



February 19, 2007

Dear Valued Client:

The American Society of Clinical Oncology (ASCO) and College of American Pathologists (CAP) recently released Guideline Recommendations for Human Epidermal Growth Factor Receptor 2 (HER-2) Testing in Breast Cancer, which were published in the *Journal of Clinical Oncology* and the *Archives of Pathology and Laboratory Medicine*.¹

The guideline recommendations recognize that accurate identification of breast cancers overexpressing HER-2 is critical for identifying patients most likely to respond to agents that target HER-2, such as trastuzumab-based therapy (Herceptin[®]), while minimizing the potential impact of serious treatment-associated side effects.

The panel recommends testing for HER-2 status on newly diagnosed breast cancer, and emphasizes that the determination of HER-2 status—via laboratory testing using immunohistochemistry (IHC) or fluorescent *in situ* hybridization (FISH)—should be performed by a CAP-accredited laboratory.

The panel recommendations for optimal HER-2 testing include:

- Initial and ongoing validation of HER-2 laboratory tests
- Annual assurance of high level of concordance between HER-2 test methods (IHC and FISH)
- Specimens showing equivocal or borderline results with one method should be tested by the alternate method
- Ongoing quality assurance parameters, including monitoring of concordance between IHC and FISH results, and participation and satisfactory performance in the appropriate proficiency testing programs.

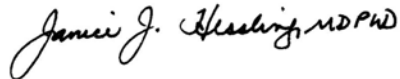
LabCorp provides unsurpassed experience in HER-2 testing. Beginning in 1991, LabCorp was the primary site for the initial clinical trials with Genentech, Inc. (A94080-4990) in the development of the HercepTest[™], the companion diagnostic test for trastuzumab therapy (Herceptin[®]). In addition, LabCorp was involved in the early development of FISH testing for HER-2 and concordance studies between IHC and FISH. Multiple clinical studies have shown greater accuracy of HER-2 results when testing is performed at high-volume reference laboratories where optimal testing algorithms are practiced and where stringent quality programs monitor other aspects of test development and quality assurance that impact testing accuracy.²⁻³

Laboratory Corporation of America Holdings (LabCorp)—including US LABS, Esoterix, DIANON Systems, and the Center for Molecular Biology and Pathology—meets the ASCO/CAP guideline recommendations for both IHC and FISH testing. The LabCorp facilities that perform HER-2 testing have each completed the recommended annual validation of HER-2 tests for 2007, with appropriate concordance of positive and negative cases. In addition, each of these laboratories has been conducting ongoing quality assurance measures for many years. These QA measures include the monitoring of

concordance between IHC and FISH, as well as enrollment and satisfactory performance in semiannual CAP Proficiency Testing for HER-2, for both IHC and FISH assays.

LabCorp clients and their patients should continue to have strong confidence in the quality of testing and the results of HER-2 tests for both IHC and FISH. LabCorp remains committed to providing high-quality results to assist you in providing exceptional patient care.

Sincerely,

A handwritten signature in black ink that reads "Janice J. Hessling, MD PhD". The signature is written in a cursive, flowing style.

Janice J. Hessling, MD PhD
Medical Director, Center for Molecular Biology and Pathology (CMBP)
Subspecialty Medical Director of Immunopathology, LabCorp/DIANON

1. Wolff AC, Hammond MEH, Schwartz JN et al. American Society of Clinical Oncology/College of American Pathologists Guideline Recommendations for Human Epidermal Growth Factor Receptor 2 Testing in Breast Cancer. *J Clin Oncology*. 2007;25(1).
2. Reddy JC, Reimann JD, Anderson SM, Klein PM. Concordance between central and local laboratory HER2 testing from a community-based clinical study. *Clin Breast Cancer*. 2006;7:153-157.
3. Perez EA, Suman VJ, Davidson NE, et al. HER2 testing by local, central, and reference laboratories in specimens from the North Central Cancer Treatment Group N9831 intergroup adjuvant trial. *J Clin Oncology*. 2006;24:3032-3038.