TruSight™ Oncology Comprehensive (EU)

Learn more about this CE-marked *in vitro* diagnostic, next-generation sequencing solution for comprehensive genomic profiling

As a global leader in next-generation sequencing (NGS) and microarray-based solutions, Illumina is dedicated to improving human health by unlocking the power of the genome. Illumina continues to innovate by offering TruSight Oncology Comprehensive (EU), a CE-marked *in vitro* diagnostic (IVD), pan-cancer comprehensive genomic profiling (CGP) panel. TruSight Oncology Comprehensive (EU) can generate a broad molecular profile of solid tumor patient samples, including formalin-fixed, paraffin-embedded (FFPE) tissue, maximizing a lab's ability to find actionable alterations that can help inform therapy decisions according to clinical guidelines.

With TruSight Oncology Comprehensive (EU), your laboratory can:

Generate a CGP report for a patient sample

- Detect DNA plus RNA variants and biomarkers signatures for multiple solid tumor types, generate a CGP report for a patient's tumor, and increase confidence in treatment decisions

Enable targeted therapies and clinical trials

- Leverage content that includes key biomarkers associated with drug labels, ESMO guidelines, and clinical trials for multiple solid tumor types
- Deliver results that inform therapy decisions according to clinical guidelines

Perform IVD testing in-house

- Implement a streamlined workflow, going from sample to report in 4–5 days
- Enable precision oncology testing while keeping data securely within your institution and eliminating the need for send-out services

About TruSight Oncology Comprehensive (EU)

- TruSight Oncology Comprehensive (EU) can be implemented easily in-house, features a streamlined workflow that proceeds from sample to report in 4–5 days, and requires as few as five FFPE slides
- The IVD test reliably detects all DNA and RNA variant categories, including single nucleotide variants (SNVs), insertions/deletions (indels), amplifications, fusions, and splice variants, and it enables analysis of the genomic signatures microsatellite instability (MSI) and tumor mutational burden (TMB)
- Illumina is advancing a companion diagnostic (CDx) roadmap with multiple indications linked to breakthrough therapies to improve patient outcomes

Frequently asked questions

Who is TruSight Oncology Comprehensive (EU) for?

TruSight Oncology Comprehensive (EU) is designed for molecular pathologists and lab directors who perform solid-tumor testing and provide results that guide oncologists in treatment decisions.

Types of institutions:

- Academic medical centers
- Large- to medium-sized hospitals
- Independent commercial laboratories

TruSight Oncology Comprehensive (EU) will be available in the following countries:

- Austria
- Belgium
- Bulgaria
- Cyprus
- Czech Republic
- Denmark
- Estonia
- Finland
- France
- Germany
- Greece
- Iceland
- Ireland
- Israel
- Italy
- Latvia
- Liechtenstein
- Lithuania
- Luxembourg
- Macedonia
- Malta
- Netherlands
- Norway
- Poland
- Portugal
- Qatar
- Romania
- Serbia
- Slovakia
- Slovenia
- South Africa
- Spain
- Sweden
- Switzerland
- United Arab Emirates
- United Kingdom

What are the IVD claims?

TruSight Oncology Comprehensive (EU) is an IVD test that uses targeted NGS to detect variants in 517 genes using nucleic acids extracted from FFPE tumor tissue samples from patients with solid malignant neoplasms using the Illumina NextSeq™ 550Dx Instrument. The test can be used to detect SNVs, multinucleotide variants, indels, and gene amplifications from DNA, and gene fusions and splice variants from RNA. The test also reports MSI status and a TMB score.

The test is intended as a CDx to identify patients with cancer for treatment with the targeted therapy listed in Table 1, in accordance with the approved therapeutic product labeling. In addition, the test is intended to provide tumor profiling information for use by qualified health care professionals in accordance with professional guidelines and is not conclusive or prescriptive for labeled use of any specific therapeutic product.

Table 1: CDx indication

Tumor type	Biomarkers	Targeted therapy
Solid tumors	*NTRK1*, *NTRK2*, *NTRK3* gene fusions	VITRAKVI® (larotrectinib)

Read the TruSight Oncology Comprehensive Package Insert to learn more.

What gene/biomarker content is included?

TruSight Oncology Comprehensive (EU) includes key biomarkers in clinical guidelines, drug labels, and clinical trials, across multiple solid tumor types and histologies (Table 2). Content includes small DNA variants (Table 3) as well as fusions (RNA), splice variants (RNA), amplifications (DNA), and complex genomic signatures (Table 4). These lists are based on content validated by Illumina.

Table 2: Subset of genomic tumor profiling biomarkers for multiple cancer types

Tumor type		Select genes with biomarkers of clinical significance[a]
	Pan-cancer	*BRAF, FGFR1, FGFR2, FGFR3,* MSI, *NTRK1, NTRK2, NTRK3, RET,* TMB
	Breast cancer	*AKT1, BRCA1, BRCA2, ERBB2, ESR1, PALB2, PIK3CA, PTEN*
	Colorectal cancer	*BRAF, ERBB2, KRAS, NRAS, POLE,* MSI
	Melanoma	*BRAF, KIT, NRAS*
	Non-small cell lung cancer	*ALK, BRAF, EGFR, ERBB2, KRAS, MET, NRG1, RET, ROS1*
	Ovarian cancer	*BRCA1, BRCA2*
	Pancreatic cancer	*BRCA1, BRCA2, KRAS, PALB2, NRG1*
	Prostate cancer	*ATM, BRCA1, BRCA2, PALB2, PTEN*

a. Genes with biomarkers of clinical significance linked to major oncology guidelines.

MSI, microsatellite instability; TMB, tumor mutational burden.

Table 3: TruSight Oncology Comprehensive (EU) panel content

Small variants: 517 genes (from DNA)											
ABL1	*BCORL1*	*CIC*	*EPHB1*	*FGF23*	*HIST1H3B*	*JUN*	*MLH1*	*PAK5*	*PRKAR1A*	*RYBP*	*TAF1*
ABL2	*BCR*	*COP1*	*ERBB2*	*FGFR1*	*HIST1H3C*	*KAT6A*	*MLLT3*	*PALB2*	*PRKCI*	*SDHA*	*TBX3*
ABRAXAS1	*BIRC3*	*CREBBP*	*ERBB3*	*FGFR2*	*HIST1H3D*	*KDM5A*	*MPL*	*PARP1*	*PRKDC*	*SDHAF2*	*TCF3*
ACVR1	*BLM*	*CRKL*	*ERBB4*	*FGFR3*	*HIST1H3E*	*KDM5C*	*MRE11*	*PAX3*	*PRKN*	*SDHB*	*TCF7L2*
ACVR1B	*BMPR1A*	*CRLF2*	*ERCC1*	*FGFR4*	*HIST1H3F*	*KDM6A*	*MSH2*	*PAX5*	*PRSS8*	*SDHC*	*TERC*
ADGRA2	*BRAF*	*CSF1R*	*ERCC2*	*FH*	*HIST1H3G*	*KDR*	*MSH3*	*PAX7*	*PTCH1*	*SDHD*	*TERT*
AKT1	*BRCA1*	*CSF3R*	*ERCC3*	*FLCN*	*HIST1H3H*	*KEAP1*	*MSH6*	*PAX8*	*PTEN*	*SETBP1*	*TET1*
AKT2	*BRCA2*	*CSNK1A1*	*ERCC4*	*FLI1*	*HIST1H3I*	*KEL*	*MST1*	*PBRM1*	*PTPN11*	*SETD2*	*TET2*
AKT3	*BRD4*	*CTCF*	*ERCC5*	*FLT1*	*HIST1H3J*	*KIF5B*	*MST1R*	*PDCD1*	*PTPRD*	*SH2D1A*	*TFE3*
ALK	*BRIP1*	*CTLA4*	*ERG*	*FLT3*	*HIST2H3A*	*KIT*	*MTOR*	*PDCD1LG2*	*PTPRS*	*SHQ1*	*TFRC*
ALOX12B	*BTG1*	*CTNNA1*	*ERRFI1*	*FLT4*	*HIST2H3C*	*KLF4*	*MUTYH*	*PDGFRA*	*PTPRT*	*SLIT2*	*TGFBR1*
AMER1	*BTK*	*CTNNB1*	*ESR1*	*FOXA1*	*HIST2H3D*	*KLHL6*	*MYB*	*PDGFRB*	*QKI*	*SLX4*	*TGFBR2*
ANKRD11	*CALR*	*CUL3*	*ETS1*	*FOXL2*	*HIST3H3*	*KMT2A*	*MYC*	*PDK1*	*RAB35*	*SMAD2*	*TMEM127*
ANKRD26	*CARD11*	*CUX1*	*ETV1*	*FOXO1*	*HNF1A*	*KRAS*	*MYCL*	*PDPK1*	*RAC1*	*SMAD3*	*TMPRSS2*
APC	*CASP8*	*CXCR4*	*ETV4*	*FOXP1*	*HNRNPK*	*LAMP1*	*MYCN*	*PGR*	*RAD21*	*SMAD4*	*TNFAIP3*
AR	*CBFB*	*CYLD*	*ETV5*	*FRS2*	*HOXB13*	*LATS1*	*MYD88*	*PHF6*	*RAD50*	*SMARCA4*	*TNFRSF14*
ARAF	*CBL*	*DAXX*	*ETV6*	*FUBP1*	*HRAS*	*LATS2*	*MYOD1*	*PHOX2B*	*RAD51*	*SMARCB1*	*TOP1*
ARFRP1	*CCND1*	*DCUN1D1*	*EWSR1*	*FYN*	*HSD3B1*	*LMO1*	*NAB2*	*PIK3C2B*	*RAD51B*	*SMARCD1*	*TOP2A*
ARID1A	*CCND2*	*DDR2*	*EZH2*	*GABRA6*	*HSP90AA1*	*LRP1B*	*NBN*	*PIK3C2G*	*RAD51C*	*SMC1A*	*TP53*
ARID1B	*CCND3*	*DDX41*	*FAM46C*	*GATA1*	*ICOSLG*	*LYN*	*NCOA3*	*PIK3C3*	*RAD51D*	*SMC3*	*TP63*
ARID2	*CCNE1*	*DHX15*	*FANCA*	*GATA2*	*ID3*	*LZTR1*	*NCOR1*	*PIK3CA*	*RAD52*	*SMO*	*TRAF2*
ARID5B	*CD274*	*DICER1*	*FANCC*	*GATA3*	*IDH1*	*MAGI2*	*NEGR1*	*PIK3CB*	*RAD54L*	*SNCAIP*	*TRAF7*
ASXL1	*CD276*	*DIS3*	*FANCD2*	*GATA4*	*IDH2*	*MALT1*	*NF1*	*PIK3CD*	*RAF1*	*SOCS1*	*TSC1*
ASXL2	*CD74*	*DNAJB1*	*FANCE*	*GATA6*	*IFNGR1*	*MAP2K1*	*NF2*	*PIK3CG*	*RANBP2*	*SOX10*	*TSC2*
ATM	*CD79A*	*DNMT1*	*FANCF*	*GEN1*	*IGF1*	*MAP2K2*	*NFE2L2*	*PIK3R1*	*RARA*	*SOX17*	*TSHR*
ATR	*CD79B*	*DNMT3A*	*FANCG*	*GID4*	*IGF1R*	*MAP2K4*	*NFKBIA*	*PIK3R2*	*RASA1*	*SOX2*	*U2AF1*
ATRX	*CDC73*	*DNMT3B*	*FANCI*	*GLI1*	*IGF2*	*MAP3K1*	*NKX2-1*	*PIK3R3*	*RB1*	*SOX9*	*VEGFA*
AURKA	*CDH1*	*DOT1L*	*FANCL*	*GNA11*	*IKBKE*	*MAP3K13*	*NKX3-1*	*PIM1*	*RBM10*	*SPEN*	*VHL*
AURKB	*CDK12*	*E2F3*	*FAS*	*GNA13*	*IKZF1*	*MAP3K14*	*NOTCH1*	*PLCG2*	*RECQL4*	*SPOP*	*VTCN1*
AXIN1	*CDK4*	*EED*	*FAT1*	*GNAQ*	*IL10*	*MAP3K4*	*NOTCH2*	*PLK2*	*REL*	*SPTA1*	*WISP3*
AXIN2	*CDK6*	*EGFL7*	*FBXW7*	*GNAS*	*IL7R*	*MAPK1*	*NOTCH3*	*PMAIP1*	*RET*	*SRC*	*WT1*
AXL	*CDK8*	*EGFR*	*FGF1*	*GPS2*	*INHA*	*MAPK3*	*NOTCH4*	*PMS1*	*RHEB*	*SRSF2*	*XIAP*
B2M	*CDKN1A*	*EIF1AX*	*FGF2*	*GREM1*	*INHBA*	*MAX*	*NPM1*	*PMS2*	*RHOA*	*STAG1*	*XPO1*
BAP1	*CDKN1B*	*EIF4A2*	*FGF3*	*GRIN2A*	*INPP4A*	*MCL1*	*NRAS*	*PNRC1*	*RICTOR*	*STAG2*	*XRCC2*
BARD1	*CDKN2A*	*EIF4E*	*FGF4*	*GRM3*	*INPP4B*	*MDC1*	*NRG1*	*POLD1*	*RIT1*	*STAT3*	*YAP1*
BBC3	*CDKN2B*	*ELOC*	*FGF5*	*GSK3B*	*INSR*	*MDM2*	*NSD1*	*POLE*	*RNF43*	*STAT4*	*YES1*
BCL10	*CDKN2C*	*EML4*	*FGF6*	*H3F3A*	*IRF2*	*MDM4*	*NTRK1*	*PPARG*	*ROS1*	*STAT5A*	*ZBTB2*
BCL2	*CEBPA*	*EMSY*	*FGF7*	*H3F3B*	*IRF4*	*MED12*	*NTRK2*	*PPM1D*	*RPS6KA4*	*STAT5B*	*ZBTB7A*
BCL2L1	*CENPA*	*EP300*	*FGF8*	*H3F3C*	*IRS1*	*MEF2B*	*NTRK3*	*PPP2R1A*	*RPS6KB1*	*STK11*	*ZFHX3*
BCL2L11	*CHD2*	*EPCAM*	*FGF9*	*HGF*	*IRS2*	*MEN1*	*NUP93*	*PPP2R2A*	*RPS6KB2*	*STK40*	*ZNF217*
BCL2L2	*CHD4*	*EPHA3*	*FGF10*	*HIST1H1C*	*JAK1*	*MET*	*NUTM1*	*PPP6C*	*RPTOR*	*SUFU*	*ZNF703*
BCL6	*CHEK1*	*EPHA5*	*FGF14*	*HIST1H2BD*	*JAK2*	*MGA*	*PAK1*	*PRDM1*	*RUNX1*	*SUZ12*	*ZRSR2*
BCOR	*CHEK2*	*EPHA7*	*FGF19*	*HIST1H3A*	*JAK3*	*MITF*	*PAK3*	*PREX2*	*RUNX1T1*	*SYK*	

Table 4: Additional content in TruSight Oncology Comprehensive (EU)

Fusions: 23 genes (from RNA)					
ALK	*EGFR*	*ETV1*	*FGFR3*	*NTRK2*	*RET*
AXL	*EML4*	*ETV4*	*KIF5B*	*NTRK3*	*ROS1*
BCL2	*ERG*	*FGFR1*	*NRG1*	*PAX3*	*TMPRSS2*
BRAF	*ESR1*	*FGFR2*	*NTRK1*	*RAF1*	
Splice variants: Two genes (from RNA)					
MET			*EGFR*		
Amplifications: Two genes (from DNA)					
ERBB2			*MET*		
Complex genomic signatures					
TMB			MSI		

What are the key attributes of the TruSight Oncology Comprehensive (EU) assay?

- Provides a kitted solution that can be implemented in-house by any lab
- Includes both DNA and RNA content and detects all variant classes, plus genomic signatures such as TMB and MSI; fusions are identified from RNA to maximize sensitivity for detection
- Enables CGP test results to be generated in only 4–5 days

How is TruSight Oncology Comprehensive (EU) different from current research use only (RUO) CGP assays, such as Oncomine Comprehensive Assay Plus RNA*?

As a CE-marked IVD test, TruSight Oncology Comprehensive (EU) is compliant with European IVD Directive (IVDD) requirements and is on course to comply with stricter IVD Regulation (IVDR) legislation; the IVD label provides labs with the benefits of IVDR preparedness and reduced liability risk, and enables easier implementation with significantly reduced test validation efforts, as compared to RUO assays.

- Illumina has built a pipeline through multiple pharmaceutical partnerships based on TruSight Oncology Comprehensive (EU), aiming to expand CDx claims
- Built on proven Illumina technology for library preparation, sequencing, and bioinformatics, TruSight Oncology Comprehensive (EU) delivers highly reliable data with maximum quality and accuracy. Its hybrid-capture library preparation enables full detection and characterization of fusion events, which are not possible with amplicon-based techniques (Figure 1)

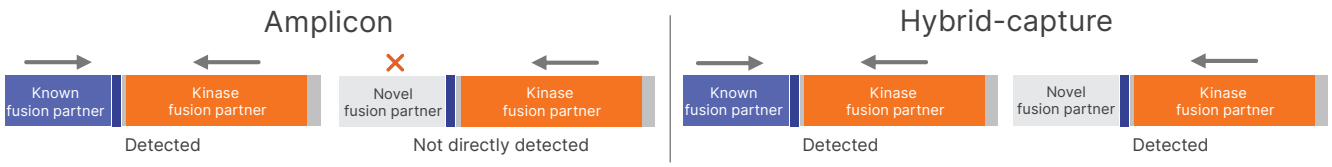

Figure 1: Hybrid–capture chemistry detects novel fusions missed by amplicon-based approaches

Amplicon-based approaches typically require confirmatory testing and do not characterize novel fusion partners. Hybrid–capture chemistry can identify both known and novel fusion partners.

* Thermo Fisher Scientific, Catalog no. A48578.

Workflow

What is the recommended sample input?

TruSight Oncology Comprehensive (EU) requires 40 ng RNA and/or 40 ng DNA extracted from FFPE tissue.

What are the workflow steps from sample preparation to final report?

The TruSight Oncology Comprehensive (EU) workflow includes four steps: sample acquisition and processing, DNA and RNA extraction, library preparation, and fully automated sequencing, analysis, and report generation (Figure 2).

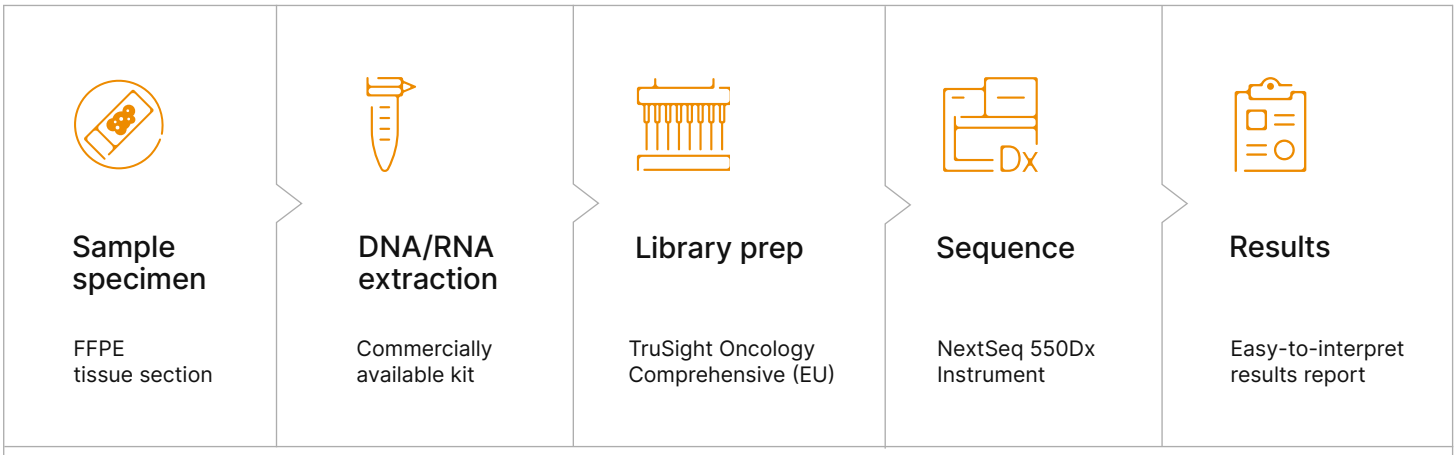

Figure 2: TruSight Oncology Comprehensive (EU) sample-to-report workflow.

Additional details:

- Specimen tissue should be fixed using formalin fixative suitable for molecular analyses; a minimum of 20% tumor cell content is recommended and ≥ 30% is optimal
- DNA and RNA extraction can be performed using commercially available extraction kits
- Library preparation takes approximately two days
- After loading the libraries on the NextSeq 550Dx instrument, the workflow is fully automated, including sequencing, base calling and QC, variant calling, interpretation, and generation of the final results report

How long is the turnaround time (TAT) from sample to report?

The TAT is 4–5 days from extracted DNA/RNA to the final results report.

What sequencing platform is needed?

TruSight Oncology Comprehensive (EU) is run on the NextSeq 550Dx instrument, an FDA-regulated and CE-marked, high-throughput sequencing platform.

What is the workflow for data analysis?

TruSight Oncology Comprehensive (EU) offers a streamlined, automated workflow from sequencing to final results report. Simply set up the sequencing run using Local Run Manager software. After the sequencing run is complete, secondary and tertiary analyses kickoff automatically and are performed on-instrument. The output is an easy-to-interpret results report.

What is the expected analysis time for a sample batch processed in a sequencing run?

The analysis time is 8–10 hours.

What is included in the final results report?

One of the key concerns when using a CGP panel is how to interpret the data and filter nonsignificant variants. TruSight Oncology Comprehensive (EU) software performs analysis and filtering as part of a fully automated workflow. The final report is easy to read and actionable.

Results Report

The Results Report is organized into two main sections (Figure 3):

1. Genomic findings with evidence of clinical significance:

Lists detected variants that have evidence of clinical significance (therapeutic, prognostic, or diagnostic) based on information in approved drug labels, guidelines, and clinical practice guidelines for the patient's tumor type.

2. Genomic findings with evidence of potential clinical significance:

Lists detected variants that:

- Have evidence of potential clinical significance (therapeutic, prognostic, or diagnostic) based on information in drug labels, guidelines, and clinical practice guidelines in another tumor type
- Match genomic and tumor type eligibility criteria for a clinical trial
- Have evidence of potential clinical significance in the primary literature for the patient's tumor type

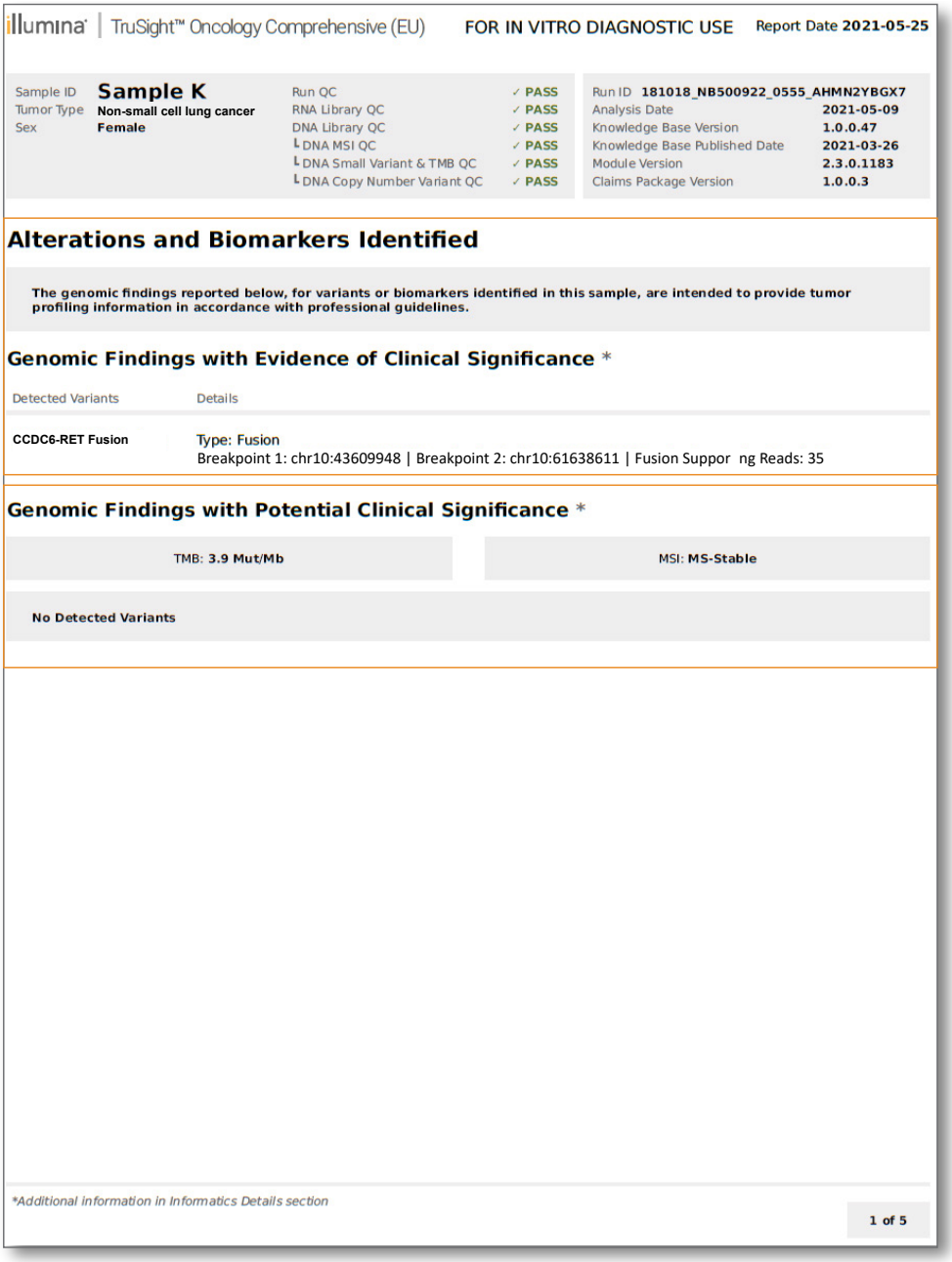

Figure 3: TruSight Oncology Comprehensive (EU) example results report

The results report includes genomic findings with evidence of clinical significance and genomic findings with evidence of potential clinical significance.

Reimbursement

What reimbursement is available for CGP tests in Europe? How does that vary by country?

National and/or regional funding is available in most Western European countries. Laboratory services are reimbursed depending on the country in which they are located, the clinical setting in which they operate, and the services they provide (Figure 4 and Table 5). Illumina has established a dedicated Market Access team that works with Payers to expand the reimbursement of CGP across Europe. In addition, Illumina is working to open access to CGP in various major European emerging markets. For further questions about the appropriate coding or reimbursement for cancer testing, customers are encouraged to:

- Consult their respective national medical society for guidance regarding managing reimbursement claims and refer to any national or regional budget holders (payers) for guidance on coding and reimbursemen (eg, national pathology societies)
- Contact their local Illumina representative, who can connect them with Illumina Market Access team. The team can provide guidance on where to find general reimbursement fee schedules, answer general reimbursement queries, or direct customers to key local institutions for further support†

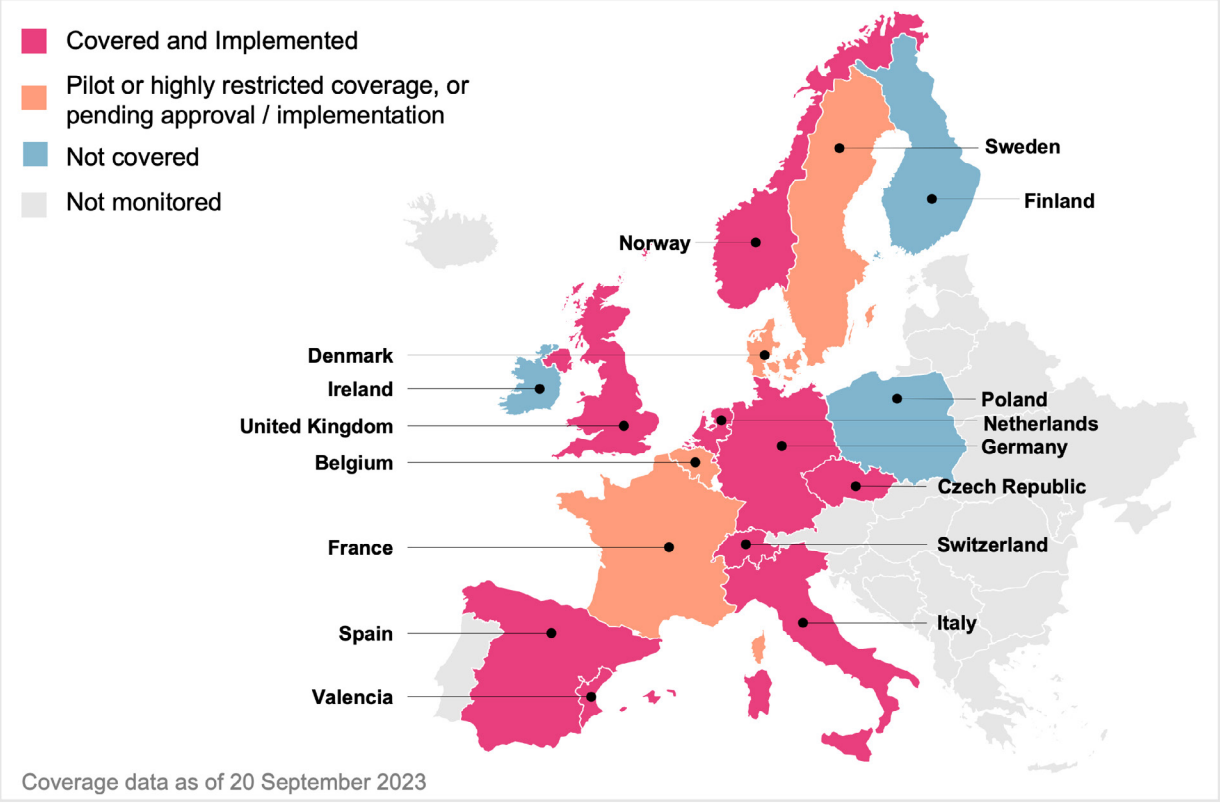

Figure 4: CGP test coverage options across Europe

† As a manufacturer of IVD products, Illumina cannot advise customers on which specific reimbursement codes to use when billing for TruSight Oncology Comprehensive (EU).

Table 5: Laboratory fee schedules

Country	Relevant fee schedules
Austria	Not applicable
Belgium	National Institute for Health and Disability Insurance
Denmark	Not applicable
England	National Genomic Test Directory
Finland	Not applicable
France	L'Assurance Maladie billing and remuneration
Germany	KBV Uniform Evaluation Standard
Israel	National Health Basket
Italy[a]	Italy: Rates for Hosipital and Outpatient Care
Netherlands[b]	Not applicable
Norway	Not applicable
Scotland	Not applicable
Spain[a]	Not applicable
Sweden	Not applicable
Switzerland	Federal Office of Public Health

a. For Italy, the national fee schedule is informative only; for Italy and Spain, coverage is defined at the regional level.
b. For the Netherlands, coverage is negotiated at the local level between hospitals and health insurers.
Not applicable indicates that no fee schedule is available; diagnostics are funded through global budget allocation to laboratory customers.

Learn more →

TruSight Oncology Comprehensive IVD Solutions

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