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PROFESSIONAL MEDICAL PRODUCTS

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TEST VAGINITE FEMLAB® FEMLAB® VAGINITIS TEST KIT

Usò Professionale
Professional Use

REF 29111 / V02-512



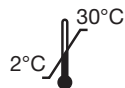
Ameritech Diagnostic Reagent Co., Ltd
K4-2 Science Technology Garden,
Economic Development Zone, Tongxiang, ZJ, China
Made in China



AR Experts BV,
Boeingavenue 209, 1119 PD Schiphol-Rijk, The Netherlands

IVD

PER USO PROFESSIONALE
FOR PROFESSIONAL USE



Tampone/Swab:



Zhejiang Gongdong Medical Technology Co., Ltd.
NO.10 Beyuan Ave., Huangyan, 318020
Taizhou, Zhejiang, China
Made in China



Shanghai International Holding Corp. GmbH (Europe)
Eiffestrasse 80, 20537 Hamburg, Germany

STERILE EO



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The FemLab® Vaginitis test kit is a screening device for use in the detection of the major forms of vaginitis in vaginal fluid specimens from women concerned about their vaginal health.

SUMMARY AND EXPLANATION OF THE FEMLAB® VAGINITIS TEST KIT

Vaginitis is defined as irritation of the vagina, a troublesome condition that affects millions of women of all ages in all parts of the world. The most common types of vaginitis are Bacterial vaginitis, Candida yeast infections, Trichomoniasis, and trachomatis. These common forms of vaginitis can usually be treated effectively with prescription or over-the-counter medication if correctly diagnosed. However, if left untreated, misdiagnosed or incorrectly treated, vaginitis can produce serious consequences such as sterility or miscarriage, and it can be a precursor to cancer. The various types of vaginitis will be discussed in detail in a later section of this package insert. The FemLab® test kit is an easy to use product that can accurately diagnose common types of vaginitis within a few minutes. The test kit is intended to be used by or under the direction of a trained medical professional. The test kit is very easy to use and only minimal training is necessary for staff level technicians to become proficient in the accurate diagnosis of vaginitis in any particular case. Such trained professionals can also easily instruct or assist patients with the use of the kit on their own. To use the kit, samples of vaginal fluids are taken on sterile swabs, and are either applied to test zones on the test kit platform, or diluted in a specially designed buffer delivery system for application to the remaining test zones. The test results are evaluated by comparing the color change results for each of the six test zones to the colors on the test cassette, and then consulting the diagnosis protocol described later in this document. Each major form of Vaginitis may be accurately diagnosed by following this methodology.

Treatment or recommended treatment regimens require the consultation of a medical professional. FemLab® is not to be used for self-diagnosis and self-treatment.

INTENDED USE

The FemLab® test kit will be used only on site in physician's offices, clinics, and hospital or professional laboratories - point of care sites - where women will visit in person to have the test performed. The test kit procedures may be performed only by trained medical professionals who have carefully read, and understand, the Instructions for Use. Samples must be tested on site, and may not be transported for testing in remote locations. The FemLab® test kit may not be used at a pharmacy, unless the pharmacy is also a professional laboratory or other point of care site, where women visit in person to have the test performed by a medical professional who has been trained in the use of the test kit. Samples may not be transported for testing in remote locations. As the FemLab® test kit is to be used as a screening tool, the diagnosis of any vaginitis condition will depend on the careful analysis of the FemLab® results as described in this document. All final diagnostic conclusions, including medical decisions regarding patient treatments, are the responsibility of the treating medical professional. The FemLab® test kit is primarily a screening tool, and any positive results should always be referred to a clinician for further evaluation and for treatment.

PRINCIPLES OF THE TEST

The FemLab® test kit has a total of seven sample application zones on the small plastic test platform. Each test zone and the color changes for each positive and negative result are described in detail in this document. The seven test zones are individual chemical and biological tests that screen for specific chemical or biological aspects of the vaginal fluid samples. These test zones can accurately differentiate between the various disease states (see Interpretation of Results later in this document). Vaginal fluid samples are collected in a three-step collection procedure; two samples are used directly on test zones, and the

third is diluted in a custom designed buffer dilution and delivery system. The test results are determined by observing color changes on each test zone following sample application. The colors are compared to a color chart on the test cassette to draw conclusions as to the results of each test. A diagnostic protocol to accurately determine the condition causing the vaginitis will be described in this document. The diagnostic protocol detailed below, and the sample collection and application instructions must be followed closely to achieve an accurate diagnosis. Descriptions of each test zone, drawings of the test cassette and recommended methods of use are shown below.

ZONE 1: PH ZONE

The normal pH of vaginal fluid is in the range 3.8 - 4.2. After application of the test fluid sample, if the pH test zone (zone 1) turns from pink to light blue-green within 1 minute, the pH is above 4.7, which indicates a positive result. If the vaginal fluid is below pH 4.7, the color remains pink, indicating normal vaginal pH. The pH zone change to a light blue-green color - an abnormally high pH - is a positive finding, consistent with bacterial vaginitis and/or trichomoniasis, microorganisms that impair the growth of the normal vaginal lactobacilli, which keep pH low.

ZONE 2A - 2B: GARDNERELLA ZONE

An enzyme activity test specifically designed to detect the presence of *Gardnerella vaginalis* bacteria and a few other infectious bacteria in vaginal fluid specimens is used in Zone 2. The development of a visible peach-to-pink-to-red color on the test swab after application of the vaginal fluid sample onto the test zone is a positive test result, indicating the presence of *Gardnerella* Bacterial vaginitis. No color change on the test swab indicates there is no *Gardnerella* infection.

ZONE 3: NITRITE ZONE

This test zone depends upon the chemical conversion of nitrate to nitrite by the action of gram-negative bacteria in the vaginal fluid. If the test procedure using the buffer diluted vaginal fluid sample turns the test zone from colorless to a pink color, this is a positive reaction consistent with the presence of a yeast infection. If no color change is observed, this indicates a lack of yeast.

ZONE 4: BLOOD ZONE

A vaginal infection may result in bleeding in the vaginal cavity. After application of the buffer diluted vaginal fluid sample onto the Blood Zone, a color change from yellow to dark green or blue is an indication of blood in the vaginal fluid. The presence of blood indicates the possibility of a infection or severe Bacterial vaginitis. A confounding factor can be the presence of menstrual blood in the sample, which may result in a false positive test. If menstrual blood may be present, this zone should be given less weight in the diagnostic scheme.

ZONE 5: PROTEIN ZONE

Application of the buffer diluted vaginal fluid sample onto the Protein Zone will result in a blue color if the protein concentration in the vaginal fluid exceeds normal levels. A blue color, a positive reaction, is consistent with the presence of Bacterial vaginitis, but also may occur with other forms of vaginitis. The infectious organisms produce pus, which will result in abnormal protein levels in the vaginal fluid.

ZONE 6: LEUKOCYTE ZONE

Application of the buffer diluted vaginal fluid sample onto the leukocyte zone will result in a color change to pink or light purple if white blood cells are present. Light purple indicates a positive result, indicating a *Trichomonas* infection, depending on the status of other test zones. If there is no color change, this indicates no *Trichomonal* infections.

PACKAGE CONTENTS AND INSTRUCTIONS FOR USE

Warnings and precautions

- Check the expiration date printed on foil pouch and carton box. Do not use the test kit after the expiration date.
 - Do not use the test kit if the foil pouch is not sealed, or if the pouch is broken.
 - Do not remove the test from foil pouch until ready to use. Once the foil pouch has been opened, the test must be used within 60 minutes.
 - To obtain accurate results, the Package Insert Instructions for Use must be read before using the test kit, and followed closely.
 - Do not use the vaginal fluid collection container if it is broken or the buffer is leaking out.
 - This product is intended only for vaginal fluid use. Do not touch or collect vaginal fluid near the cervix.
 - Do not use vaginal fluid specimens that contain blood.
 - Only use the sterile tri-pack swabs included with the test kit. Do not use sterile swabs if the package is not sealed or if the seal has been broken.
 - Patient vaginal swabs are not appropriate for any other purpose, including bacterial culture, after performing the test.
- Dispose of patient samples in biological sample disposal containers.

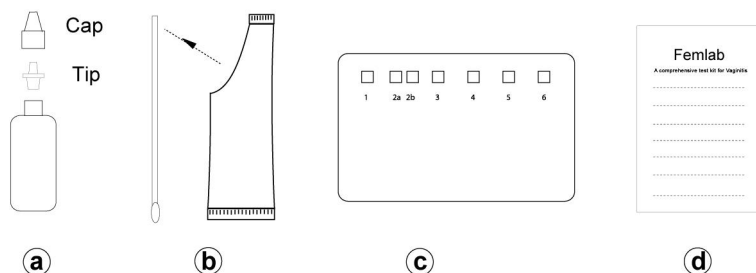
Test tray and supplies

This package contains the following items:

- Vaginal fluid specimen container with buffer solution
- Tri-pack Sterile Swab
- Instructions for Use (Package Insert)
- Test Tray

Instructions for use

This test kit is intended for use by a trained medical technician, nurse, nurse practitioner, physician's assistant, or physician, or by a patient under the guidance of one of these trained medical practitioners. The instructions for use shown below should be studied carefully and followed exactly to ensure accurate sample collection and application, and therefore reliable and accurate results.



Drawing 1 - Contents of Package

- a) Vaginal Fluid Specimen Container with Buffer Solution
- b) Tri-pack Sterile Swab
- c) Instructions for Use (Package Insert)
- d) Test Tray

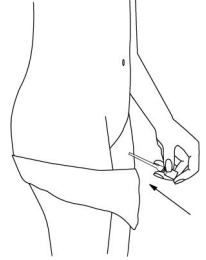
The package also contains this package insert and instructions for use. Patient records are recorded on the FemLab® cassette by circling each positive or negative finding on the cassette label.

COLLECTION OF VAGINAL FLUID SAMPLE

Open the package and identify the vaginal fluid specimen container with buffer (a), the tri-pack of three sterile swabs (b), the test tray (c) and the insert (d).

Wash hands thoroughly, and observe sterile technique while taking and testing vaginal fluid samples.

First, thoroughly swab the inner and outer labia of the patient with a sterile wipe to reduce the exterior bacterial count from the vaginal opening. Open the sterile tri-pack of sample collection swabs, and gently open the vaginal opening, and insert the swabs about two to three inches into the vagina. Do not insert near the cervix, as pH results would be inaccurate.



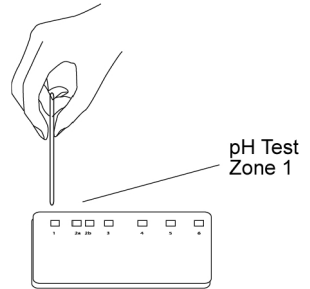
Drawing 2 - Insertion of sterile swab tri-pack into vagina

Gently stroke the inner walls of the vagina with the swabs, ensuring that the swabs are all moistened thoroughly. Leave the swabs in the vagina several minutes to ensure they are saturated with vaginal fluid.

Remove the test cassette tray from the foil pouch. Write the patient's name in the space provided on the FemLab® test cassette.

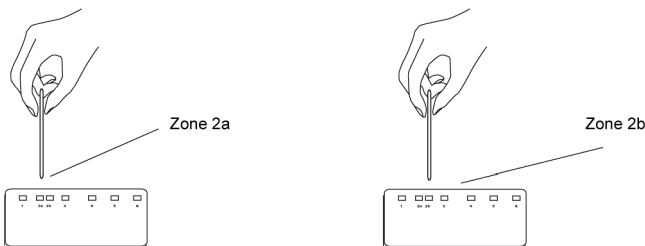
Remove the three swabs from the vagina.

Rub one swab saturated with fluid sample onto Zone 1 - the pH zone - of the test tray. Discard the swab in a biological specimen container. Read the pH color after one minute, and note the result on the Test cassette tray next to the pH Zone Result color comparison chart. Simply circle the color - either positive or negative - with an ink pen.



Drawing 3 - Application of swabs onto test Zone 1, pH Zone

While the pH Zone color is developing, take a second swab and rub onto Zone 2a six or seven times. Then, immediately rub this same swab onto Zone 2b several times. Wait 1 - 5 minutes. If the swab itself becomes peach or pink within One minute, it is a positive reading for Gardnerella. Record the Gardnerella result on the test cassette near the Gardnerella Zone Result color comparison.



Drawing 4 - Application of swabs onto test Zone 2, Gardnerella zone

Finally, take the third swab, open the vaginal fluid specimen container with buffer solution, and thoroughly mix the swab into the buffer in the container. Swirl the swab vigorously for 15 seconds, and then expunge as much liquid as possible from the swab by pressing and rotating the fiber portion against the wall of the specimen collector. Discard the swab. Screw the tip securely into the specimen container (a). Then screw the cap onto the specimen container (a).



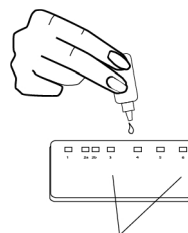
Drawing 5 - Screw the Tip and Cap onto the Specimen Container

After the specimen container (a) is tightened securely, shake vigorously up and down ten (10) times.



Drawing 6- Shake vigorously up and down ten (10) times

Squeeze the vaginal fluid collection container device above each of test zones 3 through 6. Use one drop on each of test zones 3 through 6.



Zones 3-6

Drawing 7 - Squeeze buffer solution and place the droplets into zones 3 - 6

Wait about two minutes, and then read the color results for each of the test zones 3 through 6. Promptly circle the square that most closely matches the test zone color.

Note: It is important to read the test results within two (2) to three (3) minutes after placing the droplets of specimen onto the test zones.

Discard the specimen collection container with the second and third swabs in a biological specimen container.

IMPORTANT ISSUES TO OBTAIN BEST RESULTS

- The specimen used for pH testing must be an undiluted vaginal fluid sample.
- The specimen used for Gardnerella testing must be a separate undiluted sample.
- The specimen used for the remaining tests must be diluted in the buffer solution container as directed.
- The collection of the vaginal fluid sample should be performed in a single step.
- Ensure that nothing remains inside of vagina after collection.
- Read the colors on the test cassette within the prescribed time of application of the sample, and circle the color result with a pen on the cassette to record the results.

QUALITY CONTROL

Each production lot of FemLab® cassettes is tested rigorously at the factory before packaging and shipping, with both positive and negative control reagents.

KIT STORAGE

Store the FemLab® test kit at 2-30 degrees C (35 - 86 degrees F), out of direct sunlight.

INTERFERENCE ANALYSIS

Potentially interfering chemical such as self-medication, Spermicide, Iodine and douches that commonly available in over the counter of drug store were supplemented to negative and positive vagina fluid. Then we apply such mixed solution on FemLab® Test Kit to run analysis of interference. Each chemical had 20 run. The results of studies are summarized as following;

	Negative Test	Positive Test
Iodine Potassium Decolorized Iodine Tincture Rite Aid Brand	-	+
Disposable Douche Rite Aid Brand	-	+
Spermicide Rite Aid Brand	-	+

It may be concluded from this analysis that none of self-medication in above Table interfered with the ability of FemLab® to correctly analyze both positive and negative control samples. Both the normal (negative) sample and the positive control test solution were correctly diagnosed with FemLab® irrespective of the presence of the potentially self-medication.

CROSS REACTIVE ANALYSIS

The ability of the FemLab® Test Kit to specifically detect various vaginal infection were challenged through cross reaction studies on indigenous flora to vaginal cavity such as Staphylococcus aureus, Lactobacillus spp and Group B Streptococcus that may be potential cross reacting with FemLab® device. The specificity study was done at laboratory. Negative and positive vaginal fluid samples were spike with above microorganisms then run a test on. These samples were tested on the FemLab® Test Kit. Each microorganism had 10 run. Total 30 test results are summarized into the following table.

	Negative Test	Positive Test
Staphylococcus Aureus	-	+
Lactobacillus spp.	-	+
Group B Streptococcus	-	+

The results show none of above microorganisms had cross reactivity with FemLab® Test Kits. In-vitro, those microorganisms should not have cross reaction with device.

LIMITATIONS OF THE TEST KIT

- The FemLab® test kit is to be used as a screening device. Final diagnostic results should be rendered by medical professionals, who may recommend additional laboratory or med-

ical testing to confirm any diagnosis.

- The absence of any positive results with the FemLab® test kit does not rule out the presence of vaginitis.
- Test results may be affected by improper specimen collection, handling and procedure.
- Mixed infections may occur. Therefore, a test result indicating one positive result does not rule out the presence of other infectious organisms.

INTERPRETATION OF RESULTS FROM THE FEMLAB® TEST KIT

The major forms of Vaginitis can be determined fairly accurately by a careful analysis of the FemLab® test results as recorded on the test cassette color chart. The following diagnostic protocol will provide guidance in this process.

It cannot be emphasized enough that accurate results require that the vaginal fluid sample collection methodology and test application methodology be performed according to the instructions in this document.

The diagnostic protocol will be described below in three sections: (1) Test Zone Color Interpretation - will describe generally what the color result for each test zone means; (2) Identification of Infectious Organisms - will describe the combinations of test zone results that identify a particular organism; and (3) issues of interpretation important to accurate diagnoses.

TEST ZONE COLOR INTERPRETATION

Zone 1 - pH Test Zone: A light blue-green color indicates a positive result, a pH above 4.7. This may indicate a bacterial infection and will also be present with most cases of Trichomonal vaginitis if Leukocytes, Zone 6, are also present. No color change indicates a pH below 4.7, which is normal for the vagina. This indicates the absence or very low level of bacterial infection or Trichomoniasis.

Zone 2 - Gardnerella Test Zone: A peach-pink color indicates a positive result. The Gardnerella test zone (2b) and the test swab used on Zone 2 will turn peach-pink within five minutes if a Gardnerella bacterial infection is present. A positive result specifically indicates the presence of Gardnerella bacteria. A negative result means that Gardnerella is not present, but infections from other bacteria are not ruled out by a negative result.

Zone 3 - Nitrite Test Zone: A pink color indicates a positive result. The nitrite test zone will turn to pink if the conversion of nitrate to nitrite by the action of gram-negative bacteria in the vaginal fluid occurs. This result reliably indicates the presence of Yeast infections.

Zone 4 - Blood Test Zone: A dark green or blue color indicates a positive result. The blood test zone turns from yellow to dark green if red blood cells are present in the buffer diluted vaginal sample. Menstrual blood in the sample may result in a false positive test. If menstrual blood is suspected, less weight should be given to the blood zone.

Zone 5 - Protein Test Zone: A blue color indicates a positive result. The protein test zone will turn to blue if the buffer diluted vaginal fluid sample contains protein in excess of normal values. A positive result is associated with bacterial, yeast and Trichomonal infections. Serious occurrences of these infections will produce pus which shows up as positive protein in the protein test zone. A negative protein zone result is associated with the absence or low levels of these infectious organisms.

Zone 6 - Leukocytes Test Zone: A light purple color indicates a positive result. The Leukocyte test zone, initially colorless, turns to light purple with application of the diluted vaginal fluid specimen if white blood cells are present in the sample. A positive result indicates the presence of Trichomonas parasites infection. If both leukocyte and pH tests are positive (zones 1 and 6), it is likely that Trichomonas is present. A negative leukocyte zone result indicates the absence or very low levels of Trichomonas.

IDENTIFICATION OF INFECTIOUS ORGANISMS

The following two tables (Table I and Table II) summarize the interpretation method for the FemLab® test kit.

To use the Diagnostic Protocol in Tables I and II below, compare the test zone color results on the FemLab® Test Kit to the test zones on the Tables.

The cells in Table I indicate the general positive and negative interpretations for each Zone color result.

Use this information to evaluate the possible disease states diagnosed by the FemLab® cassette results Table II shows the expected result for the four main pathogenic organisms that are causes of vaginitis.

Compare the actual FemLab® test cassette color results to the positive and negative cells on Table II. If any combination of zones on the test kit match those in Table II, the corresponding disease organism is correctly identified. If specific test zones on the FemLab® cassette are negative and the corresponding cells in Table II are positive, then that disease organism is not present. If the zones for a particular organism match, and other zones also match another organism, then this is a multiple diagnosis, and multiple organisms are present.

Table I - FemLab® Test Kit Test Zone Interpretation Table

Test Result	Positive Color	Negative Color	Positive Result Interpretation	Negative Result Interpretation
pH Zone 1	Blue-green	Pink	Bacterial Vaginitis and/or Trichomonas	No or low level bacterial infection. Trichomonas still possible
Gardnerella Zone 2	Pink	No color	Bacterial Vaginitis and/or Gardnerella	No Gardnerella infection
Nitrite Zone 3	Pink	No color	Yeast infection	No or low level yeast or bacterial infection
Protein Zone 5	Blue	Light Yellow-green	Bacterial, Yeast or Trichomonas infections, associated with severity	No color change suggests only moderate infections of any types
Leukocytes Zone 6	Pink-purple	No color	Trichomonas infection if pH (Zone 1) also positive	No color change indicates patient has no Trichomonal

Table II - FemLab® Test Kit Diagnostic Conclusions

Test Zone	Zone 1 pH	Zone 2 Gardnerella	Zone 3 Nitrite	Zone 4 Blood	Zone 5 Protein	Zone 6 Leukocytes
Bacterial Vaginitis	Positive	Positive or Negative	Negative	Negative (or Positive, severe Bacterial Vaginitis)	Negative (or Positive, severe Bacterial Vaginitis)	Negative
Yeast Vaginitis	Negative	Negative	Positive	Negative or Positive (severe Yeast Vaginitis)	Negative	Negative
Trichomonal Vaginitis	Positive (or Negative, light Trichomonal Vaginitis)	Negative	Negative	Negative	Positive or Negative	Positive
Healthy	Negative	Negative	Negative	Negative or Positive (during menstrual period)	Negative	Negative

PERFORMANCE CHARACTERISTICS - FEMLAB® CLINICAL TRIAL RESULTS

The performance of the FemLab® test kit to detect Bacterial, yeast, Trichomonas vaginitis in vaginal fluid specimens collected from symptomatic and asymptomatic patients, was determined in a multi-center study conducted at three geographically separate clinical sites. A total of 300 women were enrolled and tested. Study site personnel performed the FemLab® test according to a specific protocol, and also performed traditional tests for comparison to the FemLab® results. The study personnel performed control tests on each patient, and reported diagnoses of the most important vaginitis disease entities: Bacterial Vaginitis, Gardnerella, Yeast Vaginitis, and Trichomonas vaginitis. In addition, clinical evaluations of the severity of symptoms in the presenting patients were recorded.

The traditional tests used as control methods included commercially available pH and Gardnerella tests, wet mount microscopic evaluation of samples for Trichomonas parasites, and culture systems for detection of yeast. A pelvic exam was performed on each patient to determine overall level of vaginal health.

The clinical trial results are discussed below, first with a general comparison between results, and then specific comparisons of the ability of each method to diagnose infectious organisms. The results for each diagnosis as found by the FemLab® Test Kit are compared to the results found by the control methods, and are reported in a 2 by 2 chart from which the statistical model may be calculated.

The terms positive (+) and negative (-) are used to refer to the presence or absence of the condition of interest, the presence of an infectious diagnosis. Thus there are true positives and true negatives, where both methods of diagnosis agree. There are also two cells on each chart where the diagnoses disagree.

These proportions are described with the following terms:

Sensitivity is the proportion of true positives that are correctly identified by the test, compared to the control method.

Specificity is the proportion of true negatives that are correctly identified by the test, compared to the control method.

Sensitivity and specificity are one approach to quantifying the diagnostic ability of a diagnostic test. In clinical practice, however, the test result is all that is known, so we want to know how good the test is at predicting the abnormal condition. The comparison of sensitivity and specificity provide this means.

Performance Characteristics – Symptomatic vs. Asymptomatic Patients

As part of the clinical trial, pelvic exams were performed by gynecologists on each of the 300 patients enrolled, and the results were reported on a scale of 1 to 4. The pelvic examination reported the general condition of vaginal cavity, the color, amount and any odor of discharge, and other visible observations. The results were reported as the following;

I+: Slight discharge with no color and odor

II+: Slight discharge with redness and no odor

III+: White discharge with redness, slight odor and itching

IV+: White discharge with pus, redness, strong odor, burning and itching

Thirty eight women were found to be asymptomatic (I+). Of these women, however, 23 were also diagnosed by the hospital as having some form of vaginitis. Fifteen were found to be completely free from any form of vaginitis. FemLab® results on these asymptomatic women agreed: 21 women were found to have some form of vaginitis, and 17 were healthy.

The remainder of the trial population (262 cases) had clinical symptoms of vaginal disease, with pelvic exam reports of II+, III+ or IV+. Upon testing, only 10 of these cases were diagnosed as healthy with no form of infectious vaginitis by the hospital control methods, and by the FemLab® test, and these cases were in the II+ pelvic exam category. Thus, 96.2% of symptomatic patients had at least one, and sometimes more, diagnosis of Bacterial Vaginitis, Yeast Vaginitis, trichomoniasis infections. The conclusion that can be drawn from this analysis of the pelvic exam data is that pelvic exams are generally very accurate at predicting the presence of vaginitis, but that some forms of vaginitis are asymptomatic, and may not be diagnosed by this method alone. This suggests that pelvic exams are not sufficient in themselves in the final determination of vaginitis.

Performance Characteristics – Healthy vs. Diseased Patients

The ability of the FemLab® test kit to detect any of the various forms of vaginitis in vaginal fluid specimens collected in the multi-center study was compared to the results of the traditional tests for diagnosing any form of vaginitis.

Out of the 300 patients tested for any of the various forms of vaginitis, the FemLab® and hospital control diagnoses agreed in 284 cases, resulting in an overall agreement of 94.7%. In 18 cases (6% of the total), both FemLab® and reference methods concluded with a “Healthy” vaginal diagnosis. However, FemLab® found 7 cases with some form of vaginitis that the control methods missed, while the control methods found 9 cases with some form of vaginitis that were diagnosed “Healthy” by FemLab. These results are shown in Table III below. The significant level of overall agreement – 94.7% overall agreement - between the two methods suggests that FemLab® is very capable of diagnosing vaginitis.

Table III
Healthy Diagnosis - Comparison between FemLab® and Control Methods

		Control	Diagnosis	Method			
		Healthy	%	Diseased	%	Total	%
Femlab Diagnosis	Healthy	18	6%	9	3%	27	9%
	Diseased	7	2%	266	89%	273	91%
	Total	25	8%	275	92%	300	100%

Performance Characteristics – Bacterial Vaginitis and Gardnerella

The ability of the FemLab® test kit to detect Bacterial Vaginitis and Gardnerella in vaginal fluid specimens collected in the multi-center study was compared to the results of the control test methods for diagnosing Bacterial Vaginitis.

Bacterial Vaginitis is the most common vaginitis and has been associated with pelvic inflammatory disease, cervicitis, postoperative infection, abnormal cytology (cellular structure), and increased acquisition of human immunodeficiency virus infection and other sexually transmitted diseases. Bacterial Vaginitis can also cause obstetric complications such as preterm labor and low-birth-weight infants.

Common symptoms for Bacterial Vaginitis include: a milky, thin discharge at times; or a heavy, gray discharge and a “fishy” odor which may become more noticeable during intercourse. However, any individual may experience symptoms differently.

The performance of the FemLab® test for Bacterial Vaginitis was compared to the control group reference methods for diagnosing Bacterial Vaginitis.

Out of the 300 patients tested for Bacterial Vaginitis, the FemLab® and control method diagnoses agreed in 247 cases, resulting in an overall agreement of 82.3%. In 93 cases, both reference methods produced positive diagnoses for Bacterial Vaginitis (31% of the total). Thus, FemLab® and the control methods agreed on positive diagnoses for 93 of 104 cases that the control method found positive, yielding a sensitivity = 89.4%. (Sensitivity is the proportion of true positives that are correctly identified by the test. Specificity is the proportion of true negatives that are correctly identified by the test). Also, FemLab® and control methods agreed on negative findings 154 times out of 196 cases found negative by the control methods, yielding a FemLab® specificity of 78.6% for Bacterial Vaginitis. These results are shown in Table IV below.

Table IV

Bacterial (Bv) Vaginitis Diagnosis Comparison between FemLab® and Control Methods

			Control	Methods	Diagnosis		
		Bv +	(%)	Bv -	(%)	Total	
FemLab	Bv +	93	31%	42	14%	135	45%
Diagnosis	Bv -	11	4%	154	51%	165	55%
	Total	104	35%	196	65%	300	100%

The FemLab® test produced the following results for diagnosis of Bacterial Vaginitis: sensitivity = 89.4%; specificity = 78.6%; positive predictive value = 68.9%; negative predictive value = 93.3%; and overall agreement = 82.3%.

Performance Characteristics – Yeast Vaginitis

Yeast Vaginitis is very common. Even in asymptomatic, reproductive age women without recent yeast infection, there can be a 25-30% incidence of vaginal yeast colonization. Cultures are more often positive in women with a history of recurrent yeast infection than in asymptomatic women.

Vaginal pH is lower in yeast infections than other types of vaginitis and is usually in the range of 3.8-4.2 but almost always less than 4.5

Culture is an accurate method to diagnose yeast infections, but this only applies to symptomatic patients because there is a background of false positive diagnoses by culture methods in women without yeast problems. The cause of Yeast Vaginitis has at least two components. One is the presence of a yeast species growing in the vagina and the other is some change in the vaginal biochemical or immune environment that allows the yeast organisms to overgrow and produce symptoms. The most common yeast organism is candida albicans but other species of yeast also produce symptoms such as C. glabrata, C. tropicalis, C. guilliermondii and C. parapsilosis and others.

The performance of the FemLab® test for Yeast Vaginitis was compared to the preferred reference method for diagnosing Yeast Vaginitis - Culture media.

All of the 300 patients in the clinical trial population were evaluated for yeast infections. The FemLab® test kit diagnosis agreed with the reference control method in 260 cases (86.7% overall agreement). In the 128 cases where the hospital control methods produced a positive diagnosis for Yeast Vaginitis, the FemLab® test also showed positive results in 117 cases – fully 39% of the trial population (91.4% sensitivity). Also, in the 172 cases where the

hospital reference methods produced negative test results for Yeast Vaginitis, the FemLab® results agreed in 143 cases (83.1% specificity). (Sensitivity is the proportion of true positives that are correctly identified by the test. Specificity is the proportion of true negatives that are correctly identified by the test). Overall agreement between FemLab® and the results of the reference tests, in diagnosing both positive and negative results, was 86.7%.

Table V Yeast Vaginitis (Yv) Diagnosis
Comparison between FemLab® and Control Methods

			Control	Methods	Diagnosis		
		Yv +	(%)	Yv -	(%)	Total	
FemLab	Yv +	117	39%	29	10%	146	49%
Diagnosis	Yv -	11	4%	143	48%	154	51%
	Total	128	43%	172	57%	300	100%

Comparison To Control Methods: The FemLab® test produced the following results for diagnosis of Yeast Vaginitis: sensitivity = 91.4%; specificity = 83.1%; positive predictive value =80.1%; negative predictive value = 92.9%; and overall agreement = 86.7%.

Performance Characteristics – Trichomonas Infections

The traditional method of diagnosing trichomonal infections is a wet mount microscopic examination of vaginal secretions in saline. Careful examination may show moving organisms - trophozoites are about the size of a white blood cell with 3 flagella that cause the movement. Compared to DNA testing, which can pick up about 87% of positive Trichomonal cases, wet mount microscopy usually identifies only about half of cases. Symptoms can be similar to a yeast infection vaginitis. pH measurement of vaginal discharge for both is usually greater than 4.5.

Trichomonal Vaginitis is often asymptomatic, and even when symptoms are present, they correlate poorly with a clinical diagnosis of vaginitis. The relative lack of specificity of symptoms precludes a differential diagnosis based on symptoms. In the clinical study, Bacterial Vaginitis, Yeast infections, and Trichomoniasis were diagnosed on the basis of reference tests and the FemLab® test results. The overlap of the various diagnoses from both test methods shown on Table VII below shows the results of different test methods in patients stratified by clinical diagnosis.

The ability of the FemLab® test kit to diagnose Trichomonal infections was compared to the traditional method of wet mount microscopy used by the control laboratory.

In the trial population of 300 patients analyzed for Trichomonal Vaginitis, the FemLab® diagnosis agreed with the reference control method in 264 cases (88.0% overall agreement). In the 85 cases where the hospital control methods produced positive tests for Trichomonal Vaginitis, the FemLab® test also showed positive in 72 cases (84.7% sensitivity). (Sensitivity is the proportion of true positives that are correctly identified by the test. Specificity is the proportion of true negatives that are correctly identified by the test). In contrast, in the 215 cases where the hospital reference methods produced negative test results for Trichomonal Vaginitis, the FemLab® results were positive in 23 cases (89.3% specificity).

Table VI

Trichomonas Vaginitis (Tv) Diagnosis

Comparison between FemLab® and Control Methods

		Control	Diagnosis	Method			
		Ty+	%	Ty-	%	Total	%
Femlab Diagnosis	Ty+	72	24%	23	8%	95	32%
	Ty-	13	4%	192	64%	205	68%
	Total	85	28%	215	72%	300	100%

Comparison To Control Methods: The FemLab® test produced the following results for diagnosis of Trichomonal Vaginitis: sensitivity = 84.7%; specificity = 89.3%; positive predictive value 75.8= %; negative predictive value = 93.7%; and overall agreement = 88.0%.

Performance Characteristics – Other Vaginal Diseases

Sexually transmitted diseases such as syphilis, gonorrhea, HPV or Herpes are not detected directly by the FemLab® test kit. In some cases of such diseases, such as an aggressive Herpes infection, the FemLab® test may report pH, blood, or protein as positive due to the symptoms of the Herpes. In such cases, pelvic exams will clearly reveal the cause of the symptoms, and additional tests are widely available to confirm diagnoses. In cases of syphilis or gonorrhea also, symptoms will often be very specific for the disease state. Thus, even though FemLab® may reveal no positive results when sexually transmitted diseases are causal factors of symptomology, an accurate diagnosis of the disease state can result from additional test procedures specific for such diseases.

Performance Characteristics – Multiple Diagnoses

Significant numbers of patients in the clinical trial were diagnosed with multiple forms of vaginitis. Eleven cases were diagnosed with 3 forms of vaginitis by FemLab® – Bacterial, and Trichomonal Vaginitis. An additional two cases also had yeast infections as well as the prior three. These diagnoses were confirmed by the control methods of testing. The two cases with four diagnoses found by FemLab® also had four diagnoses by control methods. Of the remaining eleven FemLab® cases with three or more diagnoses, eight were picked up by the control methods as showing two or three diagnoses. In 11 of the 13 cases, the pelvic exam reported a IV+ result, showing severe symptoms.

Performance Characteristics – Summary

In Table VIII below, the statistical results of the comparisons between FemLab® diagnoses and control method diagnoses for the four major infectious organisms responsible for vaginitis are shown.

Statistical Measures of the Sensitivity, Specificity and Overall Agreement of the FemLab® Test kit Compared to Control Methods

Table VII

Vaginitis	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Overall Agreement	Prevalence in trial population
Bacterial Vaginitis	89.4%	78.6%	68.9%	93.3%	82.3%	31%
Trichomonal Vaginitis	84.7%	89.3%	75.8%	93.7%	88.0%	24%
Yeast Vaginitis	91.4%	83.1%	80.1%	92.9%	86.7%	39%

The Sensitivity and Specificity for each infectious organism are the key factors for evaluation of the efficacy of FemLab. The Sensitivity of the FemLab® test kit - the agreement with the control methods for the positive diagnosis of the four various disease states - ranges between 84.7% and 92.0%. This means that FemLab® can be considered very effective in the identification of the infectious organisms; a clinician can have a high degree of confidence in the results. Indeed, given the known uncertainties in the control methods of diagnosis, this level of agreement is excellent. In addition, the Specificity - the ability to obtain negative diagnosis agreement - is also very good, ranging between 78.6% and 92.0%. From the perspective of the FemLab® test kit, many of these cases can be considered misdiagnosed by the control methods, giving a clinician additional confidence in the FemLab® accuracy. In addition, many cases of FemLab® “misdiagnosis” compared to the control method for one particular disease state are in fact correctly diagnosed for another disease. For instance, many cases diagnosed with both Bacterial Vaginitis and Trichomoniasis by FemLab, only were diagnosed with Bacterial Vaginitis by the control methods. It is very possible that in fact these women did have Trichomonal infections as well, since the control method of diagnosis of Trichomoniasis - microscopic evaluation - is well known to be sensitive to technician error.

These results can be interpreted as providing a high level of confidence to a clinician for use of the FemLab® test kit as a screening method. Only a very small proportion of patients are misdiagnosed compared to the control method, and many of these are diagnosed correctly for another infection. In summary, the clinical data show clearly that FemLab® is very effective in diagnosing the major forms of vaginitis.

REF	Product code		Manufacturer	EU REP	Authorized representative in the European community
LOT	Lot number		In vitro diagnostic medical device compliant with Directive 98/79 / EC	IVD	In vitro diagnostic medical device
	Keep in a cool, dry place		Caution: read instructions (warnings) carefully		Contains sufficient for “n” tests
	Keep away from sunlight		Store between 2 and 30°C		Expiration date
	Consult instructions for use		Disposable device, do not re-use		

GIMA WARRANTY TERMS

The Gima 12-month standard B2B warranty applies.

