Technical Specifications

FOUNDATIONONE®LIQUID CDx

Intended Use

FoundationOne® Liquid CDx is a next generation sequencing based in vitro diagnostic device that analyzes 324 genes. Substitutions and insertion and deletion alterations (indels) are reported in 311 genes, copy number alterations (CNAs) are reported in 310 genes, and gene rearrangements are reported in 324 genes. The test also detects tumor fraction and the genomic signatures blood tumor mutational burden (bTMB) and microsatellite instability high (MSI-H) status. FoundationOne® Liquid CDx utilizes circulating cell-free DNA (cfDNA) isolated from plasma derived from the anti-coagulated peripheral whole blood of cancer patients. The test is intended to be used as a companion diagnostic to identify patients who may benefit from treatment with targeted therapies in accordance with the approved therapeutic product labeling. 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 malignant neoplasms.

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 genomic findings should be reflexed to routine biopsy and their tumor mutation status confirmed using an FDA-approved tumor tissue test, if feasible.

Summary of Analytical Sensitivity and Specificity[1]

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. 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)
Short Variants	Enhanced Sensitivity	0.40% VAF
	Standard Sensitivity	0.82% VAF
Rearrangements	Enhanced Sensitivity	0.37% VAF
	Standard Sensitivity	0.90% VAF
Copy Number Amplification	NA	21.7% TF
Copy Number Loss	NA	30.4% 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).

FoundationOne® Liquid CDx Gene List[1]

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 (EMSY)
C17orf39 (GID4)
CALR
CARD11
CASP8
CBFB
CBL
CCND1
CCND2
CCND3
CCNE1
CD22

FoundationOne® Liquid CDx Gene List continued →

(FoundationOne® Liquid CDx Gene List continued)

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

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]

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

1. Data on file M-GB-00001408

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medinfo.uk@roche.com 0800 3281629
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