ASSAY SPECIFICATIONS
FOR

FOUNDATIONONE LIQUID CDX

(SPEC-0004, VER. 04)

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1. Intended Use

FoundationOne Liquid CDx (F1 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 (MSI). F1 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, F1 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.

2. Device Description

The F1 Liquid CDx assay is performed exclusively as a laboratory service using circulating cfDNA isolated from plasma derived from anti-coagulated peripheral whole blood from patients with solid malignant neoplasms. The assay employs a single DNA extraction method to obtain cfDNA from plasma from whole blood. Extracted cfDNA undergoes whole-genome shotgun library construction and hybridization-based capture of 324 cancer-related genes. All coding exons of 309 genes are targeted; select intronic or non-coding regions are targeted in 21 of these genes. Additionally, select intronic or non-coding regions only are targeted in 15 genes (refer to **Table 1** for the complete list of genes targeted by F1 Liquid CDx). Hybrid-capture selected libraries are sequenced with deep coverage using the Illumina NovaSeq® 6000 platform. Sequence data are processed using a custom analysis pipeline designed to accurately detect genomic alterations, including base substitutions, indels, select copy number variants, and select genomic rearrangements. The assay detects substitutions and indels in a total of 311 genes, copy number alterations in 310 genes, and genomic rearrangements in 324 genes. The assay also detects tumor fraction and genomic signatures including MSI and bTMB. A subset of targeted regions in 75 genes is baited for increased sensitivity (**Table 1**).

Table 1: F1 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.

ABL1 [Exons 4-9]	*CARD11*	*DDR1*	***FGFR3 [Exons 7, 9 (alternative designation exon 10), 14, 18, Intron 17]***	*KDR*	***MYD88 [Exon 4]***	*PPP2R1A*	*SMARCB1*
ACVR1B	*CASP8*	***DDR2 [Exons 5,17,18]***	*FGFR4*	*KEAP1*	*NBN*	*PPP2R2A*	***SMO***
AKT1 [Exon 3]	*CBFB*	*DIS3*	*FH*	*KEL*	***NF1***	*PRDM1*	*SNCAIP*
AKT2	*CBL*	*DNMT3A*	*FLCN*	***KIT [Exons 8,9,11,12,13,17, Intron 16]***	*NF2*	*PRKAR1A*	*SOCS1*

AKT3	***CCND1***	*DOT1L*	*FLT1*	*KLHL6*	*NFE2L2*	*PRKCI*	*SOX2*
ALK [Exons 20-29, Introns 18,19]	*CCND2*	*EED*	***FLT3 [Exons 14,15,20]***	*KMT2A (MLL) [Introns 6, 8-11, Intron 7]*	*NFKBIA*	*PTCH1*	*SOX9*
ALOX12B	*CCND3*	***EGFR [Introns 7,15,24-27]***	***FOXL2***	*KMT2D (MLL2)*	*NKX2-1*	***PTEN***	*SPEN*
AMER1 (FAM123B)	*CCNE1*	*EP300*	*FUBP1*	***KRAS***	*NOTCH1*	***PTPN11***	*SPOP*
APC	*CD22*	*EPHA3*	*GABRA6*	*LTK*	*NOTCH2 {Intron 26}*	*PTPRO*	*SRC*
AR	*CD70*	*EPHB1*	*GATA3*	*LYN*	*NOTCH3*	*QKI*	*STAG2*
ARAF [Exons 4,5,7,11,13,15,16]	*CD74* {Introns 6-8}*	*EPHB4*	*GATA4*	*MAF*	***NPM1 [Exons 4-6,8,10]***	*RAC1*	*STAT3*
ARFRP1	*CD79A*	***ERBB2***	*GATA6*	***MAP2K1 (MEK1) [Exons 2,3]***	***NRAS [Exons 2,3]***	*RAD21*	***STK11***
ARID1A	*CD79B*	***ERBB3 [Exons 3,6,7,8,10,12,20,21,23,24,25]***	***GNA11 [Exons 4,5]***	***MAP2K2 (MEK2) [Exons 2-4,6,7]***	*NSD3 (WHSC1L1)*	*RAD51*	*SUFU*
ASXL1	***CD274 (PD-L1)***	*ERBB4*	*GNA13*	*MAP2K4*	*NT5C2*	*RAD51B*	*SYK*
ATM	*CDC73*	*ERCC4*	***GNAQ [Exons 4,5]***	*MAP3K1*	***NTRK1 [Exons 14,15, Introns 8-11]***	*RAD51C*	*TBX3*
ATR	***CDH1***	*ERG*	***GNAS [Exons 1,8]***	*MAP3K13*	*NTRK2 {Intron 12}*	*RAD51D*	*TEK*
ATRX	***CDK12***	***ERRFI1***	*GRM3*	*MAPK1*	***NTRK3 [Exons 16,17]***	*RAD52*	*TERC* {ncRNA}*
AURKA	***CDK4***	***ESR1 [Exons 4-8]***	*GSK3B*	*MCL1*	*NUTM1* {Intron 1}*	*RAD54L*	***TERT* {Promoter}***
AURKB	***CDK6***	*ETV4* {Intron 8}*	*H3F3A*	***MDM2***	*P2RY8*	***RAF1 [Exons 3,4,6,7,10,14,15,17**, Introns 4-8]***	*TET2*
AXIN1	*CDK8*	*ETV5* {Introns 6, 7}*	*HDAC1*	*MDM4*	***PALB2***	*RARA {Intron 2}*	*TGFBR2*
AXL	*CDKN1A*	***ETV6* {Introns 5,6}***	*HGF*	*MED12*	*PARK2*	***RB1***	*TIPARP*
BAP1	*CDKN1B*	*EWSR1* {Introns 7-13}*	*HNF1A*	*MEF2B*	*PARP1*	*RBM10*	*TMPRSS2* {Introns 1-3}*
BARD1	***CDKN2A***	***EZH2 [Exons 4,16,17,18]***	***HRAS [Exons 2,3]***	*MEN1*	*PARP2*	*REL*	*TNFAIP3*
BCL2	*CDKN2B*	*EZR* {Introns 9-11}*	*HSD3B1*	*MERTK*	*PARP3*	***RET** [Introns 7,8, **Exons 11,13-16, Introns 9-11]***	*TNFRSF14*
BCL2L1	*CDKN2C*	*FAM46C*	*ID3*	***MET***	*PAX5*	*RICTOR*	***TP53***
BCL2L2	*CEBPA*	*FANCA*	***IDH1 [Exon 4]***	*MITF*	*PBRM1*	*RNF43*	*TSC1*
BCL6	*CHEK1*	*FANCC*	***IDH2 [Exon 4]***	*MKNK1*	*PDCD1 (PD-1)*	***ROS1 [Exons 31,36-38,40, Introns 31-35]***	*TSC2*

BCOR	***CHEK2***	*FANCG*	*IGF1R*	*MLH1*	***PDCD1LG2 (PD-L2)***	*RPTOR*	*TYRO3*
BCORL1	*CIC*	*FANCL*	*IKBKE*	***MPL [Exon 10]***	***PDGFRA [Exons 12,18, Introns 7, 9, 11]***	*RSPO2* {Intron 1}*	*U2AF1*
BCR {Introns 8, 13, 14}*	*CREBBP*	*FAS*	*IKZF1*	*MRE11A*	***PDGFRB [Exons 12-21,23]***	*SDC4* {Intron 2}*	***VEGFA***
***BRAF [Exons 11-18**, Introns 7-10]*	***CRKL***	*FBXW7*	*INPP4B*	*MSH2 {Intron 5}*	*PDK1*	*SDHA*	*VHL*
***BRCA1** {Introns 2, 7, 8, 12, 16, 19, 20}*	*CSF1R*	*FGF10*	*IRF2*	*MSH3*	*PIK3C2B*	*SDHB*	*WHSC1*
***BRCA2** {Intron 2}*	*CSF3R*	*FGF12*	*IRF4*	*MSH6*	*PIK3C2G*	*SDHC*	*WT1*
BRD4	*CTCF*	*FGF14*	*IRS2*	*MST1R*	***PIK3CA [Exons 2,3,5-8,10,14,19,21 (Coding Exons 1, 2, 4-7, 9, 13,18,20)]***	*SDHD*	*XPO1*
BRIP1	*CTNNA1*	*FGF19*	*JAK1*	*MTAP*	*PIK3CB*	*SETD2*	*XRCC2*
BTG1	***CTNNB1 [Exon 3]***	*FGF23*	***JAK2 [Exon 14]***	***MTOR [Exons 19,30,39,40,43-45,47,48,53,56]***	*PIK3R1*	*SF3B1*	*ZNF217*
BTG2	*CUL3*	*FGF3*	***JAK3 [Exons 5,11,12,13,15,16]***	*MUTYH*	*PIM1*	*SGK1*	*ZNF703*
BTK [Exons 2,15]	*CUL4A*	*FGF4*	*JUN*	*MYB* {Intron 14}*	*PMS2*	*SLC34A2* {Intron 4}*	
C11orf30 (EMSY)	*CXCR4*	*FGF6*	*KDM5A*	***MYC [Intron 1]***	*POLD1*	*SMAD2*	
C17orf39 (GID4)	*CYP17A1*	***FGFR1** [Introns 1, 5, **Intron 17]***	*KDM5C*	*MYCL (MYCL1)*	*POLE*	*SMAD4*	
CALR	*DAXX*	***FGFR2** [Intron 1, **Intron 17]***	*KDM6A*	***MYCN***	*PPARG*	*SMARCA4*	

3. IVDD Product Classification

F1 Liquid CDx is classified in accordance with Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on in vitro diagnostic medical devices (IVDD) as a general IVD medical device; it is not listed in Annex II of the IVDD, nor is it a device for self-testing. For general IVD medical devices, the manufacturer self-assesses conformity with the essential requirements and prepares a Declaration of Conformity in accordance with Annex III of the Directive.

F1 Liquid CDx is CE marked according to IVDD 98/79/EC and are registered through Qarad, Foundation Medicine's Authorized Representative in the EU.

4. CE-IVD Part Number

PN-00108

5. Manufacturer

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