Announcements

**Lynch Syndrome Germline Testing Now Available at Integrated Oncology**

Integrated Oncology now offers a comprehensive menu of Lynch syndrome genetic tests. The comprehensive analysis includes both Sanger sequencing and deletion/duplication analysis by multiplex ligation-dependent probe amplification (MLPA). _EPCAM_ is available as a deletion/duplication analysis by MLPA.

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<tr>
<th>Test Name</th>
<th>Description</th>
<th>Test Options</th>
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<tr>
<td>MLH1 Comprehensive Analysis</td>
<td>Full gene sequencing and multiplex ligation-dependent probe amplification (MLPA) for detecting large duplications and deletions</td>
<td>Available as a single-gene test or in multi-gene panels</td>
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<tr>
<td>MSH2 Comprehensive Analysis</td>
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<td>MSH6 Comprehensive Analysis</td>
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<td>PMS2 Comprehensive Analysis</td>
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<tr>
<td><em>EPCAM</em> Deletion/Duplication Analysis</td>
<td>Multiplex ligation-dependent probe amplification (MLPA) for detecting large duplications and deletions</td>
<td>Available as a single-gene test</td>
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For detailed information about the Lynch syndrome gene tests, familial gene test offerings, and multi-gene panel options, see pages 4-8 of this newsletter.

**KRAS and NRAS Extended Panels Now Available at Integrated Oncology**

Integrated Oncology has extended its _KRAS_ mutation analysis test and added _NRAS_ mutation testing for colorectal cancer (CRC). Both assays will detect mutations in exons 2, 3, and 4 and cover codons 12, 13 (exon 2), codons 59, 61 (exon 3), and codons 117, 146 (exon 4). The National Comprehensive Cancer Network® (NCCN) guidelines for colon cancer now recommend that, in addition to exon 2 _KRAS_ mutation testing, _NRAS_ and non-exon 2 _KRAS_ mutation testing be performed whenever possible in patients with metastatic CRC. Patients with any known _KRAS_ or _NRAS_ mutation should not be treated with cetuximab or panitumumab. For detailed information about Integrated Oncology's _KRAS_ and _NRAS_ extended test offerings, see page 3 of this newsletter.

**Reference**


**Extended BRAF Mutation Analysis**

Integrated Oncology has expanded its _BRAF_ mutation analysis offerings. The new tests differentiate all V600 mutations of the _BRAF_ oncogene frequently found in human cancers, such as melanoma, colorectal cancer, lung cancer, thyroid cancer, and hairy cell leukemia, allowing the determination of drug response, aiding in diagnosis, and providing prognostic information. For detailed information about Integrated Oncology's _BRAF_ Mutation Analysis and _BRAF_ Mutation Analysis in Melanoma, see page 2 and 3 of this newsletter.
Updates to the Integrated Oncology Test Menu

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<tr>
<th>Test Name</th>
<th>Change (Only fields that change are included here.)</th>
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<tr>
<td>Oncology Therapeutic Panel (IntelliGEN*)</td>
<td>Specimen Formalin-fixed, paraffin-embedded (FFPE) tissue block or slides, bone marrow, fine needle aspirate (FNA), solid tumor (excision, core, FNA, or endoscopic biopsies) formalin-fixed paraffin-embedded tissue. Fixative should be neutral-buffered formalin. For solid tumor metastatic bone samples, submit a nondecalcified FFPE sample. Decalcified bone biopsies are not acceptable sample types for this test. <strong>Block:</strong> Tumor surface area of ≥2 mm² and tumor content ≥10%; ≥50% is preferred. <strong>Unstained Slides:</strong> See table below as a guide to the number of slides required to meet the DNA input requirements.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Measured Tumor Surface Area</th>
<th>Tumor Content %</th>
<th>Number of Slides Needed (Each slide cut in 10-μM sections)</th>
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<tr>
<td>≥4 mm²</td>
<td>≥50%</td>
<td>5 unstained slides and 1 H&amp;E</td>
</tr>
<tr>
<td>1-4 mm²</td>
<td>≥10%</td>
<td>10 unstained slides and 1 H&amp;E</td>
</tr>
</tbody>
</table>

**Note:**
- Tumor surface areas between 1-4 mm² with ≥10% tumor content are less likely to meet the DNA input requirements.
- Tumor surface areas between 1-4 mm² and <10% tumor or below <1 mm² will be considered QNS for analysis.
- If sending a core biopsy, if tumor is less than <0.5 cm in length it is less likely to meet the DNA input requirements.
- If sending a cell block aspirate, at least eight tumor cell clusters providing 400-800 intact tumor cells is needed, or it is less likely to meet the DNA input requirements.

**Volume** Five to 10 stained slides at 10-μM and one matching H&E-stained slide or formalin-fixed, paraffin-embedded tissue block, 1-2 mL bone marrow, 5-10 mL FNA

| Minimum Volume | 1 mL bone marrow; FNA requires sufficient cells for DNA extraction |

New BRAF, KRAS, and NRAS Procedures

**BRAF Gene Mutation Analysis**

**CPT** 81210

**Special Instructions** Please provide a copy of the pathology report. Direct any questions regarding this test to customer service at 800-345-4363. BRAF testing will be delayed if the pathology report is not received.

**Specimen** Formalin-fixed, paraffin-embedded (FFPE) tissue blocks or slides, thyroid fine needle aspirate (FNA), whole blood, or bone marrow

**Volume** FFPE tissue block or four unstained slides and one matching H&E-stained slide at 5 μM; 5-10 mL FNA in RPMI or CytoLyt container; 3-5 mL whole blood, 1-2 mL bone marrow

**Minimum Volume** Two unstained slides and one matching H&E-stained slide at 5 μM. Samples with >4 mm² and ≥50% tumor content are preferred; FNA (with sufficient cells for DNA extraction); 3 mL blood, 1 mL bone marrow

**Container** FFPE tissue block or slides, lavender-top (EDTA) tube, green-top (sodium heparin) tube, FNA in RPMI or CytoLyt container

**Storage Instructions** Ship at room temperature. If whole blood, bone marrow, or FNA in RPMI specimens are to be stored prior to shipment at 2°C to 8°C. Store FFPE block or slides, FNA in CytoLyt container at room temperature.

**Causes for Rejection** Tumor block containing no tumor; broken or stained slides; clotted or frozen whole blood or bone marrow.

**Use** BRAF is an important member of the mitogen-activated protein kinase (MAPK) pathway that influences cell proliferation. This test differentiates all V600 mutations of the BRAF oncogene frequently found in human cancers, such as melanoma, colorectal cancer, lung cancer, ovarian cancer, thyroid cancer, and hairy cell leukemia, allowing the determination of drug response, aiding the diagnosis and providing prognosis information. More than 90% of mutations are the V600E (c1799T>A) type, but other V600 mutations have been reported.

**Limitations** This assay is able to detect 5% mutation in a background of wild-type DNA. This test was developed, and its performance characteristics determined, by LabCorp. It has not been cleared or approved by the US Food and Drug Administration (FDA).

**Methodology** SNaPshot Multiplex PCR (primer extension-based method)

**BRAF Gene Mutation Analysis, Melanoma**

**CPT** 81210

**Special Instructions** Please provide a copy of the pathology report. Direct any questions regarding this test to customer service at 800-345-4363. **BRAF** testing will be delayed if the pathology report is not received.

**Specimen** Formalin-fixed, paraffin-embedded (FFPE) tissue block or slides

**Volume** FFPE tissue block or slides, 8-10 mL FNA in RPMI or CytoLyt container

**Minimum Volume** Four unstained slides at 5 μM and one matching H&E-stained slide at 5 μM

**Container** Formalin-fixed, paraffin-embedded (FFPE) tissue blocks or slides

**Storage Instructions** Ship at room temperature. Store FFPE block or slides at room temperature.

**Causes for Rejection** Tumor block containing insufficient tumor tissue; broken or stained slides.

**Use** The US Food and Drug Administration (FDA) has approved TKI inhibitor vemurafenib and dabrafenib for the first-line treatment of patients with unresectable or metastatic melanoma whose tumors have a **BRAF** V600E mutation, and trametinib for tumors with either V600E or V600K mutations. These mutations make up greater than 90% of identified **BRAF** mutations. In addition, pembrolizumab and nivolumab have been approved by the FDA for treatment for disease progression after treatment with ipilimumab and V600 mutation positive patients with unresectable or metastatic melanoma with disease progression and prior treatment with a **BRAF** inhibitor. The NCCN guideline also suggests using both pembrolizumab and nivolumab as options for first-line treatment as both drugs have higher response rates and less toxicity compared to ipilimumab. **BRAF** is an important member of
the mitogen-activated protein kinase (MAPK) pathway that influences cell proliferation. *BRAF* mutations are found in approximately 50% of melanoma tumors.

**Limitations** This assay is able to detect 5% mutation in a background of wild-type DNA.

**Methodology** Amplification refraction mutation-specific system (ARMSS) polymerase chain reaction (PCR)

**NRAS** Gene Mutation Analysis, Extended

**CPT** 81479

**Special Instructions** Please provide a copy of the pathology report. Direct any questions regarding this test to customer service at 800-345-4363. NRAS testing will be delayed if the pathology report is not received.

**Specimen** Formalin-fixed, paraffin-embedded (FFPE) tissue or slides.

**Volume** Formalin-fixed, paraffin-embedded tissue block or one unstained slide and one matching H&E-stained slide at 5 μM.

**Minimum Volume** Two unstained slides and one matching H&E-stained slide at 5 μM. Samples with >4 mm² and ≥50% tumor content are preferred.

**Container** Formalin-fixed, paraffin-embedded (FFPE) tissue blocks or slides

**Storage Instructions** Maintain blocks/slides at room temperature.

**Causes for Rejection** Tumor block containing insufficient tumor tissue; broken or stained slides.

**Use** NRAS is a guanosine triphosphate (GTP)-binding protein involved in downstream receptor signaling, which is critical for cell proliferation, survival, and differentiation. Mutations in the NRAS oncogene are frequently found in human cancers. They are common in melanomas, colorectal cancer, and thyroid cancer. This assay detects NRAS mutations in exons 2, 3, and 4, allowing the determination of drug response.

**Limitations** This assay is able to detect 5% mutation in a background of wild-type DNA. This test was developed, and its performance characteristics determined, by LabCorp. It has not been cleared or approved by the US Food and Drug Administration (FDA).

**Methodology** SNaPshot Multiplex PCR (primer extension-based method)

**New Lynch Syndrome Germline Procedures**

**EPCAM** Deletion/Duplication Analysis

**CPT** Call client services.

**Synonym** Lynch Syndrome

**Test Includes** Deletion/duplication analysis of the terminal region of the *EPCAM* gene

**Specimen** Whole blood

**Volume** 7 mL

**Minimum Volume** 4 mL

**Container** Lavender-top (EDTA) tube

**Storage Instructions** Maintain specimen at room temperature.

**Causes for Rejection** Container broken or leaking; container not labeled; improper anticoagulant

**Use** Can confirm a clinical diagnosis of HNPCC and allow early diagnosis in family members, guiding preventive measures. Hereditary nonpolyposis colorectal cancer (HNPCC) is an autosomal-dominant, genetically heterogeneous syndrome caused by heterozygous mutations in mismatch repair genes (MMR). HNPPC is estimated to account for 4% to 6% of colorectal cancer and is characterized by early onset, a predominant proximal location of colon cancer, multiple primary cancers, and significantly improved survival when compared stage for stage to sporadic colon cancer survival rates. *EPCAM* gene accounting for an estimated 1% to 3% of all detectable HNPCC syndrome mutations. Studies indicate that large deletions in the end of this gene can lead to a loss of MSH2 expression and result in HNPCC. Genetic testing can confirm the diagnosis of HNPPC and can also identify presymptomatic individuals among the patient’s relatives.

**Limitations** This assay targets exons 8 and 9 of the *EPCAM* gene. This MLPA analysis will not detect deletions or duplications of the *EPCAM* gene that do not include exons 8 or 9 and may not detect certain other genomic rearrangements, such as translocations, inversions, or some partial exon rearrangements. Mosaic variants are not reliably detected

**RAS Pathway Mutation Profile (KRAS, NRAS), Extended**

**CPT** 81275; 81403; 81479

**Synonyms** Extended RAS Pathway Mutation Profile

**Special Instructions** Please provide a copy of the pathology report. Direct any questions regarding this test to customer service at 800-345-4363. NRAS testing will be delayed if the pathology report is not received.

**Specimen** Formalin-fixed, paraffin-embedded (FFPE) tissue block or four unstained slides and one matching H&E-stained slide at 5 μM.

**Minimum Volume** Two unstained slides at 5 μM and one matching H&E-stained slide. Samples with >4 mm² and ≥50% tumor content are preferred.

**Container** Formalin-fixed, paraffin-embedded (FFPE) tissue blocks or slides

**Storage Instructions** Ship at room temperature.

**Causes for Rejection** Tumor block containing insufficient tumor tissue; broken or stained slides.

**Use** KRAS and NRAS are guanosine triphosphate (GTP)-binding proteins involved in downstream receptor signaling, which is critical for cell proliferation, survival, and differentiation. Mutations in the KRAS and NRAS oncogene are frequently found in human cancers. They are common in pancreatic, colorectal, lung, bile duct, and thyroid cancer, as well as in melanomas. This assay detects KRAS and NRAS mutations in exons 2, 3, and 4, allowing the determination of drug response.

**Limitations** This assay is able to detect 5% mutation in a background of wild-type DNA. This test was developed, and its performance characteristics determined by LabCorp. It has not been cleared or approved by the US Food and Drug Administration (FDA).

**Methodology** SNaPshot Multiplex PCR (primer extension-based method)

**HEREDITARY NONPOLYPOSIS COLORECTAL CANCER (HNPPC): MLH1 (KNOWN MUTATION)**

**CPT** Call Client Services.

**Synonym** Lynch Syndrome

**Special Instructions** This option is available when the mutation is known and can be documented by the ordering physician. If the mutation cannot be documented, please order 511615. Specimens must be accompanied by a completed consent form. In the case of family tests (ie, known mutations), please submit the result report of the first patient tested in the family (the index case), if not performed at a LabCorp facility. Other family members are subsequently tested for the specific mutation found in the first patient tested.

**Specimen** Whole blood; DNA is accepted (Call 800-345-4363 for DNA collection information.)

**Volume** 2 mL

**Container** Lavender-top (EDTA) tube

**Collection** Samples may be stored for brief periods at 4°C. Ship overnight at room temperature.

**Storage Instructions** Maintain specimen at room temperature.

**Causes for Rejection** Container broken or leaking; container not labeled or label not legible; improper anticoagulant

**Use** Identify who in a family harbors the familial mutation and is at high risk of the disease and who does not harbor the familial mutation and is not at increased risk of the disease. Family testing for known familial
mutations can identify presymptomatic mutation carriers within affected families who are at high risk of developing the familial disease.

**Limitations** This method does not reliably detect mosaic variants; large deletions; large duplications, inversions, or other rearrangements; deep intronic variants; it may be affected by allele dropout; it may not allow determination of the exact numbers of T/A or microsatellite repeats; and it does not allow any conclusion as to whether two heterozygous variants are present on the same or on different chromosome copies. This test was developed, and its performance characteristics determined, by LabCorp. It has not been cleared or approved by the US Food and Drug Administration (FDA).

**Methodology** DNA sequencing

**Additional Information** Once a mutation is identified in an index patient, family members can be tested for the presence of that specific mutation (single-amplicon testing). Please note, if additional amplicons are required for family testing, the patient will be charged for each additional amplicon.

### Hereditary Nonpolyposis Colorectal Cancer (HNPCC): MSH2 (Known Mutation)

**CPT** Call Client Services  
**Synonym** Lynch Syndrome

**Special Instructions** This option is available when the mutation is known and can be documented by the ordering physician. If the mutation cannot be documented, please order 511632. Specimens must be accompanied by a completed consent form. 

In the case of family tests (ie, known mutations), please submit the result report of the first patient tested in the family (the index case), if not performed at a LabCorp facility. Other family members are subsequently tested for the specific mutation found in the first patient tested.

**Specimen** Whole blood; DNA is accepted (Call 800-345-4363 for DNA collection information.)

**Volume** 2 ml

**Container** Lavender-top (EDTA) tube

**Collection** Samples may be stored for brief periods at 4°C. Ship overnight at room temperature.

**Storage Instructions** Maintain specimen at room temperature.

**Causes for Rejection** Container broken or leaking; container not labeled or label not legible; improper anticoagulant

**Use** Identify who in a family harbors the familial mutation and is at high risk of the disease and who does not harbor the familial mutation and is not at increased risk of the disease. Family testing for known familial mutations can identify presymptomatic mutation carriers within affected families who are at high risk of developing the familial disease. 

**Limitations** This method does not reliably detect mosaic variants; large deletions; large duplications, inversions, or other rearrangements; deep intronic variants; it may be affected by allele dropout; it may not allow determination of the exact numbers of T/A or microsatellite repeats; and it does not allow any conclusion as to whether two heterozygous variants are present on the same or on different chromosome copies. This test was developed, and its performance characteristics determined, by LabCorp. It has not been cleared or approved by the US Food and Drug Administration (FDA).

**Methodology** DNA sequencing

**Additional Information** Once a mutation is identified in an index patient, family members can be tested for the presence of that specific mutation (single-amplicon testing). Please note, if additional amplicons are required for family testing, the patient will be charged for each additional amplicon.

### Hereditary Nonpolyposis Colorectal Cancer (HNPCC): PMS2 (Known Mutation)

**CPT** Call Client Services  
**Synonym** Lynch Syndrome

**Special Instructions** This option is available when the mutation is known and can be documented by the ordering physician. If the mutation cannot be documented, please order 511630. Specimens must be accompanied by a completed consent form. 

In the case of family tests (ie, known mutations), please submit the result report of the first patient tested in the family (the index case), if not performed at a LabCorp facility. Other family members are subsequently tested for the specific mutation found in the first patient tested.

**Specimen** Whole blood; DNA is accepted (Call 800-345-4363 for DNA collection information.)

**Volume** 2 ml

**Container** Lavender-top (EDTA) tube

**Collection** Samples may be stored for brief periods at 4°C. Ship overnight at room temperature.

**Storage Instructions** Maintain specimen at room temperature.

**Causes for Rejection** Container broken or leaking; container not labeled or label not legible; improper anticoagulant

**Use** Identify who in a family harbors the familial mutation and is at high risk of the disease and who does not harbor the familial mutation and is not at increased risk of the disease. Family testing for known familial mutations can identify presymptomatic mutation carriers within affected families who are at high risk of developing the familial disease.

**Limitations** This method does not reliably detect mosaic variants; large deletions; large duplications, inversions, or other rearrangements; deep intronic variants; it may be affected by allele dropout; it may not allow determination of the exact numbers of T/A or microsatellite repeats; and it does not allow any conclusion as to whether two heterozygous variants are present on the same or on different chromosome copies. This test was developed, and its performance characteristics determined, by LabCorp. It has not been cleared or approved by the US Food and Drug Administration (FDA).
**MLH1 Comprehensive Analysis**

**CPT** 81292; 81294  
**Synonym** Lynch Syndrome  
**Test Includes** This comprehensive test includes both Sanger sequencing and deletion/duplication analysis by MLPA of the MLH1 gene. The sequencing portion of this test covers all coding nucleotides plus at least two and typically 20 flanking intronic nucleotides upstream and downstream of each coding exon, covering the conserved donor and acceptor splice sites, as well as typically 20 flanking nucleotides in the 5'/3' UTR. The deletion/duplication analysis can detect single exon, multi-exon, and full gene deletions or duplications.  
**Specimen** Whole blood  
**Volume** 7 mL  
**Minimum Volume** 4 mL  
**Container** Lavender-top (EDTA) tube  
**Storage Instructions** Maintain specimen at room temperature.  
**Causes for Rejection** Container broken or leaking; container not labeled; improper anticoagulant  
**Use** Can confirm a clinical diagnosis of HNPCC and allow early diagnosis in family members, guiding preventive measures. Hereditary nonpolyposis colorectal cancer (HNPCC) is an autosomal-dominant, genetically heterogeneous syndrome caused by heterozygous mutations in mismatch repair genes (MMR). HNPCC is estimated to account for 4% to 6% of colorectal cancer and is characterized by early onset, a predominant proximal location of colon cancer, multiple primary cancers, and significantly improved survival when compared to stage for stage to sporadic colon cancer survival rates. HNPCC has been linked to mutations in the genes MLH1, MSH2, PMS2, and MSH6, which are involved in DNA mismatch repair. Genetic testing can confirm the diagnosis of HNPCC and can also identify presymptomatic individuals among the patient’s relatives.  
**Limitations** Sequencing cannot detect variants in regions not covered by this analysis, such as variants in noncoding or deep intronic regions and may not reliably detect changes in repetitive elements, such as microsatellite repeats. Sequence analysis may also be affected by allele drop-out due to the presence of a rare variant under a primer site. MLPA is designed to detect single exon, multi-exon, and full gene deletions or duplications. MLPA may not detect certain genomic rearrangements, such as translocations, inversions, or some partial exon rearrangements. This assay cannot determine exact breakpoints of deletions or duplications detected. Mosaic variants are not reliably detected by either sequencing or MLPA. These analyses also cannot determine whether two or more heterozygous changes are located on the same or different chromosomes. This test was developed, and its performance characteristics determined, by LabCorp. It has not been cleared or approved by the US Food and Drug Administration (FDA).  
**Methodology** DNA sequencing and multiplex ligation-dependent probe amplification (MLPA)  

**MLH1/MSH2 Comprehensive Analysis**

**CPT** 81292; 81294; 81295; 81297  
**Synonym** Lynch Syndrome  
**Test Includes** This comprehensive test includes both Sanger sequencing and deletion/duplication analysis by MLPA of the MLH1 and MSH2 genes. The sequencing portion of this test covers all coding nucleotides plus at least two and typically 20 flanking intronic nucleotides upstream and downstream of each coding exon, covering the conserved donor and acceptor splice sites, as well as typically 20 flanking nucleotides in the 5'/3' UTR. The deletion/duplication analysis can detect single exon, multi-exon, and full gene deletions or duplications.  
**Specimen** Whole blood  
**Volume** 7 mL  
**Minimum Volume** 4 mL  
**Container** Lavender-top (EDTA) tube  
**Storage Instructions** Maintain specimen at room temperature.  
**Causes for Rejection** Container broken or leaking; container not labeled; improper anticoagulant  
**Use** Can confirm a clinical diagnosis of HNPCC and allow early diagnosis in family members, guiding preventive measures. Hereditary nonpolyposis colorectal cancer (HNPCC) is an autosomal-dominant, genetically heterogeneous syndrome caused by heterozygous mutations in mismatch repair genes (MMR). HNPCC is estimated to account for 4% to 6% of colorectal cancer and is characterized by early onset, a predominant proximal location of colon cancer, multiple primary cancers, and significantly improved survival when compared to stage for stage to sporadic colon cancer survival rates. HNPCC has been linked to mutations in the genes MLH1, MSH2, PMS2, and MSH6. Genetic testing can confirm the diagnosis of HNPCC and can also identify presymptomatic individuals among the patient’s relatives.  
**Limitations** Sequencing cannot detect variants in regions not covered by this analysis, such as variants in noncoding or deep intronic regions and may not reliably detect changes in repetitive elements, such as microsatellite repeats. Sequence analysis may also be affected by allele drop-out due to the presence of a rare variant under a primer site. MLPA is designed to detect single exon, multi-exon, and full gene deletions or duplications. MLPA may not detect certain genomic rearrangements, such as translocations, inversions, or some partial exon rearrangements. This assay cannot determine exact breakpoints of deletions or duplications detected. Mosaic variants are not reliably detected by either sequencing or MLPA. These analyses also cannot determine whether two or more heterozygous changes are located on the same or different chromosomes. This test was developed, and its performance characteristics determined, by LabCorp. It has not been cleared or approved by the US Food and Drug Administration (FDA).  
**Methodology** DNA sequencing and multiplex ligation-dependent probe amplification (MLPA)  

**MLH1/MSH2/MSH6 Comprehensive Analysis**

**CPT** 81292; 81294; 81295; 81297  
**Synonym** Lynch Syndrome  
**Test Includes** This comprehensive test includes both Sanger sequencing and deletion/duplication analysis by MLPA of the MLH1, MSH2, and MSH6 genes. The sequencing portion of this test covers all coding nucleotides plus at least two and typically 20 flanking intronic nucleotides upstream and downstream of each coding exon, covering the conserved donor and acceptor splice sites, as well as typically 20 flanking nucleotides in the 5'/3' UTR. The deletion/duplication analysis can detect single exon, multi-exon, and full gene deletions or duplications.  
**Specimen** Whole blood  
**Volume** 7 mL  
**Minimum Volume** 4 mL  
**Container** Lavender-top (EDTA) tube  
**Storage Instructions** Maintain specimen at room temperature.  
**Causes for Rejection** Container broken or leaking; container not labeled; improper anticoagulant  
**Use** Can confirm a clinical diagnosis of HNPCC and allow early diagnosis in family members, guiding preventive measures. Hereditary nonpolyposis colorectal cancer (HNPCC) is an autosomal-dominant, genetically heterogeneous syndrome caused by heterozygous mutations in mismatch repair genes (MMR). HNPCC is estimated to account for 4% to 6% of colorectal cancer and is characterized by early onset, a predominant proximal location of colon cancer, multiple primary cancers, and significantly improved survival when compared to stage for stage to sporadic colon cancer survival rates. HNPCC has been linked to mutations in the genes MLH1, MSH2, PMS2, MSH6, and EPCAM. Genetic testing can confirm the diagnosis of HNPCC and can also identify presymptomatic individuals among the patient’s relatives.  
**Limitations** Sequencing cannot detect variants in regions not covered by this analysis, such as variants in noncoding or deep intronic regions and may not reliably detect changes in repetitive elements, such as microsatellite repeats. Sequence analysis may also be affected by allele drop-out due to the presence of a rare variant under a primer site. MLPA is designed to detect single exon, multi-exon, and full gene deletions or duplications. MLPA may not detect certain genomic rearrangements, such as translocations, inversions, or some partial exon rearrangements. This assay cannot determine exact breakpoints of deletions or duplications detected. Mosaic variants are not reliably detected by either sequencing or MLPA. These analyses also cannot determine whether two or more heterozygous changes are located on the same or different chromosomes. This test was developed, and its performance characteristics determined, by LabCorp. It has not been cleared or approved by the US Food and Drug Administration (FDA).  
**Methodology** DNA sequencing and multiplex ligation-dependent probe amplification (MLPA)
primary cancers, and significantly improved survival when compared stage for stage to sporadic colon cancer survival rates. HNPCC has been linked to mutations in the genes MLH1, MSH2, PMS2, and MSH6, which are involved in DNA mismatch repair. Genetic testing can confirm the diagnosis of HNPCC and can also identify presymptomatic individuals among the patient’s relatives.

Limitations Sequencing cannot detect variants in regions not covered by this analysis, such as variants in noncoding or deep intronic regions and may not reliably detect changes in repetitive elements, such as microsatellite repeats. Sequence analysis may also be affected by allele drop-out due to the presence of a rare variant under a primer site. MLPA is designed to detect single exon, multi-exon, and full gene deletions or duplications. This assay cannot determine whether two or more heterozygous changes are located on the same or different chromosomes. This test was developed and, and its performance characteristics determined, by LabCorp. It has not been cleared or approved by the US Food and Drug Administration (FDA).

Methodology DNA sequencing and multiplex ligation-dependent probe amplification (MLPA)

**MLH1/MSH2/MSH6/PM2 Comprehensive Analysis**

- **CPT** 81292; 81294; 81295; 81297; 81298; 81300; 81317; 81319
- **Synonym** Lynch Syndrome
- **Test Includes** This comprehensive test includes both Sanger sequencing and deletion/duplication analysis by MLPA of the MLH1, MSH2, MSH6, and PM2 genes. The sequencing portion of this test covers all coding nucleotides plus at least two and typically 20 flanking intronic nucleotides upstream and downstream of each coding exon, covering the conserved donor and acceptor splice sites, as well as typically 20 flanking nucleotides in the 5’ and 3’ UTR. The deletion/duplication analysis can detect single exon, multi-exon, and full gene deletions or duplications.
- **Specimen** Whole blood
- **Volume** 7 mL
- **Minimum Volume** 4 mL
- **Container** Lavender-top (EDTA) tube
- **Storage Instructions** Maintain specimen at room temperature.
- **Causes for Rejection** Container broken or leaking; container not labeled; improper anticoagulant
- **Use** Can confirm a clinical diagnosis of HNPCC and allow early diagnosis in family members, guiding preventive measures. Hereditary nonpolyposis colorectal cancer (HNPCC) is an autosomal-dominant, genetically heterogeneous syndrome caused by heterozygous mutations in mismatch repair genes (MMR). Genetic testing can confirm the diagnosis of HNPCC and can also identify presymptomatic individuals among the patient’s relatives.

**MSH2 Deletion/Duplication Analysis**

- **CPT** Call Client Services
- **Synonym** Lynch Syndrome
- **Specimen** Whole blood
- **Volume** 7 mL
- **Minimum Volume** 4 mL
- **Container** Lavender-top (EDTA) tube
- **Storage Instructions** Maintain specimen at room temperature.
- **Causes for Rejection** Container broken or leaking; container not labeled; improper anticoagulant
- **Use** This test is intended for individuals who have had previous negative sequencing of the MSH2 gene and have not had previous deletion/ duplication analysis or who have a family member with an identified large deletion or duplication of the MSH2 gene. If testing for a known family mutation, please submit a copy of the laboratory report from the index family member documenting the familial mutation.
some partial exon rearrangements. This assay cannot determine exact breakpoints of deletions or duplications detected.

This test was developed, and its performance characteristics determined, by LabCorp. It has not been cleared or approved by the US Food and Drug Administration (FDA).

**Methodology** Mulitplex ligation-dependent probe amplification (MLPA)

### MSH6 Comprehensive Analysis

**CPT** 81298; 81300  
**Synonym** Lynch Syndrome  
**Test Includes** This comprehensive test includes both Sanger sequencing and deletion/duplication analysis by MLPA of the MSH6 gene. The sequencing portion of this test covers all coding nucleotides plus at least two and typically 20 flanking intronic nucleotides upstream and downstream of each coding exon, covering the conserved donor and acceptor splice sites, as well as typically 20 flanking nucleotides in the 5’ and 3’ UTR. The deletion/duplication analysis can detect single exon, multi-exon, and full gene deletions or duplications.

**Specimen** Whole blood  
**Volume** 7 mL  
**Minimum Volume** 4 mL  
**Container** Lavender-top (EDTA) tube  
**Storage Instructions** Maintain specimen at room temperature.  
**Causes for Rejection** Container broken or leaking; container not labeled; improper anticoagulant  
**Use** Can confirm a clinical diagnosis of HNPCC and allow early diagnosis in family members, guiding preventive measures. Hereditary nonpolyposis colorectal cancer (HNPCC) is an autosomal-dominant, genetically heterogeneous syndrome caused by heterozygous mutations in mismatch repair genes (MMR). HNPCC is estimated to account for 4% to 6% of colorectal cancer and is characterized by early onset, a predominant proximal location of colon cancer, multiple primary cancers, and significantly improved survival when compared stage for stage to sporadic colon cancer survival rates. HNPCC has been linked to mutations in the genes MLH1, MSH2, PMS2, MSH6, and EPCAM. Genetic testing can confirm the diagnosis of HNPCC and can also identify presymptomatic individuals among the patient’s relatives.

**Limitations** Sequencing cannot detect variants in regions not covered by this analysis, such as variants in noncoding regions or deep intronic regions and may not reliably detect changes in repetitive elements, such as microsatellite repeats. Sequence analysis may also be affected by allele drop-out due to the presence of a rare variant under a primer site. MLPA is designed to detect single exon, multi-exon, and full gene deletions or duplications. MLPA may not detect certain genomic rearrangements, such as translocations, inversions, or some partial exon rearrangements. This assay cannot determine exact breakpoints of deletions or duplications detected. Mosaic variants are not reliably detected by either Sanger sequencing or MLPA. These analyses also cannot determine whether two or more heterozygous changes are located on the same or different chromosomes.

This test was developed, and its performance characteristics determined, by LabCorp. It has not been cleared or approved by the US Food and Drug Administration (FDA).

**Methodology** DNA sequencing and multiplex ligation-dependent probe amplification (MLPA)

### MSH6 Deletion/Duplication Analysis

**CPT** Call Client Services  
**Synonym** Lynch Syndrome  
**Specimen** Whole blood  
**Volume** 7 mL  
**Minimum Volume** 4 mL  
**Container** Lavender-top (EDTA) tube  
**Storage Instructions** Maintain specimen at room temperature.  
**Causes for Rejection** Container broken or leaking; container not labeled; improper anticoagulant  
**Use** This test is intended for individuals who have had previous negative sequencing of the MSH6 gene and have not had previous deletion/duplication analysis or who have a family member with an identified large deletion or duplication of the MSH6 gene. If testing for a known family mutation, please submit a copy of the laboratory report from the index family member documenting the familial mutation.

**Limitations** MLPA is designed to detect single exon, multi-exon, and full gene deletions or duplications. MLPA may not detect certain genomic rearrangements, such as translocations, inversions, mosaic variants, or some partial exon rearrangements. This assay cannot determine exact breakpoints of deletions or duplications detected.

This test was developed, and its performance characteristics determined, by LabCorp. It has not been cleared or approved by the US Food and Drug Administration (FDA).

**Methodology** Multiplex ligation-dependent probe amplification (MLPA)

### PMS2 Comprehensive Analysis

**CPT** 81317; 81319  
**Synonym** Lynch Syndrome  
**Test Includes** This comprehensive test includes both Sanger sequencing and deletion/duplication analysis by MLPA of the PMS2 gene. The sequencing portion of this test covers all coding nucleotides plus at least two and typically 20 flanking intronic nucleotides upstream and downstream of each coding exon, covering the conserved donor and acceptor splice sites, as well as typically 20 flanking nucleotides in the 5’ and 3’ UTR. The deletion/duplication analysis can detect single exon, multi-exon, and full gene deletions or duplications.

**Specimen** Whole blood  
**Volume** 7 mL  
**Minimum Volume** 4 mL  
**Container** Lavender-top (EDTA) tube  
**Storage Instructions** Maintain specimen at room temperature.  
**Causes for Rejection** Container broken or leaking; container not labeled; improper anticoagulant  
**Use** Can confirm a clinical diagnosis of HNPCC and allow early diagnosis in family members, guiding preventive measures. Hereditary nonpolyposis colorectal cancer (HNPCC) is an autosomal-dominant, genetically heterogeneous syndrome caused by heterozygous mutations in mismatch repair genes (MMR). HNPCC is estimated to account for 4% to 6% of colorectal cancer and is characterized by early onset, a predominant proximal location of colon cancer, multiple primary cancers, and significantly improved survival when compared stage for stage to sporadic colon cancer survival rates. HNPCC has been linked to mutations in the genes MLH1, MSH2, PMS2, and MSH6, which are involved in DNA mismatch repair. Genetic testing can confirm the diagnosis of HNPCC and can also identify presymptomatic individuals among the patient’s relatives.

**Limitations** Sequencing cannot detect variants in regions not covered by this analysis, such as variants in noncoding or deep intronic regions and may not reliably detect changes in repetitive elements, such as microsatellite repeats. Sequence analysis may also be affected by allele drop-out due to the presence of a rare variant under a primer site. MLPA is designed to detect single exon, multi-exon, and full gene deletions or duplications. MLPA may not detect certain genomic rearrangements, such as translocations, inversions, or some partial exon rearrangements. This assay cannot determine exact breakpoints of deletions or duplications detected. Mosaic variants are not reliably detected by either Sanger sequencing or MLPA. These analyses also cannot determine if two or more heterozygous changes are located on the same or different chromosomes. Due to the presence of the pseudogene PMS2CL, which has not been associated with Lynch syndrome, this assay cannot determine the location, ie, in PMS2 or PMS2CL, of any large deletions or duplications of exons 12 to 15 of the PMS2 gene detected by deletion/duplication analysis.

This test was developed, and its performance characteristics determined, by LabCorp. It has not been cleared or approved by the US Food and Drug Administration (FDA).

**Methodology** DNA sequencing and multiplex ligation-dependent probe amplification (MLPA)

### PMS2 Deletion/Duplication Analysis

**CPT** Call client services.  
**Synonym** Lynch Syndrome  
**Specimen** Whole blood  
**Volume** 7 mL  
**Minimum Volume** 4 mL  
**Container** Lavender-top (EDTA) tube  
**Storage Instructions** Maintain specimen at room temperature.  
**Causes for Rejection** Container broken or leaking; container not labeled; improper anticoagulant  
**Use** This test is intended for individuals who have had previous negative sequencing of the PMS2 gene and have not had previous deletion/
duplication analysis or who have a family member with an identified large deletion or duplication of the PMS2 gene. If testing for a known family mutation, please submit a copy of the laboratory report from the index family member documenting the familial mutation.  

**Limitations**  
MLPA is designed to detect single exon, multi-exon, and full gene deletions or duplications. MLPA may not detect certain genomic rearrangements, such as translocations, inversions, mosaic variants, or some partial exon rearrangements. This assay cannot determine exact breakpoints of deletions or duplications detected. Due to the presence of the pseudogene PMS2CL, which has not been associated with Lynch syndrome, this assay cannot determine the location, ie, in PMS2 or PMS2CL, of any large deletions or duplications of exons 12 to 15 of the PMS2 gene detected by deletion/duplication analysis.

This test was developed, and its performance characteristics determined, by LabCorp. It has not been cleared or approved by the US Food and Drug Administration (FDA).

**Methodology**  
Multiplex ligation-dependent probe amplification (MLPA)