FREQUENTLY ASKED QUESTIONS

What is CRC?
CRC (CRC) 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 CRCs.¹

How does CRC form?
Most CRCs 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.² Some polyps can develop 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 CRC be prevented? If detected, can it be treated?
CRC is often considered the most preventable, yet least prevented cancer in the United States,³ and it is highly treatable when caught early. Precancerous polyps can take 10 to 15 years to develop from benign to malignant,⁴ so early identification and removal (through routine screening) can effectively prevent cancer from ever forming. In addition, because most polyps and early-stage cancers cause no symptoms, the only way to detect them early is through screening. The good news is that for people whose CRC is detected at an early (localized) stage, the five-year survival rate is greater than 90 percent.⁵

Unfortunately, 23 million Americans age 50 and over do not get screened for CRC as recommended.⁶ Data shows that more than half of CRC-related deaths could be avoided with regular screening⁷; however, the lack of patient compliance with screening has resulted in more than 60 percent of all CRC cases not being detected until the late stages, making treatment difficult and the five-year survival rate a mere 12 percent.⁸

Who should be screened for CRC?
The American Cancer Society recommends that all Americans at average risk for CRC begin screening at age 50,⁹ while those at increased or high risk, such as those with a family history, should begin screening before age 50.¹⁰ African Americans have the highest CRC incidence and mortality rates of all racial groups in the United States¹¹ and research shows that African-Americans are diagnosed at a younger average age than other people. Therefore, some experts suggest that African-Americans should begin their screening at age 45.¹² 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 the sample is analyzed for blood and certain DNA alterations that are associated with cancer or precancer. 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 screening test. Cologuard looks for both altered DNA and blood biomarkers known to be associated with CRC and precancer in the stool.

**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 and picked up by the stool it passes through the colon. Cologuard is designed to detect these altered DNA and blood biomarkers released into the stool. At the Exact Sciences lab, stool 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.

Important labeling information:
• A negative Cologuard test result does not guarantee absence of cancer or advanced adenoma. Patients with a negative Cologuard test result should be advised to continue participating in a colorectal cancer screening program with another recommended screening method. The screening interval for this follow-up has not been established.
• Cologuard may produce false negative or false positive results. A false positive result occurs when Cologuard produces a positive result, even though a colonoscopy will not find cancer or precancerous polyps. A false negative result occurs when Cologuard does not detect a precancerous polyp or colorectal cancer even when a colonoscopy identifies the positive 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.

Note: The performance of Cologuard has been established in a cross sectional study (i.e., single point in time). Programmatic performance of Cologuard (i.e., benefits and risks with repeated testing over an established period of time) has not been studied. Performance has not been evaluated in adults who
have been previously tested with Cologuard. Non-inferiority or superiority of Cologuard programmatic sensitivity as compared to other recommended screening methods for CRC and AA has not been established.

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, the doctor will schedule a follow-up colonoscopy. 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.

What scientific data supports Cologuard?

The DeeP-C Pivotal Study included 10,000 patients between the ages of 50 and 84 who were at average risk for CRC. 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 of the DeeP-C Pivotal Study were to determine the sensitivity and specificity of Cologuard for CRC. The secondary endpoints were to compare the sensitivity and specificity of Cologuard to FIT for CRC and pre-cancerous polyps.

Key published data of Cologuard vs. FIT shows:
- Sensitivity of Cologuard in detecting patients with CRC 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%.

How do patients get Cologuard?
Cologuard is prescribed by a healthcare provider. Patients should speak with their healthcare provider to determine if Cologuard is appropriate for them.

How do patients use Cologuard?
After the healthcare provider orders Cologuard, the patient receives the Cologuard kit in the mail, which includes two collection containers—one to collect stool for sDNA testing; the second for blood testing. After collecting a stool sample in the collection container and tube, the patient pours a solution into both to preserve the integrity of the sample as it is transported to the lab. Using the pre-paid mailer provided, the patient then ships the Cologuard kit back to the lab via UPS. The kit also includes a step-by-step guide for collecting the stool sample and preparing the kit for shipment. Patients also have access to a support hotline and website provided by Exact Sciences.

Important labeling information:
- Patients should not provide a sample for Cologuard if they have diarrhea or if they have blood in their urine or stool (e.g., from bleeding hemorrhoids, bleeding cuts or wounds on their hands, rectal bleeding, or menstruation).
• To ensure the integrity of the sample, the laboratory must receive the patient specimens within 72 hours of collection. Patients should send stool samples to the laboratory according to the instructions stated in the Cologuard Patient Guide.

• Patients should be advised of the caution listed in the Cologuard Patient Guide. Patients should NOT drink the preservative liquid.

**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. If the test comes back positive, the doctor will refer the patient for a colonoscopy. If the test is negative, the patient should speak with his or her physician to discuss next steps in the screening process and protocol.

**What are Cologuard's indications for use?**
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.

**Is Cologuard an appropriate screening method for people over the age of 75?**
CRC screening guideline recommendations vary for persons over the age of 75. The decision to screen persons over the age of 75 should be made on an individualized basis in consultation with a healthcare provider. Cologuard test results should be interpreted with caution in older patients as the rate of false positive results increases with age.

**Who should not use Cologuard?**
Cologuard was not clinically evaluated for the following types of patients:

- Patients with a history of CRC, adenomas or other related cancers
- Patients who have had a positive result from another CRC screening method within the last 6 months
- Patients who have been diagnosed with a condition that is associated with high risk for CRC. 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 CRC
- Patients who have been diagnosed with a relevant familial (hereditary) cancer syndrome, such as Hereditary non-polyposis CRC 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.

**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. Patients should be careful when opening and closing the lids to avoid the risk of hand strain.

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 is available for $599 and is covered by Medicare. Exact Sciences received a final National Coverage Determination for Cologuard in October 2014 and a final reimbursement price of $492.72 from the Centers for Medicare and Medicaid Services (CMS). Cologuard is also covered by a number of private insurers.

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. The Centers for Medicare and Medicaid Services assessment is that Cologuard be performed every three years for patients 50 and older who do not have symptoms of CRC and who do not have an increased risk of CRC. Medicare covers Cologuard for individuals age 50-85 fitting these criteria once every three years at no cost to patients.

Where can I find more information on Cologuard?
To learn more, visit www.CologuardTest.com or 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.

Caution: Federal law restricts this device to sale by or on the order of a licensed healthcare practitioner.