USER MANUAL

32 SAMPLES

Research Use Only Components of SOPHiA DDM™ Dx RNAtarget Oncology Solution

For Research Use Only (RUO)
Not for use in diagnostic procedures

SOPHiA GENETICS™

SUMMARY INFORMATION

Product Name	SOPHiA DDM™ Dx RNAtarget Oncology Solution, Research Use Only Components
Product Type	Bundle Solution
Product Family	Molecular kit + analytics
Algorithm ID	ILL1XGR1S2_FFPE_NextSeq
Sequencer	Illumina® - NextSeq® 550
Gene Panel ID	ROS_v1
Product Version	v1.0
Sample Type	RNA isolated from formalin-fixed, paraffin embedded (FFPE) tissue specimens
Release Version	1.0.0
Document ID	SG-08861
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RUO

PRODUCT CODES

	FULL PRODUCT CODE	BOX 1	BOX 2	LIBRARY PREPARATION KIT
REF	BS0119ILLCSRY07-32	B1.L1.0019.C-32	B2.0019.C-48	6C0233

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REVISION HISTORY

DOCUMENT ID/VERSION	DATE	DESCRIPTION OF CHANGE
SG-08861 -1.0	January 2026	• Initial Version

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1. GENERAL STATEMENT OF THE TEST PRINCIPLE(S)/ PROCEDURE

Fusion genes are important clinical biomarkers in oncology that guide diagnosis, inform prognosis, and support treatment decisions[1]. For example, up to 17% of solid tumors are characterized by gene fusions. Gene fusions are among the most successful targets of precision cancer medicine with many therapeutics targeting fusion proteins in routine clinical use. The most comprehensive way to detect fusions is using RNA-based Next Generation Sequencing (NGS) assays, which can detect novel and known fusion events.

The SOPHiA DDM™ Dx RNAtarget Oncology Solution (ROS) is an NGS-based test developed by SOPHiA GENETICS intended for the qualitative detection, annotation, and pre-classification of gene fusions or exon skipping events and incorporates a multi-gene panel appropriate for different solid tumor types. The product is intended for processing and analyzing RNA samples extracted from patient FFPE biopsy or surgical resection Lung Cancer tissue specimens. The NGS kit and protocol is designed for users to process 10 ng – 200 ng (recommended 50 ng) of RNA for NGS library construction, hybridization-based capture enrichment of 13 genes (as defined in the Intended Purpose), and sequencing using the Illumina® NextSeq® 550 platform.

The secure cloud-based SOPHiA DDM™ Dx mode, hosting a customized bioinformatics pipeline, allows the users to upload the NGS data and obtain a SOPHiA DDM™ Dx ROS Solution Report as a PDF. The report describes the detected fusion and exon skipping events in a sample, the sample quality score and status. Only the fusions events involved in the 11 target genes and the exon skipping events (MET ex14, EGFRvIII) in the 2 target genes defined in the Intended Purpose will be reported in the IVD Report. The list of transcripts involved in clinically relevant gene fusions are displayed in Table 1 below.

Table 1. List of transcripts involved in clinically relevant fusions

Gene	RefSeq ID	Gene	RefSeq ID	Gene	RefSeq ID
ALK	NM_004304	H4	NM_021624	PLAG1	NM_002655
ATIC	NM_004044	HIP1	NM_005338	PPFIBP1	NM_003622
BCR	NM_004327	HLA-A	NM_002116	PRKAR1A	NM_002734
C2orf22	NM_152391	HOOK3	NM_032410	PWWP2A	NM_001130864
CARS	NM_001014437	KIAA1598	NM_001127211	RANBP2	NM_006267
CCDC6	NM_005436	KIF5B	NM_004521	RET	NM_020975
CD74	NM_001025159	KLC1	NM_001394837	RNF213	NM_001256071
CLIP1	NM_001247997	KLK2	NM_005551	ROS1	NM_002944
CLTC	NM_004859	KTN1	NM_001079521	SDC4	NM_002999
CNTRL	NM_007018	LMNA	NM_170707	SEC31A	NM_001077207
DCTN1	NM_004082	LRIG3	NM_153377	SLC34A2	NM_006424
EGFR	NM_005228	MET	NM_000245	STRN	NM_003162
EML4	NM_019063	MSN	NM_002444	TFG	NM_006070
ERC1	NM_178040	MYO5A	NM_001382347	TP53	NM_000546
ETV6	NM_001987	NACC2	NM_144653	TPM3	NM_152263

Gene	RefSeq ID	Gene	RefSeq ID	Gene	RefSeq ID
EZR	NM_001111077	NCOA4	NM_001145263	TPM4	NM_003290
FGFR1	NM_023110	NPM1	NM_002520	TPR	NM_003292
FGFR2	NM_000141	NRG1	NM_013964	TRIM24	NM_015905
FGFR3	NM_000142	NSD1	NM_022455	TRIM27	NM_006510
FGFR4	NM_213647	NTRK1	NM_002529	TRIM33	NM_015906
FOP	NM_001111067	NTRK2	NM_006180	VCL	NM_014000
FRMD3	NM_174938	NTRK3	NM_001012338	ZCCHHC8	NM_017612
GOLGA5	NM_005113	PCM1	NM_006197	ZMYM2	NM_197968

This table is based on COSMIC[2] or ChimerDB databases[3], for which annotation is provided in the report. For any fusion involving a transcript outside of this list only genomic coordinates will be provided.

As further described in Appendix I, an additional Research Use Only (RUO) feature is available, i.e., a Quality (QA) Report, which includes quality metrics for each sample.

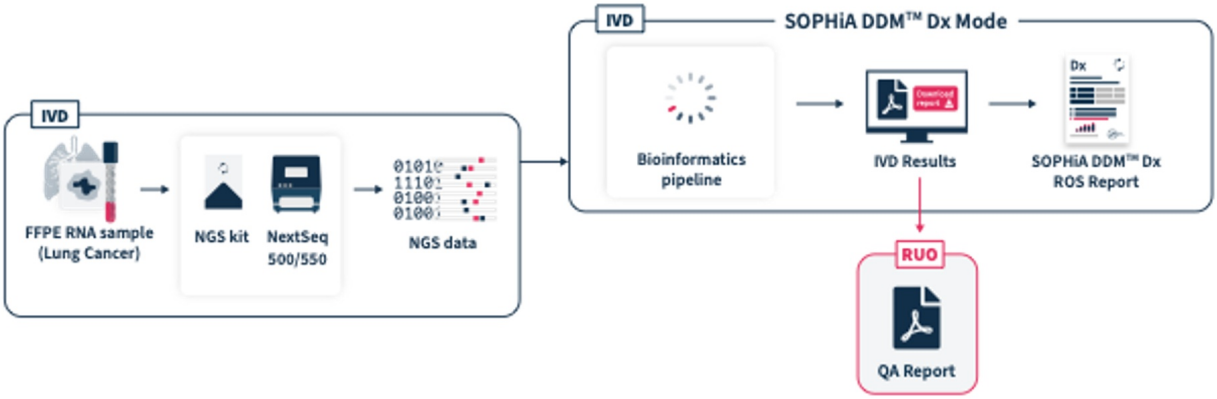
Note that the results of a genetic analysis should only be interpreted by a qualified expert in molecular genetics such as European registered Clinical Laboratory Geneticist (ErCLG) certified by the European Board of Medical Genetics (EBMG).

2. PRODUCT COMPONENTS

SOPHiA DDM™ Dx ROS is a complete solution that bundles the target enrichment kit with the analytical power of AI and is used in combination with an IVD accessory, the cloud-based SOPHiA DDM™ Dx mode. The product consists of two components: The library preparation and capture kit (SOPHiA GENETICS™ Dx RNA Library Prep Kit IV – 32 reactions) and the analytical bioinformatics pipeline used in combination with SOPHiA DDM™ Dx mode.

- The kit is composed of reagents and protocols to support the preparation and enrichment of targeted, Illumina®-compatible libraries from RNA extracted from Lung Cancer FFPE samples, suitable for enrichment and sequencing on an Illumina® NextSeq® 550 sequencer.
- The main purpose of the bioinformatics pipeline is to perform read filtering, alignment and fusion and exon skipping detection (secondary analysis) and annotation (tertiary analysis), to establish SOPHiA DDM™ Dx ROS fusion and exon skipping detection.
- SOPHiA DDM™ Dx mode hosts the bioinformatics pipeline and serves as the graphical user interface for the upload of Next-Generation Sequencing (NGS) sequencing data and the generation and download of the SOPHiA DDM™ Dx ROS Report. Refer to the SOPHiA DDM™ Dx mode User Manual for operational instructions.

Figure 1. Product Components Overview



SOPHiA DDM™ Dx ROS also includes the QA Report as Research Use Only (RUO). All details about the RUO features and results for SOPHiA DDM™ ROS RUO analyzes are available in this document.

3. ANALYSIS DESCRIPTION AND PARAMETERS

Quality (QA) Report

As a result of the analysis the user will have access to a QA Report where quality metrics computed for each sample are displayed. The subset of metrics particularly important for evaluating data quality include:

a. Original size (in megabytes) of the input fastq files.

b. Fastq file size after downsampling (if the original file size is above 200mb).

c. Percentage of uniquely mapped reads.

d. Percentage of reads mapping to the target regions. Target regions include exons outside of the scope of the IVD claims that are part of the product design.

e. Molecule coverage depth for all the genes in the panel. This includes genes outside of the scope of the IVD claims that are part of the product design.

f. Molecule coverage of the control gene.

4. LIMITATIONS, WARNINGS, AND PRECAUTIONS FOR RESEARCH USE ONLY APPLICATIONS

4.1 WARNINGS

- The additional features of the RNAtarget Technology (including, but not limited to, SNV/indel/delin detection, expression fold changes measurement, 5'-3' gene coverage imbalance) available via the desktop application Platform are for Research Use Only, and have not been validated for analytical performance. Not for use in diagnostic procedures.
- Any Research Use Only functionality is for information only and is not intended to be used for diagnosis. The RUO functions have not been fully validated within the scope of the IVD product. Using the RUO functions is up to the discretion of the clinician and will need to be assessed independently
- The data provided in the Quality Report (available for download from the SOPHiA DDM™ Dx mode Platform is for information only and is not intended to be used for diagnosis purposes.
- The content of the QA Report is not limited to metrics relevant to the IVD claims for this product.
- The section of the QA report containing the molecular coverage displays information for all genes included in the panel, which includes genes outside of the scope of the IVD claims.
- The percentage of reads mapped to the target region is based on a definition of target region that includes genes outside of the scope of the IVD claims.
- In the QA Report, only the metrics most relevant for the IVD scope of the product, listed in Section 13.1, were validated using simulated data.
- All metrics related to mapping and coverage are computed from the main bam file obtained by aligning the reads in paired mode. As the main bam files resulting from single- and paired-end alignments are not identical, subtle differences in the coverage and mapping rates are expected between the mapped reads used for fusion calling (using single-end alignment) and the rates reported in the QA Report.
- Low on-target rate (significantly below 70%) may be associated with low sample quality or technical problems when executing the capture workflow (e.g., omission of probe addition).
- High average group size values (>10 reads) might indicate sample quality issues or technical problems during workflow execution.

5. SYMBOLS

Symbol	Title
	Consult instructions for use
	Catalog number
	Batch code (Lot Number)
	Caution
	Manufacturer
	Temperature Limit
	Use-by date
	European Conformity
	Authorized Representative in the European Community
	Research Use Only
	Contains sufficient for <n> tests
	Importer
	Date of manufacture
	Refer to **Warnings and Precautions** in "Section 5. Kit Materials and Methods"
	Refer to **Warnings and Precautions** in "Section 5. Kit Materials and Methods"

6. SUPPORT

In case of difficulty using SOPHiA DDM™ Dx mode, please consult the troubleshooting section of the SOPHiA DDM™ Dx mode User Manual available on SOPHiA DDM™ Dx mode or contact our support line by telephone at +41 21 694 10 60 or e-mail support@sophiagenetics.com. Please visit www.sophiagenetics.com for further details. Support may also be reached via web request from the Dashboard screen in the Support section of SOPHiA DDM™ Dx mode.

Document Approvals

Approved Date: 29 Jan 2026

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