



HER2 (ERBB2) Testing

Effective Date: January 18, 2016

Performing Department: Molecular Pathology

South Bend Medical Foundation Molecular Diagnostics Laboratory currently follows guidelines for HER2 testing, both fluorescence in situ hybridization (FISH) and immunohistochemistry (IHC), as documented in current recommendations for human epidermal growth factor receptor 2 testing released jointly in 2013 by the American Society of Clinical Oncology and The College of American Pathologists. Based on these guidelines, The Medical Foundation Molecular Laboratory adopted the test algorithm which applies HER2 IHC testing first, followed by reflex FISH testing when the IHC result is indeterminate or equivocal (1). This was done to optimize turnaround time (IHC is faster than FISH), and it allowed pathology staff the opportunity to use the IHC stained material to guide FISH testing. However, over the last year, data from The Medical Foundation Laboratory indicated that the updated interpretation criteria for HER2 IHC slides have resulted in an unexpected increase in the number of cases being classified as 2+ equivocal, an observation seen also by other laboratories. In 2014, Rakha et al (2) noted that, "this guidance, if followed as stated, will lead to a substantive increase in the proportion of cases classified as 2+", mirroring The Medical Foundation experience. In 2015 ASCO/CAP guideline authors acknowledged this concern and indicated that a technical modification of the 2013 practice guideline is forthcoming (3).

However, there are two acceptable HER2 test algorithms in the current 2013 ASCO/CAP document (1). In order to minimize this effect caused by the updated HER2 IHC scoring criteria, The Medical Foundation Molecular Laboratory will switch to the second algorithm which applies FISH HER2 testing first, followed by HER2 by IHC when the FISH result is indeterminate or equivocal.

This change will go into effect January 18, 2016.

1. Wolff AC, Hammond ME, Hicks DG et al. 2013. Recommendations for human epidermal growth factor receptor 2 testing in breast cancer: American Society of Clinical Oncology/College of American Pathologists clinical practice guideline update. *J Clin Oncol.* 31: 3997-4013.
2. Rakha EA, Starczynski J, Lee AH et al. 2014. The updated ASCO/CAP guideline recommendations for HER2 testing in the management of invasive breast cancer: a critical review of their implications for routine practice. *Histopathol* 64, 609-615.
3. Hammond ME and Hicks DG. 2015. American Society of Clinical Oncology/College of American Pathologists Human Epidermal Growth Factor Receptor 2 Testing Clinical Practice Guideline Upcoming Modifications. Proof that Clinical Practice Guidelines are Living Documents. *Arch Pathol Lab Med* 139, 970-971.