**IGH-BCL2 Fusion, t(14;18) for Follicular Lymphoma (Formalin-Fixed Tissue) by FISH**

**Indications for Ordering**
Diagnosis of follicular lymphoma (FL) in conjunction with clinical, morphologic, and flow cytometric data

**Test Methodology**
- Fluorescence in-situ hybridization (FISH)
- Dual color, dual fusion probes detect t(14;18) or IGH-BCL2 gene rearrangement

**Tests to Consider**
Typical testing strategy
FL can often be diagnosed using the combination of morphology, immunohistochemistry (IHC), immunophenotyping, and clinical presentation
- Lymph node biopsy with morphologic and IHC evaluation
- Leukemia/lymphoma phenotyping by flow cytometry
- CD5 negative and CD10 positive suggests FL
- Bone marrow (BM) evaluation for staging – marrow involvement is common

Chromosome analysis by FISH – may be useful when the above combination does not yield a diagnosis
- Presence of IGH-BCL2 fusion, t(14;18) supports a diagnosis of FL

**Primary test**
*IGH-BCL2 Fusion, t(14;18) by FISH 2001536*
- Most sensitive method to detect IGH-BCL2 fusion in formalin-fixed, paraffin-embedded (FFPE) tissue specimens

**Related tests**
- Leukemia/Lymphoma Phenotyping by Flow Cytometry 2008003
  - Aids in diagnosis of hematopoietic neoplasms
- Chromosome FISH, Interphase 2002298
  - Specific FISH probe for t(14;18) must be requested
- Chromosome Analysis, Bone Marrow 2002292
  - Diagnosis, prognosis, and monitoring of lymphoma in BM
- Chromosome Analysis, Solid Tumor 2002296
  - May identify additional, useful cytogenetic abnormalities in tissues that are not targeted by FISH assays

**Disease Overview**

**Incidence** – most common non-Hodgkin B-cell lymphoma

**Signs/symptoms**
- Early – usually asymptomatic
- Advanced
  - Peripheral and central lymphadenopathy
  - Splenomegaly
  - BM involvement
  - B symptoms – fever, night sweats, weight loss

**Diagnostic criteria for FL**
- Morphology
  - Lymph node – neoplastic mixture of centrocytes and centroblasts recapitulating germinal centers of secondary lymphoid follicles
  - BM – paratrabecular lymphoid aggregates
- Flow cytometry
  - CD5 negative; CD10 positive monoclonal B cells

**Genetics**
*Gene – IGH-BCL2*

**Structure/function**
- Translocation juxtaposes the immunoglobulin enhancer region (*IGH*, 14q32) with the BCL-2 oncogene (18q21)
- Translocation causes overexpression of BCL-2, an anti-apoptotic protein, which prevents normal cell death

**Test Interpretation**

**Results**
- Positive – presence of the t(14;18) translocation substantiates a diagnosis of FL
  - 20% or more of the cells examined were abnormal
- Negative – absence of t(14;18) translocation

**Limitations**
- *IGH-BCL2* fusion, t(14;18) by FISH has not been validated for tissue fixed in alcohol-based or nonformalin fixatives
- Negative result does not exclude the possibility of translocations involving other partners nor rule out FL