Alberta Health Services

# Laboratory Bulletin

**Date:** **October 13, 2010**

**To:** **<u>All Zones</u> - Physicians, Laboratory Directors and Managers**

**From:** **<u>AHS Laboratory Services – Edmonton Zone</u>**
**Molecular Pathology Laboratory - University of Alberta Hospital (UAH)**

**Re:** **Change in methodology for Cancer Microsatellite Instability Assay**

## PLEASE POST OR DISTRIBUTE AS WIDELY AS APPROPRIATE

**Key Message:**

The University of Alberta Hospital - Molecular Pathology Laboratory is changing the methodology for our Cancer Microsatellite Instability Assay from ***ten singleplex microsatellite loci to five multiplex mononucleotide microsatellite loci***. The result categories, MSS, MSI-L and MSI-H, remain the same.

**Background:**

Microsatellites are short stretches of DNA, typically between 1 and 6 nucleotides in length. During replication, DNA polymerase may stutter on these repetitive sequences creating mismatched loops in the affected strand. These are normally repaired by mismatch repair (MMR) proteins. However, loss of function in one or more MMR proteins prevents repair of these loops and changes in microsatellite length become incorporated into all newly synthesized DNA. This change in length is known as microsatellite instability (MSI). Approximately 15% of all colorectal cancers are MSI positive and in the most common hereditary form, Lynch Syndrome, 85-90% are MSI positive. However, 10-15% of sporadic colorectal cancers also demonstrate MSI, making MSI a sensitive but non-specific marker for Lynch Syndrome.

**Test Indications:**

Please refer to the Amsterdam Criteria (Gastroenterology, 1999;116:1453-1456) and Revised Bethesda Guidelines (J Nat Cancer Inst. 2004,96:261-268) for testing colorectal tumours for MSI.

**Methodology:**

Samples are evaluated for MSI by fluorescent multiplex amplification of 5 microsatellite loci within DNA extracted from corresponding normal and tumour tissue. The distinctive amplicon patterns generated for each marker within normal and tumour DNA is compared and the presence of specific differences between them is classified as MSI.

**Rationale for Change:**

The new assay format is a ***more efficient, cost effective method***. This format is more easily capable of handling a significant increase in test volume should there be a change in the screening criteria of patients.

**Sample Requirement:**

A completed Molecular Pathology requisition accompanied by:
- representative tissue blocks from normal (uninvolved) tissue and tumour tissue
- one hematoxylin and eosin stained slide from each block submitted
- any associated Anatomical Pathology reports

**Turnaround Time:**

Currently four weeks from receipt of sample to reporting.

**Result Reporting:**

Microsatellite stable (MSS): no instability observed in any of the markers analyzed
Low frequency instability (MSI-L): instability detected in 1 of the 5 markers analyzed
High frequency instability (MSI-H): instability detected in 2 or more of the 5 markers analyzed

**Inquiries and feedback may be directed to:**

Dr. John Coffin, Laboratory Scientist, Molecular Pathology Laboratory at (780) 407-3181
Dr. Atilano Lacson, Divisional Director of Anatomical Pathology at (780) 407-2716
Dr. Fiona Bamforth, Acting Director of Molecular Pathology at (780) 407-8851

**This bulletin has been reviewed and approved by Dr. Robert Rennie, Edmonton Zone Clinical Department Head**