Mutation Surveyor Change Log

Version 5.1.2

Corrected the Following Bugs

Feature	Affected	Algorithm Change	Risk
Create SCF	Fix Create SCF Tool Max Output Length	No	Low
Custom Report	Fix cDNA Numbering for Custom Nomenclature in Custom Report	No	Low
Custom Report	Fix Custom Report Sorting Function	No	Low
Het-Indel Detection Tool	Fix Alignment to Reference issue for some samples with complex Het-Indels	Yes	Medium
Het-Indel Detection Tool	Improve Support for the Manual Addition of Longer Insertions and Deletions	No	Low
Mutation Calls	Fix Mutation Call edit issue in GAD for some unpaired reverse samples	No	Low
Mutation Calls	Fix Change in Mutation Call after Project Restart Using Same Settings	Yes	Medium
Mutation Calls	Fix missed Mutation Call issue with Ref trace and no Score Trim	Yes	High
Project Reviewer	Fix trace display in Project Reviewer at regions of insertions	No	Low
	Other minor bug fixes	No	Low

Version 5.1.1

Corrected the Following Bugs

Feature	Affected	Algorithm Change	Risk
Alignment	Beckman CEQ8000 GeXP software SCF and ESD format support	Yes	Low
Alignment	Processing of Raw Trace Files Results in Failed Alignment	Yes	Medium
Alignment	Grouping of Certain Reverse Trace Files Into Same Contig Results in Short Synthetic Reference Trace	Yes	Medium
Custom Report	Some Reported Variants Missing from Custom Report	No	Low
	Other minor bug fixes	No	Low

Version 5.1.0

Added and Updated the Following Features

Feature	Affected	Algorithm Change	Risk
Alignment	Heterozygous Indel detection improvements	Yes	Medium
Custom Report	Support mitochondrial forensic nomenclature	No	Low
Database	Add Delete Mutation and Add to Database options	No	Low
Digital Rights Management	Support local annual subscription licensing of Mutation Surveyor	No	Low
Het-Indel Detection Tool	Indel Quality Score	No	Low
Track Manager	Update Track Manager	No	Low

Corrected the Following Bugs

Feature	Affected	Algorithm Change	Risk
Alignment	Fix Issue with 2D Mutation Calls Being Considered Independent Due to Spacing Issue for GenBank Alignment In Reverse Trace Files	Yes	Medium
Alignment	Fix issue related to missed homozygous insertion/duplication call due to irregular peak heights	Yes	High
Alignment	Contig direction/pairing issues	Yes	Medium
Custom Report	Fix VCF output issue for minus strand genes when project is run with "Orient GenBank Files in Chromosome Direction" selected	No	Low
Custom Report	Fix issue related to Undo Deletion and Undo Confirmation in Custom Report failing to restore mutation call text color	No	Low
Custom Report	Custom Report Display Issues for negatives	No	Low
Custom Report	Fix blank Exon column in One Mutation Per Row format of Custom Report when using SEQ files	No	Low
Export GAD	Fix issue with Export GAD option to Output POI for indels	No	Low
Graphic Analysis Display	Fix incorrect Phred Score Display for 1D Data	No	Low
Het-Indel Detection Tool	Missed Het-Indel after fixing missed SNP	Yes	Medium
Mutation Calls	cDNA numbering issues in introns between UTRs	Yes	Medium
Mutation Calls	Fix issue regarding reported variant and overlapping mutations calls for same position	Yes	Medium
Output	Fix issue with Het_Indel Detection Tool display setting adjustments not being applied to print output	No	Low
Reported Variant	Imported Track Data Missing for mtDNA	No	Low

Annotation			
	Other minor bug fixes	No	Low

Version 5.0.1

Added and Updated the Following Features

Feature	Affected	Algorithm Change	Risk
AutoRun	Add VCF output to AutoRun's Custom Report output options	No	Low
Database	Distinguish between two artifact entries at same chromosome location but different trace location/contig	No	Low
Graphic Analysis Display	Display Phred Score for Reference Trace Files	No	Low
Project Reviewer	Project Reviewer Trace Pane Update to allow adjustment in number of traces in view	No	Low
Project Reviewer	Add zoom options to Project Reviewer	No	Low
Reports	Updates to Clinical Report	No	Low
Reports	Enhancements to the Clinical Report	No	Low

Corrected the Following Bugs

Feature	Affected	Algorithm Change	Risk
Advanced GBK Editor	Advanced GBK file editor saves gene transcript and mrna transcript in two different locations	No	Low
Advanced GBK Editor	mRNA Transcripts from 5.0 Advanced GBK File Editor Missing Exon Information	No	Low
Advanced GBK Editor	Auto Create ROI fix for genes with more than 6 exons	No	Low
Alignment	Fix a multithreading issue causing a different number of unmatched traces between projects with DMD gene	Yes	High
Custom Report	Saving Custom Report .xls file also saves blank .log file	No	Low
Custom Report	VCF Format fixes	Yes	Medium
Custom Report	Custom Report Column Issue	No	Low
Custom Report	Custom Report Quality Failure Coloring Missing for ROI Coverage and Quality (ROI) Columns	No	Low
Export GAD	Change Header File Issue in Export GAD	No	Low
Graphic Analysis Display	Trace pane scroll bar missing when project does not have track annotation	No	Low
Graphic Analysis Display	Amino Acid Translation Missing from some mtDNA Genes	Yes	Medium

Graphic Analysis Display	Some nucleotides outside of comparison region are duplicated in graphical views	No	Low
Graphic Analysis Display	Track pane display settings not saved for projects without track information	No	Low
Graphic Analysis Display	Track pane display settings not remembered between 2D and 1D contigs	No	Low
Graphic Analysis Display	Fix issue related to an inability to add substitutions when Check 2D Small Peaks is selected	No	Low
Het-Indel Detection Tool	Heterozygous insertion allele issue with certain reference traces	Yes	High
Mutation Calls	Fix issue with improper automatic deletion of mutation call	No	Low
Mutation Calls	Added by computer function adds incorrect call	Yes	High
Mutation Calls	Incorrect annotation related to .seq file	Yes	Medium
Mutation Calls	Incorrect heterozygous duplication call with GenBank, Reference, and Sample Files Loaded in project.	Yes	High
Mutation Calls	Missed Heterozygous Deletion	Yes	High
Mutation Calls	Missed SNP in MS 5.0 due to extra heterozygous indel call	Yes	High
Mutation Calls	Editing Duplication Mutation Call fixes	Yes	High
Output	Fix Access Violation in module ntdll.dll issue for opening some projects	No	Low
Output	dbSNP Comments No Longer Populated in Comments Column of Mutation Table	No	Low
Output	Project save size issue	No	Low
Output	AA and transcript issues with overlapping genes in GenBank file	No	Low
Reported Variant Annotation	dbSNP info from NCBI not displayed in Mutation Surveyor	No	Low
Reported Variant Annotation	Some reported GenBank variants do not appear in Mutation Table	Yes	Medium
Reports	Nucleotide Position Shifted by One Basepair Using Output Trace Data Option	No	Low
Reports	Amino acid translation not populated in Vertex Report	Yes	Medium
Reports	Clinical Report Displays Incorrect Calls for Heterozygous Duplications	Yes	Medium
Settings	Can't Select Delete Indels Outside of ROI Option	No	Low
Settings	Automatic GBK Download translation issue	Yes	Medium
Tools	2D Filename Match Editor Integer Error	No	Low
Track Manager	Track Pane Does Not Display Mutant Alleles for Positions with Multiple Alleles	No	Low
Track Manager	Microsoft Windows Display text size issue	No	Low

	Other minor bug fixes	No	Low

Version 5.0.0

Added and Updated the Following Features

Feature	Affected	Algorithm Change	Risk
Alignment	Improve GenBank Search on Server	No	Low
Custom Report	Assign Comments to Traces	No	Low
Customer Reports	Emory Report - Lock Sample File in View	No	Low
Database	Create Variant Knowledge Base	Yes	Medium
Database	Remember Deleted Artifacts	Yes	Medium
Graphic Analysis Display	Add nucleotide string search	No	Low
Graphic Analysis Display	Display Chromosome Coordinates	No	Low
Het-Indel Detection Tool	Deconvolute Heterozygous indels when neither allele matches GenBank	Yes	High
HLA	Add HLA Tool	No	Low
Methylation	Include added variations outside of comparison region to methylation report	No	Low
Nomenclature	Update HGVS nomenclature in custom report for three letter termination codon	No	Low
Reports	Add VCF Output	No	Low
Settings	Calculate Phred Score Before Alignment	No	Low
Settings	Add "Check Gene Direction" option	No	Low
Track Manager	Import Tracks, including prediction information (dbNSFP, ClinVar)	No	Low
User Management	Add User Login Option	No	Low
User Management	Generate User Login History Report	No	Low
User Management	Add Audit Trail	No	Low

Corrected the Following Bugs

Feature	Affected	Algorithm Change	Risk
Alignment	Lane quality of unmatched traces differs between runs	No	Low
Alignment	Issue with some Unmatched traces that have het-indels	Yes	Medium

Alignment	Gap in reference and sample traces due to unmatched forward trace	No	Low
Alignment	Number of matched .seq files differs between projects	No	Low
Custom Report	Custom Report Negative SNP Duplication issue	No	Low
Custom Report	Manual Comments missing for some Table Formats	No	Low
Custom Report	Missing somatic mutation from various mutation reports related to dbSNP	Yes	Medium
Custom Report	Custom Report settings conflict with Russian Version of Windows 7	No	Low
Export GAD	Export GAD as JPG captures progress bar for all mutations in samples	No	Low
Graphic Analysis Display	CpG Islands incorrectly marked as TpG using methylation function	Yes	Medium
Graphic Analysis Display	"With Indel Change" Option Causing Amino Acid Discrepancy	Yes	Medium
Graphic Analysis Display	Check 2D small peaks displaying information for 1 direction	Yes	Medium
Graphic Analysis Display	Truncated amino acid sequence in GAD using muliple seq files per contig	No	Low
Graphic Analysis Display	Fix issue with saving Phred score to project	No	Low
Het-Indel Detection Tool	Fix for detection of heterozygous deletion in traces with compressed nucleotides	Yes	Medium
Mutation Calls	Saved .SGP project freezes when re-opened	No	Low
Mutation Calls	Access Violation Error message after adding mutation	No	Low
Mutation Calls	Incorrect HGVS nomenclature for known duplication in EGFR gene	Yes	High
Mutation Calls	Issue related to "Use Amplicon ID to Construct Contig" and synthetic reference traces causing different mutation calls	Yes	Medium
Nomenclature	c.DNA index in GAD incorrect for heterozygous duplications	Yes	Medium
Project Reviewer	Possible conflict in Project Reviewer Report with Reference Traces	No	Low
Project Reviewer	Project Reviewer Errors Associated with Negative Reference File	No	Low
Reported Variant Annotation	Mutation displays different c. number between reports	Yes	Medium

Version 4.0.11

Corrected the Following Bugs

Feature	Affected	Algorithm	Risk

		Change	
Alignment	Short reference traces could cause sample traces to be in separate contigs	Yes	Medium
Mutation Calls	False Positive due to noise in Reference Trace	Yes	High

Version 4.0.10

Corrected the Following Bugs

Feature	Affected	Algorithm Change	Risk
Alignment	Hypervariable GenBank/Reference trace alignment issue	No	Low

Version 4.0.9

Added and Updated the Following Features

Feature	Description	Algorithm Change	Risk
Project Reviewer Report	Legend “button” added to icon toolbar Show/hide “annotation” pane button added. Legend and color codes are now a separate window that can be moved/hidden, sequence annotation is a separate pane	No	Low
Settings	ND Filename Match Editor/Extract SGP/Mutation Assembly/Show Hide GAD Panes Previous settings for tools are contained in settings.ini file and remembered for subsequent projects	No	Low
Setups- Text based network license	LSM 2.0.9 product information display LSM 2.0.9 is able to display client computer name and user name	No	Low
Setups	Register.exe contains a “remove” button allowing users to remove local license information from machine	No	Low
Settings	Load/Save settings button added to project settings dialog box Project settings can be saved as an .ini file and loaded into project, defaultsettings.ini file updated to local folder	No	Low

Corrected the Following Bugs

Feature	Affected	Algorithm Change	Risk
Alignment	Synthetic reference creation of methylated datasets	Yes	Medium

	containing sample and reference files Methylated reference / sample pairs create synthetic sample and add file to contig		
Export GAD	Revisions to export GAD JPG and mutation parameters Incorrect information associated with negative mutations fixed, export GAD files display correct information for negative mutations	No	Low
Alignment	Alignment of traces to large GenBank files-maximum length extended to 10Mbp Traces align to GenBank files 10Mbp or less	Yes	Medium
Alignment	Sequence files resulting in improper contig grouping Contig issues related to poor sequence files resolved to group into correct contigs	Yes	Medium
Mutation Calls	Patch added to ends of trace to normalize peaks and make mutation calls near the end of trace Some missed calls near the ends of trace due to sequence ending may now be called	Yes	High
Mutation Calls	False positive mutation calls due to noise in reference traces False positives due to noise eliminated	Yes	High

Version 4.0.8

Added and Updated the Following Features:

- Support for Adobe Acrobat 10

- Show/Hide Grid in GAD

- Add c.dna numbering to Mutation Table

- Enhance Comment template

- Custom Report Color Improvements

Corrected the Following Bugs:

- Unmatched Traces Issue

- ROI Coverage/Quality not saved properly to project

- Missing Reported SNP color

- Synthetic Trace Issue for multiple SEQ files in one Contig

- Alignment to wrong repeat region

- Custom Report's "Mutation Summary" Priorities

- Save Images of Negative Mutations from Export GAD

- Other minor bug fixes

Version 4.0.7

Added and Updated the Following Features:

- Add c.dna numbering to Main Display

- Modify Mutation Projects reads GB files

- Export Custom Report Excel cells as text format instead of general format option

Corrected the Following Bugs:

- Custom Report Access Violation fix

- Some annotation missing for second project when using Modify Mutation Projects is used to merge projects

- dbSNP reported on R sample, but not F sample.

- N recorded in GenBank file, missed hom delN in samples

- Project Reviewer Report crash

- Export GAD Current Mutation Only termination bug

- Unmatched Traces Issue

- Project Reviewer Backwards Compatibility Issue

- Negative dbSNP identifier lost from mutation table and Custom Report

- Other minor bug fixes

Version 4.0.6

Added and Updated the Following Features:

- Launch MS without the Printers installed

Corrected the Following Bugs:

- Amplicon ID value in Custom Report is affected by "use amplicon ID..." option in Settings

- Mutation Calls shown in Mutation Table when trace is Low Quality

- Modify Mutation Projects error with SNP_tags when GBK files are same

- Amplicon ID may not be working properly

- S/N Ratio score fixed

- Reports show wrong references amino acid for translation table 2

- Projects aligned to multiple GenBank files in Project Reviewer

- Some Missed heterozygous indels

- ROI Quality score change

- ROIs missing when Amplicon ID is used to construct contigs but are not defined in GenBank

- Fetching Wrong SNP Tag

- SNP Tag not fetched for some insertions

- Legacy NC accession nucleotides read as minus positions

- Overlapping Genes in GBK causes CDS arrow to not be displayed correctly in GAD

- Crash fix for High Noise Samples

- Traces Aligning to the wrong location of GenBank reference because of similar homology, example 2

- Trace with Repetitive sequence aligns to wrong region

- Other minor bug fixes

Version 4.0.5

Added and Updated the Following Features:

- Changes to Advanced GBK File Editor to Better Handle Minus Strand Genes

- Changes to Mutation Surveyor Settings/Report to Better Handle Minus Strand Genes

- Compatibility for Large Genes with ROIs and more than 200 sample traces

- Compatibility for many variations with many SNP Tags and more than 400 sample traces

- Calculating quality scores for ROIs Update. A penalty score is factored into the ROI Quality score when the Aligned Region (Comparison Region) does not contain the entire ROI. Adjust the quality score by the percent overlap of the Aligned Region and the ROI. For example, if length of ROI is 63 and length of

overlap between Aligned Region and ROI is 8, percent overlap is 8/63 = 0.127. Current Quality Score (ROI) is 88, new score would be 88 (0.127) = 11. In previous versions, the ROI score was very high, even though only a small portion of ROI was good quality.

- Insertion and Deletion output changes to Custom Report's XML format

Corrected the Following Bugs:

- Custom Report Printing Margins Issue

- Custom Report Color-coding Priority Issue with Reported Variations

- GAD Substitution Calls are Shifted

- New Custom Report settings not saved

- Reprocess data crash

- Modify Project Saving

- Software version number is not displayed in report headers

- Modify Mutation Projects error with SNP_tags when GBK files differ

- Reading ESD files, possible indel present, crash when uploading

- Clinical Report Header fix

- Clinical Report call replication fix

- Other minor bug fixes

Version 4.0.4

Added and Updated the Following Features:

- Extend Create SCF tool capacity to more than 1200 nucleotides

- Improve 1 Directional sensitivity for substitutions when 2 Directional setting is selected

Corrected the Following Bugs:

- HGVS report-3.2,3.24 saved project does not display c. numbers correctly

- Improve generation of synthetic reference for samples with mixed nucleotides

- Exons of Amino Acid Display in GAD for v3.97 projects are not displayed properly

- Other minor bug fixes

Version 4.0.3

Added and Updated the Following Features:

- Print GAD - increase nucleotide range to 16 bps

- Add Percentage of Conserved and Mutant in Heterozygous Indel Tool

- Increase detection sensitivity when raw reads have low relative intensity

Corrected the Following Bugs:

- Fix basecaller issue related to IUPAC calls

- Traces Aligning to the wrong location of GenBank reference because of similar homology

- Custom Report INI file, CDS +/- 50 bp--External exception EFFACE generated by Custom Report

- SNP tags from v3.97 were not displayed

- Missed mutation with sharp peaks when minor allele is not centered under major allele

- Show Direction of yellow arrow of CDS

- Other minor bug fixes

Version 4.0.0

Added and Updated the Following Features:

- Text Base Security - Previous versions of Mutation Surveyor could only be secured by hardware keys (parallel port or USB port). In this version, the software can be secured with or without hardware keys. Our network licensing option with hardware keys is not compatible with 64-bit operating systems and Windows 7 - the server computer could not be one of these. With more institutions switching to virtual systems, hardware keys are not always a desirable option because additional hardware would be needed to read the USB key (for example a digi-hub). Text-based security helps with these issues. Local licensing security by a text-based key is different than local licensing security by hardware keys. The hardware keys could be moved from computer-to-computer. The local text-based key is locked to a single computer.

- Custom Report's Signal Strength reads sample file header, BasePatch Normalization no longer displayed

- Exon and mtDNA Gene Annotation Displayed for GBK files

- Display Amplicon ID in Custom Report

- Custom Report, display nucleotide, mRNA and protein accession numbers

- forensic mtDNA nomenclature for insertions and deletions

- Save all reports as XLSX

- Custom Report One mutation per row Custom sorting of information by column HGVS style for nt cDNA style for a.a.-no p. before mutation

- MutAutoRun saving over network

- Increase Alignment Speed and Improve Accuracy - 1) Alignment algorithm adjusted to increase speed. Prior to v4.0 dynamic programming was used to search only one 24mer to find other traces that might be in same contig, then do modified Smith-Waterman to complete the matching. Now we use multiple 12mers to find a cluster of 12mers between multiple traces, if mismatch we use 6mer in a local region. 2) A modified Mexican Hat Wavelet formula (1-|x/w|^1.25) was added to assist calling bases in regions that are noisy and have spacing issues, such as homopolymer stretches that have broad peaks. The Mexican Hat Wavelet sharpens peaks, helping to distinguish the number of peaks within a broadened peak. The trace may have only 1 peak called, but might actually be two bases, and the Mexican Hat Wavelet helps to align these regions more accurately. When the BasePatch option is not selected, the original basecalls are displayed in the electropherograms. When the BasePatch option is selected, the basecall results from applying the Mexican Hat Wavelet formula are displayed in the electropherograms. "A" bases are more often wide than other bases at the beginning, and we set relative width to 1.25 to call A bases, other nucleotides are treated as relative width of 1. False positives, especially Indels at beginning and end of traces, might be reduced by as much as 70%. 3) Score Trim in versions prior to v4.0 was relative to the Phred-like score (in this score, the peak spacing is of main concern). In version 4.0, both the Phred-like score and Signal/Noise ratio are evaluated, and the lowest score is used to define results. For example, 20 = 1/20 (5%) and 15 = 1/15 (7%). Lane Quality is relative to Signal/Noise ratio, so the Score Trim is now a combination of the Lane Quality in the local region and Phred-like score. The Comparison Start and End bars are moved inward relative to this new Score Trim value. This helps to reduce false positive calls made at the beginning and end of traces by not including these low quality regions in the comparison.

- Circular Genome Support - traces that overlap origin now align to both sides of origin

- Project includes Original and Edited GenBank Files - If custom SNP tags are added to positions, then the GenBank file is edited. The Edited and Original GenBank file can now be extracted from the SGP by using the Extract SGP tool.

- Increase throughput from 400 traces to 2000 traces

- Add BasePatch Tool

Corrected the Following Bugs:

- Advanced GBK File Editor, Nomenclature of some insertion/deletions is causing variation line to be omitted in seq file

- Some Seq Files not working

- Compression of repeat nucleotides in electropherogram during alignment

- Print Clinical Report Out of Range Error

- High Quality Traces not Matching error

- Custom SNP Tag Color-coding Discrepancy

- Amino Acid Display is Wrong for mtDNA

- BasePatch causing abnormal program termination

- Print GAD giving access violation when printing Word Doc

- Remember Last Directory

- FASTA Files not loaded

- Amino acid change not reported - Mutation calls are identified by frame number, not nucleotide number. For the same nucleotide position, amino acid change was reported for some, but not others due to the frame number issue. This was related to c.1 position.

- False Negatives Fix

- Other minor bug fixes

Description of Risk Categories

- Low – cosmetic; such as changes to the graphic user interface and reporting options (no algorithm change).
- Medium – includes minor algorithm changes that may affect sample grouping and final reports.
- High – includes significant algorithm changes that may result in alignment and mutation call detection differences.