FDA Questions to the Panel

Molecular and Clinical Genetics Panel
Galleri
GRAIL, Inc.
September 23, 2026

FDA is seeking input on the benefit-risk assessment for Galleri when indicated as the sponsor has proposed:

> *The Galleri® test is a qualitative, next-generation sequencing (NGS)-based in vitro diagnostic test intended to detect cancer-specific methylation patterns in cell-free DNA isolated from peripheral whole blood. Galleri is intended for screening for the early detection of multiple types of cancer, in adults aged 50 years or older. The test is also intended for the prediction of Cancer Signal Origin in individuals with a Cancer Signal Detected test result.*
>
> *A test result of Cancer Signal Detected, including a predicted Cancer Signal Origin, may indicate the presence of an invasive solid tumor or hematologic malignancy and should be followed by a diagnostic workup recommended by qualified healthcare professionals. A test result of No Cancer Signal Detected does not rule out the presence of cancer, and individuals should continue with guideline-recommended single-cancer screening tests.*
>
> *This test is performed at GRAIL, Inc. Prescription only.*

We have the following discussion questions for the Panel to address during the Advisory Committee Meeting:

1. The FDA Executive Summary and panel presentation described Galleri performance by overall 12-month episode sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), 12-month episode sensitivity per cancer type, and 12-month episode sensitivity by stage, as reported in the clinical studies (PATHFINDER 2 and NHS-Galleri).

    a. Please discuss the clinical significance of the results for patients and providers in the intended use setting, considering Galleri performance:
        i. Overall
        ii. Per cancer type
        iii. For cancer types with current guideline-recommended screening (i.e., breast, colorectal, lung, cervical, and prostate)
        iv. For cancer types without current guideline-recommended screening.

    In your discussion, please also discuss the clinical significance of any inter-study variability observed between PATHFINDER 2 and NHS-Galleri on the test's performance estimates.

    b. Please discuss whether Galleri performance by stage (overall and per cancer type) supports the proposed indications for use of "early" detection of multiple types of cancer.
        i. If no, please discuss whether Galleri performance supports an alternate indication for the detection of multiple types of cancer, absent the "early" characterization.

ii. If yes, please identify the cancer types for which Galleri performance supports "early" detection, and discuss how "early" detection should be described in the test labeling (e.g., by cancer stage, intent for curative treatment available)

c. Please discuss whether there are any cancer types where Galleri's cancer type detection performance presents new risks (e.g., due to uncertainty in performance estimates) and for which risk mitigations may be needed. Where applicable, discuss what types of mitigations (e.g., labeling warnings or limitations) may be effective.

2. Taking into consideration current guideline-recommended screening methods and the demonstrated performance of Galleri to detect multiple cancer types, including cancers with and without guideline-recommended screening, please discuss how test performance and use, including benefits, risks, and limitations, should be communicated to providers and patients to support shared decision-making in determining whether to use Galleri?

   For reference, the following statement is currently proposed to be included in the Galleri Indications for Use:

   A test result of No Cancer Signal Detected does not rule out the presence of cancer, and individuals should continue with guideline-recommended single-cancer screening tests.

   The following statements are proposed to be listed in the Precautions and Limitations section of the Galleri labeling:

   - *The Galleri test is not a replacement for existing recommended single-cancer screening tests or diagnostic modalities for cancer.*
   - *A result of No Cancer Signal Detected does not rule out the presence of cancer. Individuals should continue with guideline-recommended single-cancer screening*

3. If the device is approved based on existing data, please discuss whether one or multiple post-approval studies to gather additional information about benefits and risks of Galleri would be beneficial. Please discuss the types of information that would be important to collect during such studies.