

## FREQUENTLY ASKED QUESTIONS

### **What is colorectal cancer?**

Colorectal cancer is cancer of the large intestine (colon), the lower part of the digestive system. Rectal cancer is cancer of the last several inches of the colon. Together, they're often referred to as colorectal cancers.<sup>1</sup>

### **How does colorectal cancer form?**

Most colorectal cancers develop slowly over several years. Before cancer develops, a polyp—a non-cancerous growth—usually appears on the inner lining of the colon or rectum. Some polyps can change into cancer, but not all do. If a polyp turns into cancer, it can eventually begin to grow into the wall of the colon or rectum.

### **Can colorectal cancer be prevented? If detected, can it be treated?**

Colorectal cancer is often considered the most preventable, yet least prevented cancer in the United States,<sup>2</sup> and it is highly treatable when caught early. Precancerous polyps may take 10 to 15 years to transform from benign to malignant<sup>3</sup> making screening and early detection keys to survival. One of the main reasons for late-stage detection is the lack of patient compliance with screening. In fact, more than half of colorectal cancer-related deaths could be avoided with regular screening.<sup>4</sup> For those whose cancer is detected at an earlier stage, the five-year survival rate can be greater than 90%.<sup>5</sup>

### **Who should be screened for colorectal cancer?**

The American Cancer Society recommends that all Americans age 50 and older be regularly screened for colorectal cancer.<sup>6</sup> About nine out of 10 people diagnosed with colorectal cancer are at least 50 years old.<sup>6</sup> However, 23 million Americans age 50 and over do not get screened for CRC as recommended.<sup>7</sup> Patients should speak with their physicians about their individual risk factors including family history to determine the screening program that is right for them.

### **What screening options are available to patients?**

There are a variety of screening options available, including:

**Colonoscopy** – Colonoscopy is an exam that lets a doctor look closely at the inside of the entire colon and rectum. While the patient is sedated, the doctor uses a thin flexible lighted tube that has a tiny video camera on the end, called a colonoscope, which is inserted into the colon and sends pictures to a TV screen. Colonoscopy usually requires one day of bowel preparation and diet restriction and another day for the procedure itself. Colonoscopies may be used for screening, surveillance or diagnostic purposes.

**Stool DNA Test (sDNA)** – Offered by a health care provider, this noninvasive test allows the patient to collect a sample of their stool in the privacy of their home and then send it to a lab where certain DNA alterations that are associated with cancer or precancer can be detected. A negative test result means that the test did not detect abnormal DNA and/or blood in the sample. A positive Cologuard test means that the test detected abnormal DNA and/or blood that could be caused by advanced adenomas or cancer in the colon or rectum. Any positive result should be followed by a diagnostic colonoscopy.

**Fecal Occult Blood Test (FOBT)** – There are two types of FOBT stool tests. One uses the chemical guaiac to detect blood. The other, a fecal immunochemical test (FIT), uses antibodies to detect blood in the stool. A patient receives a test kit from their healthcare provider. After the stool sample is collected by the patient, either in their home or in their doctor’s office, the patient uses a stick or brush to obtain a small amount of stool. The test kit is returned to the doctor or a lab, where the stool samples are checked for the presence of blood.

### **What is Cologuard®?**

Cologuard, developed by Exact Sciences, is the first and only FDA-approved, noninvasive, stool DNA colorectal cancer screening test. Cologuard is a screening test that detects both altered DNA and blood biomarkers known to be associated with colorectal cancer and precancer in the stool. Cologuard is available through a healthcare provider. If the test yields a positive result, the patient is referred for diagnostic colonoscopy.

### **How does Cologuard detect cancer and precancer?**

Every day, cells are shed from the colon wall. As part of this process, normal cells along with abnormal cells from cancer or precancer are shed from the colon. The stool picks up those cells as it passes through the colon. Cologuard is designed to detect altered DNA and blood biomarkers released in the stool. During the Cologuard screening process, patients are instructed to collect a stool sample—for sDNA testing and blood testing—which are analyzed at the lab in an automated system to yield a single test result.

### **How does Cologuard compare to Fecal Immunochemical Test (FIT)?**

FIT only detects blood in the stool, however, not all polyps or lesions actively bleed, and bleeding may be intermittent. Cologuard is designed to detect blood and DNA associated with cancer and precancer, which may indicate the presence of cancer or precancer. In a large prospective study, Cologuard has been shown to improve detection of cancer and precancerous polyps, compared to a leading FIT (OC FIT-CHEK® from Polymedco). Cologuard detects multiple markers from cells that are exfoliated into stools continuously.

### **How is Cologuard different than colonoscopy?**

Cologuard is noninvasive and does not require a change in medication, dietary restrictions or bowel preparation prior to taking the test. If the test yields a positive result, a follow-up colonoscopy is recommended. Cologuard is not intended to replace the use of colonoscopy but rather serve as another tool for clinicians to offer patients in an effort to get them screened.

### **Who should use Cologuard?**

Cologuard is intended for the qualitative detection of colorectal neoplasia associated DNA markers and for the presence of occult hemoglobin in human stool. A positive result may indicate the presence of colorectal cancer (CRC) or advanced adenoma (AA) and should be followed by diagnostic colonoscopy. Cologuard is indicated to screen adults of either sex, 50 years or older, who are at typical average-risk for CRC. Cologuard is not a replacement for diagnostic colonoscopy or surveillance colonoscopy in high risk individuals.

### **Who should not use Cologuard?**

Cologuard was not clinically evaluated for the following types of patients:

- Patients with a history of colorectal cancer, adenomas or other related cancers

- Patients who have had a positive result from another colorectal cancer screening method within the last 6 months
- Patients who have been diagnosed with a condition that is associated with high risk for colorectal cancer. These include but are not limited to:
  - Inflammatory Bowel Disease (IBD)
  - Chronic ulcerative colitis (CUC)
  - Crohn’s disease
  - Familial adenomatous polyposis (FAP)
  - Family history of colorectal cancer
  - Patients who have been diagnosed with a relevant familial (hereditary) cancer syndrome, such as Hereditary non-polyposis colorectal cancer syndrome (HNPCCC or Lynch Syndrome), Peutz-Jeghers Syndrome, MYH-Associated Polyposis (MAP), Gardner’s syndrome, Turcot’s (or Crail’s) syndrome, Cowden’s syndrome, Juvenile Polyposis, Cronkhite-Canada syndrome, Neurofibromatosis, Familial Hyperplastic Polyposis.

**What scientific data supports Cologuard?**

Detailed data from Exact Sciences’ prospective, 90-site, 10,000-patient pivotal study, “Multitarget Stool DNA Testing for Colorectal Cancer Screening,” was published in April 2014 in the *New England Journal of Medicine*. To view the study results, visit: <http://www.cologuardtest.com/hcp/about-cologuard/performance-effectiveness>.

The DeeP-C Pivotal Study included 10,000 patients between the ages of 50 and 84 who were at average risk for colorectal cancer. Patients were recruited across the United States at 90 sites. It compared the performance of Cologuard and a leading FIT (OC FIT-CHEK® from Polymedco) using colonoscopy as the reference method. FIT is a noninvasive commercially available test to screen for blood in the stools.

The primary endpoints were to determine the sensitivity and specificity of Cologuard for colorectal cancer. The secondary endpoints were to compare the sensitivity and specificity of Cologuard to FIT for colorectal cancer and pre-cancerous polyps.

Key published data of Cologuard vs. FIT shows:

- Sensitivity of Cologuard in detecting patients with colorectal cancer was 92% versus 74% for FIT;
- Cologuard detected 69% of the most advanced precancerous polyps;
- Cologuard achieved a specificity of 87% versus FIT specificity at 95%.

**Are there any risks to using the Cologuard collection kit?**

The risks related to using the Cologuard collection kit are low. No serious adverse events were reported among 10,023 people in the study.

**How do patients get Cologuard?**

Cologuard is available to patients through a healthcare provider. A patient will then receive the Cologuard kit in the mail at their home. Patients can speak with their healthcare providers to determine if Cologuard is appropriate.

**How is the sample collected?**

The Cologuard kit includes a sample container and a tube to collect a single stool sample for DNA and biomarker testing, and a solution that acts as a buffer that helps to preserve the DNA as it is transported to the lab. The kit also includes a step-by-step guide for collecting the stool sample and preparing the kit for shipment. Patients will also have access to a support hotline and website provided by Exact Sciences.

### **What happens to the sample once the kit leaves the patient's home?**

Once a patient completes the Cologuard stool collection process, they ship it directly to the lab via UPS. At the lab, the samples are processed through a series of sophisticated, automated procedures to isolate specific DNA targets and detect the presence of blood. A negative test result means that the test did not detect altered DNA and/or blood in the sample. A positive Cologuard test means that the test detected altered DNA and/or blood that could be caused by advanced adenomas or cancer in the colon or rectum. Any positive result should be followed by a diagnostic colonoscopy.

### **How long does it take to get the results back?**

Results from the Cologuard screening test are turned around in as little as two weeks from receipt of the sample at the lab. Patients learn of their results directly from the prescribing healthcare provider.

### **Where can patients get Cologuard if their healthcare provider does not currently offer it?**

Patients can be connected with a healthcare provider via Exact Sciences at 1-844-870-8870.

### **How much does Cologuard cost? Will insurance cover it?**

The Cologuard test will cost \$599. Cologuard is the first product to take part in the joint FDA and CMS parallel review pilot program in which both agencies simultaneously review medical devices to help reduce the time between FDA approval and Medicare coverage. A final National Coverage Determination is expected to be posted in October/November of this year after a public comment period.

### **Can people get Cologuard even if it is not covered by insurance yet?**

For more information, visit [www.CologuardTest.com](http://www.CologuardTest.com) or call 1-844-870-8870. Cologuard is currently going through the coverage determination process with Centers for Medicare and Medicaid Services (CMS). A reimbursement price is expected to be determined by CMS by Q4 of 2014.

### **How often will patients have to use Cologuard?**

The testing interval has not yet been determined. It is important for patients to speak with their healthcare provider about the established screening guidelines and where Cologuard fits into screening schedules for each individual patient.

### **Where can I find more information on Cologuard?**

To learn more, visit [www.CologuardTest.com](http://www.CologuardTest.com) or [www.exactsciences.com](http://www.exactsciences.com), where you can sign up for the company's eNewsletter or call 1-844-870-8870. Or visit the informational site on colon cancer and the importance of screening and early detection at [www.beseengetscreened.com](http://www.beseengetscreened.com).

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<sup>1</sup> Diseases and Conditions: Colon Cancer. Mayo Clinic. August 22, 2013.

<http://www.mayoclinic.org/diseases-conditions/colon-cancer/basics/definition/con-20031877>

<sup>2</sup> JNCI J Natl Cancer Inst (2009) 101 (18): 1225-1227. doi: 10.1093/jnci/djp273 First published online: August 21, 2009 <http://jnci.oxfordjournals.org/content/101/18/1225.full.pdf+html>

<sup>3</sup> American Cancer Society Colorectal Cancer Prevention and Early:

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Detection: <http://www.cancer.org/acs/groups/cid/documents/webcontent/003170-pdf.pdf>

<sup>4</sup> Centers for Disease Control and Prevention (CDC): “Colorectal Cancer Screening Saves Lives” brochure. [http://www.cdc.gov/cancer/colorectal/pdf/SFL\\_brochure.pdf](http://www.cdc.gov/cancer/colorectal/pdf/SFL_brochure.pdf)

<sup>5</sup> American Cancer Society Colorectal Cancer Facts & Figures 2011-2013  
<http://www.cancer.org/acs/groups/content/@epidemiologysurveillance/documents/document/acspc-028312.pdf>

<sup>6</sup> American Cancer Society recommendations for colorectal cancer early detection  
<http://www.cancer.org/cancer/colonandrectumcancer/moreinformation/colonandrectumcancerearlydetection/colorectal-cancer-early-detection-acs-recommendations>

<sup>7</sup> Centers for Disease Control and Prevention (CDC): “Vital Signs: Colorectal Cancer Screening”  
<http://www.cdc.gov/vitalsigns/colorectalcancerscreening/>