Technical Specifications

FOUNDATIONONE®LIQUID CDx

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, including rearrangements and copy number losses only in *BRCA1* and *BRCA2*. 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. Additionally, FoundationOne Liquid CDx is intended to provide tumor mutation profiling for substitutions and indels to be used by qualified health care professionals in accordance with professional guidelines in oncology for patients with solid malignant neoplasms.

Table 1: Companion diagnostic indications

TUMOR TYPE	BIOMARKER(S) DETECTED	THERAPY
Non-Small Cell Lung Cancer (NSCLC)	*EGFR* exon 19 deletions and *EGFR* exon 21 L858R subsitution	IRESSA® (gefitinib), TAGRISSO® (osimertinib) or TARCEVA® (erlotinib)
Prostate Cancer	*BRCA1, BRCA2* alterations	Rubraca® (rucaparib)

A negative result from a plasma specimen does not mean that the patient's tumor is negative for genomic findings. Patients 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 and complete product specifications.

ALTERATION TYPE	BAIT SET REGION	MEDIAN LIMIT OF DETECTION (LOD)	LOD RANGE QUARTILE 1-3	LIMIT OF BLANK (VARIANT DETECTION RATE IN HEALTHY DONORS)[1]
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 Losses	NA	30.4% TF	NA	0%

VAF = variant allele frequency; TF = tumor fraction

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

[1] 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 Gene List →

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]
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
GNA11
[Exons 4,5]
GNA13
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 (WHSC1L1)
NT5C2
NTRK1
[Exons 14,15]
NTRK2
NTRK3
[Exons 16,17]
P2RY8
PALB2
PARK2
PARP1
PARP2
PARP3
PAX5
PBRM1
PDCD1 (PD-1)
PDCD1LG2 (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
SOCS1
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	BAIT SET REGION	MEDIAN LIMIT OF DETECTION (LOD)
Copy Number Amplification	NA	21.7% TF
MSI	NA	0.8% Unstable loci
bTMB (component indels)	NA	1.00% VAF
bTMB (component subs)	NA	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 microsaetellitle 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 (EMSY)
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
CXCR4
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
ERRFI1
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
GATA6
GNA11 ***[Exons 4, 5]***
GNA13
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
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]***
MUTYH
*MYB** *[Intron 14]*
MYC ***[Intron 1]***
MYCL (MYCL1)
MYCN
MYD88 ***[Exon 4]***

Professional Service Gene List continued →

(Information Provided as a Professional Service Continued)

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

PDCD1 (PD-1)

PDCD1LG2 (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

TGFBR2

TIPARP

*TMPRSS2**
[Introns 1-3]

TNFAIP3

TNFRSF14

TP53

TSC1

TSC2

TYRO3

U2AF1

VEGFA

VHL

WHSC1

WT1

XPO1

XRCC2

ZNF217

ZNF703

† Visit foundationmedicine.com to create an online account. ‡ Current as of August 2020. Please visit foundationmedicine.com for the most up-to-date gene list.

References:
1. FoundationOne Liquid CDx Technical Information. For full label refer to www.F1LCDxLabel.com
2. Data on File, Foundation Medicine, Inc., 2020

FoundationOne®Liquid CDx is for prescription use only and is a qualitative next-generation sequencing based *in vitro* diagnostic test for advanced cancer patients with solid tumors. The test analyzes 324 genes utilizing circulating cell-free DNA and is FDA-approved to report short variants in 311 genes and as a companion diagnostic to identify patients who may benefit from treatment with specific therapies (listed in Table 1 of the Intended Use) in accordance with the approved 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 test does not guarantee a patient will be matched to a treatment. A negative result does not rule out the presence of an alteration. Patients who 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 complete risk information, please visit www.F1LCDxLabel.com.

FOUNDATION MEDICINE®

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