failed" is shown after a clean instrument procedure, the message appears only briefly.	This is a rare issue that only occurs if the sequencing instrument detects a lane clog after performing a clean instrument procedure. If a lane clog occurs and you do not see the error message, you are notified to perform a clean instrument procedure when you start a run.
		Mitigation: Contact Technical Support for help to fix a clog.

¹Mitigation is included if applicable.

View the correct orientation of transcripts that are transcribed from the reverse strand

You can view the direction of transcripts and get correct exon numbers with the Broad Institute Integrative Genomics Viewer (IGV) or with other genome browsers, such as the UCSC Human Genome Browser.

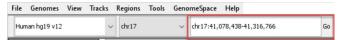
Enable IGV

Pre-requisite:

- Java™ Web Start version 8 (64-bit) installed. If you are running Java™ 9 or later, you must also have Java™ 8 for the JNLP to work correctly to view variants in IGV.
- 1. Run Configure Java.
- 2. In the Java Control Panel, in the Security tab, click Edit Site List.
- 3. In the **Exception Site List**, click **Add**, enter the Genexus™ Software URL, for example, https://<your server address>, then click **OK**.
- Click **OK** to close the Control Panel.

View a coverage graph in IGV

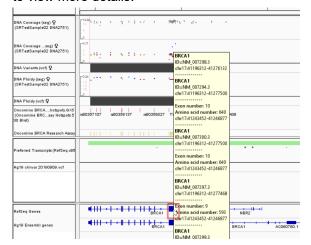
- 1. In Genexus™ Software, click the **Variants** tab.
- 2. In the row of the variant of interest, in the Locus column, copy the locus for the variant.
- 3. In the Variant ID column, click the link for the variant of interest.
- 4. In the **Gene Browser** that opens below the variants table, click **View in IGV**.
- 5. In the warning message that appears at the bottom of the screen, click **Keep**.
- 6. At the bottom of the screen, click the name of the file.
- 7. In the warning message dialog box that appears, click **Continue**.
- 8. In the Security Warning dialog box that appears, accept the risk, then click **Run**. The transcript is shown in IGV in a new window.
- 9. In IGV, in the search box, paste the locus that you copied in step 2, then click Go.



10. Use the tools in the top right of the screen to expand and shrink the view of the tracks.



11. In the Sequence pane, view the direction of the transcript and place the pointer over an exon of interest to view more details.



For more information about IGV, see the IGV User Guide.

System Requirements

Genexus™ Software 6.6 has a browser-based interface that can be viewed using Google™ Chrome™ version 90 and above (version 90 has been tested) and is best viewed with a

1440 x 900 screen resolution. The software is accessed on an independent client computer with a private web server.

Package and version information

Release Date	28 October 2021
Release Version	6.6

Software packages versions in 6.6

These tables list the versions for each of the latest packages and plugins for Genexus™ Software.

Packages

Package	Version
ts-algorithm-516	6.6
ts-apache2	6.6
ts-assaydev-ampliseq-coca-541-v4	6.6
ts-assaydev-ampliseq-coca3b-541-v2	6.6
ts-assaydev-ampliseq-coca3b-gx7-v1	6.6
ts-assaydev-ampliseqhd-coca-541-v4	6.6
ts-assaydev-ampliseqhd-coca3b-gx7-v1	6.6
ts-assaydev-analysis516	6.6
ts-assaydev-assets	6.6
ts-assaydev-crawler	6.6
ts-assaydev-factory-template	6.6
ts-assaydev-genxscriptupdates	6.6
ts-assaydev-grws	6.6
ts-assaydev-igvservlet	6.6
ts-assaydev-iruploader	6.6
ts-assaydev-manager	6.6
ts-assaydev-ocrp516	6.6

Package	Version
ts-assaydev-ovat-plugin516	6.6
ts-assaydev-purificationscriptupdates	6.6
ts-assaydev-reportbuilder	6.6
ts-assaydev-seeddata	6.6
ts-assaydev-server516	6.6
ts-assaydev-ui	6.6
ts-config	6.6
ts-deeplaser	6.6
ts-fonts	6.6
ts-genxupdates	6.6
ts-immune-repertoire	6.6
ts-java11	6.6
ts-postgresql	6.6
ts-purificationupdates	6.6
ts-reference-delta	6.6
ts-software-update	6.6
ts-tomcat8	6.6
ts-variome-data-calculator	6.6

Plugins

Plugin	Version
customersupportarchive	6.6
coverageanalysis	6.6
molecularcoverageanalysis	6.6
sampleid	6.6

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3 June 2022