iQ®200 SERIES
Urine Microscopy Systems

Memory Joggers for Edit-Free Release

Edit Free Release:

Allows the user to automatically release (Auto Release) results obtained by the software and the APR® without human intervention, according to user defined parameters. User-defined criteria for specific demographic locations and age ranges can be entered according to the laboratory specific parameters. If a specimen results matches any criteria from the Auto-Release or any Exception screen, that specimen will be displayed on the Work List for review.

Reviewing the Yellow:

- The RBC, WBC and SQEPS are auto-released based on a user-defined Particle Verification Range (PVR).
- All other particles are reviewed on a user-defined threshold.
- When reviewing categories, apply the 50 % rule
- Samples run in full edit

50% Rule and/or Clinical Significance in relation to abnormal threshold:

- If more than 50% or "most" of the images are correct, it is not necessary to re-classify the incorrect images.
- If equal to or more than 50% of the images are incorrect, it is necessary to re-classify the images appropriately.
- **Exception:** More stringent re-classification of images is an option when considering the clinical significance in relation to the abnormal threshold.

RED & GREEN go out the door,
YELLOW requires a little bit more!

Below the minimum verification value = normal

Results need to be reviewed by the operator

Above the maximum verification value = abnormal

Urine Culture Indicator Checklist:

Note any RED result in this section prompts the user to look for BACT in the background of other images whereas an adjustment of the grade may be warranted.

BACT in the background (WBC, WBCC, SQEP, MUCS):

- One or two BACT in the total backgrounds or one or Two BACT individual isolated images = Trace (Rare)
- More BACT than above noted but not in 1/2 of backgrounds = Few (1+)
- BACT in about 1/2 backgrounds = Mod (2+)
- BACT in most of the backgrounds = Many (3+)

Configurations vary: Some may not report Trace (Rare), whereas the Trace (Rare) and Few (1+) descriptions are combined into Few (1+). Some users report BACT "Present" with no grades.

UNCL Category:

- If Prompted to review, re-classify all Renals. Transitionals & Casts

All other identifiable particles in the UNCL category are already accounted for and used in the instrument's calculations for the determination of grades and counts. These particles simply were not the best examples and therefore, not put in a classified category. The instrument "knows what they are". Some users may not report certain particle types.

Special Considerations:

High Concentration and/or Possible Amorphous Flags:

- May require an iQ200 dilution re-run if:

1. **The Urine Chemistries do not match microscopic results as expected.**
2. **An unexpected count/grade is obtained.**

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Other Considerations:

The Image Encyclopedia is an important tool to help new users or occasional users definitively identify particles.

Some iQ200 images resemble traditional microscopic images, others vary slightly, such as:

Size: Diameter of particles may be estimated by placing and leaving the cursor tool tip over the image box.

NSE: Note presence of nucleus and nuclear-cytoplasm ratio (N-C ratio) for both REEP and TREP.

TRCH: Note the pear-shape and "tail". These most often appear in the WBC category.

Pre-dilution on the iQ200:

1. **Grossly bloody**
2. **Viscous/milky**
3. **Dense/grossly amorphous**
4. **Short sample**

A good rule is "if you can't see through it, do something to it".

Manual microscopic confirmations:

Basic confirmations:

1. **Motility of TRCH**
2. **Cellular Casts**
3. **FAT/OVFB – use polarized light**

Some users can identify cell type for cellular casts without using manual confirmation. Some may use the CELL category to report mixed cell casts or as a generic cell cast report.

Sperm (SPRM):

Sperm confirmation is not required on a routine basis. When a decision is made by the user to confirm SPRM, for example in a medical-legal case, a manual confirmation must be performed using an original or non-used specimen container.

If you have any questions, Please feel free to contact Iris Diagnostics:

818-709-1244, select option 2,
800-776-4747, select option 2,
or email: callcenter@proiris.com.

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Diagnostics Division

300-5451 A

Memory Joggers for Chemistry/Microscopy Correlation White Blood Cell (WBC)/Leukocyte Esterase (LE)

Introduction

Microscopy and chemistry tests are complementary. The standard of care regarding urinalysis usually prescribes three components: physical examination, chemical examination and microscopic examination. All three components are usually required because there may be extenuating circumstances requiring a comprehensive evaluation to make a diagnostic decision.

When comparing macroscopic (physical/chemistry) and microscopic urinalysis results, it is important to note that such a comparison is not intended to ensure that results produce an exact match. **If results do not match, there may be logical reasons for this occurrence.** In addition to factors presented below, it is also important to be aware of any limitations or interferences that may occur for any chemistry strip.[1]

Dry strip urine chemistry methods provide qualitative or semi-quantitative measurements for various parameters. These methods are not designed to offer quantitative results.

Positive Chemical Test for LE/No WBCs in the Microscopic Exam:

- "Five types of cells can be present in urine: neutrophils, lymphocytes, eosinophils, basophils and monocytes (macrophages). Because neutrophils predominate in the peripheral blood, they are the white blood cell most often observed in urine."[2]
- "Because leukocytes readily lyse in urine, discrepancies can occur between the number of cells seen microscopically and the LE screening test."[2]
- "An alkaline environment or hypotonic urine (SG ≤1.010) enhances cell lysis."[2]
- "A positive LE test, despite few or no white blood cells present microscopically, can occur because of WBC lysis and disintegration."[2]
- "Also, different populations of WBCs have varying quantities of cytoplasmic granules and therefore differing amounts of leukocyte esterase. In fact, lymphocytes have no leukocyte esterase."[2]
- To provide optimal results, samples must be well mixed prior to aliquoting at the collection site and prior to running the samples. Intact WBCs easily "settle out". Inadequate mixing of the sample may cause cells to be unevenly distributed in the assayed sample. This may lead to discordant results.

Intact WBCs in the Microscopic Exam/ No LE on Chemistry Pad:

- "When increased WBCs appear in the urine, but the LE chemistry test is negative, it is important to consider that the WBCs present may not be of the granulocytic series-thus producing negative results (ex: lymphocytes)."[2]
- "Although the LE screening tests usually detects 10-25 white blood cells per microliter; the amount of esterase present may be insufficient to produce a positive response."[2]
  - (10-25 WBCs/uL ≈ 2-4.5 WBCs/hpf. 15 WBCs/uL ≈ 3 WBCs/hpf).
- "Note that owing to hydration, hypotonic urine could cause the leukocyte esterase to be diluted such that it is below the detection limit of the LE reaction."[2]
- The analytical output from urine chemistry and urine microscopy systems are not identical and should be used in a complementary manner to make a final diagnosis.
- **"Note: *Diagnostics or therapeutic decisions should not be based on any single result or method*".**[3]

Preanalytical Variables:

- All urine chemistry strips have limitations.
- "Specimen collection, specimen handling, specimen integrity, interfering substances and patient factors are common causes of inaccurate test results. Some of the preanalytical variables that can contribute to false-positive and false-negative results are listed below."[4] **Note: *Refer to the specific strips package insert for more detailed information.***

Possible False-positive LE Chemistry Reactions[2,3,4]

- — Preservatives; formaldehyde; formalin
- — Contamination by oxidizing agents and detergents, formalin
- — Therapeutic pigments
- — Beet digestion
- — Vaginal contamination of urine
- — Refer to actual strip package insert for detailed limitations

Possible False-negative LE Chemistry Reactions[2,3,4]

- — High concentrations of protein, glucose, cephalexin and gentamycin may diminish the color response
- — High specific gravity
- — Strong oxidizing agents (soaps and detergents)
- — Refer to the actual strip package insert for detailed limitations

If you have any questions, feel free to contact Iris Diagnostics or your Local Iris Representative. Our contact information is listed as follows:

(800) 776-4747, Option 2 (Within the U.S.A.)
(818) 709-1244, Option 3 (Within the U.S.A.)
or email: support@proiris.com.

References:

1. iChem®VELOCITY™ Operator's Manual; Iris Diagnostics.
2. *Fundamentals of Urine and Body Fluid Analysis*; Nancy Brunzel; Third Edition.
3. iChem®VELOCITY™ package insert; Iris Diagnostics.
4. Becton Dickinson; Troubleshooting Preanalytical Variables In Urinalysis Testing; VS9012; 4/11.

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300-5464 A

Memory Joggers for Chemistry/Microscopy Correlation
Red Blood Cell (RBC)/Blood

Introduction

Microscopy and chemistry tests are complementary. The standard of care regarding urinalysis usually prescribes three components: physical examination, chemical examination and microscopic examination. All three components are usually required because there may be extenuating circumstances requiring a comprehensive evaluation to make a diagnostic decision.

When comparing macroscopic (physical/chemistry) and microscopic urinalysis results, it is important to note that such a comparison is not intended to ensure that results produce an exact match. **If results do not match, there may be logical reasons for this occurrence.** In addition to factors presented below, it is also important to be aware of limitations or interferences that may occur for any chemistry strip.[1]

Dry strip urine chemistry methods provide qualitative or semi-quantitative measurements for various parameters. These methods are not designed to offer quantitative results.

Positive Chemical Test for Blood/No RBCs in the Microscopic Exam:

- "Specimens may have a positive chemical test for blood, but the microscopic examination reveals no RBCs. This can be explained by the fact that RBCs readily lyse and disintegrate in hypotonic or alkaline urine; such lysis can also occur within the urinary tract before urine collection."[2]
- "As a result, urine specimens can be encountered that contain only hemoglobin from RBCs that are no longer intact or microscopically visible."[2]
- "It is important to note that other substances, such as myoglobin, microbial peroxidases, and strong oxidizing agents can cause a positive blood chemical test."[2]
- To provide optimal results, samples must be well mixed prior to aliquoting at the collection site and prior to running the sample. Intact RBCs easily "settle out". Inadequate mixing of the sample may cause cells to be unevenly distributed in the assayed sample. This may lead to discordant results.

Intact RBCs in the Microscopic Exam/ No Blood on Chemistry Pad:

- "In specimens in which RBCs are present microscopically, but the chemical screen for blood is negative, ascorbic acid interference (degree of interference varies with reagent strip brand) should be suspected. If ascorbic acid is ruled out, it is possible that the formed elements observed are not RBCs, but a "look alike" component such as yeast or monohydrate calcium oxalate crystals."[2]
- "Lysis of red blood cells with the release of hemoglobin is enhanced in alkaline or dilute urine (Specific Gravity ≤1.010)."[2]
- "Note that smoking as well as normal exercise has also been associated with hematuria. Anticoagulant drugs and drugs that induce a toxic reaction, such as sulfonamides, can also cause increased numbers of RBCs in the urine sediment."[2]
- The analytical output from urine chemistry and urine microscopy systems are not identical and should be used in a complementary manner to make a final diagnosis.
- **"Note: *Diagnostic or therapeutic decisions should not be based on any single result or method."*[3]**

Preanalytical Variables:

- All urine chemistry strips have limitations.
- "Specimen collection, specimen handling, specimen integrity, interfering substances and patient factors are common causes of inaccurate test results. Some of the preanalytical variables documented in literature that can contribute to false-positive and false-negative results for any strip are listed below."[4] **Note: *Refer to the specific strip package insert for more detailed information.***

Possible False-positive Blood Chemistry Reactions[2,3,4]

- Menstrual contamination
- Bacterial peroxidases
- Strong oxidizing agents (Presence of chlorine bleach)
- Preservatives (formalin) and cleaning agents such as hypochlorite
- Refer to actual strip package insert for detailed limitations

Possible False-negative Blood Chemistry Reactions[2,3,4]

- Reducing agents such as ascorbic acid (level of interference varies according to the strip), uric acid, glutathione and gentistic acid; pH 5
- High nitrite can delay the reaction; MESNA
- Refer to actual strip package insert for detailed limitations

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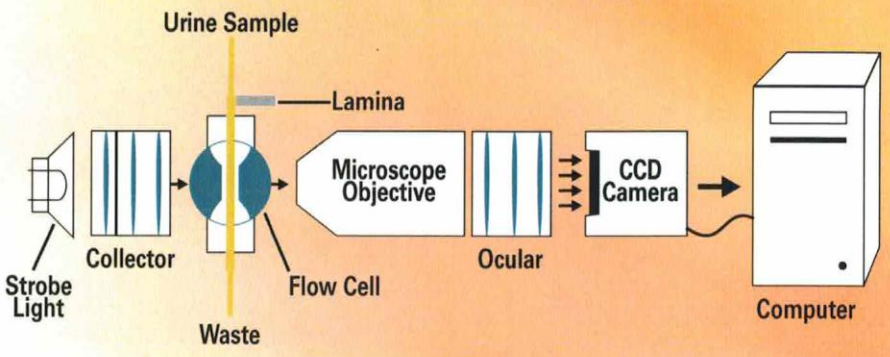
300-5463 B

Analysis Process

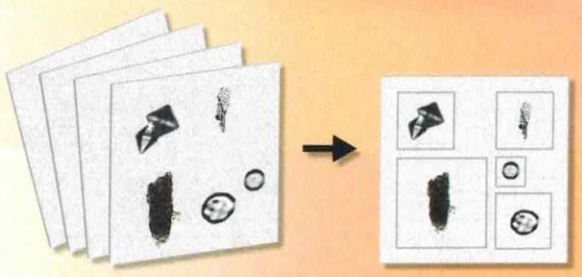
Flow Capture

To enable digital image (morphology) capture, the urine specimen undergoes a patented hydrodynamic focusing process. This process, implemented in our patented flowcell, thins the urine stream to a 5 μ/ml thickness at the focal plane of the microscope objective.



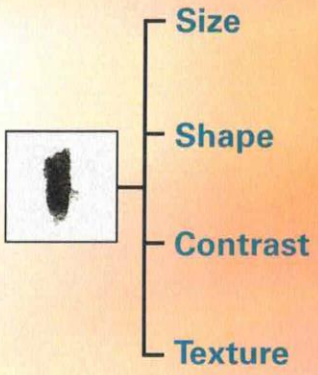
Particle Detection & Isolation

Patented algorithms isolate individual cells in the field of view. The fluid dynamics in the flowcell orientates and constrains the position of the urine particles into a layer at the microscopic focal plane. This process orientates and controls the position of the urine particles into a layer which is compatible with a microscopic field of view to allow consistent image capture. The system takes 24 pictures per second, looking at 500 pictures.



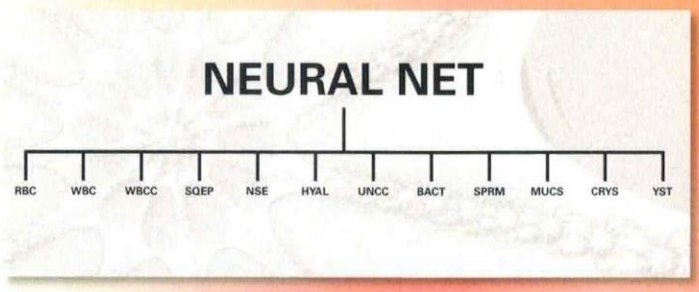
Particle Segmentation

Isolated urine particles are analyzed for specific features including size, contrast, shape and texture. Each feature is then categorized using a series of patented and proprietary algorithms based on known variables. The various individual features of each urine particle are converted to numerical values.



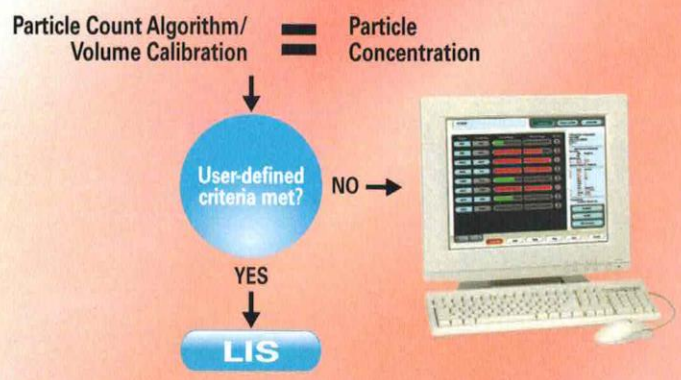
Particle Classification

The neural network is called Auto-Particle Recognition (APR™) and is designed to auto-classify urine particles. The matrix of numerical values that describes each urine particle is inputted into the neural network. The neural network logic has been developed through the analysis of over 26,000 images. APR™ classifies each particle into 1 of 12 categories. Urine particles may be further sub-classified by the operator into 27 additional categories.



Quantitative Result Reporting

After the APR™ sorts various urine particles into known categories, the concentration for each category is determined. The particle type and concentration compare to the user-defined auto-release criteria. Auto-released results are sent directly to the LIS; all other results are verified and released by the operator.



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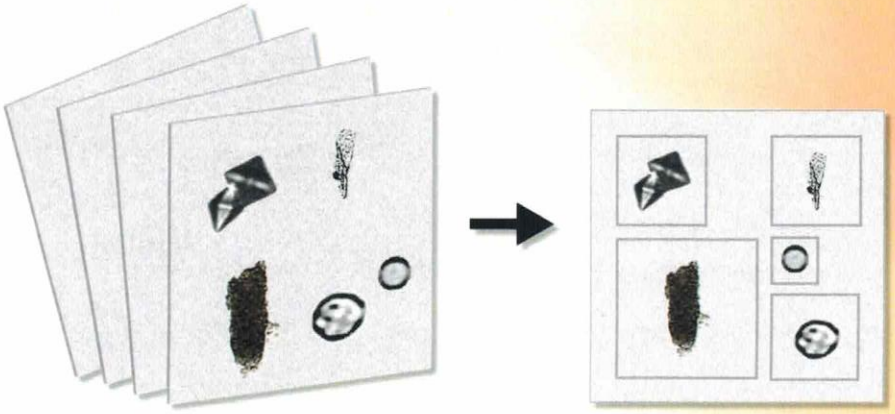
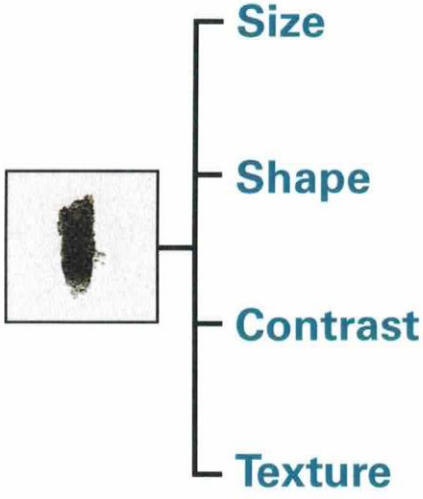
300-9352 C

Advanced Technology with the iQ®200 Series





Automated Morphology.
Iris Diagnostics, the leader in complete urinalysis and body fluids testing, uses patented core technologies in all of the iQ 200 Series products to generate state-of-the-art pictures.

Flow-Imaging
Isolating individual cells in the field of view enables urine particles to be digitally captured is the essence of Flow Imaging Technology.

Auto-Particle Recognition (APR™)
APR auto-classifies urine particles into 1 of 12 categories. Urine particles may be further sub-classified by the operator into 27 additional categories.

Charge-Coupled Device (CCD) Imaging
CCD provides digital pictures or morphology of urine particles which maybe verified, stored and attached to the report.

Integrated Urine Microscopy and Urine Chemistry
The iQ 200 Series of products provide integrated urine microscopy and urine chemistry results on one screen which may be released to the LIS with one touch.

Automated Body Fluids Software
This software provides the tools needed to perform automated, walk-away analysis of red blood cells and nucleated cells in a variety of body fluids.

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Key	Category
RBC	Red blood Cell
DRBC	Dysmorphic Red Blood Cell
WBC	White Blood Cell
WBCC	White Blood Cell Clump
BACT	Bacteria
BYST	Budding Yeast
HYST	Yeast with Pseudo Hyphae
SQEP	Squamous Epithelial
TREP	Transitional Epithelial
REEP	Renal Epithelial
OVFB	Oval Fat Body
FAT	Fat
MUCS	Mucous
RBCC	Red Blood Cell Clump
SPRM	Sperm
TRCH	Trichomonas
NSE	Non-Squamous Epithelial
UNCC	Unclassified Cast
HYAL	Hyaline Cast
EPIC	Epithelial Cast
WBCT	White Blood Cell Cast
RBCT	Red Blood Cell Cast
GRAN	Granular Cast
CELL	Cellular Cast
BROAD	Broad Cast
FATC	Fatty Cast
WAXY	Waxy Cast
UNCX	Unclassified Crystal
TP04	Triple Phosphate Crystal
CAOX	Calcium Oxalate Crystal
CAPH	Calcium Phosphate Crystal
CACB	Calcium Carbonate Crystal
URIC	Uric Acid Crystal
LEUC	Leucine Crystal
CYST	Cystine Crystal
TYRO	Tyrosine Crystal
AMOR	Amorphous Crystal
ART	Artifact
UNCL	Unclassified