CINtec® Histology Test
Frequently Asked Questions

High-grade disease can’t hide anymore
CINtec® Histology Test

FAQ Topics:

- MEDICAL VALUE
- PROTOCOL
- PRICE
- OTHER
MEDICAL VALUE Questions - CLICK for Answers

What is the difference between 510(k) CINtec® Histology and the original Class I CINtec® products?

Why move from a validated laboratory developed test (LDT) for p16 to the new 510(k) CINtec® Histology test?

Why add CINtec® Histology to your cervical testing menu?

Can other p16 clones be substituted for evaluation of cervical biopsies?

Why is the CINtec® Histology product registered as a 510(k) device and not a PMA?

Is there new scientific evidence supporting use of CINtec® Histology for clinical evaluation of cervical biopsies?

What are the views from cervical cancer experts and medical societies regarding CINtec® Histology?

If CINtec® Histology is used to aid in evaluation of precancerous cervical lesions, what tests are run to confirm cervical cancer?

What peer-reviewed publications are available that discuss why CINtec® Histology should be used?
Why is the new 510(k) CINtec® Histology test priced higher than the original Class I CINtec® products?
<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Why must VENTANA OptiView DAB IHC Detection Kit be used in the 510(k)-cleared CINtec® Histology assay?</td>
<td></td>
</tr>
<tr>
<td>Can VENTANA ultraView detection be used with the 510(k) CINtec® Histology product and can it be run on a VENTANA BenchMark XT automated staining instrument?</td>
<td></td>
</tr>
<tr>
<td>What is the stability/expiry dating for the new 510(k) CINtec® Histology product?</td>
<td></td>
</tr>
<tr>
<td>If currently using the Class I CINtec® p16 Histology product, is there a need to validate the 510(k) CINtec® Histology product?</td>
<td></td>
</tr>
<tr>
<td>What information is available to pathologists to help correctly interpret the CINtec® Histology test?</td>
<td></td>
</tr>
</tbody>
</table>
**OTHER Questions - CLICK for Answers**

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Where is CINtec® Histology testing offered for sendouts?</td>
<td></td>
</tr>
<tr>
<td>What is the difference between CINtec® Histology and CINtec® PLUS Cytology?</td>
<td></td>
</tr>
<tr>
<td>Can CINtec® Histology also be used on cervical cytology specimens?</td>
<td></td>
</tr>
<tr>
<td>When will CINtec® PLUS Cytology (used on cervical cytology specimens)</td>
<td>be available in the U.S.?</td>
</tr>
<tr>
<td>What is the difference between CINtec® Histology and the HPV ASR probes</td>
<td>that Roche offers?</td>
</tr>
<tr>
<td>What is the cobas® HPV Test used for and how does it fit with the Roche</td>
<td>Cervical Cancer Screening and Diagnostic Portfolio?</td>
</tr>
</tbody>
</table>
CINtec® Histology is now 510(k) cleared at the request of the FDA. In order to achieve this clearance, a clinical study was conducted to support the 510(k) clearance claims for CINtec® Histology. In addition, CINtec® Histology is validated as a complete assay (antibody + detection + instrument), not just the antibody. This provides an increased level of confidence in the assay with a clear indication of use in aiding the diagnosis of cervical precancer.

1. The CERvical Tissue Adjunctive aNalysis Study (CERTAIN). Roche data on file.
CINtec® Histology utilizes the E6H4 p16 clone, which is supported by over a hundred peer-reviewed publications and recommended by professional societies including the World Health Organization (WHO).\textsuperscript{2} In addition, the 510(k) FDA clearance is backed by one of the largest immunohistochemistry (IHC) clinical studies on record. No other clone is supported by this level of clinical validation/data, or has 510(k) clearance by the FDA. CINtec® Histology is the only p16 IHC test with proven performance.\textsuperscript{1, 3, 4, 5, 6}

1. The CERrvical Tissue Adjuctive aNalysis Study (CERTAIN). Roche data on file.
While interpreting cervical biopsies on the H&E-stained slide alone may be familiar, CINtec® Histology may provide for a more confident diagnosis along with H&E. CINtec® Histology can serve as a locator tool by highlighting CIN lesions that may not have been identified on the initial review of the H&E-stained slide. In addition, CINtec® Histology may help in the differential diagnosis when a suspicious area is identified on the H&E-stained slide.³

In the Roche 510(k) clinical study (the CERTAIN study),¹ CINtec® Histology is shown to help improve consistency of diagnosis across pathologists. In addition to the CERTAIN study, other studies have shown that the CINtec® Histology test, when used in conjunction with H&E, significantly improves interobserver agreement compared to H&E alone.⁴

1. The CERrvical Tissue Adjctive aNalysis Study (CERTAIN). Roche data on file.
CINtec® Histology (and the E6H4 clone) is the only 510(k)-cleared IVD product on the market for objective biomarker evaluation of cervical biopsy specimens. More than 100 peer-reviewed publications and 4 major clinical studies support the medical value of CINtec® Histology. The E6H4 clone is exclusive to Roche. There are many other p16 clones, all of which are labeled for research use only (RUO). None of them has been validated for clinical use and should not be promoted or used in the clinical cervical cancer-testing space.
CINtec® Histology is used as an adjunct to H&E. Based on this criteria, the FDA recommended CINtec® Histology be registered as a Class II medical device (510(k) de novo).
The clinical study supporting the CINtec® Histology 510(k) clearance (the CERTAIN study)¹ was the largest immunohistochemistry (IHC) study conducted thus far for clinical evaluation of cervical biopsies. There is a significant amount of valuable data generated from this study. A number of peer-reviewed publications describing the CERTAIN study and its conclusion will be forthcoming.

1. The CERVical Tissue Adjunctive aNalysis Study (CERTAIN). Roche data on file.
In 2012, the LAST (Lower Anogenital Squamous Terminology) recommendations were developed by an interdisciplinary team led by the College of American Pathologists (CAP) and the American Society for Colposcopy and Cervical Pathology (ASCCP). The LAST recommendations indicate that only p16 IHC (CINtec® Histology) has sufficient scientific and medical evidence to be used along with H&E in evaluation of cervical biopsies.\(^5\) The LAST recommendations were adopted by the World Health Organization (WHO) in 2014.\(^6,7\)

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Invasive cervical cancer has very distinct histological characteristics that may be readily identified using H&E alone. However, cervical precancerous lesions can be challenging to identify by histological assessment of H&E alone. Some lesions could be small and/or look like a benign mimic and be missed on the H&E. CINtec® Histology provides objective information to help identify cervical precancer by highlighting areas of interest. Just as important, it can help rule out cervical disease within cervical biopsies. This allows the pathologist to re-review these corresponding areas in more detail on the H&E-stained slide of the cervical biopsy to render a final diagnosis. This is why the addition of the objective biomarker information provided by CINtec® Histology is critical to driving consistency in diagnosis.²⁴

There are a large number of peer-reviewed publications that support the scientific and medical value of CINtec® Histology (clone E6H4). Some of the key publications include Bergeron et al., which supported the CE/IVD clinical registration of CINtec® Histology outside the U.S., as well as Ordi et al. and Galgano et al., both of which further describe the value of CINtec® Histology. Darragh et al. describes the CAP/ASCCP LAST recommendations for use of p16 IHC (CINtec® Histology) in the evaluation of cervical biopsies.
Generally we price our higher-medical-value assays at a premium due to the much greater investment in resources needed to meet the stringent criteria for 510(k) clearance or PMA approval from the FDA. The FDA required that CINtec® Histology be taken to a 510(k), given how the assay is used in the market today. Thus, we had to reevaluate the pricing of CINtec® Histology to reflect the 510(k) status it now has.
When optimizing the CINtec® Histology assay for 510(k) clearance, the best staining was found to occur with the OptiView DAB IHC Detection Kit. Thus, OptiView detection was used for the CINtec® Histology clinical validation studies supporting our 510(k) clearance. Other high-medical-value tests that use OptiView Detection include the VENTANA ALK (D5F3) CDx Assay and the VENTANA PD-L1 (SP142) Assay.
CINtec® Histology was FDA cleared and clinically validated on the VENTANA BenchMark ULTRA IHC/ISH instrument using the OptiView DAB IHC Detection Kit. Running the assay on any other instrument or with any other detection kit has not been 510(k) cleared by the FDA.
The 510(k) CINtec® Histology product’s stability/expiry dating is 24 months from date of manufacture (same as the current Class I CINtec® p16 Histology dispenser-based product). Customers will receive product with a minimum of 12 months dating.
The 510(k) CINtec® Histology product uses a new protocol (The CINtec® Histology procedure is used solely on the VENTANA BenchMark ULTRA instrument) that is tied to the 510(k) product. It is recommended that your laboratory perform validation studies according to your established procedures and requirements.
In addition to the Interpretation Guide and the Compendium & Staining Atlas, there is online education for pathologists—CINtec® Histology Interpretation on Roche Diagnostics University—to provide a more detailed understanding of how to use and interpret the CINtec® Histology test. This online education consists of 4 modules that can be reviewed at https://usdiagnostics.roche.com/en/education/overview.html
Our CINtec® Histology user base is extensive (hundreds of labs). We can help identify a suitable laboratory partner to meet your needs.
CINtec® PLUS Cytology is an immunocytochemistry (ICC) test used to identify the co-expression of p16 and Ki-67 in cervical cytology specimens. Co-expression of these two biomarkers in the same cell indicates the cell cycle is deregulated. CINtec® PLUS Cytology is not currently available in the U.S.
CINtec® Histology is indicated for use on formalin-fixed, paraffin-embedded (FFPE) cervical biopsy specimens. This product has not been validated for use on cytology specimens.
The CINtec® PLUS Cytology test will be a Class III PMA device and is not expected to be available in the U.S. until 2020.
HPV mRNA ISH probes are analyte-specific reagents for labs to independently create and validate LDTs. The HPV mRNA ISH probes are supported by analytical data only for the detection of specific HPV mRNA genotypes in formalin-fixed, paraffin-embedded (FFPE) tissue. The HPV mRNA ISH probes are not supported by any clinical data, recommendations for use in specific FFPE tissues, or recommendations on how to automate/use the product.

The CINtec® Histology product is supported by full 510(k) requirements as mandated by the FDA (e.g., clinical verification and validation, stain interpretation, as well as analytical verification and validation). The product labeling and claims indicate specific use of the product on cervical tissue and how to use the product. Furthermore, CINtec® Histology is supported by medical society recommendations.5,7


The **cobas®** HPV Test is FDA approved for screening for HPV in cervical cytology specimens. It is a PCR-based test that identifies the 14 most prevalent high-risk HPV (hrHPV) genotypes associated with cervical cancer. It is the only clinically validated, FDA-approved assay that simultaneously reports pooled hrHPV results and individual HPV 16 and HPV 18 results in a single test.

Should a woman have an abnormal Pap cytology screening result and/or be positive for hrHPV (particularly HPV 16 or HPV 18), it is likely that the woman will undergo colposcopy and cervical biopsy. The cervical biopsy is stained with H&E and a second serial section is stained with CINtec® Histology. The final diagnosis of cervical precancer is based on the combined evaluation of the H&E-stained slide along with the CINtec® Histology-stained slide.
References

1. The CERrvical Tissue Adjuctive aNalysis Study (CERTAIN). Roche data on file.


