## The revised Bethesda Guidelines for testing colorectal tumors for microsatellite instability (MSI).

Tumors from individuals should be tested for microsatellite instability in the following situations:

- 1. Colorectal cancer diagnosed under the age of 50 years of age.
- 2. Presence of synchronous, metachronous colorectal, or other HNPCC-associated tumors<sup>\*</sup>, regardless of age.
- 3. Colorectal cancer with the MSI-H<sup>†</sup> histology<sup>€</sup> diagnosed in a patient who is less than 60 years of age.
- 4. Colorectal cancer diagnosed with one or more first-degree relatives with an HNPCC-related tumor, with one of the cancers being diagnosed under age 50 years.
- 5. Colorectal cancer diagnosed in two or more first or second degree relatives with HNPCC-related tumor, regardless of age.

<sup>\*</sup> Hereditary Nonpolyposis Colorectal Cancer (HNPCC)-related tumors include colorectal, endometrial, stomach, ovarian, pancreas, bladder, ureter and renal pelvis, biliary tract, brain (usually glioblastoma as seen in Turcot Syndrome), sebaceous gland adenomas and keratoacanthomas in Muir-Torre syndrome, and carcinoma of the small bowel.

<sup>†</sup> MSI-H = high microsatellite instability in tumors refers to changes in two or more of the five NCI-recommended panels of microsatellite markers. MSI-L = low microsatellite instability in tumors refers to changes in only one of the five NCI-recommended panels of microsatellite markers.

<sup>€</sup> Presence of tumor infiltrating lymphocytes, Crohn's-like lymphocytic reaction, mucinous/signet ring differentiation, or medullary growth pattern.

There was no consensus on whether to include the age criteria in point (3) above; participants voted to keep age 60 years in the guidelines.