



**TECHNICAL SPECIFICATIONS  
FOR**

**FOUNDATIONONE CDX  
(SPEC-0001, VER. 02)**

**FOUNDATION MEDICINE, INC.  
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**APPROVALS**

<b>REVIEWER TITLE</b>	<b>PRINTED NAME/APPROVAL SIGNATURE</b>	<b>DATE</b>
VP, Regulatory Affairs	Christine Vietz / 	23 Oct 2019

**REVISION HISTORY**

<b>VERSION NUMBER</b>	<b>EFFECTIVE DATE (DD MMM YYYY)</b>	<b>DOCUMENT/REVISION AUTHOR</b>	<b>REVISION DESCRIPTION</b>
01	27 MAR 2019	Juan Liao	Initial Release

02	23-Oct-2019	Juan Liao	Updated Intended Use and Device Description to add LOH as a biomarker reported by the assay; removed manufacturing facilities
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## 1. GENERAL DESCRIPTION

### 1.1. Intended Use

FoundationOne CDx (F1CDx) is a next generation sequencing based in vitro diagnostic device for detection of substitutions, insertion and deletion alterations (indels), and copy number alterations (CNAs) in 324 genes and select gene rearrangements, as well as genomic signatures including microsatellite instability (MSI), tumor mutational burden (TMB), and for selected forms of ovarian cancer, loss of heterozygosity (LOH) score, using DNA isolated from formalin-fixed paraffin embedded (FFPE) tumor tissue specimens. The test is intended as a companion diagnostic to identify patients who may benefit from treatment with therapies in accordance with approved therapeutic product labeling. Additionally, F1CDx 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.

### 1.2. Device Description

F1CDx is performed at Foundation Medicine, Inc. The assay includes reagents, software, instruments and procedures for testing DNA extracted from FFPE tumor samples.

The assay employs a DNA extraction method from routine FFPE biopsy or surgical resection specimens, which undergoes whole-genome shotgun library construction and hybridization-based capture of all coding exons from 309 cancer-related genes, 1 promoter region, 1 non-coding RNA (ncRNA), and select intronic regions from 34 commonly rearranged genes, 21 of which also include the coding exons (refer to **Table 1** and **Table 2** below for complete list of genes included in F1CDx). In total, the assay therefore detects alterations in a total of 324 genes. Using the Illumina® HiSeq 2500 or 4000 platform, hybrid-capture–selected libraries will be sequenced to high uniform depth (targeting > 500X median coverage with > 99% of exons at coverage > 100X). Sequence data is processed using a customized analysis pipeline designed to detect all classes of genomic alterations, including base substitutions, indels, copy number alterations (amplifications and homozygous deletions), and selected genomic rearrangements (e.g., gene fusions). Additionally, genomic signatures including MSI, TMB, and for selected forms of ovarian cancer, LOH score will be reported.

Test results are provided in an interpretive report. If a clinically relevant alteration is found in any one of the genes, the report will identify the gene and alteration and will provide the relevant scientific background that is specific to the patient's cancer.

**Table 1. Genes with full coding exonic regions included in F1CDx for the detection of substitutions, indels, and CNAs**

<i>ABL1</i>	<i>BRAF</i>	<i>CDKN1A</i>	<i>EPHA3</i>	<i>FGFR4</i>	<i>IKZF1</i>	<i>MCL1</i>	<i>NKX2-1</i>	<i>PMS2</i>	<i>RNF43</i>	<i>TET2</i>
<i>ACVR1B</i>	<i>BRCA1</i>	<i>CDKN1B</i>	<i>EPHB1</i>	<i>FH</i>	<i>INPP4B</i>	<i>MDM2</i>	<i>NOTCH1</i>	<i>POLD1</i>	<i>ROS1</i>	<i>TGFBR2</i>
<i>AKT1</i>	<i>BRCA2</i>	<i>CDKN2A</i>	<i>EPHB4</i>	<i>FLCN</i>	<i>IRF2</i>	<i>MDM4</i>	<i>NOTCH2</i>	<i>POLE</i>	<i>RPTOR</i>	<i>TIPARP</i>
<i>AKT2</i>	<i>BRD4</i>	<i>CDKN2B</i>	<i>ERBB2</i>	<i>FLT1</i>	<i>IRF4</i>	<i>MED12</i>	<i>NOTCH3</i>	<i>PPARG</i>	<i>SDHA</i>	<i>TNFAIP3</i>
<i>AKT3</i>	<i>BRIP1</i>	<i>CDKN2C</i>	<i>ERBB3</i>	<i>FLT3</i>	<i>IRS2</i>	<i>MEF2B</i>	<i>NPM1</i>	<i>PPP2R1A</i>	<i>SDHB</i>	<i>TNFRSF14</i>
<i>ALK</i>	<i>BTG1</i>	<i>CEBPA</i>	<i>ERBB4</i>	<i>FOXL2</i>	<i>JAK1</i>	<i>MEN1</i>	<i>NRAS</i>	<i>PPP2R2A</i>	<i>SDHC</i>	<i>TP53</i>
<i>ALOX12B</i>	<i>BTG2</i>	<i>CHEK1</i>	<i>ERCC4</i>	<i>FUBP1</i>	<i>JAK2</i>	<i>MERTK</i>	<i>NT5C2</i>	<i>PRDM1</i>	<i>SDHD</i>	<i>TSC1</i>
<i>AMER1</i>	<i>BTK</i>	<i>CHEK2</i>	<i>ERG</i>	<i>GABRA6</i>	<i>JAK3</i>	<i>MET</i>	<i>NTRK1</i>	<i>PRKAR1A</i>	<i>SETD2</i>	<i>TSC2</i>
<i>APC</i>	<i>C11orf30</i>	<i>CIC</i>	<i>ERRF11</i>	<i>GATA3</i>	<i>JUN</i>	<i>MITF</i>	<i>NTRK2</i>	<i>PRKCI</i>	<i>SF3B1</i>	<i>TYRO3</i>
<i>AR</i>	<i>CALR</i>	<i>CREBBP</i>	<i>ESR1</i>	<i>GATA4</i>	<i>KDM5A</i>	<i>MKNK1</i>	<i>NTRK3</i>	<i>PTCH1</i>	<i>SGK1</i>	<i>U2AF1</i>
<i>ARAF</i>	<i>CARD11</i>	<i>CRKL</i>	<i>EZH2</i>	<i>GATA6</i>	<i>KDM5C</i>	<i>MLH1</i>	<i>P2RY8</i>	<i>PTEN</i>	<i>SMAD2</i>	<i>VEGFA</i>
<i>ARFRP1</i>	<i>CASP8</i>	<i>CSF1R</i>	<i>FAM46C</i>	<i>GID4 (C17orf39)</i>	<i>KDM6A</i>	<i>MPL</i>	<i>PALB2</i>	<i>PTPN11</i>	<i>SMAD4</i>	<i>VHL</i>
<i>ARID1A</i>	<i>CBFB</i>	<i>CSF3R</i>	<i>FANCA</i>	<i>GNA11</i>	<i>KDR</i>	<i>MRE11A</i>	<i>PARK2</i>	<i>PTPRO</i>	<i>SMARCA4</i>	<i>WHSC1</i>
<i>ASXL1</i>	<i>CBL</i>	<i>CTCF</i>	<i>FANCC</i>	<i>GNA13</i>	<i>KEAP1</i>	<i>MSH2</i>	<i>PARP1</i>	<i>QKI</i>	<i>SMARCB1</i>	<i>WHSC1L1</i>
<i>ATM</i>	<i>CCND1</i>	<i>CTNNA1</i>	<i>FANCG</i>	<i>GNAQ</i>	<i>KEL</i>	<i>MSH3</i>	<i>PARP2</i>	<i>RAC1</i>	<i>SMO</i>	<i>WT1</i>
<i>ATR</i>	<i>CCND2</i>	<i>CTNNB1</i>	<i>FANCL</i>	<i>GNAS</i>	<i>KIT</i>	<i>MSH6</i>	<i>PARP3</i>	<i>RAD21</i>	<i>SNCAIP</i>	<i>XPO1</i>
<i>ATRX</i>	<i>CCND3</i>	<i>CUL3</i>	<i>FAS</i>	<i>GRM3</i>	<i>KLHL6</i>	<i>MST1R</i>	<i>PAX5</i>	<i>RAD51</i>	<i>SOCS1</i>	<i>XRCC2</i>
<i>AURKA</i>	<i>CCNE1</i>	<i>CUL4A</i>	<i>FBXW7</i>	<i>GSK3B</i>	<i>KMT2A (MLL)</i>	<i>MTAP</i>	<i>PBRM1</i>	<i>RAD51B</i>	<i>SOX2</i>	<i>ZNF217</i>
<i>AURKB</i>	<i>CD22</i>	<i>CXCR4</i>	<i>FGF10</i>	<i>H3F3A</i>	<i>KMT2D (MLL2)</i>	<i>MTOR</i>	<i>PDCD1</i>	<i>RAD51C</i>	<i>SOX9</i>	<i>ZNF703</i>
<i>AXIN1</i>	<i>CD274</i>	<i>CYP17A1</i>	<i>FGF12</i>	<i>HDAC1</i>	<i>KRAS</i>	<i>MUTYH</i>	<i>PDCD1LG2</i>	<i>RAD51D</i>	<i>SPEN</i>	
<i>AXL</i>	<i>CD70</i>	<i>DAXX</i>	<i>FGF14</i>	<i>HGF</i>	<i>LTK</i>	<i>MYC</i>	<i>PDGFRA</i>	<i>RAD52</i>	<i>SPOP</i>	
<i>BAP1</i>	<i>CD79A</i>	<i>DDR1</i>	<i>FGF19</i>	<i>HNF1A</i>	<i>LYN</i>	<i>MYCL</i>	<i>PDGFRB</i>	<i>RAD54L</i>	<i>SRC</i>	
<i>BARD1</i>	<i>CD79B</i>	<i>DDR2</i>	<i>FGF23</i>	<i>HRAS</i>	<i>MAF</i>	<i>MYCN</i>	<i>PDK1</i>	<i>RAF1</i>	<i>STAG2</i>	
<i>BCL2</i>	<i>CDC73</i>	<i>DIS3</i>	<i>FGF3</i>	<i>HSD3B1</i>	<i>MAP2K1</i>	<i>MYD88</i>	<i>PIK3C2B</i>	<i>RARA</i>	<i>STAT3</i>	
<i>BCL2L1</i>	<i>CDH1</i>	<i>DNMT3A</i>	<i>FGF4</i>	<i>ID3</i>	<i>MAP2K2</i>	<i>NBN</i>	<i>PIK3C2G</i>	<i>RB1</i>	<i>STK11</i>	
<i>BCL2L2</i>	<i>CDK12</i>	<i>DOT1L</i>	<i>FGF6</i>	<i>IDH1</i>	<i>MAP2K4</i>	<i>NF1</i>	<i>PIK3CA</i>	<i>RBM10</i>	<i>SUFU</i>	
<i>BCL6</i>	<i>CDK4</i>	<i>EED</i>	<i>FGFR1</i>	<i>IDH2</i>	<i>MAP3K1</i>	<i>NF2</i>	<i>PIK3CB</i>	<i>REL</i>	<i>SYK</i>	
<i>BCOR</i>	<i>CDK6</i>	<i>EGFR</i>	<i>FGFR2</i>	<i>IGF1R</i>	<i>MAP3K13</i>	<i>NFE2L2</i>	<i>PIK3R1</i>	<i>RET</i>	<i>TBX3</i>	
<i>BCORL1</i>	<i>CDK8</i>	<i>EP300</i>	<i>FGFR3</i>	<i>IKBKE</i>	<i>MAPK1</i>	<i>NFKBIA</i>	<i>PIM1</i>	<i>RICTOR</i>	<i>TEK</i>	

**Table 2. Genes with select intronic regions for the detection of gene rearrangements, a promoter region and a ncRNA gene.**

<i>ALK</i> introns 18, 19	<i>BRCA1</i> introns 2, 7, 8, 12, 16, 19, 20	<i>ETV4</i> intron 8	<i>EZR</i> introns 9- 11	<i>KIT</i> intron 16	<i>MYC</i> intron 1	<i>NUTM1</i> intron 1	<i>RET</i> introns 7-11	<i>SLC34A2</i> intron 4
<i>BCL2</i> 3'UTR	<i>BRCA2</i> intron 2	<i>ETV5</i> introns 6, 7	<i>FGFR1</i> intron 1, 5, 17	<i>KMT2A</i> ( <i>MLL</i> ) introns 6-11	<i>NOTCH2</i> intron 26	<i>PDGFRA</i> introns 7, 9, 11	<i>ROS1</i> introns 31-35	<i>TERC</i> ncRNA
<i>BCR</i> introns 8, 13, 14	<i>CD74</i> introns 6- 8	<i>ETV6</i> introns 5, 6	<i>FGFR2</i> intron 1, 17	<i>MSH2</i> intron 5	<i>NTRK1</i> introns 8-11	<i>RAF1</i> introns 4-8	<i>RSPO2</i> intron 1	<i>TERT</i> Promoter
<i>BRAF</i> introns 7- 10	<i>EGFR</i> introns 7, 15, 24-27	<i>EWSR1</i> introns 7-13	<i>FGFR3</i> intron 17	<i>MYB</i> intron 14	<i>NTRK2</i> Intron 12	<i>RARA</i> intron 2	<i>SDC4</i> intron 2	<i>TMPRSS2</i> introns 1- 3

1.3. IVDD Product Classification

F1CDx has been 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 self-declared IVD medical device; it is not listed in Annex II of the IVDD, nor is it a device for self-testing.

F1CDx is CE marked according to IVDD 98/79/EC and is registered through Qarad, Foundation Medicine’s Authorized Representative in the EU.

1.4. CE-IVD Part Number

PN-00106



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