1. Thank you for contacting the National Center for Ethics in Health Care with your ethical concerns regarding informed consent for screening tests for hereditary nonpolyposis colorectal cancer (HNPCC), aka Lynch syndrome. In formulating this response, your concerns were discussed by Center staff, and prior consultations, relevant VA documents, and policies were reviewed.

2. You describe the following situation:

The VA Genomic Medicine Program is preparing to implement standard pathologic screening for histologic markers of HNPCC in all resected colorectal tumor tissue from patients undergoing colon cancer surgery (about 4,000/year in the VA). The screen will be performed on tissue removed at surgery. The screening identifies patients for further testing with DNA sequencing which is considerably more expensive. Although the practice of screening for HNPCC is relatively new, it is considered the standard of care by the American College of Medical Genetics and American Society of Human Genetics and is being adopted by other major medical centers.

There are two screening methods: 1) Microsatellite instability (MSI) which compares alleles in a specified set of polymorphic markers between tumor DNA and normal tissue; and 2) Immunohistochemical staining (IHC) which looks at gene products from tumor DNA. Neither test has the sensitivity to definitively identify patients with HNPCC; definitive diagnosis is achieved with germ line DNA
sequencing. MSI identifies approximately 67% and IHC approximately 89% of colon cancer patients as not having HNPCC (Lynch, et al. 2007).

The treatment and follow up in patients with HNPCC is more intense than for patient without HNPCC. The screening tests are specific to the possibility of HNPCC and do not identify other genetic abnormalities or vulnerabilities.

3. **Ethics Questions:** Given the value of obtaining the patient’s informed consent for all treatments and procedures and value of placing the least burden on patients and staff to obtain fully adequate consent; what is the most ethical way to obtain informed consent for HNPCC screening?

4. **Ethics Discussion:** Adequate informed consent requires that the patient, or surrogate if the patient lacks decision-making capacity, be told and understand the meaning and implications their treatment, which in the case of surgery for colon cancer may include HNPCC screening. The information needed for adequate informed consent includes the expected benefits and known risks of the test, indications for the test, reasonable alternatives and the clinical rationale for why doing the test is recommended over alternatives (VA Handbook 1004.01 13.a.(4-5)). HNPCC screening has implications for further testing and follow-up treatment. Treating clinicians should individualize the information conveyed in informed consent and treatment discussions based on their knowledge of patient.

Documentation must indicate that an adequate informed consent process took place between the patient and clinician before testing occurred. The more serious the consequences of the test, the more explicit the documentation required to ensure that the informed consent process met all criteria.

Informed consent for testing can be obtained and documented in accordance with VHA Handbook 1004.01 in three different ways depending on the nature of the test: 1) Oral consent is obtained for the overall treatment plan and testing is considered part of that plan. Clinicians document consent for the treatment plan in the electronic record; 2) Oral consent is obtained for a specific test. The clinician documents informed consent for the specific test in the electronic medical record specifically; and 3) Signature consent for a specific test is obtained and documented in the electronic record along with a copy of the signed informed consent form.
Oral consent the overall treatment plan - Consent for tests which are “low risk and are within broadly-accepted standards of medical practice” can be obtained as part of an oral consent to the overall treatment plan and documented as such in the record (VHA Handbook 1004.01 13.a.(1)(a)). Pathologic testing for histologic markers is routinely performed on all surgically resected or biopsy tissues and is within broadly-accepted standards of medical practice. HNPCC screening meets this standard as it is low risk and is the standard of care recommended by the ACMG and ASHG (Joint Test and Technology Transfer Committee Working Group, 2000). It is not necessary to delineate all of the specific histologic tests that will be performed as part of pathologic evaluation of resected tissue, as this cannot be known until the pathologist has examined the tissue sample.

Specific oral consent - Specific consent is required for tests that “are particularly sensitive and may have consequences that the patient might reasonably want to avoid” (VHA Handbook 1004.01 subpara. 13.a.(1)(b)). Consent for such tests can be obtained orally and signature consent is not required. Still, clinicians are required to document consent for such tests in the patient's electronic medical record in addition documentation of the overall treatment plan. Tests requiring specific documentation of consent include, “. . . tests to identify illicit drug use, alcohol intoxication, HIV, Hepatitis C, Hepatitis B, Methicillin-Resistant Staphylococcus Aureus (MRSA), sexually-transmitted diseases, and inheritable genetic abnormalities” (VHA Handbook 1004.01 subpara. 13.a.(1)(b)). Screening tests for HNPCC lack the specificity to show definitively if a patient has HNPCC. Rather, positive results indicate a need for further testing.

Signature consent – Handbook 1004.01 requires that the patient’s signature consent must be obtained for treatments and procedures that:
1. Can be reasonably expected to produce significant pain or discomfort to the patient;
2. Can be reasonably expected to produce pain or discomfort to the patient that is substantial enough to require sedation, anesthesia, or narcotic analgesia;
3. Can be reasonably considered to have a significant risk of complication or morbidity;
4. Require injections of any substance into a joint space or body cavity (excluding the intravascular space); or
5. Are listed in Appendix A.

HPNCC screening does not meet these criteria for signature consent

5. **Summary:** HNPCC screening is part of processing a specimen that the patient has consented to having sampled. It does not add pain or discomfort, is low risk, is part of routine processing, and does not definitively test for a heritable condition. Therefore, consent for HNPCC screening can be obtained and documented as part of a patient's consent to the resection as part of their overall treatment plan.

Guidelines for informing patients about HNPCC screening as part of the consent process to the treatment plan can be found in VHA Handbook 1004.01 13.a.(2-15), these include discussion of the expected benefits and known risks of the test, indications for the test, reasonable alternatives and the clinical rationale for why doing the test is recommended over alternatives.

Note that for patients who screen positive, specific consent would be required for the DNA sequencing test to confirm or rule out HNPCC. This is a test specifically for a heritable condition. The consent can be obtained orally but must be documented as a specific consent to the test in the patient's electronic record (VHA Handbook 1004.01 subpara .13a.(1)(b)).

6. **Center Opinion:** Clinicians can obtain consent to screen colectomy patients with colon cancer for HNPCC as part of the treatment plan discussion. They can document consent for HNPCC screening by documenting that patients' consent to the treatment plan. Neither documentation of specific oral consent nor written signature consent beyond that required for the tissue sampling are required for HNPCC screening. For patients who screen positive, specific consent would be required for the DNA sequencing test to confirm or rule out HNPCC, a test specifically for a heritable condition. The consent can be obtained orally but must be documented as a specific consent to the test in the patient's electronic record (VHA Handbook 1004.01 subpara. 13.a.(1)(b)).

7. x Should you have questions regarding these comments, or wish the National Center for Ethics in Health Care to assist with any of the proposed options please
contact Douglas Olsen. He can be reached at 202-461-4120 or douglas.olsen@va.gov.

8. x

References


VHA Handbook 1004.01 *Informed Consent for Clinical Treatments and Procedures*