# 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.

FoundationOne® Liquid CDx is a single-site assay performed at Foundation Medicine, Inc. in Cambridge, MA.

## 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

FOUNDATION MEDICINE®



Roche Products Limited
Hexagon Place, 6 Falcon Way, Shire Park, Welwyn Garden City, Hertfordshire AL7 1TW,
Registered in England 100674
medinfo.uk@roche.com 0800 3281629
Roche Products Limited is the sole licensed distributor of Foundation Medicine, Inc. products in the UK

M-GB-00000169 Date of Preparation September 2020