

# **DRAGEN v3.8.9**

## **Software Release Notes**

## Introduction

These release notes detail the key changes to software components for the Illumina® DRAGEN™ Bio-IT Platform v3.8.9.

Changes are relative to DRAGEN™ v3.8.4. If you are upgrading from a version prior to DRAGEN™ v3.8.4, please review the release notes for a list of features and bug fixes introduced in subsequent versions.

DRAGEN™ Installers, User Guide and Release Notes are available here:

[https://support.illumina.com/sequencing/sequencing\\_software/dragen-bio-it-platform.html](https://support.illumina.com/sequencing/sequencing_software/dragen-bio-it-platform.html)

The 3.8.9 software package includes:

- DRAGEN™ SW for x86 Centos 7 - dragen-3.8.9-7.el7.x86\_64.run

The following configurations are also available on request:

- Amazon Machine Image (AMI)
- RPM packages for Centos 7 for Amazon Web Services (AWS)

Deprecated platforms:

- Support for IBM PPC has been deprecated since DRAGEN™ v3.7
- Support for Intel CentOS 6 has been deprecated since DRAGEN™ v3.8

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## Added Functionality

None.

## Issues Resolved

Issues found on v3.8.4 or affecting v3.8.4, that are fixed in v3.8.9

Defect ID	Component	Description
SET-1965 DRAGEN-12187	Amplicon	Fix a hang encountered during Amplicon processing on NextSeq2K instruments, due to a race condition in instrument specific multi-sample-mapper mode
DRAGEN-12855	Amplicon	Fix for the generated hang diag file filling up the /var volume, due to a crash in an Amplicon run, by removing the per-base logs in hang diag file
SET-973 DRAGEN-11624	Expansion Hunter	Fix to allow Expansion Hunter processing of inputs that have multiple libraries (RGLB) for one sample (RGSM)
DRAGEN-12405	Methylation	Fix for an incorrect alignment, which happens only when multi-pass alignment and fastq list are used with Methylation, due to MD tag being calculated from wrong alignment
DRAGEN-11983	Somatic T/N	Fix a segfault in the somatic variant caller, due to incorrect handling of a haplotype that starts with an indel not being clipped.
DRAGEN-11791	Somatic T/N	Fix to use the correct AF for somatic AF call threshold, when variants with AF less than --vc-af-call-threshold appear in VCF for somatic T/N
DRAGEN-12640	Somatic	Fix a crash during somatic analysis on some samples, due to a bug in the Eigen library for Single Value Decomposition
DRAGEN-12454	SNV VC	Fix a watchdog timeout while generating a systematic noise file.
SET-2035 DRAGEN-12390	SNV VC	Fix HMM hangs in the small VC, due to no space left in DRAM pool
SET-1971	SNV VC	Fix for unexpected MT variant calls, by using extra HMM bandwidth
SET-2030 DRAGEN-14034	SNV VC	Fix for HMM hangs encountered, due to incorrect update to region free list
SET-2356 DRAGEN-14979	SNV VC / Somatic	Fix incorrect variant calls that happen due to a 16bit variable overflow for very large coverage
DRAGEN-12168	HT Builder	Fix for potential HT build failure, due to an undefined behavior from uninitialized snp file name
DRAGEN-11998	HT Builder, Graph HT	Fix for alt-awareness not working when the HT is built with an alt aware reference with a pop alts liftover sam
DRAGEN-12860	CNV	Fix for a DRAGEN HWAL error and hang when CNV is enabled, due to a hardware gzipped race condition
SET-1779 DRAGEN-13351	CNV	Fix for a CNV deletion call on chrY for female samples
DRAGEN-11862	Somatic CNV	Fix the OutlierBafFraction QC metric that is miscalculated for tumor-only runs
DRAGEN-12408	Somatic CNV	Fix a crash during Somatic CNV analysis due to invalid purity selection in VAF modeling

SET-1674 DRAGEN-13070	BCL	Fix for the wrong index length in 'Top_Unknown_Barcodes.csv' when demultiplexing using bcl-convert
DRAGEN-12124	BCL	Fix a crash when --bcl-only-read 1 is specified and UMI ranges are specified in OverrideCycles
DRAGEN-11944	BCL	Fix an issue where non-contiguous bases are output to fastq, introduced by new TrimUMI,0 and CreateFastqForIndexReads,1 options. Cases are sequences of YNU, UNY or UNU in a genomic read when TrimUMI is disabled, and INU, UNI, and UNU in an index read when TrimUMI is disabled and CreateFastqForIndexReads is enabled.
DRAGEN-13409	BCL	Fix for bcl-convert producing incorrect data when Read 1 size is less than 25 cycles
DRAGEN-14380	BCL	Fix crash when config.xml is present in BaseCalls on aggregated-bcl input (HiSeq/MiSeq)
DRAGEN-12479 DRAGEN-12739	Metrics	Fix for full_res coverage report not output when metrics compression is enabled, due to a wigToBigWig crash during metrics file compression
DRAGEN-12103	Combine GVCF	Fix for 0 sized gVCF output file, when enable-vcf-compression is true
DRAGEN-14538	CRAM	Fix for wrong "span" value(s) generated in the CRAM index, leading to invalid index, encountered on containers with multiple refs, where the references with exactly one record aligned against them

## Known Issues

Known issues of the DRAGEN™ v3.8.9 release

Defect ID	Component	Issue Type	Description	Remedy / Workaround
DRAGEN-11376	System	Support	Support for CentoOS6 has been deprecated and not available for DRAGEN™ v3.8 and later	Upgrade system to CentOS7
DRAGEN-13977	System	Compatibility	dragen_drv does not compile on Ubuntu linux kernel 5.8.0	Ubuntu is not officially supported. Contact customer support to have engineering team provide updated driver files
DRAGEN-11718	Small VC	Run time	Germline WGS runtime is ~10% slower than v3.7 on AWS instances, due to the enabling of Joint Detection of Overlapping Variants	None
DRAGEN-11729	BCL	Usability	BCL conversion for very high sample counts (>50k) may require >128GB system RAM	256GB RAM is recommended for very high sample count BCL conversion up to 150k samples
SET-929 DRAGEN-1370	BCL	Usability	BCL convert may fail to complete and assert	None. BCL already prints a warning that corrupt files are detected. Future releases will improve the detection and

			when some bcl files are truncated	handling of the specific type of corruption
DRAGEN-11800	Graph Mapper	Run time	Graph based mapper run time up to ~5% slower than legacy	None. Improved accuracy may lead to more work for the small VC.
DRAGEN-11801	DNA Amplicon	Bug	Amplicon caller does not exit with non-zero code when `vc-target-bed` argument is missing. Run completes with calls outside target region.	User must ensure to specify both `vc-target-bed` and `amplicon-target-bed`
DRAGEN-11636	License	Bug	License manager crash due to license .gbin file corruption has been observed for on-site systems. Rare occurrence	Delete gbin files and re-install licenses
DRAGEN-11514	Installer	Stability	Installation failure has been observed, due to inability to allocate hugepage memory buffers. Rare occurrence	Stop running programs. Sync memory. Re-run installer
DRAGEN-11511	HWAL	Stability	Timeout writing to hardware crash has been observed on Phase 1 on-site servers only. Rare occurrence that coincide only with concurrent dragen_info usage.	System power cycle is required
DRAGEN-15271	HWAL	Stability	Timeout writing to hardware crash has been observed on AWS, because of a prior crash	Re-run the sample on new instance succeeds
DRAGEN-15228	Map/Align	Stability	A very rare variation in alignment output for same inputs has been observed in nightly testing	None. For information only. Root cause has not been established. The variation
DRAGEN-15706	SNV VC	Bug	Integer 32bit overflow for very high depth samples, when using option "--vc-dragstr-pcr-params" to read pcr-model-0.log input files	None. This feature or usage mode is a special mode employed only on NextSeq2K on-instrument analysis, and rarely when attempting to improve run time for re-processing very high coverage (500x) samples.
DRAGEN-15473	CYP2D6	Accuracy	Some rare CYP2D6 calls are discordant with 3 <sup>rd</sup> party tool GeTRM	None. For informational purposes only. Accuracy improvements are continually made to future DRAGEN versions
DRAGEN-14794	Metrics	Usability	QC region coverage metrics reports more aligned reads than WGS coverage metrics	For informational purposes only. The separate coverage stats are based on slightly different definitions, which can be confusing to users. See user guide for details. Future DRAGEN version

				3.10 will consolidate the coverage metric to avoid confusion
DRAGEN-14526	Methylation	Usability	Duplicates are not reported in mapping metrics when using multi-pass methylation.	For informational purposes only. This metric is calculated in the recommended single-pass methylation mode.
DRAGEN-12601	Methylation	Bug	Multi-pass methylation mapper intermittently produces non-deterministic global alignments	This issue is specific to the "multi-pass" mode of the methylation mapper hardware. The Recommended usage mode for Methylation is the faster "single-pass" mode, which does not have this issue.
DRAGEN-12735	Hardware Trimmer	Usability	The system allows incorrect use of <code>*-read-trimmers=adapter</code> by allowing a run without specifying the required adapter file, leading to a silent failure	Ensure that the adapter sequence file is specified on the command line
DRAGEN-12718	Sort/Dupmark	Usability	High coverage samples such as 500x may run out of available system memory during processing in sort/dupmark step	Workaround by using <code>--dupmark-version=sort</code> , which is slightly slower but uses less memory

## SW Installation Procedure

- Download the desired installer from the Illumina support website and unzip the package
- The archive integrity can be checked using: `./<DRAGEN 3.8.9 .run file> --check`
- Install the appropriate release based on your Linux OS with the command: `sudo sh <DRAGEN 3.8.9 .run file>`
- Please follow the installer instructions. Server power cycle may be required after installation, depending on the currently installed version. If an updated FPGA shell image needs to load from flash, this is only achieved with power cycle.
  - A power cycle is required when upgrading from v3.3.7 or older
  - A power cycle is required when downgrading to v3.3.7 or older
  - A power cycle is not required when upgrading from a release after v3.3.7
- Procedure to downgrade to v3.3.7 or older:
  - Requires the following three steps. The prior .mcs file needs to be flashed manually:
    - Install the prior release: `sudo sh <DRAGEN 3.3.7 .run file>`
    - `program_flash /opt/edico/bitstream/07*/*.mcs`
    - Power cycle