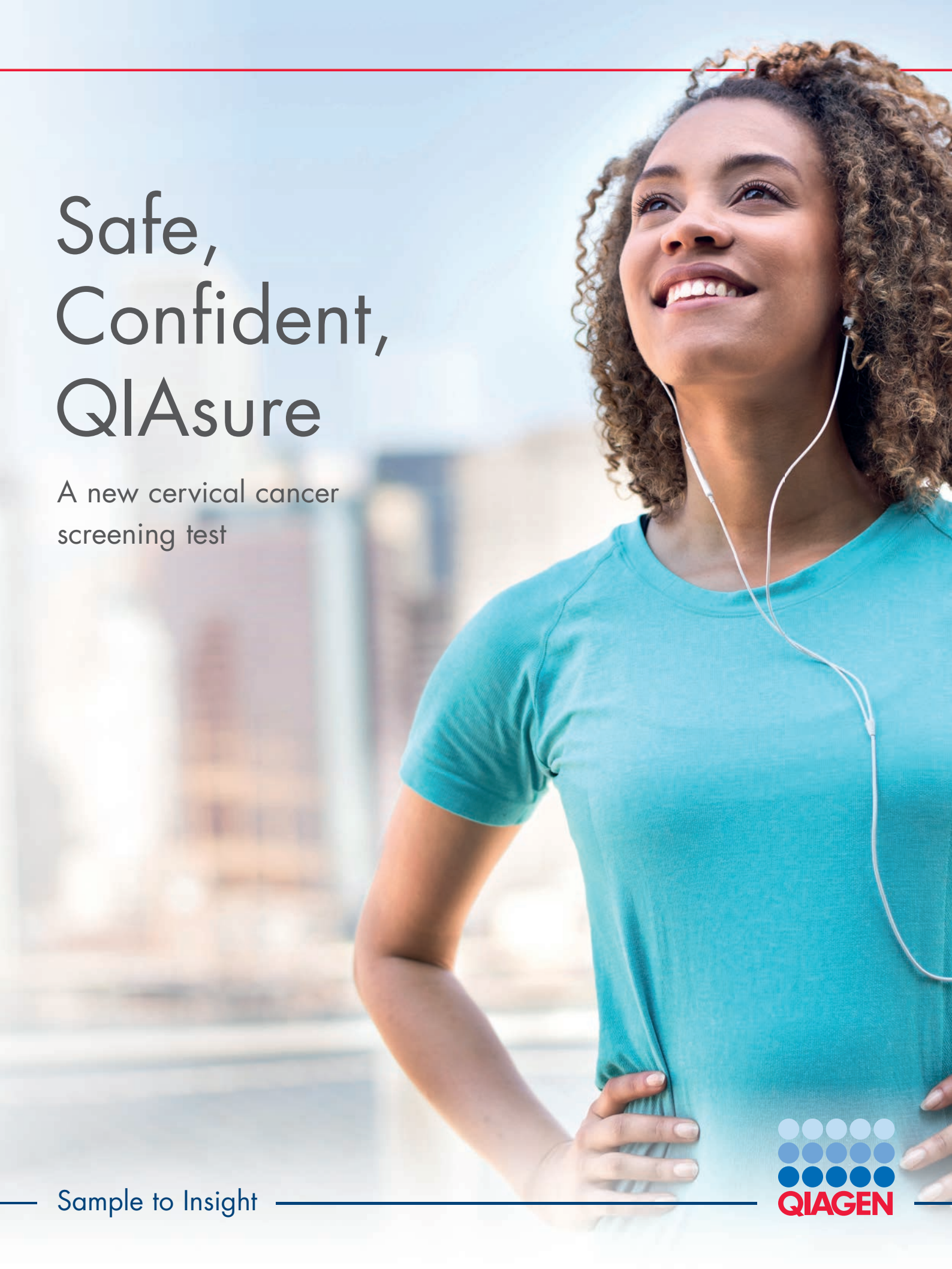

Safe, Confident, QIAsure

A new cervical cancer screening test

Sample to Insight

QIAGEN

QIAsure: A breakthrough solution in Women's Health

We are at a turning point in the battle against cervical cancer. The global human papillomavirus (HPV) epidemic has led to a rise in cervical cancer incidence worldwide. It is now the second most common cancer among women aged 15 to 44, affecting more than 500,000 women a year (1). Fortunately, cervical cancer is nearly 100% preventable through early detection of precancer before the disease becomes a danger to a patient's life or reproductive health. QIAGEN, the developer of the gold-standard HPV screening test *digene*® HC2 High-Risk HPV DNA Test®, brings to market the QIAsure Methylation Test—a new cervical cancer screening test that gives clinicians molecular insight into whether an HPV infection is actively transforming cervical cells into cancer.

Why QIAsure?

Today, women have an 80% chance in their lifetimes of contracting high-risk HPV (hrHPV), the causal agent of cervical cancer. Advances in technology have created effective methods for detection of hrHPV. However, only 10% of women with hrHPV will develop long-lasting HPV infections that put them at risk for development of cervical cancer (2). There is growing need for an accurate triage test to see beyond HPV for clinical assurance that the patient has no short-term risk of cervical cancer.

What is QIAsure?

QIAsure is a quantitative methylation specific PCR (qMSP) test that lets clinicians see what's happening at a molecular level so they can determine whether a hrHPV positive patient is at short-term risk of developing cervical cancer. QIAsure detects the presence of biomarkers associated with cervical carcinoma and advanced transforming cervical intraepithelial neoplasia (CIN), to objectively discern passive HPV infections from ones that need immediate attention.

QIAsure can be used to triage a positive hrHPV test on the same specimen used for the HPV test. It can also be used as a confirmatory test to an atypical squamous cells of undetermined significance (ASC-US) cytology result. QIAsure looks for methylation of host cell genes *FAM19A4* and *miR124-2* in cervical cells. Methylation of these genes indicates carcinogenic cell transformation and high short-term risk of developing cervical cancer; absence of methylation indicates low short-term risk of developing cervical cancer.

With these molecular insights, QIAsure can eliminate overtreatment by identifying women who need immediate treatment and those who need monitoring.

Key benefits:

Accuracy
QIAsure is a quantitative methylation-specific PCR test with high sensitivity and 100% accuracy in detecting biomarkers associated with cervical carcinoma in patients.

Objective results
QIAsure provides objective results on whether a patient has a hrHPV infection that's actively transforming cervical cells into cancer.

Simple sample
QIAsure can be performed on the same sample (self-sample or physician/gynecologist collected) as the primary screening HPV test.

Saves time & money
QIAsure can help reduce unnecessary colposcopies and cervical treatments.

Convenience
QIAsure can be performed on self-samples collected by the patient without a speculum exam, making it easy and convenient to be tested early and often.

Peace of mind
QIAsure provides test negative patients with peace of mind that they have a low short-term risk of cervical cancer.

Transforming information into insight

QIAsure transforms information into insight through DNA methylation analysis that objectively determines the presence of biomarkers associated with cervical precancer and cancer. QIAsure can be performed in the PCR lab through industry-standard methods of sample prep/extraction and automation platforms for analysis (clinically validated for Rotor-Gene® Q MDx instrument). Using a qMSP test, QIAsure can detect the presence of carcinogenic cervical cells and advanced transforming CIN lesions. QIAsure has been clinically proven to detect the transformation of cervical cells and advanced transforming CIN 2/3 lesions, even in patients with normal cytology.

Scientific Process & Clinical Data

Abnormal patterns of DNA methylation have been implicated in various cancers, including cervical cancer where promoter hypermethylation of the tumor suppressor genes *FAM19A4* and/or *miR124-2* indicates the presence of precancer or cancer (3–10). QIAsure examines promoter hypermethylation in bisulfite-converted DNA isolated from cervical specimens using a multiplex real-time PCR test. Positive results correlate with the presence of carcinogenic cells and advanced transforming CIN lesions.

In clinical trials, QIAsure testing was performed on physician-collected cervical specimens from 258 hrHPV-positive women including 117 without evidence of CIN 2 or worse after 18 months follow-up (CIN≤1), 42 with CIN 2, 30 with CIN 3, 50 with squamous cell carcinoma, and 10 with adenocarcinoma. QIAsure detected 100% of carcinomas (squamous cell carcinoma and adenocarcinoma) in these samples, but varied in detection of other grades of CIN, from 88.9% in CIN 3+ to lower sensitivity for CIN 1/2. *FAM19A4* and *miR124-2* methylation analysis specifically detects advanced transforming CIN lesions (10). CIN 2/3 with low levels of *FAM19A4* and *miR124-2* methylation have low short-term progression risk for cancer. These patients can be managed by close surveillance rather than treated.

Independent research from leading cervical cancer scientists confirms the effective use of *FAM19A4/miR124-2* methylation analysis for detection of cervical carcinomas and advanced CIN 2/3 lesions (4–9). In a subgroup of women over 30 years (n=287), the CIN 3+ sensitivity and specificity for *FAM19A4* methylation (88.3% and 62.1%) was greater than that of cytology (85.0% and 47.6%) and HPV 16/18 genotyping (70% and 57.7%) (9). DNA methylation analysis of *FAM19A4/miR124-2* has an equal performance and high sensitivity for identifying high-grade CIN and cervical cancer in hrHPV positive brush- and lavage-collected self-samples.

Table 1. QIAsure assay positivity rates

Clinical endpoint	Fraction	Positivity rate (95% CI)
All carcinomas	69/69	100.0% (94.0–100.0)
Adenocarcinoma	10/10	100.0% (69.0–100.0)
Squamous cell carcinoma	59/59	100.0% (94.0–100.0)
CIN 3+	88/99	88.9% (81.0–93.7)
CIN 3	19/30	63.3% (45.1–78.4)
CIN 2	22/42	52.4% (37.5–66.8)
≤CIN 1	33/117	28.2% (20.8–37.0)

QIAsure detects 100% of cervical carcinomas*

*QIAsure has 100% accuracy in detecting biomarkers associated with cervical carcinoma in patients.

Meeting your need for clinical assurance

Current cervical screening algorithms lack an objective and accurate test to identify cervical precancer and cancer before it becomes a threat to the patient's health. The current clinical focus on hrHPV testing and genotyping lets clinicians know whether a patient *could* develop cervical cancer; however hrHPV infection is a risk factor, not an indicator of cervical cancer. Further testing is needed to identify patients who need immediate follow-up and treatment versus close surveillance.

QIAsure provides an effective triage test in cervical screening to fulfill the need for more actionable molecular insight into whether a patient has cervical precancer or cancer. It can separate out patients with hrHPV infections that are transforming into cancer from patients who have low short-term risk of developing cancer. This means QIAsure can guide surveillance and treatment decisions, and prevent women with non-transforming infections from receiving unnecessary treatments.

Clinical Examples

Sophie (age 32) undergoes primary screening for HPV and discovers she is at risk for cervical cancer due to detection of hrHPV. QIAsure is performed on the same sample to detect the presence of precancer or cancer. QIAsure produces a negative result and the clinician schedules a six-month follow-up appointment. QIAsure separates transforming hrHPV infections from non-transforming infections so that Sophie can be confident she is safe from cancer.

Clinical examples, continued

Veronica (age 30) has a high-risk HPV infection and returns for her six-month follow-up appointment. A pap smear discovers abnormal cytology and she undergoes colposcopy to look for CIN lesions. CIN 1 and 2 are present; however the level of short-term risk is unclear since there is no molecular insight into whether the lesions are actively transforming into cancer or could subside on their own. The patient and clinician discuss options for treatment since treatment could inhibit Veronica's ability to carry a pregnancy to term. QIAsure is performed providing the clinician more insight into what's happening at a molecular level and providing critical information to make the best clinical decision.

Emma (age 34) has hrHPV, but normal cytology. A confirmatory QIAsure test is performed and produces a positive result, indicating the presence of transforming precancer. Emma is sent straight to colposcopy and treated for CIN 3. If she hadn't had the QIAsure test, she would have had to wait 6 months before being re-tested, putting her life and reproductive health at risk. QIAsure identifies transforming hrHPV infections that can be missed by cytology and genotyping so that Emma is safe from dangerous precancer that could have rapidly progressed to cancer.

Clinical implications

QIAsure can deliver objective assurance that women are safe from cervical cancer following a positive hrHPV result or an abnormal cytology result. The high sensitivity and specificity of QIAsure offers reassurance for absence of cervical cancer in test negative women; a positive test identifies women who need immediate treatment. Unlike cytology, *FAM19A4/miR124-2* methylation analysis on hrHPV-positive cervical specimens detects 100% of biomarkers associated with cervical cancer, and identifies advanced transforming CIN2/3.

QIAsure bridges a gap in cervical screening as an accurate and objective triage test that can be performed on the same sample used for hrHPV testing. It is a unique and effective method to see beyond HPV and gain molecular insights into whether a hrHPV infection is actively transforming into cervical cancer. It provides clinicians with a new way to detect the presence of cervical precancer and make informed decisions about follow-up treatment.

Moreover, QIAsure provides peace of mind for patients so they can live their lives safe, confident, and sure of their reproductive health.

QIAGEN and cervical cancer prevention

QIAGEN is a worldwide leader in innovative Sample to Insight® solutions for molecular diagnostics, applied testing, advanced genomics, and clinical and academic research. QIAGEN is committed to the highest standards of performance and service excellence to create real-world value for our customers and real-world human impact for millions of patients across the world.

Since the launch of the *digene* HPV Test in 1999, QIAGEN has been at the forefront of advanced HPV screening and cervical cancer prevention. Considered the gold standard for HPV testing, the *digene* HPV Test uses advanced molecular technology to provide a highly accurate means of identifying women at risk for cervical cancer. For almost 20 years, clinicians around the world have used the *digene* HPV Test to routinely screen more than 100 million women for the presence of HPV. QIAGEN is deeply committed to helping women in developing nations around the world gain access to essential cervical cancer screening through its QIAGEN*cares* and *care*HPV® initiatives.

QIAGEN is excited to bring its newest Women's Health solution to market—QIAsure, a qMSP triage test for objective detection of cervical precancer and cancer.

Ordering Information

Product	Content	Cat no.
QIAsure Methylation Test	For 72 reactions: 2 Master Mixes, 2 Calibrators.	616014
Related Products		
Rotor-Gene® Q MDx 5plex HRM System	Real-time PCR cycler and High Resolution Melt analyzer with 5 channels (green, yellow, orange, red, crimson) plus HRM channel, laptop computer, software, accessories: includes 1-year warranty on parts and labor, installation and training	9002033
Rotor-Gene Q MDx 5plex HRM Platform	Real-time PCR cycler and High Resolution Melt analyzer with 5 channels (green, yellow, orange, red, crimson) plus HRM channel, laptop computer, software, accessories: includes 1-year warranty on parts and labor, installation and training not included	9002032
Rotor-Gene AssayManager®	Software for routine testing in combination with the Rotor-Gene Q and QIAsymphony® RGQ instruments; single license software for installation on one computer	9022739

For more information about QIAsure, visit **www.qiagen.com/qiasure**.

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