VITROS Products Chemistry

INSTRUCTIONS FOR USE

mALB

VITROS Chemistry Products mALB Reagent

Microalbumin

REF **680 1740**

Intended Use

For *in vitro* diagnostic use only.

VITROS Chemistry Products mALB Reagent is used on the VITROS 5,1 FS Chemistry System, the VITROS 4600 Chemistry System and the VITROS 5600 Integrated System to quantitatively measure albumin concentration in human urine (mALB). Measurement of urinary albumin aids in the diagnosis of diabetic nephropathy, hypertension and cardiovascular disease.

Summary and Explanation of the Test

Microalbuminuria is characterized by urinary albumin excretion above normal levels in the absence of clinically detectable nephropathy. [1, 2, 3] Mildly increased excretion of albumin has been recognized to be a predictor of impending development of clinical renal disease in patients with hypertension or diabetes mellitus. [4] Microalbuminuria is noted to be present if urinary albumin is in the range of 30–300 mg/ 24 h. [5]

Principles of the Procedure

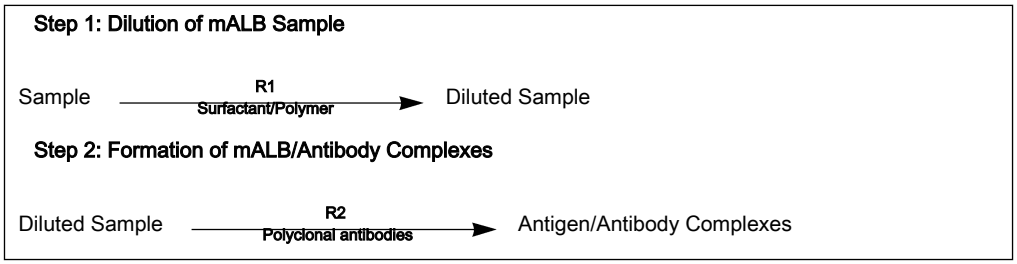
The quantitative measurement of urine albumin is performed using the VITROS Chemistry Products mALB Reagent in conjunction with the VITROS Chemistry Products Calibrator Kit 24 on the VITROS 5,1 FS/4600 Chemistry Systems and the VITROS 5600 Integrated System. The VITROS Chemistry Products mALB Reagent is a dual chambered package containing ready-to-use liquid reagents. Samples, calibrators and controls are mixed with Reagent 1 containing a polymer and surfactant. Addition of antisera specific for human albumin (Reagent 2) produces an immunochemical reaction yielding antibody/antigen complexes. The light scattering properties of the antibody/antigen complexes increase solution turbidity proportional to albumin concentration in the sample. The turbidity is measured spectrophotometrically at 340 nm. Once a calibration has been performed for each reagent lot, the urinary albumin concentration in each unknown sample can be determined using the stored calibration curve and the measured absorbance obtained in the assay of the sample.

Test Type and Conditions

Test Type	VITROS System	Approximate Incubation Time	Temperature	Wavelength	Reaction Sample Volume
Blanked Endpoint	5600, 4600, 5,1 FS	Incubation 1: 5 minutes Incubation 2: 5 minutes	37 °C (98.6 °F)	340 nm	12 µL

Not all products and systems are available in all countries.

Reaction Scheme



Warnings and Precautions

For *in vitro* diagnostic use only.

WARNING: *This product contains sodium azide. Disposal of reagents into sinks with copper or lead plumbing should be followed with plenty of water to prevent formation of potentially explosive metallic azides.*

WARNING: *Take care when handling materials and samples of human origin. Since no test method can offer complete assurance that infectious agents are absent, consider all clinical specimens, controls, and calibrators potentially infectious. Handle specimens, solid and liquid waste, and test components in accordance with local regulations and CLSI Guideline M29[6] or other published biohazard safety guidelines.*

For specific warnings and precautions for calibrators, quality control materials, and other components, refer to the Instructions for Use for the appropriate VITROS product, or to other manufacturer's product literature.

Reagents

Reactive Ingredients

Reagent 1 (R1): None
Reagent 2 (R2): Goat antisera to human albumin 1 mL/mL

Other Ingredients

Reagent 1 (R1): Preservative, polymer, buffers, inorganic salt, surfactant, protein
Reagent 2 (R2): Preservative, buffer, inorganic salt

Reagent Handling

Caution: **Do not use reagent packs with damaged or incompletely sealed packaging.**

- Inspect the packaging for signs of damage.
- Be careful when opening the outer packaging with a sharp instrument so as to avoid damage to the individual product packaging.
- The reagents are supplied ready for use.
- Avoid agitation, which may cause foaming or the formation of bubbles.

Reagent Preparation

1. Remove from storage.
2. Immediately load into Supply 3.

IMPORTANT: *Do not loosen or remove caps prior to loading.*

Reagent Storage and Stability

VITROS Chemistry Products mALB Reagent is stable until the expiration date on the carton when it is stored and handled as specified. Do not use beyond the expiration date.

Reagent	Storage Condition		Stability
Unopened	Refrigerated	2–8 °C (36–46 °F)	Until expiration date
Opened	On-analyzer	System turned on	≤ 4 weeks

Verify performance with quality control materials:

- If the system is turned off for more than 30 minutes.
- After reloading reagents that have been removed from Supply 3 and stored for later use.

Specimen Collection, Preparation and Storage

Specimens Recommended

Urine

IMPORTANT: *Certain collection devices have been reported to affect other analytes and tests[7]. Owing to the variety of specimen collection devices available, Ortho-Clinical Diagnostics is unable to provide a definitive statement on the performance of its products with these devices. Confirm that your collection devices are compatible with this test.*

Specimens Not Recommended

Acidified specimens

Urine

Specimen Collection and Preparation

Collect specimens using standard laboratory procedures.[8]

Note:	For details on minimum fill volume requirements, refer to the operating instructions for your system.

Patient Preparation

No special patient preparation is necessary.

Special Precautions

IMPORTANT:	*Contamination of urine specimens with residual serum or plasma present on the surface of gloves, sample cups, caps, vial stoppers or disposable tips may result in falsely elevated urinary albumin values. Take precautionary measures to prevent contamination, e.g. wear clean gloves when handling urine specimens, calibrators, controls and consumables.*

Centrifuge specimens prior to analysis.

Specimen Handling and Storage

- Handle and store specimens in stoppered containers to avoid contamination and evaporation.
- Mix samples by gentle inversion and bring to room temperature, 18–28 °C (64–82 °F), prior to analysis.

Specimen Storage and Stability

Storage	Temperature	Stability
Room temperature	18–28 °C (64–82 °F)	≤ 1 day
Refrigerated	2–8 °C (36–46 °F)	≤ 7 days
Frozen[9]	≤-20 °C (≤-4 °F)	Not recommended

Testing Procedure

Materials Provided

VITROS Chemistry Products mALB Reagent

Materials Required but Not Provided

- VITROS Chemistry Products Calibrator Kit 24
- Quality control materials, such as VITROS Chemistry Products mALB Performance Verifiers I and II
- VITROS Chemistry Products FS Diluent Pack 2 (BSA/Saline)

Operating Instructions

- Check reagent inventories at least daily to ensure that quantities are sufficient for the planned workload.
- For additional information, refer to the operating instructions for your system.

IMPORTANT:	*Bring all fluids and samples to room temperature, 18–28 °C (64–82 °F), prior to analysis.*

Sample Dilution

IMPORTANT:	*DO NOT MANUALLY DILUTE SAMPLES. Refer to the system's operating instructions for more information on the On-Analyzer Dilution Procedure.*

If urinary albumin concentrations exceed the system’s measuring (reportable) range:

On-Analyzer Dilution

1. Dilute the sample with saline from VITROS Chemistry Products FS Diluent Pack 2 (BSA/saline).
2. Reanalyze.
3. An initial three-fold (1 part sample plus 2 parts saline) dilution is recommended. Do not exceed a dilution factor of 6 (1 part sample plus 5 parts saline). If a dilution factor greater than 6 is required, use an alternate urine protein method such as VITROS Chemistry Products UPRO Slides.

Calibration

Required Calibrators

VITROS Chemistry Products Calibrator Kit 24

Calibrator Preparation, Handling, and Storage

Refer to the Instructions for Use for VITROS Chemistry Products Calibrator Kit 24.

Calibration Procedure

Refer to the operating instructions for your system.

When to Calibrate

Calibrate:

- When the reagent lot number changes.
- When critical system parts are replaced due to service or maintenance.
- When government regulations require.
  For example, in the USA, CLIA regulations require calibration or calibration verification at least once every six months.

The VITROS mALB assay may also need to be calibrated:

- If quality control results are consistently outside acceptable range.
- After certain service procedures have been performed.

For additional information, refer to the operating instructions for your system.

Calculations

Absorbance is measured at 340 nm after each incubation step (blank, endpoint) and the response calculated from the difference in absorbance values. Once a calibration has been performed for each reagent lot, urinary albumin concentration in the unknown samples can be determined using the stored calibration curve and the calculated response obtained in the assay of each sample.

Validity of a Calibration

Calibration parameters are automatically assessed by the system against a set of quality parameters detailed in the Review Assay Data screen (found via Options → Review/Edit Calibrations → Review Assay Data). Failure to meet any of the pre-defined quality parameters results in a failed calibration. The calibration report should be used in conjunction with quality control results to determine the validity of a calibration.

Measuring (Reportable) Range

Conventional Units (mg/dL)	SI Units (mg/L)
0.6–19.0	6.0–190.0

For out-of-range samples, refer to “Sample Dilution.”

Traceability of Calibration

The values assigned to the VITROS Chemistry Products Calibrator Kit 24 for urinary albumin are traceable to the BAM-IRMM-LGC (Bundesanstalt für Materialforschung und -prüfung/Institute for Reference Methods and Materials/Laboratory of the Government Chemist) ERM-DA470 Reference Material. [10]

Quality Control

Quality Control Material Selection

IMPORTANT: *VITROS Chemistry Products mALB Performance Verifiers are recommended for use with the VITROS Chemistry and Integrated Systems. Evaluate the*

performance of other commercial control fluids for compatibility with this assay before using for quality control.

Control materials other than VITROS Chemistry Products mALB Performance Verifiers may show a difference when compared with other microalbumin methods if they:

- Depart from a true human matrix.
- Contain high concentrations of preservatives, stabilizers, or other nonphysiological additives.

Quality Control Procedure Recommendations

- Choose control levels that check the clinically relevant range.
- Analyze quality control materials in the same manner as patient samples, before or during patient sample processing.
- To verify system performance, analyze control materials:
  - After calibration.
  - According to local regulations or at least once each day that the assay is being performed.
  - After specified service procedures are performed. Refer to the operating instructions for your system.
- If control results fall outside your acceptable range, investigate the cause before deciding whether to report patient results.
- For general quality control recommendations, refer to CLSI *Statistical Quality Control for Quantitative Measurements: Principles and Definitions; Approved Guideline-Third Edition*[11] or other published guidelines.
- For additional information, refer to the operating instructions for your system.

Quality Control Material Preparation, Handling, and Storage

Refer to the Instructions for Use for VITROS Chemistry Products mALB Performance Verifier I and II or to other manufacturer's product literature.

Results

Reporting Units and Unit conversion

The VITROS 5,1 FS/4600 Chemistry and VITROS Integrated Systems may be programmed to report mALB results in conventional or SI units.

Conventional Units	SI Units
mg/dL	mg/L (mg/dL x 10)

Limitations of the Procedure

Known Interferences

The VITROS mALB method was screened for interfering substances following NCCLS Protocol EP7.[12] The substances listed in the table, when tested at the concentrations indicated, caused the bias shown.

Interferent*	Interferent Concentration		mALB Concentration		Bias**	
			Conv. (mg/dL)	SI (mg/L)	Conv. (mg/dL)	SI (mg/L)
Furosemide	60 mg/dL	1.8 mmol/L	2.4	23.8	-0.5	-4.7
Sulfamethoxazole	120 mg/dL	4.7 mmol/L	2.3	23.3	0.5	5.0

*It is possible that other interfering substances may be encountered. These results are representative; however, your results may differ somewhat due to test-to-test variation. The degree of interference at concentrations other than those listed might not be predictable.

**The bias is an estimate of the maximum difference observed.

Other Limitations

- Contamination of urine specimens with residual serum or plasma present on the surface of gloves, sample cups, caps, vial stoppers or disposable tips may result in falsely elevated urinary albumin values. Take precautionary measures to prevent contamination, e.g. wear clean gloves when handling urine specimens, calibrators, controls and consumables.
- No antigen excess effect was observed for samples with urinary albumin concentration up to 800 mg/dL (8000 mg/L).
- Urine samples should not be acidified.
- Certain drugs and clinical conditions are known to alter urinary albumin concentration in vivo. For additional information, refer to one of the published summaries.[13, 14]

Expected Values

Reference Interval

The upper reference limit is the 97.5th percentile of results from an internal study of random urine specimens from 129 apparently healthy adults.

Conventional Units (mg/dL)	SI Units (mg/L)
< 1.7	< 16.7

The American Diabetes Association has recommended the following guidelines:

Category	24-h collection (mg/24h)	Timed collection (µg/min)	Spot collection (µg/mg creatinine)
Normal	< 30	< 20	< 30
Microalbuminuria	30–300	20–200	30–300
Clinical albuminuria	> 300	> 200	> 300

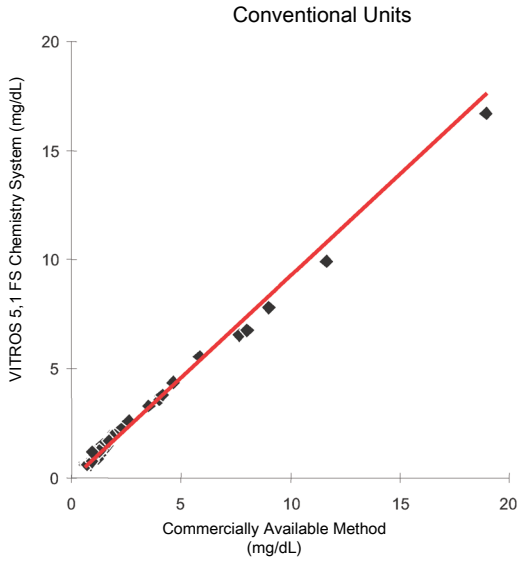
Because of variability in urinary albumin excretion, two of three specimens collected within a 3- to 6-month period should be abnormal before considering a patient to have crossed one of these diagnostic thresholds. Exercise within 24 h, infection, fever, congestive heart failure, marked hyperglycemia, and marked hypertension may elevate urinary albumin excretion over baseline values. [5]

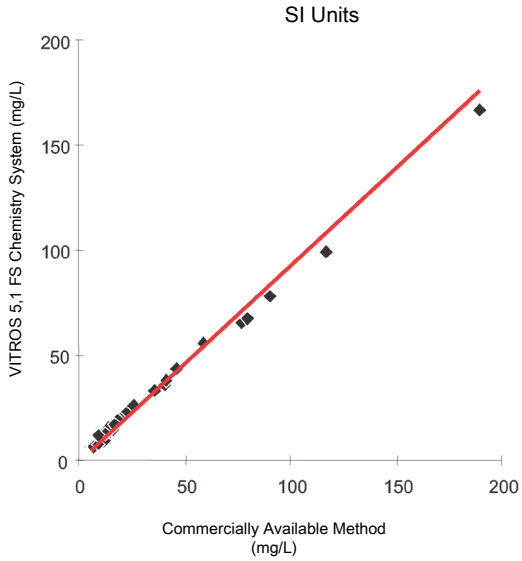
Performance Characteristics

Method Comparison

The plots and data below show the results of a method comparison study with urine samples analyzed on the VITROS 5,1 FS Chemistry System and a commercially available system.

The table also shows the results of comparisons with urine samples on the VITROS 5600 Integrated System and the VITROS 5,1 FS Chemistry System. The testing followed NCCLS Protocol EP9. [15]





				Conventional Units (mg/dL)			SI Units (mg/L)		
	n	Slope	Correlation Coefficient	Range of Sample Conc.	Intercept	Sy.x	Range of Sample Conc.	Intercept	Sy.x
5,1 FS† System vs. commercially available method*	61	0.93	0.977	0.61–16.71	0.03	0.16	6.13–167.09	0.32	1.62
5600 vs. 5,1 FS†	108	1.02	0.999	0.6–17.6	0.0	0.22	6.0–176.0	0.0	2.20

* Dade Behring N Antiserum to Human Albumin assay

† Analytical processing hardware and software algorithms on the VITROS 4600 Chemistry System are designed to the same specifications as those applied to the VITROS 5,1 FS Chemistry System. Assay performance on the VITROS 4600 System has been demonstrated to be comparable to that on the VITROS 5,1 FS System. All performance characteristics for VITROS 5,1 FS System are therefore applicable to the VITROS 4600 System.

Precision

Precision was evaluated with quality control materials and a human urine pool on the VITROS 5,1 FS Chemistry System following NCCLS Protocol EP5. [16]

Precision was also evaluated with quality-control materials on the VITROS 5600 Integrated System following NCCLS Protocol EP5. [17]

These results are guidelines. Variables such as instrument maintenance, environment, reagent storage/handling, control material reconstitution, and sample handling can affect the reproducibility of test results.

	Conventional Units (mg/dL)			SI Units (mg/L)					
System	Mean Conc.	Within Day SD*	Within Lab SD**	Mean Conc.	Within Day SD*	Within Lab SD**	Within Lab CV%**	No. Observ.	No. Days
5,1 FS†	4.4	0.05	0.07	43.6	0.50	0.73	1.67	88	22
	7.9	0.11	0.26	78.7	1.09	2.58	3.28	88	22
	2.6	0.03	0.07	25.8	0.34	0.73	2.83	88	22
5600	4.4	0.06	0.06	44.2	0.58	0.64	1.36	88	22
	8.4	0.10	0.10	84.1	0.97	1.02	1.19	88	22

* Within Day precision was determined using two runs per day with two replications per run.

** Within Lab precision was determined using a single lot of reagents and at least four calibrations.

† Analytical processing hardware and software algorithms on the VITROS 4600 Chemistry System are designed to the same specifications as those applied to the VITROS 5,1 FS Chemistry System. Assay performance on the VITROS 4600 System has been demonstrated to be comparable to that on the VITROS 5,1 FS System. All performance characteristics for VITROS 5,1 FS System are therefore applicable to the VITROS 4600 System.

Specificity

Substances That Do Not Interfere

The substances listed in the table, at the concentrations shown, were tested according to NCCLS Protocol EP7. [12] Bilirubin and hemoglobin were tested at mALB concentrations of approximately 2.5 mg/dL (25 mg/L) and 10.0 mg/dL (100 mg/L) and found not to interfere, bias <0.38 mg/dL (<3.8 mg/L) at 2.5 mg/dL mALB and bias <1.5 mg/dL (<15 mg/L) at 10.0 mg/dL mALB. The remaining compounds listed in the table were tested at a mALB concentration of approximately 2.5 mg/dL (25 mg/L) and found not to interfere, bias <0.38 mg/dL (<3.8 mg/L).

Compound	Concentration	
Acetaminophen	140 mg/dL	9.3 mmol/L
Ammonia	570 mg/dL	334.7 mmol/L
Amoxicillin	200 mg/dL	5.5 mmol/L
Ascorbic acid (L)	500 mg/dL	28.4 mmol/L
Bilirubin	26 mg/dL	0.44 mmol/L
Bovine Serum Albumin (BSA)	10 mg/dL	0.1 g/L
Calcium	30 mg/dL	7.5 mmol/L
Ceftriaxone	550 mg/dL	9.9 mmol/L
Creatinine	300 mg/dL	26.5 mmol/L
Glucose	4000 mg/dL	222.0 mmol/L
Hemoglobin	250 mg/dL	2.5 g/L
Human IgG	200 mg/dL	2 g/L
Ibuprofen	50 mg/dL	2.4 mmol/L
Magnesium	60 mg/dL	24.7 mmol/L
Propranolol	55 mg/dL	2.1 mmol/L
Salicylic acid	100 mg/dL	7.3 mmol/L
Trimethoprim	2 mg/dL	69 µmol/L
Urea	3000 mg/dL	499.5 mmol/L
Uric Acid	120 mg/dL	7.1 mmol/L

References

1. Mogensen, C.E., et. al., “Early Changes in Kidney Function, Blood Pressure and the Stages in Diabetic Nephropathy,” in *Prevention and Treatment of Diabetic Nephropathy*, H. Keen and M. Legrain, ed. Boston, MTP Press, pp. 57-83, 99-105, (1983).
2. Mogensen, C.E., C.K. Christensen and E. Vittinghus, “The Stages in Diabetic Renal Disease, with Emphasis on the Stage of Incipient Diabetic Nephropathy,” *Diabetes*, 32:Suppl. 2, 64-78, (1983).
3. Viberti, G.C., et. al., “Proteinuria in Diabetes Mellitus: Role of Spontaneous and Experimental Variation of Glycemia,” *Kidney International*, 21:714-20, (1982).
4. Burtis C, Ashwood, ER (ed). *Tietz Textbook of Clinical Chemistry*, 3rd ed. Philadelphia, PA; WB Saunders Co; 484; 1999.
5. American Diabetes Association. “Standards of Medical Care for Patients with Diabetes Mellitus” *Diabetes Care*, 23:Suppl. 1, S32-42, (2000).
6. CLSI. *Protection of Laboratory Workers from Occupationally Acquired Infections; Approved Guideline – Third Edition.* CLSI document M29-A3 (ISBN 1-56238-567-4). CLSI, 940 West Valley Road, Suite 1400, Wayne, PA 19087-1898 USA; 2005.
7. Calam RR. Specimen Processing Separator Gels: An Update. *J Clin Immunoassay*. 11:86–90; 1988.
8. NCCLS. *Urinalysis and Collection, Transportation, and Preservation of Urine Specimens; Approved Guideline – Second Edition*. NCCLS document GP16-A2 (ISBN 1-56238-448-1). CLSI, 940 West Valley Road, Suite 1400, Wayne, PA 19087-1898 USA; 2001.
9. Manley, et al. Decreases in Albumin/Creatinine and N-Acetylglucosaminidase/Creatinine Ratios in Urine Samples Stored at -20 °C, *Clin Chem*, 38/11, 2294–2299; 1992.
10. European Commission. *The Certification of a Matrix Reference Material for Immunochemical Measurement of 15 Serum Proteins, ERM-DA470*. Report EUR 15243 EN and 16882 EN, European Communities, 2004.
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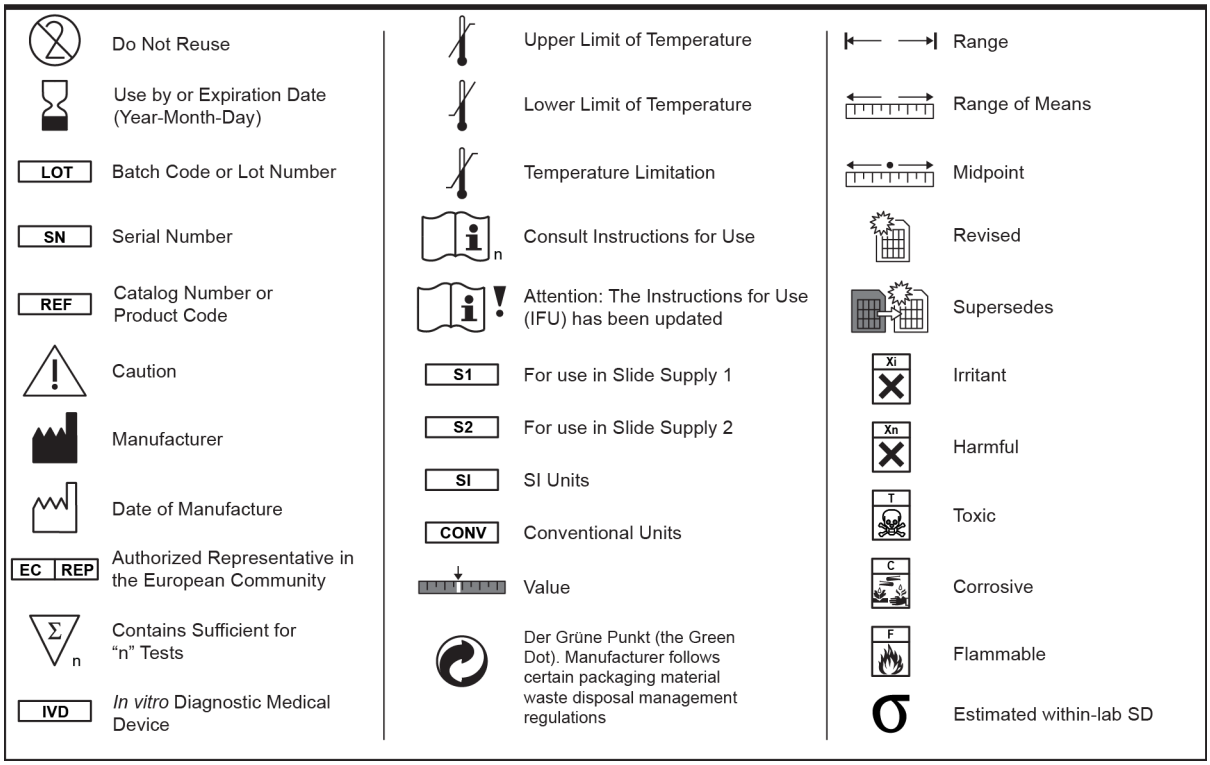
12. NCCLS. *Interference Testing In Clinical Chemistry*; Proposed Guideline. NCCLS document EP7-A [ISBN 1-56238-480-5]. CLSI, 940 West Valley Road, Suite 1400, Wayne, PA 19087-1898 USA; 2002.
13. Young DS. *Effects of Drugs on Clinical Laboratory Tests*. Ed. 4 Washington, D.C.: AACC Press; 2000.
14. Friedman RB, Young DS. *Effects of Disease on Clinical Laboratory Tests*. Washington, D.C.; AACC Press; 1997.
15. NCCLS. *Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline.* NCCLS document EP9-A2 [ISBN 1-56238-472-4]. CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA; 2002.
16. NCCLS. *Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline - Second Edition*. NCCLS Document EP5-A (ISBN 1-56238-368-X). CLSI, 940 West Valley Road, Suite 1400, Wayne PA, USA, 19087-1898, 2004.

17. NCCLS. *Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline – Second Edition*. NCCLS document EP5-A2 [ISBN 1-56238-542-9]. CLSI, 940 West Valley Road, Suite 1400, Wayne, PA 19087-1898 USA, 2004.

Glossary of Symbols

The following symbols may have been used in the labeling of this product.



Revision History

Date of Revision	Version	Description of Technical Changes*
2014-05-28	8.0	• Specificity: corrected spelling of Acetaminophen • Glossary of Symbols: added Date of Manufacture
2013-08-05	7.0	Specificity: updated data for Hemoglobin
2012-02-28	6.0	Glossary of Symbols: updated
2010-11-01	5.0	Added information for the VITROS 4600 Chemistry System
2009-04-24	4.1	Method Comparison – minor correction
2009-03-11	4.0	• Added information for the VITROS 5600 Integrated System • Test Type and Conditions – Added statement • Traceability of the Calibration – Updated data • Method Comparison – Added information on sample types • References – Updated • Glossary of Symbols – Updated • Minor wording and formatting changes
2005-04-25	3.0	• Specimen Storage and Stability – updated data • References – updated 9
2004-11-08	2.0	Amended Intended Use statement.

Date of Revision	Version	Description of Technical Changes*
2004-09-24	1.0	First release of document

* The change bars indicate the position of a technical amendment to the text with respect to the previous version of the document.

When this Instructions For Use is replaced, sign and date below and retain as specified by local regulations or laboratory policies, as appropriate.

Signature

Obsolete Date

CE

EC REP

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Ortho Clinical Diagnostics

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