

Technical Specifications



Intended Use

FoundationOne Liquid CDx is a qualitative next generation sequencing based *in vitro* diagnostic test that uses targeted high throughput hybridization-based capture technology to detect and report substitutions, insertions and deletions (indels) in 311 genes, rearrangements in four (4) genes, and copy number alterations in three (3) genes. FoundationOne Liquid CDx utilizes circulating cell-free DNA (cfDNA) isolated from plasma derived from anti-coagulated peripheral whole blood of cancer patients collected in FoundationOne Liquid CDx cfDNA blood collection tubes included in the FoundationOne Liquid CDx Blood Sample Collection Kit. The test is intended to be used as a companion diagnostic to identify patients who may benefit from treatment with the targeted therapies listed in Table 1 in accordance with the approved therapeutic product labeling.

Table 1: Companion diagnostic indications

TUMOR TYPE	BIOMARKER(S) DETECTED	THERAPY
Non-small cell lung cancer (NSCLC)	<i>ALK</i> rearrangements	ALECENSA® (alectinib)
	<i>EGFR</i> Exon 19 deletions and <i>EGFR</i> Exon 21 L858R substitution	IRESSA® (gefitinib) TAGRISSO® (osimertinib) TARCEVA® (erlotinib)
	<i>MET</i> single nucleotide variants (SNVs) and indels that lead to <i>MET</i> exon 14 skipping	TABRECTA® (capmatinib)
Prostate cancer	<i>BRCA1</i> , <i>BRCA2</i> , <i>ATM</i> alterations	LYNPARZA® (olaparib)
	<i>BRCA1</i> , <i>BRCA2</i> alterations	RUBRACA® (rucaparib)
Ovarian cancer	<i>BRCA1</i> , <i>BRCA2</i> alterations	RUBRACA® (rucaparib)
Breast cancer	<i>PIK3CA</i> mutations C420R, E542K, E545A, E545D [1635G>T only], E545G, E545K, Q546E, Q546R; and H1047L, H1047R, and H1047Y	PIQRAY® (alpelisib)

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Additionally, FoundationOne Liquid CDx is intended to provide tumor mutation profiling to be used by qualified health care professionals in accordance with professional guidelines in oncology for patients with solid malignant neoplasms. A negative result from a plasma specimen does not mean that the patient's tumor is negative for genomic findings. Patients with the tumor types above who are negative for the mutations listed in Table 1 should be reflexed to routine biopsy and their tumor mutation status confirmed using an FDA-approved tumor tissue test, if feasible. Genomic findings other than those listed in Table 1 are not prescriptive or conclusive for labeled use of any specific therapeutic product. FoundationOne Liquid CDx is a single-site assay performed at Foundation Medicine, Inc. in Cambridge, MA.



Summary of Analytical Sensitivity and Specificity for FDA-Approved Content

Results from our Limit of Detection (LoD) study are shown below, indicating the median variant allele frequency or tumor fraction at which the test has shown 95% probability of detection.¹ Results are also included from the Limit of Blank (LoB) study, which evaluated variant calling in healthy donors. Please refer to our product labeling for a list of the 75 genes baited for enhanced sensitivity are noted in bold in the gene list on the next page.

ALTERATION TYPE	BAIT SET REGION	MEDIAN LIMIT OF DETECTION (LOD)	LOD RANGE QUANTILE 1-3*	LIMIT OF BLANK (VARIANT DETECTION RATE IN HEALTHY DONORS) [†]
Short Variants	Enhanced Sensitivity	0.40% VAF	0.33% - 0.50% VAF	0.82%
	Standard Sensitivity	0.82% VAF	0.70% - 0.98% VAF	
Rearrangements	Enhanced Sensitivity	0.37% VAF	0.26% - 0.47% VAF	0%
	Standard Sensitivity	0.90% VAF	NA	
Copy Number Amplifications	NA	21.7% TF	19.8%-25.2% TF	0%

VAF = variant allele frequency; TF = tumor fraction

* The accuracy of %VAF / %TF have not been analytically validated

† Calculated as the number of unique variants detected at least once across all replicates divided by the total number of unique variants included in the analysis



FoundationOne Liquid CDx FDA-Approved Gene List[‡]

As part of its FDA-approved intended use, FoundationOne Liquid CDx interrogates 311 genes, including 309 genes with complete exonic (coding) coverage and 2 genes with only select non-coding coverage (indicated with *). **Select genes and select exons (indicated in bold)** are captured with increased sensitivity.

ABL1 Exons 4-9	ACVR1B	AKT1 Exon 3	AKT2	AKT3	ALK Exons 20-29, Introns 18, 19	ALOX12B
AMER1 (FAM123B)	APC	AR	ARAF Exons 4, 5, 7, 11, 13, 15, 16	ARFRP1	ARID1A	ASXL1
ATM	ATR	ATRX	AURKA	AURKB	AXIN1	AXL
BAP1	BARD1	BCL2	BCL2L1	BCL2L2	BCL6	BCOR
BCORL1	BRAF Exons 11-18	BRCA1 Introns 2, 7, 8, 12, 16, 19, 20	BRCA2 Intron 2	BRD4	BRIP1	BTG1
BTG2	BTK Exons 2, 15	C11orf30 (EMSY)	C17orf39 (GID4)	CALR	CARD11	CASP8
CBFB	CBL	CCND1	CCND2	CCND3	CCNE1	CD22
CD274 (PD-L1)	CD70	CD79A	CD79B	CDC73	CDH1	CDK12
CDK4	CDK6	CDK8	CDKN1A	CDKN1B	CDKN2A	CDKN2B
CDKN2C	CEBPA	CHEK1	CHEK2	CIC	CREBBP	CRKL
CSF1R	CSF3R	CTCF	CTNNA1	CTNNB1 Exon 3	CUL3	CUL4A
CXCR4	CYP17A1	DAXX	DDR1	DDR2 Exons 5, 17, 18	DIS3	DNMT3A
DOT1L	EED	EGFR	EP300	EPHA3	EPHB1	EPHB4
ERBB2	ERBB3 Exons 3, 6, 7, 8, 10, 12, 20, 21, 23, 24, 25	ERBB4	ERCC4	ERG	ERRFI1	ESR1 Exons 4-8
EZH2 Exons 4, 16, 17, 18	FAM46C	FANCA	FANCC	FANCG	FANCL	FAS
FBXW7	FGF10	FGF12	FGF14	FGF19	FGF23	FGF3
FGF4	FGF6	FGFR1	FGFR2	FGFR3 Exons 7, 9 (alternative designation exon 10), 14, 18	FGFR4	FH
FLCN	FLT1	FLT3 Exons 14, 15, 20	FOXL2	FUBP1	GABRA6	GATA3
GATA4	GATA6	GNAI1 Exons 4, 5	GNAI3	GNAQ Exons 4, 5	GNAS Exons 1, 8	GRM3
GSK3B	H3F3A	HDAC1	HGF	HNF1A	HRAS Exons 2, 3	HSD3B1
ID3	IDH1 Exon 4	IDH2 Exon 4	IGF1R	IKBKE	IKZF1	INPP4B
IRF2	IRF4	IRS2	JAK1	JAK2 Exons 14	JAK3 Exons 5, 11, 12, 13, 15, 16	JUN
KDM5A	KDM5C	KDM6A	KDR	KEAP1	KEL	KIT Exons 8, 9, 11, 12, 13, 17
KLHL6	KMT2A (MLL)	KMT2D (MLL2)	KRAS	LTK	LYN	MAF
MAP2K1 (MEK1) Exons 2, 3	MAP2K2 (MEK2) Exons 2-4, 6, 7	MAP2K4	MAP3K1	MAP3K13	MAPK1	MCL1
MDM2	MDM4	MED12	MEF2B	MEN1	MERTK	MET
MITF	MKNK1	MLH1	MPL Exon 10	MRE11A	MSH2	MSH3
MSH6	MST1R	MTAP	MTOR Exons 19, 30, 39, 40, 43-45, 47, 48, 53, 56	MUTYH	MYC	MYCL (MYCL1)
MYCN	MYD88 Exon 4	NBN	NF1	NF2	NFE2L2	NFKBIA
NKX2-1	NOTCH1	NOTCH2	NOTCH3	NPM1 Exons 4-6, 8, 10	NRAS Exons 2, 3	NSD3 (WHSC1L)
NT5C2	NTRK1 Exons 14, 15	NTRK2	NTRK3 Exons 16, 17	P2RY8	PALB2	PARK2
PARP1	PARP2	PARP3	PAX5	PBRM1	PCD1 (PD-1)	PCD1LG2 (PD-L2)
PDGFRA Exons 12, 18	PDGFRB Exons 12-21, 23	PDK1	PIK3C2B	PIK3C2G	PIK3CA Exons 2, 3, 5-8, 10, 14, 19, 21 (Coding Exons 1, 2, 4-7, 9, 13, 18, 20)	PIK3CB
PIK3R1	PIM1	PMS2	POLD1	POLE	PPARG	PPP2R1A
PPP2R2A	PRDM1	PRKAR1A	PRKCI	PTCH1	PTEN	PTPN11
PTPRO	QKI	RAC1	RAD21	RAD51	RAD51B	RAD51C
RAD51D	RAD52	RAD54L	RAF1 Exons 3, 4, 6, 7, 10, 14, 15, 17	RARA	RB1	RBM10
REL	RET Exons 11, 13-16	RICTOR	RNF43	ROS1 Exons 31, 36-38, 40	RPTOR	SDHA
SDHB	SDHC	SDHD	SETD2	SF3B1	SGK1	SMAD2
SMAD4	SMARCA4	SMARCB1	SMO	SNCAIP	SOC3	SOX2
SOX9	SPEN	SPOP	SRC	STAG2	STAT3	STK11
SUFU	SYK	TBX3	TEK	TERC* ncRNA	TERT* Promoter	TET2
TGFBR2	TIPARP	TNFAIP3	TNFRSF14	TP53	TSC1	TSC2
TYRO3	U2AF1	VEGFA	VHL	WHSC1	WT1	XPO1
XRCC2	ZNF217	ZNF703				



Summary of Analytical Sensitivity and Specificity for Professional Services Content

Results from our Limit of Detection (LoD) study are shown below, indicating the median variant allele frequency, tumor fraction or unstable loci at which the test has shown 95% probability of detection.² Please refer to our product labeling for a list of the 75 genes baited for enhanced sensitivity and complete product specifications.

ALTERATION TYPE	MEDIAN LIMIT OF DETECTION (LOD)
MSI	0.8% Unstable loci
bTMB (component indels)	1.00% VAF*
bTMB (component subs)	1.00% VAF*

VAF = variant allele frequency; TF = tumor fraction

* The accuracy of %VAF / %TF have not been analytically validated

In our Limit of Blank study, which evaluated variant calling in healthy donors, 1,735 unique variants were included in the analysis for a total of 137,065 data points. A total of 18 false positives were observed across 4 unique short variants. The LoB was determined to be the ideal value of zero for short variants, rearrangements and CNAs. The false positive rate was shown to be 0% for rearrangements and CNAs and 0.013% (~1 in 8,000) for short variants (substitutions and indels).²



Information Provided as a Professional Service

As a professional service, FoundationOne Liquid CDx interrogates 324 genes, including 309 genes with complete exonic (coding) coverage and 15 genes with only select non-coding coverage (indicated with an *); **75 genes (indicated in bold)** are captured with increased sensitivity and have complete exonic (coding) coverage unless otherwise noted. The test also detects tumor fraction and the genomic signatures blood mutational burden (bTMB) and microsatellite instability high (MSI-H) status.

ABL1 Exons 4-9	ACVR1B	AKT1 Exon 3	AKT2	AKT3	ALK Exons 20-29, Introns 18, 19	ALOX12B
AMER1 (FAM123B)	APC	AR	ARAF Exons 4, 5, 7, 11, 13, 15, 16	ARFRP1	ARID1A	ASXL1
ATM	ATR	ATRX	AURKA	AURKB	AXIN1	AXL
BAP1	BARD1	BCL2	BCL2L1	BCL2L2	BCL6	BCOR
BCORL1	BCR* Introns 8, 13, 14	BRAF Exons 11-18, Introns 7-10	BRCA1 Introns 2, 7, 8, 12, 16, 19, 20	BRCA2 Intron 2	BRD4	BRIP1
BTG1	BTG2	BTK Exons 2, 15	C11orf30 (EMS1)	C17orf39 (GID4)	CALR	CARD11
CASP8	CBFB	CBL	CCND1	CCND2	CCND3	CCNE1
CD22	CD70	CD74* Introns 6-8	CD79A	CD79B	CD274 (PD-L1)	CDC73
CDH1	CDK12	CDK4	CDK6	CDK8	CDKN1A	CDKN1B
CDKN2A	CDKN2B	CDKN2C	CEBPA	CHEK1	CHEK2	CIC
CREBBP	CRKL	CSF1R	CSF3R	CTCF	CTNNA1	CTNNB1 Exon 3
CUL3	CUL4A	CXCR	CYP17A1	DAXX	DDR1	DDR2 Exons 5, 17, 18
DIS3	DNMT3A	DOT1L	EED	EGFR Introns 7, 15, 24-27	EP300	EPHA3
EPHB1	EPHB4	ERBB2	ERBB3 Exons 3, 6, 7, 8, 10, 12, 20, 21, 23, 24, 25	ERBB4	ERCC4	ERG
ERRF1	ESR1 Exons 4-8	ETV4* Intron 8	ETV5* Introns 6, 7	ETV6* Introns 5, 6	EWSR1* Introns 7-13	EZH2 Exons 4, 16, 17, 18
EZR* Introns 9-11	FAM46C	FANCA	FANCC	FANCG	FANCL	FAS
FBXW7	FGF10	FGF12	FGF14	FGF19	FGF23	FGF3
FGF4	FGF6	FGFR1 Introns 1, 5, Intron 17	FGFR2 Intron 1, Intron 17	FGFR3 Exons 7, 9 (alternative designation exon 10), 14, 18, Intron 17	FGFR4	FH
FLCN	FLT1	FLT3 Exons 14, 15, 20	FOXL2	FUBP1	GABRA6	GATA3
GATA4	GATA6	GNAI1 Exons 4, 5	GNAI3	GNAQ Exons 4, 5	GNAS Exons 1, 8	GRM3
GSK3B	H3F3A	HDAC1	HGF	HNF1A	HRAS Exons 2, 3	HSD3B1
ID3	IDH1 Exon 4	IDH2 Exon 4	IGF1R	IKBKE	IKZF1	INPP4B
IRF2	IRF4	IRS2	JAK1	JAK2 Exon 14	JAK3 Exons 5, 11, 12, 13, 15, 16	JUN
KDM5A	KDM5C	KDM6A	KDR	KEAP1	KEL	KIT Exons 8, 9, 11, 12, 13, 17, Intron 16
KLHL6	KMT2A (MLL) Introns 6, 8-11, Intron 7	KMT2D (MLL2)	KRAS	LTK	LYN	MAF

(Information Provided as a Professional Service Continued)

MAP2K1 (MEK1) Exons 2, 3	MAP2K2 (MEK2) Exons 2-4, 6, 7	MAP2K4	MAP3K1	MAP3K13	MAPK1	MCL1
MDM2	MDM4	MED12	MEF2B	MEN1	MERTK	MET
MITF	MKNK1	MLH1	MPL Exon 10	MRE11A	MSH2 Intron 5	MSH3
MSH6	MST1R	MTAP	MTOR Exons 19, 30, 39, 40, 43-45, 47, 48, 53, 56	MUTYHMYB* Intron 14	MYC Intron 1	
MYCL (MYCL1)	MYCN	MYD88 Exon 4	NBN	NF1	NF2	NFE2L2
NFKBIA	NKX2-1	NOTCH1	NOTCH2 Intron 26	NOTCH3	NPM1 Exons 4-6, 8, 10	NRAS Exons 2, 3
NSD3 (WHSC1L1)	NT5C2	NTRK1 Exons 14, 15, Introns 8-11	NTRK2 Intron 12	NTRK3 Exons 16, 17	NUTM1* Intron 1	P2RY8
PALB2	PARK2	PARP1	PARP2	PARP3	PAX5	PBRM1
PDCC1 (PD-1)	PDCC1LG2 (PD-L2)	PDGFRA Exons 12, 18, Introns 7, 9, 11	PDGFRB Exons 12-21, 23	PDK1	PIK3C2B	PIK3C2G
PIK3CA Exons 2, 3, 5-8, 10, 14, 19, 21 (Coding Exons 1, 2, 4-7, 9, 13, 18, 20)	PIK3CB	PIK3R1	PIM1	PMS2	POLD1	POLE
PPARG	PPP2R1A	PPP2R2A	PRDM1	PRKAR1A	PRKCI	PTCH1
PTEN	PTPN11	PTPRO	QKI	RAC1	RAD21	RAD51
RAD51B	RAD51C	RAD51D	RAD52	RAD54L	RAF1 Exons 3, 4, 6, 7, 10, 14, 15, 17, Introns 4-8	RARA Intron 2
RB1	RBM10	REL	RET Introns 7, 8, Exons 11, 13-16, Introns 9-11	RICTOR	RNF43	ROS1 Exons 31, 36-38, 40, Introns 31-35
RPTOR	RSPO2* Intron 1	SDC4* Intron 2	SDHA	SDHB	SDHC	SDHD
SETD2	SF3B1	SGK1	SLC34A2* Intron 4	SMAD2	SMAD4	SMARCA4
SMARCB1	SMO	SNCAIP	SOCS1	SOX2	SOX9	SPEN
SPOP	SRC	STAG2	STAT3	STK11	SUFU	SYK
TBX3	TEK	TERC* ncRNA	TERT* Promoter	TET2	TGFB2	TIPARP
TMPRSS2* Introns 1-3	TNFAIP3	TNFRSF14	TP53	TSC1	TSC2	TYRO3
U2AF1	VEGFA	VHL	WHSC1	WT1	XPO1	XRCC2
ZNF217	ZNF703					

† Current as of July 2021. Please visit foundationmedicine.com for the most up-to-date gene list.

FoundationOne®CDx and FoundationOne®Liquid CDx are qualitative next-generation sequencing based in vitro diagnostic tests for advanced cancer patients with solid tumors and are for prescription use only. FoundationOne CDx utilizes FFPE tissue and analyzes 324 genes as well as genomic signatures. FoundationOne Liquid CDx analyzes 324 genes utilizing circulating cell-free DNA and is FDA-approved to report short variants in 311 genes. The tests are companion diagnostics to identify patients who may benefit from treatment with specific therapies in accordance with the therapeutic product labeling. Additional genomic findings may be reported and are not prescriptive or conclusive for labeled use of any specific therapeutic product. Use of the tests does not guarantee a patient will be matched to a treatment. A negative result does not rule out the presence of an alteration. Some patients may require a biopsy for testing with FoundationOne CDx when archival tissue is not available which may pose a risk. Patients who are tested with FoundationOne Liquid CDx and are negative for companion diagnostic mutations should be reflexed to tumor tissue testing and mutation status confirmed using an FDA-approved tumor tissue test, if feasible. For the complete label, including companion diagnostic indications and important risk information, please visit www.FICDxLabel.com and www.FILCDxLabel.com.

References:

1. FoundationOne Liquid CDx Technical Information. For full label refer to www.FILCDxLabel.com
2. Data on File, Foundation Medicine, Inc., 2020

