



Title: DRAGEN Software v3.10.14 Customer Release Notes  
Part Number: 20106908  
Document Number: 200039779, Rev. 00  
Effective Date: June 9, 2023  
Page **1** of **9**

# **DRAGEN v3.10.14**

## **Software Release Notes**



## Introduction

These release notes detail the key changes to software components for the Illumina® DRAGEN™ Bio-IT Platform v3.10.14.

Changes are relative to DRAGEN™ v3.10.12. If you are upgrading from a version prior to DRAGEN™ v3.10.12, 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 3.10.14 software package includes installers for the on-site server:

- DRAGEN™ SW Intel Centos 7 - dragen-3.10.14-8.el7.x86\_64.run
- DRAGEN™ SW Intel Oracle 8 - dragen-3.10.14-8.el8.x86\_64.run

The following configurations are also available on request:

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

Deprecated platforms:

- Support for DRAGEN Server v1 FPGA cards have been deprecated since DRAGEN™ v3.10
- Support for Ubuntu has been deprecated since DRAGEN™ v3.9
- Support for Intel CentOS 6 has been deprecated since DRAGEN™ v3.8

## Contents

Overview .....	3
Issues Resolved.....	3
Known Issues.....	4
SW Installation Procedure.....	8



## Overview

Below is a summary of the changes included in this DRAGEN™ v3.10.14 patch release.

## Issues Resolved

Issues resolved on DRAGEN™ v3.10.14, compared to v3.10.12

Component	Defect ID	Description
CNV	DRAGEN-17488	Call amplifications and deletions for most of panel. Make low validation flag in TSO500 solid CNV deletion calls configurable.
CNV	DRAGEN-18424	If TSO500 software renames PON filename (moves or copies it), then DRAGEN will not detect the PON as valid. This change allows workflows to rename files.
CNV	DRAGEN-24599	NTC (control sample, water) was tested and had extremely low coverage, causing CNV to ASSERT. Detect such scenario and complete gracefully, and emit QC metrics indicating low coverage.
CNV	DRAGEN-24599	CNV VCFs should not report CN for TSO500 pipelines. NTC sample has MAD == 0, so no scoring model can be applied. The fix ties reporting of CN to the TSO500 flag instead of the scoring model used.
PhenoHRD	DRAGEN-22810	PhenoHRD should not raise an exception in this case where non-HRD samples have feature set to HRD. This change handles it as QC failure instead.
PhenoHRD	DRAGEN-23768	Add reporting of overall LOH
PhenoHRD	DRAGEN-23769	Add calling of absolute copy number for all CNV
RNA	DRAGEN-25253	Fix for RNA fusion call differences between 3.10.9 vs 3.10.12 PAX8-PPARG fusion recovery. Make the rna-gf-cleanup-shared-read filter less aggressive for paired reads.
RNA	DRAGEN-24640	AC016683.6;PAX8-PPARG fusion detection. Enable merge of intron with close-by exons in fusion breakpoint. Adjust intron bps to enable merging.
Somatic VC	DRAGEN-22841	MNV detection fails to detect events longer than 10BP when the SNV caller uses kmer length = 10 haplotype.
Somatic VC	DRAGEN-24258	Change the behavior of MNV output for TSO500. Instead of merging SNVs and only keeping MNVs, output both SNVs and MNVs in the final VCF. The info fields now contain the MNV group info, so that it is still possible to see if a SNV was part of a group.



Somatic VC	DRAGEN-22216	Ignore strand bias in agreeing mate pairs.
Somatic VC	DRAGEN-24893	Adjust VC pruning fraction settings for UMI solid and liquid, to rescue missing insertions.
System	DRAGEN-22328	Fix hang when DRAGEN assert on negative BCL input test.
System	DRAGEN-18840	Fix hang when PhenoHRD throws an exception.
RHEL8	DRAGEN-22634	Fix for networking becoming non-functional due to an issue with the DRAGEN DKMS install process updating to Oracle 8.6 (RHEL v8.6) or later, on a DRAGEN server.

## Known Issues

Known issues of the DRAGEN™ v3.10.14 release

Component/s	Defect ID	Issue Description	Remedy / Workaround
Amplicon	DRAGEN-16254	Excessive RNA Amplicon runtime on large samples	RNA Amplicon run time is very long when the coverage is significantly higher than expected for typical Amplicon samples
Paralog Caller	DRAGEN-19244	Hang on large number of alignments for same fragment	A hang on very high depth input when certain callers such as Paralog/CYP2D6/Expansion Hunter are run from BAM without map/align. The recommendation is to run these callers with map/align enabled.
Azure Cloud	DRAGEN-23138	Intermittent crashes when DRAGEN is streaming ORA input files from BLOB on Azure	Download input files locally before processing
BaseSpace	DRAGEN-18531	Downsampling does not allow expansion hunter launch when sample-sex is set to unknown	No workaround. Expansion Hunter requires a sample sex, user may not specify unknown. User can specify male/female or "auto" to autodetect. Downsampling does not work with "auto".
BCL	DRAGEN-20064	BCL convert aborts with an empty [BCLConvert_Data] section in v2 sample sheets	BCL convert aborts when there is empty [BCLConvert_Data] or [BCLConvert_Settings] sections in v2 sample sheets. Workaround, add entries to the sections.
BCL	DRAGEN-19323	BCL Strict Mode does not abort when *.bci lane file corrupted via truncation	No workaround. The strict mode check misses some input error modes.

BCL	DRAGEN-19292	BCL report fastq_list.csv contains incorrect file paths when ORA-interleaved compression format is used	No workaround. When "dragen-interleaved" compression format is used, the fastq_list.csv file contains two files (instead of one single interleaved file) under the "Read1File" and "Read2File" columns
BCL	DRAGEN-17015	Incorrect Error Message for Missing BCL Input Directory	Ignore the incorrect error message when --bcl-input-dir is missing
BCL	DRAGEN-16555	Minimum Adapter Overlap setting not working	Whether it's set to a valid or invalid value, an error message is displayed. No workaround
BCL	DRAGEN-15944	DRAGEN BCL logs insufficient warning when corrupt files supplied	In the rare event of a corrupt aggregated bcl. bgzf input file, the customer will correctly receive an error message of the lane and the cycle that is corrupted, but not the specific file name.
Biomarkers TMB	DRAGEN-20062	TMB accuracy failures in WES T/O	Nonsyn TMB metrics are not meeting requirements for Tumor-Only samples. No workaround
RNA Gene Fusion	DRAGEN-19957	DRAGEN Amplicon fails on an RNA sample	RNA samples may hang/fail when they are sequenced with extremely high depth. Workaround: Downsample to a reasonable depth. The added depth of excessive duplicates has no impact on accuracy
Compression	DRAGEN-10783	BAM input to DNA mapper: Deflate engine error: 0x9080 on stream 1	Extremely low repeatability. A re-run will pass
Dedup/UMI	DRAGEN-16412	Probabilistic UMI output is different from run to run	There is a run-run variation in the UMI probabilistic model. Non-prob model (non-random UMI) does not have run-to-run variation. The variation leads to ~2 reads being missing from output. This impact shall be a very small fraction.
DNA Alignment	DRAGEN-16468	Bam generated from file conversion CRAM -> BAM with hg19_alt_masked_v2 reference has invalid header	Reproducible issue that has been shown to have existed since v3.7 or earlier. When converting from CRAM to BAM using DRAGEN "file-conversion" method, the BAM has an invalid header due to a bug in the CRAM reader. No workaround. Re-header the file
DNA Alignment	DRAGEN-16467	Germline workflow is slower with graph hash table	DRAGEN run time is roughly 6.3% slower with graph aligner and graph reference is used, compared to non-graph. The increased run time is in both mapper and variant caller phases. No workaround



DNA Alignment	DRAGEN-16308	read trimmer adapter trimming sigabort during RecomputeTags::computeTags	Reproducible when running different read trimmers back-back. Workaround to run dragen_reset
DNA Alignment	DRAGEN-15151	Large run to run variation of mapper run time for EH	Up to 20% run time variation seen for mapper phase
Down sampling, UMI	DRAGEN-17082	When downsampling is used with UMIs via "enable-down-sampler=true", the BAM does not contain SA tags	No workaround. Issue is specific to the use case combination of UMI collapsing and use of down sampler.
Dup Marking	DRAGEN-16399	Assertion `pos < m_num_bits' failed, in Dupmark:: DupmarkTable::getDuplicates()	Crash in duplicate marking when there are more than 4G read pairs, which can happen when reads of multiple replicates are combined into one read group through manual BAM file editing. The system has a physical limit. Not a regression from prior releases
GVCF Genotyper	DRAGEN-17499	Empty msVCF output with whole contig gg-regions bed file	Empty output is produced when the gg-regions contain the whole chromosomes. Workaround is to drop whole regions from the regions bed file.
HW GRAPH	DRAGEN-13717	RNA VC hits ERROR: Invalid node flags	Issue is a HW graph error and rare (happens once every 6-9 months in routine VC testing). The assertion check / trap will remain in place so that invalid results will not be produced for end user. If seen in field, recommendation is to re-run sample as it is expected to pass.
Infra	DRAGEN-25358	dragen_hugepagctl conflicts with other programs that allocate hugepages	Drivers such as Infiniband requires hugepages, but conflicts with DRAGEN. dragen_hugepagectl script could be manually modified to reserve additional hugepages
Infra	DRAGEN-24514	DRAGEN hang after crash - generic issue	No workaround. DRAGEN can hang when a crash is encountered at a specific place software.
Infra	DRAGEN-23138	SIGBUS error when DRAGEN Streaming from ORA issue on Azure	No workaround. A SIGBUS error has been seen, root cause not identified.
Infra	DRAGEN-16498	AWS f1.4x   LICENSE_MSG   Challenge get token error: Get instance ID failed (Unable to retrieve AWS identity signature)	Timeout while retrieving AWS instance ID has been observed. The rate of occurrence has been too low to measure. This leads to failure in the licensing and DRAGEN job exits, run fails. Re-run would pass

Methyl-Seq	DRAGEN-15796	md5sum discordance b/w cloud and local runs	Impacts multi-pass mode and specific dataset. Single pass mode has been the recommended mode and does not have the issue. Multi-pass will be deprecated in future.
Metrics	DRAGEN-15950	A run-run variation in scRNA output	Some datasets have run-to-run variations in the mapping metrics Q30 metrics field. The issue affects only the metrics output and not the caller output
Nirvana, Somatic, BaseSpace	DRAGEN-19921	DRAGEN Somatic App – Redundant .annotated.json.gz files created with Nirvana enabled	Two identical files are produced. "hard-filtered.vcf.annotated.json.gz" and "hard-filtered.annotations.json.gz". One can be ignored.
Ora compr, UMI	DRAGEN-17533	Exception when using Ora inputs for map/align and Ora input for "--umi-source".	The "umi-source" option does not support Ora input. The workaround is to supply FASTQ file as "umi-source"
RNA Alignment	DRAGEN-18224	RNA VC FP resulting from inappropriate duplicate marking	No workaround. Observed false positive RNA variant calls in low quality FFPE samples, due to an issue in duplicate marking.
RNA Gene Fusion	DRAGEN-26197	Fusion detection is found to be heavily impacted by the background bias.	No workaround. For future improvement
RNA Gene Fusion	DRAGEN-23035	Fusion Call differences between Non-DRAGEN and DRAGEN TSO Software	No workaround. Some fusion call differences are observed between Non-DRAGEN and DRAGEN callers, which is a result of different aligners
RNA VC, Force GT	DRAGEN-18375	Native DRAGEN RNA VC fails with EFATAL: Caught signal Segmentation fault (11)	No workaround. A segfault has been observed in Force GT when RNA sample is processed with Force GT enabled in the variant calling
SNV Somatic	DRAGEN-19389	Variants not normalized in VCF	No workaround. For non-UMI modes, low call threshold introduces multi allelic calls that are not being normalized in the VCF
SNV Somatic	DRAGEN-18272	DRAGEN VCF index file doesn't match tabix and won't work with tabix to parse using regions "chr1"	No workaround. DRAGEN GVCF can produce a tabix index that won't work with tabix tool.
SNV VC	DRAGEN-16149	Germline MNV - phased calls with same PS and GT and within distance threshold are not getting combined into MNVs	Some phased calls are not getting combined into MNVs to MNV output. Full support for germline MNV is planned for a subsequent release



Somatic	DRAGEN-16319	Elevated SNP and INDEL FP on ICGC datasets	The impact of the issue is an elevated number of FPs for ICGC datasets in 3.10 compared to 3.9: a 5-6% increase in the SNP FPs and a 25%-30% increase in the INDEL FPs.
SV	DRAGEN-25620	Missing SV fusion calls when there are a high number of SV candidates	No workaround. Fusion recall degrade in samples with very high SV candidates (> 65k). Minimal impact for clinical samples.
SV	DRAGEN-24748	Nextera library prep artefacts gets called as intrachromosomal SV breakends in poor quality DNA samples	No workaround.
SV	DRAGEN-20127	PML-RARA fusion called as non-PASS even after contamination adjustment	Clinically actionable, orthogonally validated PML-RARA fusion in AML sample not called in tumour/normal analysis. Workaround: Tumour-in-normal contamination adjustment rescue the variant, but is non-PASS
Trimming	DRAGEN-19075 , SET-3449	Discrepancy of Adaptor Trimming between Fastq ToolKit and DRAGEN Fastq Toolkit	The commonly used 3' trimmers work as intended, but the hidden/rarely used 5' trimmers require their sequences be reversed.
UMI	DRAGEN-17082	When UMI is downsampled, the BAM does not have SA tag	No workaround. When running DRAGEN from fastq with downsampling, UMI collapsed BAM does not have Supplementary alignments (or SA tag)

## SW Installation Procedure

- Download the desired installer from the Illumina support website and unzip the package
- The archive integrity can be checked using: `./<DRAGEN 3.10.14 .run file> --check`
- Install the appropriate release based on your Linux OS with the command: `sudo sh <DRAGEN 3.10.14 .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



## Release History

Revision	Release Reference	Originator	Description of Change
00	CN 1087770	Cobus De Beer	Initial release