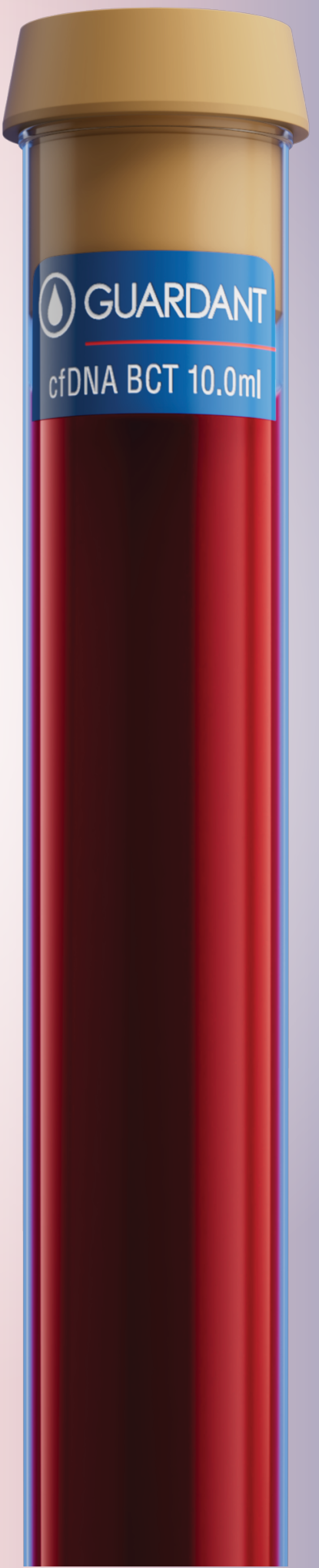
shield™

Multi-Cancer Detection



The Shield MCD Test Fact Sheet

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Developed by GUARDANT™

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shield™
Multi-Cancer Detection

GUARDANT

What is the Shield MCD test?

The Shield Multi-Cancer Detection (MCD) test is a qualitative, laboratory developed test intended to detect cancer-derived methylation-based signals in cell-free DNA (cfDNA) from blood. Shield MCD is intended for multi-cancer screening in individuals age 45 years or older, without a known diagnosis of cancer. The target cancers for the Shield MCD test include bladder, breast, colorectal, esophageal, stomach, liver, lung, ovarian, pancreatic, and prostate. The Shield MCD test is not indicated for use in pregnant women. The Shield MCD test is for prescription use only.

How does the Shield MCD test work?

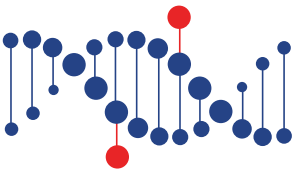
To better understand how the Shield MCD test works, it is important to understand two key concepts:

- What is cell-free DNA (cfDNA)?
- What is DNA methylation, and how can changes in it help detect cancer?

What is Cell free DNA (cfDNA)?

Cells in our body can release small amounts of their genetic material (DNA) into the bloodstream, known as cell free DNA (cfDNA)[1]. Cancer cells, if present, can also shed their genetic material, known as circulating tumor DNA (ctDNA) into the blood[1]. One of the features that distinguishes ctDNA from normal cfDNA is the pattern of methylation, a type of modification to the DNA[2]. From just a blood draw, the Shield MCD test analyses DNA methylation patterns to differentiate normal DNA from ctDNA and to determine if cancer may be present[6].

What is DNA methylation, and how can changes in it help detect cancer?



Methylation is a natural chemical modification that acts as a "tag" on DNA[1]. Depending on where these tags are located, they can turn genes on or off. In cancer cells, these DNA tags often differ from those found in normal cells[2]. For example, genes that should be active in healthy cells may be turned off by methylation, which can contribute to cancer development[3,4]. By analyzing these altered methylation patterns in circulating cell-free DNA (cfDNA), it is possible to detect signals that may be associated with cancer[5]. In addition, methylation patterns can vary by cancer type[1,4], and identifying these patterns in cfDNA may help indicate where a cancer may have originated[1,4].

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How does the Shield MCD test work?

The Shield MCD test was developed using more than 10,000 blood samples from individuals with cancer and over 7,000 samples from individuals without cancer[6]. These samples were used to train a computer system to recognize differences between cancer-related DNA methylation patterns and normal DNA methylation.

Step 1: Teaching the system to identify cancer signals[6]

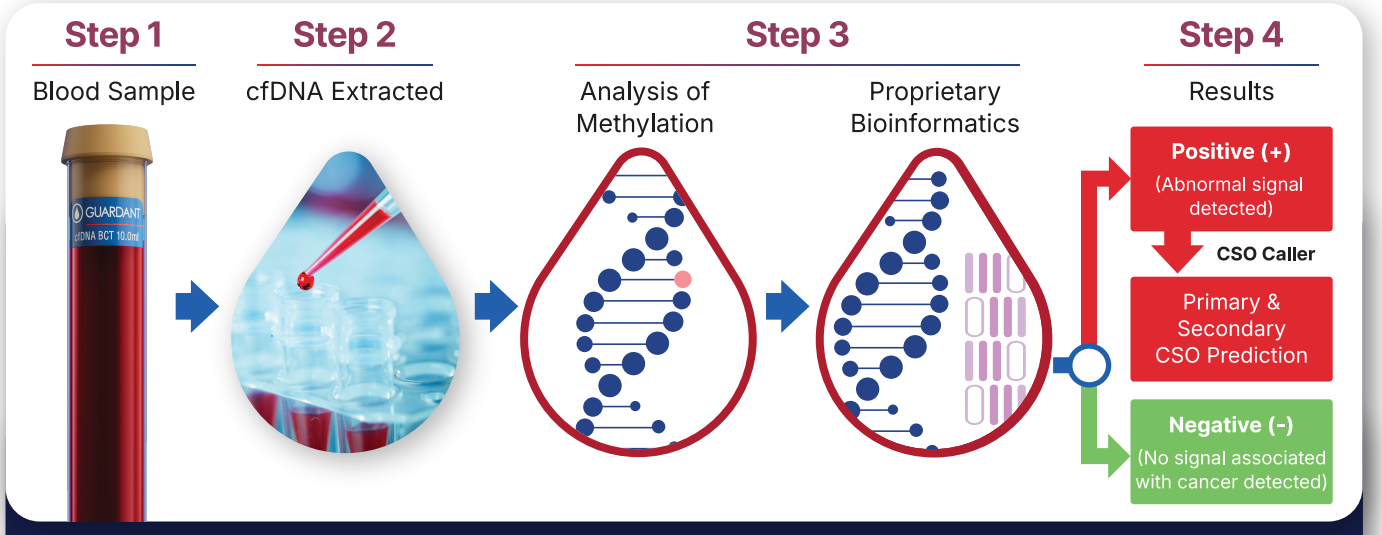
- A **multi-cancer classifier** (a type of computer model) was trained to tell the different DNA methylation patterns between samples coming from people with cancer and those from healthy individuals.
- The goal was to enable the test to distinguish, with high confidence, between abnormal signals associated with cancer and normal variations.
- For any sample given, the Shield MCD test result is positive if the methylation score for the sample exceeds the pre-defined locked threshold. The Shield MCD test result is negative when the methylation score is below the threshold.

Step 2: Teaching the system to identify the cancer's origin[6]

- If a cancer signal was detected, an additional step, called the Cancer Signal of Origin (CSO) model, was applied.
- This model was trained to recognize and differentiate DNA methylation patterns from 10 specific solid tumors (bladder, breast, colorectal, esophageal, stomach, liver, lung, ovarian, pancreatic, prostate).
- When a positive (abnormal) signal was detected, the CSO model reported the top two most likely cancer types — a primary prediction and a secondary prediction.
- By using a large and diverse dataset, the Shield MCD test was able to learn subtle differences in DNA methylation patterns across many cancers.

The Shield MCD test workflow

The following outlines simplified steps in blood sample processing for the Shield MCD test[6]:



Step 1 — **Blood Sample**
Blood is collected and sent to Guardant Health's clinical laboratory for processing.

Step 2 — **cfDNA Extraction**
Cell-free DNA in the blood, which may or may not include circulating tumor DNA (ctDNA), is extracted from the sample for analysis.

Step 3 — **Methylation analysis and Bioinformatics**
Methylated DNA is separated from unmethylated DNA and analyzed for patterns that may be associated with cancer. Tens of thousands of combinations of methylation patterns are evaluated through our advanced data processing bioinformatics.

Step 4 — **Results**
When an abnormal methylation signal is detected, suggesting the presence of ctDNA, the result is considered positive. In this case, the report includes a cancer signal of origin (CSO), a prediction for where in the body the tumor may be located. (continued next page)

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Step 4

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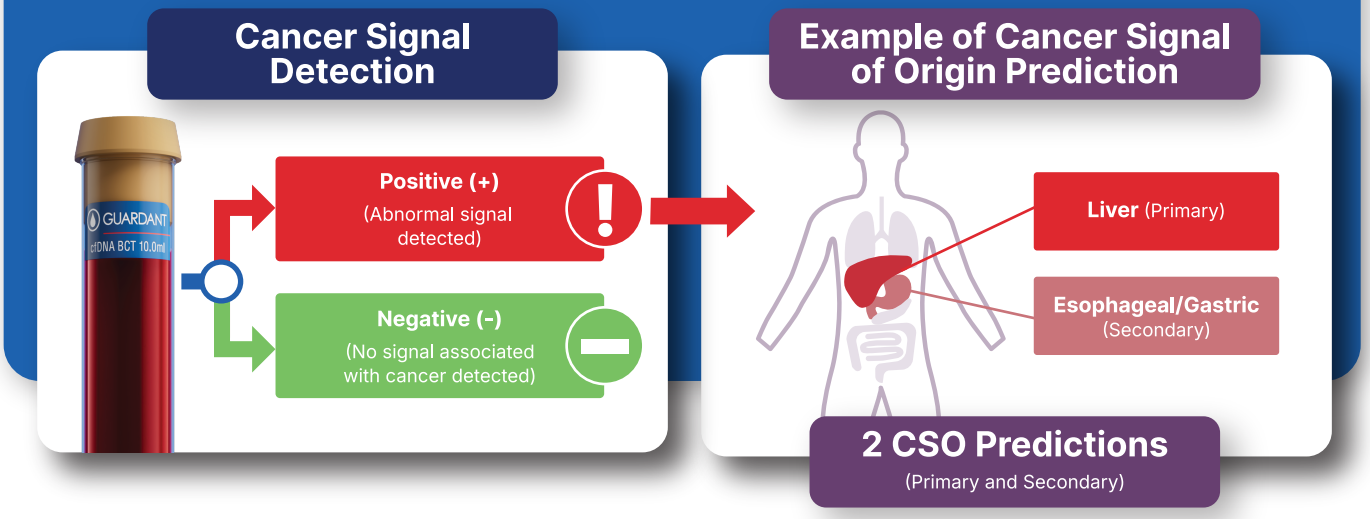
When the methylation analysis does not detect a signal that suggests the presence of ctDNA, the test result is considered negative.



Shield MCD test results

Sample Shield MCD Test Report

NEGATIVE

Your Result is Negative

A negative result means a signal associated with cancer was not detected. A negative result does not completely rule out the possibility of cancer.

Please contact the healthcare provider who ordered this test and continue to participate in recommended cancer screening tests.

POSITIVE

Your Multi-Cancer Detection (MCD) Test Result is Positive

A positive result means an abnormal signal was detected. Although a positive result raises concern for the presence of cancer, **it is not a diagnosis of cancer.** In fact, most people with a positive result do not have cancer. The Predicted Cancer Signal of Origin (CSO) offers information about the tissue type or organ that may be associated with the positive result detected by this test. The CSO may help your healthcare provider decide next steps in your clinical evaluation.

Primary Predicted CSO	Secondary Predicted CSO
Colorectal	Esophageal/Gastric(Stomach)

Your Next Steps

- Contact the healthcare provider who ordered the test regarding any clinically indicated follow-up.

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Clinical Trials

Clinical validation study:

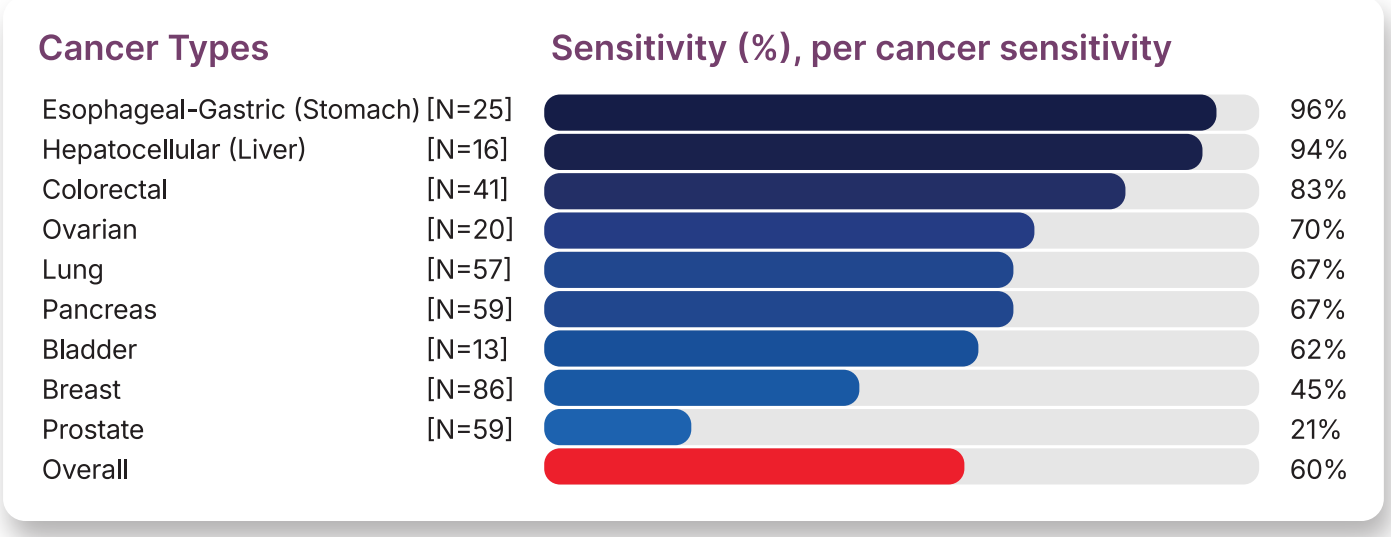
The Shield MCD test performance was validated in a blinded case-control cohort of plasma samples from adults with treatment naive cancer or from people who reported themselves to be free of cancer with 1 year of follow-up. Individuals >45 years old of various races and ethnicities were included. There were 814 cases and controls evaluated in the study[6].

These results were reported at the 2025 American Society of Clinical Oncology (ASCO) Meeting.

This case-cohort study reported three key findings:

(1) Sensitivity: The ability of the test to correctly identify people who have cancer

- The overall sensitivity of Shield MCD in this study was **60% for the detection of all 10 cancers** included (bladder, breast, colorectal, esophageal, gastric (stomach), liver, lung, ovarian, pancreatic, and prostate)[6,7].
- The sensitivity for detecting the **6 most aggressive cancers, defined as shortest survival rate by SEER**[8] (esophageal, stomach, liver, lung, ovarian and pancreatic) was **74%**[6,7].
- Sensitivity according to cancer type is shown in the figure below[6]:



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(2) Specificity: The ability of the test to correctly identify patients who do not have cancer

- The specificity for Shield MCD in this trial was **99%**[6]. That is, for 100 healthy participants, the test correctly identified 99 as cancer-free but incorrectly suggested that one blood sample from one cancer-free individual had an abnormal signal associated with cancer. This has the same meaning as a 1% false positive rate.

(3) Cancer Signal of Origin (CSO) prediction: A prediction for where in the body the abnormal signal may have originated and where the tumor may be located

A primary prediction and secondary prediction were given.

- Overall, **CSO accuracy was 93%**[6], considering both the primary and secondary predictions.

Real world performance of the Shield MCD test

A real-world study was conducted to assess the performance of the Shield MCD test on 9,251 individuals, with a 12-month follow-up. In this setting, the Shield MCD test showed 41% positive predictive value (PPV) for any solid tumor at 99% specificity[7] PPV is the probability that an abnormal signal (positive test) is associated with the presence of cancer.

Ongoing large-scale evaluation of the Shield MCD test in collaboration with the United States National Cancer Institute (NCI)

Based on its performance in predicting the presence and location of cancer, the Shield MCD test was selected for evaluation in the Vanguard study, led by the United States National Cancer Institute (NCI).

This study will assess the Shield MCD test for cancer screening in a prospective interventional study of 24,000 healthy individuals. One-third of the volunteers will be recruited into the Shield MCD test arm. The primary aim of the study is to assess the feasibility of cancer screening with MCD tests[7,9].

Laboratory and test information:

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Important safety information:

The Shield MCD test (a laboratory developed test) is a qualitative test intended to detect cancer derived alterations in cell-free DNA from blood. The Shield MCD test is intended for multi-cancer screening in individuals age 45 or older, without a known diagnosis of cancer. The target cancers for the Shield MCD test include bladder, breast, colorectal, esophageal / gastric (also called stomach), liver (also called hepatocellular), lung, ovarian, pancreatic, and prostate. The Shield MCD test is not indicated for use in pregnant women. Individuals with positive results should follow healthcare provider recommendations for diagnostic follow-up and evaluation. The Shield MCD test is intended to complement, not replace guideline recommended cancer screening tests. A negative result does not eliminate the possibility that cancer is present or will occur in the future. Individuals should continue to participate in age-appropriate guideline directed cancer screening programs. These findings should be interpreted in the context of other clinical information, and laboratory and imaging studies as clinically indicated by a qualified medical professional. The Shield MCD test is available by prescription only.

All information in this fact sheet is correct as of **April 2026**.

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