CENOGENICS CORPORATION
CHEMVIEW-10™

INTENDED USE

Cenogenics' CHEMVIEW-10™ is a visual qualitative and semiquantitative test for the determination of urobilinogen, glucose, ketones (acetoacetic acid), bilirubin, protein, nitrite, pH, blood, specific gravity and leukocytes in urine.

SUMMARY AND PRINCIPLES OF THE PROCEDURE

The CHEMVIEW-10™ strip contains solid phase reagent areas affixed to a plastic support and provided in a dry reagent format. Qualitative or semiquantitative determination of each analyte is made by a visual comparison with the color chart provided at each concentration range.

UROBILINOGEN: The test is based on the diazotization reaction of 4-Methoxybenzene diazonium salt and urinary urobilinogen in a strong acid medium. The color changes range from pink to brown-red. GLUCOSE: This test is based on a sequential enzyme reaction. First, glucose oxidase catalyzes the formation of gluconic acid and hydrogen peroxide from the oxidation of glucose. A second enzyme, peroxidase, catalyzes t he reaction of hydrogen peroxide with potassium iodide chromogen to oxidize the chromogen to colors ranging from blue through greenish-brown and brown to dark-brown.

KETONES: This test is based on the reaction of acetoacetic acid in the urine with nitroprusside. The resulting color ranges from tan when no reaction takes place to purple for positive reaction.

BILIRUBIN: This test is based on the coupling of bilirubin with 2,4-dichlorobenzene diazonium salt in a strong acid medium. The color changes from light tan to pinkish-purple.

PROTEIN: The test is based on the color change of the indicator, tetrabromophenol blue, in the presence of protein. A positive reaction is indicated by a color change from yellow through green and then to greenish-blue.

NITRITE: This test is based on the reaction of p-arsanilic acid and nitrite (which is derived from dietary nitrate in the presence of bacteria) in urine to form a diazonium compound. The diazonium compound in turn couples with N-(1-naphthyl)ethylenediamine in an acidic medium. The resulting color is pink.

Any degree of pink color is considered positive.

pH: This test is based on double indicators (methyl red and bromothymol blue) which give a broad range of color covering the entire urinary pH range. Colors range from orange through greenish-yellow and green to blue.

BLOOD: This test is based on the pseudoperoxidase activity of hemoglobin which catalyzes the reaction of 3,3'5.5'-tetramethylbenzidine and buffered organic peroxide, 2,5-

dimethylhexane-2,5-dihydroperoxide. The resulting color ranges from greenish-yellow through bluish-green to dark blue.

SPECIFIC GRAVITY: This test is based on the pKa change of certain pretreated polyelectrolytes in relation to ionic concentration. In the presence of an indicator, color ranges from deep blue in urines of low ionic concentration through green and yellow-green in urines of increasing ionic concentration.

LEUKOCYTES: This test reveals the presence of granulocyte esterases. The esterases cleave a derivatized thiazole amino acid ester to liberate derivatized hydroxy thiazole. This thiazole then reacts with a diazonium salt to produce a purple product.

CLIA COMPLEXITY:

Waived

REAGENTS

Reagent strips are packaged in a desiccated plastic vial. The vial must always be tightly capped to assure product stability.

Reagent content is based on dry weight at the time of impregnation of 100 strips:

UROBILINOGEN	4-Methoxybenzenediazonium	2.5mg
	Citric acid	30.0 mg
GLUCOSE	Glucose oxidase	451 unit
	Peroxidase	186 unit
	Potassium iodide	10.0 mg
KETONES	Sodium nitoprusside	20.0 mg
	Magnesium sulfate	246.5 mg
BILIRUBIN	2,4-Dichlorobenzenediazonium	3.0 mg
	Oxalic acid	30.0 mg
PROTEIN	Tetrabromphenol blue	0.3 mg
	Citric acid	110.0 mg
	Trisodium citrate	46.0 mg
NITRITE	p-Arsanilic acid	5.0 mg
	N-(1-naphthyl)ethylenediamine	6.0 mg
pH	Methyl red	0.04 mg
	Bromthymol blue	0.5 mg
BLOOD	2,5-Dimethylhexane-2,5-dihydroperoxide	40.0 mg
	3.3,'5,5'-Tetramethylbenzidine	3.7 mg
SPECIFIC GRAVITY	Bromthymol blue	1.2 mg
	Diethylenetriaminepentaacetic acid	12.0 mg
LEUKOCYTES	2-Phenylthiazole amino acid ester	1.0 mg
	Diazonium salt	0.7 mg

MATERIALS PROVIDED

Desiccated vial containing 100 CHEMVIEW-10™ test strips Color chart, Product instructions

MATERIAL REQUIRED BUT NOT PROVIDED

Specimen collection container

STORAGE

Store at room temperature between 15°C and 30°C. Do not store test strips in refrigerator or freezer. Do not expose test strips to moisture, heat or light.

PRECAUTIONS

1. Do not use test beyond the expiration date.
2. Reagent strips should always be stored in their desiccated vial and should be kept tightly capped.
3. Protect reagent strips from moisture, heat and light.
4. Handle all specimens of human origin as if capable of transmitting disease.
5. For in vitro diagnostic use.

SPECIMEN COLLECTION

Collect urine in a clean, dry, unused container. Test urine as soon as possible after collection. If testing can not be performed within an hour after voiding, refrigerate the specimen immediately and allow to come to room temperature before testing. It is important to use a fresh, well-mixed, uncentrifuged urine for best results.

TEST PROCEDURE

1. Remove a CHEMVIEW-10™ test strip from the bottle and replace the cap immediately.
2. Examine the strip for any discoloration or darkening of the reagent pads. If present, deterioration may be indicated, discard the strip.
3. Dip the strip completely into a well-mixed, uncentrifuged urine specimen for no more than one second. Remove excess urine by tapping the plastic film gently against the rim of the urine container or by gently blotting the edge on absorbent paper.
4. Under a good light source, compare the test results with the color chart provided on the test bottle label. Keep the test strip in horizontal position to avoid interaction of the chemical from excessive urine. Read test results within 30 -60 seconds. Changes in color that appear only along the edges of the area or after more than two minutes are not significant.

RESULTS

The results are obtained by direct comparison of test strip with the color chart printed on the bottle label.

QUALITY CONTROL

Reaction of reagent strips should be confirmed by testing known positive and negative specimens or multiple analyte controls containing normal and abnormal amounts of each of the analytes being tested.

LIMITATIONS

Substances that cause abnormal urine color, such as drugs containing azo dyes, nitrofurantoin and riboflavin may affect the readability of reagent areas on urinalysis reagent strips. The color development on the reagent pad may be masked, or a color reaction may be produced on the pad that could be interpreted visually as a false positive. It is therefore recommended that in case of doubt the test should be repeated after withdrawal of the medication.

UROBILINOGEN: A complete absence of urobilinogen in the specimen being tested cannot be demonstrated by the strip. Normal urine specimens ordinarily give a slight pink color. Higher concentration of formalin may give false negative result. This test is not a reliable method for the detection of prophobilinogen.

GLUCOSE: Reactivity of the test decreases as the specific gravity and/or pH of urine increases, and may also vary with temperature. Ascorbic acid (more than 50mg/dl) and ketone bodies (more than 40mg/dl) may cause a false negative for a specimen containing a small amount of glucose (100mg/dl), however, the combinations of such ketone levels and low glucose levels are metabolically improbable in screening.

KETONES: Normal urine specimens ordinarily yield negative results with this reagent. False positive results may occur with highly pigmented urine specimens or those containing large amounts of levodopa metabolities.[2]

BILIRUBIN: Normally no bilirubin is detectable in urine by even the most sensitive methods. Since the bilirubin in specimens is sensitive to light, exposure of the urine specimens to light for a long period time may result in a false negative. Ascorbic acid concentration of 25–50mg/dl may also cause false negatives. Even trace amounts of bilirubin are sufficiently abnormal to require further investigation. False positive results may be obtained in the presence of diagnostic or therapeutic dyes in the test urine.

PROTEIN: The minimum sensitivity of this test is 5 – 10mg/dl of protein in urine. Highly buffered alkaline urines (pH 9) may give false positive results.[2] The interpretation of results is also difficult in turbid urine specimens.

NITRATE: Any degree of uniform pink color development should be considered positive, however, pink spots or pink edges should not be interpreted as a positive result. Color development is not proportional to the number of bacteria present. The nitrite test detects only nitrate reducing bacteria. Occasionally bacteria will be present that do

not reduce nitrate to nitrite, therefore, resulting in a negative test. A first morning mid stream specimen is recommended.[2] Sensitivity of the nitrite test is decreased with high specific gravity or ascorbic acid concentration of 25mg/dl or greater.

pH: This pH test indicates the pH values only within the range of 5 to 9. Certain drugs, such as those used for hypertension and heart trouble (Acetazolamides) may cause alkaline urine.[2] Excessive urine on the test strip may wash the acid buffer from the neighboring protein reagent onto the pH area and change the pH reading to an acid pH although the urine being tested is originally neutral or alkaline. This is called the "run-over" phenomenon.

BLOOD: A false positive can sometimes occur when bacteria are present in the urine. Ascorbic acid or protein may reduce the reactivity of the blood test. Strong oxidizing substances, such as hypochlorites, may produce a false positive result. Urine from menstruating females may yield a positive result.

SPECIFIC GRAVITY: Elevated specific gravity readings may be obtained in the presence of moderate quantities (100mg-700mg/dl) of protein, specific gravity is increased with the glucose in the urine.

LEUKOCYTES: The test result may not always be consistent with the leukocyte cell number by the microscopic examination.[9] Positive results may be found in high humidity and high temperature conditions, and if bottle is not kept tightly capped. Positive results may occasionally be found with the random specimens from females due to contamination of the specimens by vaginal discharge. High concentration of glucose, high specific gravity, high level of albumin, high concentration of formaldehyde, or presence of blood may cause decreased test results. High concentration of oxalic acid or a trace amount of oxidizing agents may cause false negative results. Low specific gravity (1.010 and under) or pH 6.5 ≥ may cause a false positive.

EXPECTED VALUES

UROBILINOGEN: In this test strip, the normal urobilinogen range is 0.1 to 1.0mg/dl (1mg/dl is approximately equal to 1Ehrlich unit/dl).[4] If results exceed the concentration of 2.0mg/dl, the patient and/or the urine specimen should be evaluated further.

GLUCOSE: Normally no glucose is detectable in urine, although a minute quantity of glucose is excreted by the normal kidney. Approximately 100mg glucose/dl of urine is detectable in this test strip. Concentrations of 100mg/dl may be considered as abnormal if found consistently.

KETONES: Ketone bodies should not be detected in normal urine specimens with this reagent. The concentrations given: ± (5mg/dl), + (10mg/dl), ++(50mg/dl), +++(100mg/dl) correlate well with teacetoacetic acid concentration in urine. The sensitivity of this test is 5mg acetoacetic acid per 100ml of urine. Detectable levels of ketone may occur with frequent vomiting, diarrhea, digestive disturbances, pregnancy, or severe physical exercise.[6]

BILIRUBIN: No bilirubin is detectable in urine of healthy persons by even the most sensitive methods. Elevated bilirubin in urine always indicates disease and is the earliest sign of liver cell disease and /or biliary obstruction. The signs of "+" (0.5mg/dl), "++" (1.0mg/dl), and "+++" (3.0mg.dl) signify the qualitative severity of the liver damage or bile obstruction. Even trace amounts of bilirubin are sufficiently significant to require further investigation.

PROTEIN: Normal urine specimens ordinarily contain some protein (O-4mg/dl); therefore, only persistent elevated levels of urine protein indicate kidney or urinary tract disease. The persistent results of a trace level or greater indicates significant proteinuria, and thus further clinical testing is needed to evaluate the significance of results. The concentration given: "+" (30mg/dl); "++" (100mg/dl); "+++" (300mg/dl), "++++" (1000mg/dl) correlate well with the albumin concentrations in urine. Pathologic proteinuria generally gives persistent values of over 30mg/dl.

NITRITE: Testing of urine for nitrite is a test for bacteria in urine. Any degree of pink color after 30 seconds indicates clinically significant bacteriuria. Bacteriuria is generally due to infection of the kidneys, ureters, bladder or urethra.

pH: Normal urine is slightly acid with a pH of 6. Urine pH values generally range from 5 to 8. The pH of urine is an important indicator of certain metabolic, kidney, gastrointestinal and respiratory factors.

BLOOD: Hemolysis is a natural process of recycling old or damaged red cells. But when hemoglobin appears in urine, it indicates kidney disease or urinary tract disorder. The practical detection limit of this test is approximately 5 to 10 erythrocytes per microliter of urine. Blood may be found in the urine of menstruating females. This test is highly sensitive to hemoglobin (it is slightly less so to intact erythrocytes) and thus complements the microscopic examination.

SPECIFIC GRAVITY: Random urine specimens from adults may vary in specific gravity from 1.003 to 1.040. Twenty-four hour urines from normal adults with normal diets and normal fluid intake will have a specific gravity of 1.016 – 1.022. This test permits determination of urine SG between 1.000 and 1.030.

LEUKOCYTES: Normally no leukocytes are detectable in urine. Individually observed trace results may be of questionable clinical significance.

PERFORMANCE CHARACTERISTICS

Specific performance characteristics of the CHEMVIEW-10™ product is based both on clinical and laboratory studies. A study performed at two clinical sites involving 94 patient samples compared CHEMVIEW-10™ to a competitor's strip. 100% agreement within one color block was obtained for all analytes except protein. Protein gave a greater than 95% agreement. The lower agreement may be reflective of the technician's interpretation of the negative versus trace color block with both the

CHEMVIEW-10™ and the competitive strip. Parameters of importance to the user are sensitivity, limits of test, specificity, accuracy, precision and stability. Sensitivity and limits of tests are the generally detectable levels of each test described previously. The sensitivity depends upon several factors; the variability of color perception; the presence or absence of inhibitory factors typically found in urine, the specific gravity, ascorbic acid, pH, and lighting conditions when the product is read visually. The tests have been developed to be specific for the constituent to be measured with the exception of interferences listed previously. Exact agreement between visual results and instrumental results might not be found because of the inherent differences between the perception of the human eye and the optical system of the instruments. It is for this reason that each user is encouraged to develop his own standards for performance. The stability test has been developed by statistical procedure for various environmental conditions.

UROBILINOGEN: This test can detect urobilinogen in concentrations as low as 0.1mg/dl (approximately 0.1EU/dl); therefore, most normal urines may give a slight pink reaction.

GLUCOSE: The test has a sensitivity of 100mg of glucose in 100ml of urine, and is specific for glucose. No substance excreted in urine other than glucose is known to give a positive result. False negative results may be obtained with the presence of levodopa, ascorbic acid, glutathione, and dipyrone. If the test color appears somewhat mottled at the higher glucose concentrations, match the darkest color to the color blocks.

KETONES: The reaction of this reagent pad is caused by acetoacetic acid in urine. Acetone or beta-hydroxybutyric acid is not significant to this test. Ordinarily, the reagent area detects 5.0mg of acetoacetic acid in 100ml urine. Some high specific gravity and low pH urines may give reactions up to and including trace level (5.0mg/dl).

BILIRUBIN: The test has a sensitivity of 0.5mg/dl. Bilirubin in urine indicates liver disease before any clinical signs are usually evident.

PROTEIN: The test is more sensitive to albumins than to gamma-globulins, Bence-Jones proteins, and mucoproteins; such proteins do not interfere with the reaction of albumin.

NITRITE: This test has a sensitivity of 0.05mg/dl nitrite ion in urine of normal specific gravity and moderate levels of ascorbic acid. The test is specific for nitrite and independent of urinary pH of any other substance normally excreted in urine. Comparison of the reacted area against a white background may aid in the detection of low levels of nitrite.

pH: This test produces distinct color changes from orange to blue over the pH value 5 – 9. Values will be read to within 1 unit; however, an accurate reading may be confused because of slight variations caused by the pigments in the urine.

BLOOD: This test is slightly more sensitive to free hemoglobin and myoglobin than to intact erythrocytes. The test is generally capable of detecting 0.015mg/dl free hemoglobin or 5 to 10 intact red blood cells per microliter urine. The sensitivity may be

reduced in urines with high specific gravity and ascorbic acid content. The appearance of green spots on the reagent test area indicates the presence of intact erythrocytes in the urine.

SPECIFIC GRAVITY: This test permits determination of urine specific gravity of 1.000, 1.005, 1.010, 1.015, 1.020, 1.025 and 1.030. Highly buffered alkaline urines may cause low reading of result.

LEUKOCYTES: The test is generally capable of detecting 20-25WBC/µl as a trace.

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