REP-2-020 Attachment F - Patient Informed Consent for BRCA Testing

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Reason for Revision	

Revision Log

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Electronic Signatures

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Patient Informed Consent for Hereditary Breast and Ovarian Cancer Testing

PLEASE NOTE: A signed Physician Acknowledgement of NY Informed Consent for Genetic Testing must be on file at Eurofins NTD, LLC to permit testing and processing.

Test Specific Information (check those that apply)

❑ **MM071 *BRCA1/BRCA2* Gene Sequencing Panel**

In-solution hybridization of all coding exons is performed on the patient's genomic DNA. Direct sequencing of the captured regions is performed using next generation sequencing. The patient's gene sequences are then compared to a standard reference sequence. Potentially causative variants and areas of low coverage are Sanger-sequenced. Sequence variations are classified as pathogenic, likely pathogenic, benign, likely benign, or variants of unknown significance. Variants of unknown significance may require further studies of the patient and/or family members.

Limitations:
- Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis.
- Large deletions/duplications will not be detected by this analysis.
- Results of molecular analysis should be interpreted in the context of the patient's clinical/biochemical phenotype.
- Clinical sensitivity is unknown. Analytical sensitivity is approximately 99%.

❑ **MM072 BRCA1/BRCA2 Deletion/Duplication Panel**

DNA isolated from peripheral blood is hybridized to a CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes which cover the entire genomic region.
Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside of EGL Genetics, please submit a copy of the sequencing report with the test requisition.
Please note that a "backbone" of probes across the entire genome is included on the array for analytical and quality control purposes. Rarely, off-target copy number variants causative of disease may be identified that may or may not be related to the patient's phenotype. Only known pathogenic off-target copy number variants will be reported. Off-target copy number variants of unknown clinical significance will not be reported.

Limitations:
- Detection is limited to duplications and deletions. The CGH array will not detect point or intronic mutations.
- Results of molecular analysis must be interpreted in the context of the patient's clinical and/or biochemical phenotype.

❑ **MM070 *BRCA1/BRCA2* Gene Sequencing and Deletion/Duplication Panel**

Both BRCA1/BRCA2 gene sequencing and deletion/duplication panels described above are performed.

General Information, Limitations, and Risks:

- Mutations in the genes *BRCA1* and *BRCA2* cause hereditary breast and ovarian cancer syndrome (HBOC), an autosomal dominant cancer predisposition syndrome. Mutations in these genes are rare and account for only a small percentage of cancers; about 5-10% of all breast cancers and 10-15% of ovarian cancers are due to mutations in the *BRCA1* or *BRCA2* genes. Individuals with mutations in these genes, however, are at a significantly increased risk for developing breast, ovarian, and other cancers than those in the general population. This test is indicated for the following individuals: males or females with a personal or family history of breast and/or ovarian cancer that could be consistent with HBOC.
- This analysis can have the following outcomes:
  - **Positive:** A pathogenic variant (disease-causing) could be identified in one or more of the genes being tested for and the person is identified as being affected.
  - **Negative:** No pathogenic variant is identified. This reduces the risk of being affected by the diseases specifically tested for, but does not eliminate it completely.
  - **Inconclusive:** Due to technical issues the results were inconclusive and the test might need repeating. Results may also be inconclusive due to the identification of a variant of unknown significance.
- DNA-based studies performed are specific to the condition indicated above. The accuracy of genetic testing is limited by the methods employed, the clinical diagnosis, and the nature of the specific condition for which testing is requested. In some cases, the test will detect an abnormality, called a mutation, in the gene. In other cases the test is unable to identify an abnormality although an abnormality may still exist. This event may be due to the current lack of knowledge of the complete gene structure or an inability of the current technology to identify certain types of changes (mutations) in a gene. These analyses may not detect pathogenic

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variants in the promoter or other regulatory regions. Sequence analysis will not detect large deletions and duplications. Deletion/duplication analysis will not detect point mutations or some intronic mutations.

- These tests are currently available for clinical laboratory testing; however, improvements will be made as scientific knowledge advances. As with any complex genetic test, there is always a small possibility of a failure or error in sample analysis. Possible diagnostic errors include sample mix-ups, genotyping errors, rare genetic variants that interfere with analysis, and other sources. Extensive measures are taken to try to avoid these errors. The methods are not 100% accurate due to the possibility of rare genetic variations in the DNA of an individual or due to the complexity of the testing itself. A low error rate, approximately 1 in 1000 samples, is generally estimated to exist in a laboratory.
- This DNA test requires a blood sample which has risks associated with obtaining the sample. Additional samples may be needed if the sample is damaged in shipment or inaccurately submitted.
- It is the responsibility of the referring physician or health care provider to understand the specific use and limitations of the testing ordered, and to educate the patient regarding these limitations. Additional information describing indications, methodology and detection can be found on the EGL website at: https://www.egl-eurofins.com/
- Accurate interpretation of test results is dependent upon the patient's clinical diagnosis or family medical history and upon reported family relationships being true biological relationships. An erroneous clinical diagnosis in the patient or family member can lead to an incorrect interpretation in the laboratory result. Genetic testing in family members can sometimes reveal that true biological relationships are not consistent with the reported biological relationships. For example, non-paternity may be detected, which means that the stated or assumed father of an individual is not the true biological father.
- It is the responsibility of the referring physician or health care provider to understand the specific use and limitations of the testing ordered, including the above referenced information, and to educate the patient regarding these limitations.
- Due to the complexity of DNA testing and potential implications of test results, results will be reported directly to the patient's ordering provider, who will then review and discuss the test results with me.
- Patient-identifying results and information at Eurofins NTD, LLC will remain confidential and may only be released to other parties with my expressed written consent or as permitted or required by applicable law.
- I understand no tests other than those authorized shall be performed on my sample and that the sample shall be discarded within sixty days after being taken. However Eurofins NTD, LLC performs research and development studies to improve and to validate existing and new tests and to advance biomedical knowledge. I and my heirs will not receive payments, benefits, or rights to any resulting products or discoveries. Patient permission is requested for the use of patient de-identified sample in research and development studies and is entirely voluntary.
- If I have additional questions, I understand that I may wish to obtain further professional genetic counseling prior to consenting to this testing.

My signature below acknowledges my voluntary participation in DNA-based testing ordered by my physician for Hereditary Breast and Ovarian Cancer Syndrome (HBOC) in an attempt to determine whether I am at increased risk to be affected by the condition. My signature verifies that I have been appropriately counseled about the testing process and the different possible outcomes.

_____	_____	_____
Patient/Guardian Signature	Printed Name	Date

Physician/Counselor/Clinician Statement:

I have explained Hereditary Breast and Ovarian Cancer Syndrome (HBOC) testing to the patient/parent/guardian. The consent form and limitations of genetic testing were reviewed with the patient/parent/guardian. I accept responsibility for pre- and post-test genetic counseling. I will use my independent professional judgment and the patient's best interests in advising the patient/parent/guardian regarding DNA test results, the use and limitations of same, and any research study, clinical trial, drug, treatment or device brought to my attention by Eurofins NTD, LLC or others.

_____	_____	_____
Healthcare Provider Signature	Printed Name	Date

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A signed physician acknowledgement of NY informed consent for genetic testing must be on file at Eurofins NTD, LLC to permit testing and processing.

This Patient Informed Consent form is to be maintained by the physician in the patients' medical file. DO NOT Return to Eurofins, NTD, LLC.

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