AMIK2

cobas®

Amikacin

Order information

REF	CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
04791959 190	ONLINE TDM Amikacin 75 Tests	System-ID 07 6926 6	Roche/Hitachi **cobas c** 311, **cobas c** 501/502
03375781 190	Preciset TDM II Calibrators CAL A-F (6 x 5 mL) Diluent (1 x 10 mL)	Codes 743-748	
04521536 190	TDM Control Set Level I (2 x 5 mL) Level II (2 x 5 mL) Level III (2 x 5 mL)	 Code 310 Code 311 Code 312	

English

System information

For **cobas c** 311/501 analyzers:

AMIK2: ACN 456

For **cobas c** 502 analyzers:

AMIK2: ACN 8456

Intended use

In vitro test for the quantitative determination of amikacin in serum and plasma on Roche/Hitachi **cobas c** systems.

Summary

Amikacin is a semi-synthetic aminoglycoside that exhibits bactericidal activity against a wide range of pathogens, including many organisms resistant to other aminoglycosides.[1,2,3,4] Amikacin is active in vitro against gram-negative organisms, penicillinase and non-penicillinase producing staphylococci. The strength of this drug is due primarily to its high degree of resistance to aminoglycoside-inactivating enzymes.[5] Determination of serum or plasma drug levels is required to achieve optimum therapeutic efficacy and minimize toxicity.[6]

Test principle

Kinetic interaction of microparticles in solution (KIMS) as measured by changes in light transmission.

The assay is a homogeneous immunoassay based on the principle of measuring changes in scattered light or absorbance which result when activated microparticles aggregate. The microparticles are coated with amikacin and rapidly aggregate in the presence of an amikacin antibody solution. When a sample containing amikacin is introduced, the aggregation reaction is partially inhibited, slowing the rate of the aggregation process. Antibody bound to sample drug is no longer available to promote microparticle aggregation, and subsequent particle lattice formation is inhibited. Thus, a classic inhibition curve with respect to amikacin concentration is obtained, with the maximum rate of aggregation at the lowest amikacin concentration. By monitoring the change in scattered light or absorbance, a concentration-dependent curve is obtained.

Reagents - working solutions

R1 Anti-amikacin antibody (mouse monoclonal) and human-sourced material in buffer with preservative

R2 Conjugated amikacin derivative microparticles, human-sourced material, and preservative

R1 is in position A and R2 is in position B.

Precautions and warnings

For in vitro diagnostic use.
Exercise the normal precautions required for handling all laboratory reagents.
Disposal of all waste material should be in accordance with local guidelines.
Safety data sheet available for professional user on request.

For USA: For prescription use only.

All human material should be considered potentially infectious. All products derived from human blood are prepared exclusively from the blood of donors tested individually and shown to be free from HBsAg and antibodies to HCV and HIV.
The testing methods applied were FDA-approved or cleared in compliance with the European Directive 98/79/EC, Annex II, List A.
However, as no testing method can rule out the potential risk of infection with absolute certainty, the material should be handled with the same level of care as a patient specimen. In the event of exposure, the directives of the responsible health authorities should be followed.[7,8]

Reagent handling

Ready for use

Carefully invert reagent container several times prior to use to ensure that the reagent components are mixed.

Storage and stability

Shelf life at 2-8 °C:	See expiration date on **cobas c** pack label
On-board in use and refrigerated on the analyzer :	12 weeks

Do not freeze.

Specimen collection and preparation

For specimen collection and preparation only use suitable tubes or collection containers.

Only the specimens listed below were tested and found acceptable.
Serum: Collect serum using standard sampling tubes.
Plasma: K_2- or K_3-EDTA or Na or Li heparin plasma.

Stability:	8 hours capped at 15-25 °C
	48 hours capped at 2-8 °C
	4 weeks capped at -20 °C

The sample types listed were tested with a selection of sample collection tubes that were commercially available at the time of testing, i.e. not all available tubes of all manufacturers were tested. Sample collection systems from various manufacturers may contain differing materials which could affect the test results in some cases. When processing samples in primary tubes (sample collection systems), follow the instructions of the tube manufacturer.

Centrifuge samples containing precipitates before performing the assay.

Do not induce foaming of specimens. Specimens should not be repeatedly frozen and thawed.

Invert thawed specimens several times prior to testing.

Usual sampling time varies dependent upon desired measurement of peak or trough values.[9]

Materials provided

See “Reagents – working solutions” section for reagents.

Materials required (but not provided)

See “Order information” section

General laboratory equipment

Assay

For optimum performance of the assay follow the directions given in this document for the analyzer concerned. Refer to the appropriate operator’s manual for analyzer-specific assay instructions.

The performance of applications not validated by Roche is not warranted and must be defined by the user.

Application for serum and plasma

Deselect Automatic Rerun for these applications in the Utility menu, Application screen, Range tab.

AMIK2

Amikacin

cobas®

cobas c 311 **test definition**

Assay type	2-Point End		
Reaction time /Assay points:	10 / 10-26		
Wavelength (sub/main)	– /700 nm		
Reaction direction	Increase		
Unit	µg/mL		
Reagent pipetting		Diluent (H_2O)	
R1	167 µL	–	
R2	50 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	2.0 µL	–	–
Decreased	2.0 µL	–	–
Increased	2.0 µL	–	–

cobas c 501/502 **test definition**

Assay type	2-Point End		
Reaction time /Assay points:	10 / 16-38		
Wavelength (sub/main)	– /700 nm		
Reaction direction	Increase		
Unit	µg/mL		
Reagent pipetting		Diluent (H_2O)	
R1	167 µL	–	
R2	50 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	2.0 µL	–	–
Decreased	2.0 µL	–	–
Increased	2.0 µL	–	–

Calibration

Calibrator	S1-6: Preciset TDM II Calibrators
Calibration mode	RCM
Calibration frequency	6-point calibration • after reagent lot change • every 6 weeks • as required following quality control procedures

Traceability: This method has been standardized against USP reference standards. The calibrators are prepared to contain known quantities of amikacin in normal human serum.

ACTION REQUIRED

Due to potential carryover from the last calibrator (Cal F) into the first quality control sample (Level 1) following calibration, assaying a non-reportable blank quality control sample is required prior to assaying the controls. The blank quality control sample should be programmed in the first position followed by quality control levels 1-3. Use Multiclean (Cat. No. 04708725 190) as the blank quality control sample.

The blank quality control sample is not required when assaying controls without calibration.

Quality control

For quality control, use control materials as listed in the "Order information" section.

In addition, other suitable control material can be used.

The control intervals and limits should be adapted to each laboratory's individual requirements. Values obtained should fall within the defined limits. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

Follow the applicable government regulations and local guidelines for quality control.

Calculation

Roche/Hitachi **cobas c** systems automatically calculate the analyte concentration of each sample.

Conversion factor:[10] µg/mL x 1.71 = µmol/L

Limitations - interference

Criterion: Recovery within ± 10 % of initial value at amikacin levels of approximately 5.0 and 30 µg/mL (8.6 and 51.3 µmol/L).

Serum/Plasma

Icterus:[11] No significant interference up to an I index of 50 for conjugated bilirubin and unconjugated bilirubin (approximate conjugated and unconjugated bilirubin concentration: 50 mg/dL or 855 µmol/L).

Hemolysis:[11] No significant interference up to an H index of 1000 (approximate hemoglobin concentration: 1000 mg/dL or 621 µmol/L).

Lipemia (Intralipid):[11] No significant interference up to an L index of 2000. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

No significant interference from triglycerides up to 800 mg/dL (9.0 mmol/L).

Rheumatoid factors: No interference from rheumatoid factors up to 100 IU/mL.

Total protein: No interference from 2 g/dL to 12 g/dL protein.

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[12]

For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

ACTION REQUIRED

Special Wash Programming: The use of special wash steps is mandatory when certain test combinations are run together on Roche/Hitachi **cobas c** systems. The latest version of the carry-over evasion list can be found with the NaOHD-SMS-SmpCln1+2-SCCS Method Sheets. For further instructions refer to the operator's manual. **cobas c** 502 analyzer: All special wash programming necessary for avoiding carry-over is available via the **cobas** link, manual input is not required.

Where required, special wash/carry-over evasion programming must be implemented prior to reporting results with this test.

Limits and ranges

Measuring range

0.8-40 µg/mL (1.4-68.4 µmol/L)

Manually dilute samples above the measuring range 1 + 1 with the Preciset TDM II Diluent (0 µg/mL) and reassay. Multiply the result by 2 to obtain the specimen value.

Lower limits of measurement

Lower detection limit of the test

0.8 µg/mL (1.4 µmol/L)

The lower detection limit represents the lowest measurable analyte level that can be distinguished from zero. It is calculated as the value lying 2 standard deviations above that of the 0 µg/mL calibrator (standard 1 + 2 SD, repeatability, n = 21).

Expected values

Although optimum values may vary, peak serum values of amikacin in the range of 20 to 25 µg/mL (34.2 to 42.8 µmol/L) and trough values in the range of 5 to 10 µg/mL (8.6 to 17.1 µmol/L) are generally accepted for therapeutic effectiveness. Toxicity is associated with peak levels greater than 35 µg/mL (59.9 µmol/L) and trough values greater than 10 µg/mL (17.1 µmol/L).[6] The most serious toxic effect is permanent damage to the vestibular division of the eighth cranial nerve, which has been reported to occur most frequently in patients with renal failure. Since amikacin is inherently stable, is not metabolized, and is excreted primarily by glomerular filtration, the presence of renal impairment drastically alters its pharmacokinetics. If dosage regimens are not adjusted, excess accumulation leading to ototoxicity and further renal impairment could be

encountered.[13,14,15,16] While serum levels can be toxic, indiscriminately low dosages of amikacin will result in ineffective treatment for many strains of gram-negative bacteria. Organisms which are resistant to amikacin will often show increased resistance to all other available aminoglycosides. This observation[17] points out the possibility that the indiscriminate use of low dosages of amikacin could engender the emergence of drug-resistant organisms and possibly render the drug ineffective in treating infectious disease.[5,18]

Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges.

Specific performance data

Representative performance data on the analyzers are given below. Results obtained in individual laboratories may differ.

Precision

Precision was determined using human samples and controls in a modified NCCLS EP5-A protocol (repeatability n = 63, intermediate precision n = 63). The following results were obtained on a Roche/Hitachi **cobas c** 501 analyzer.

Serum/Plasma

Repeatability	*Mean*		*SD*		*CV*
	µg/mL	*µmol/L*	*µg/mL*	*µmol/L*	*%*
Control 1	5.07	8.67	0.14	0.24	2.7
Control 2	14.4	24.6	0.16	0.27	1.1
Control 3	28.2	48.2	0.27	0.46	1.0
HS 1	4.98	8.52	0.13	0.22	2.6
HS 2	32.6	55.7	0.31	0.53	0.9

Intermediate precision	*Mean*		*SD*		*CV*
	µg/mL	*µmol/L*	*µg/mL*	*µmol/L*	*%*
Control 1	5.07	8.67	0.19	0.32	3.8
Control 2	14.4	24.6	0.19	0.32	1.3
Control 3	28.2	48.2	0.36	0.62	1.3
HS 1	4.98	8.52	0.17	0.29	3.5
HS 2	32.6	55.7	0.41	0.70	1.3

Method comparison

Serum/plasma

Amikacin values for human serum and plasma samples obtained on a Roche/Hitachi **cobas c** 501 analyzer (y) were compared with those determined with the corresponding reagent on a Roche/Hitachi 917 analyzer (x) and on a COBAS INTEGRA 700 analyzer (x).

Roche/Hitachi 917 analyzer	Sample size (n) = 57
Passing/Bablok[19]	Linear regression
y = 0.988x - 0.078 µg/mL	y = 0.986x - 0.033 µg/mL
τ = 0.981	r = 1.000

The sample concentrations were between 1.1 and 37.4 µg/mL (1.88 and 64.0 µmol/L).

COBAS INTEGRA 700 analyzer	Sample size (n) = 53
Passing/Bablok[19]	Linear regression
y = 0.950x - 0.195 µg/mL	y = 0.949x - 0.327 µg/mL
τ = 0.934	r = 0.993

The sample concentrations were between 1.4 and 39.8 µg/mL (2.39 and 68.1 µmol/L).

Analytical specificity

The following compounds were tested for cross-reactivity.

Compound	Concentration Tested (µg/mL)	% Cross-reactivity
Amphotericin	20	ND
Ampicillin	90	ND
Carbenicillin	500	ND
Cephalexin	500	ND
Cephalosporin C	500	ND
Cephalothin	60	ND
Chloramphenicol	300	ND
Clindamycin	5	ND
Erythromycin	200	ND
Ethacrynic acid	500	ND
5-Fluorocytosine	700	ND
Furosemide	100	ND
Fusidic acid	500	ND
Gentamicin	100	ND
Kanamycin A	25	ND
Kanamycin B	25	ND
Lincomycin	30	ND
Methotrexate	23	ND
Methylprednisolone	500	ND
Neomycin	100	ND
Netilmycin	80	ND
Oxytetracycline	40	ND
Penicillin V	50	ND
Prednisolone	500	ND
Rifampin	320	ND
Spectinomycin	200	ND
Streptomycin	200	ND
Sulfadiazine	1500	ND
Sulfamethoxazole	2000	ND
Tetracycline	40	ND
Tobramycin	100	ND
Trimethoprim	120	ND
Vancomycin	400	ND

ND = not detectable

Tests were performed on 16 drugs. No significant interference with the assay was found.

Acetaminophen	Doxycycline
Acetyl cysteine	Ibuprofen
Acetylsalicylic acid	Levodopa
Ampicillin-Na	Methyldopa + 1.5 H_2O
Ascorbic acid	Metronidazole
Ca-Dobesilate	Phenylbutazone
Cefoxitin	Rifampicin
Cyclosporine	Theophylline

References

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A point (period/stop) is always used in this Method Sheet as the decimal separator to mark the border between the integral and the fractional parts of a decimal numeral. Separators for thousands are not used.

Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard.

CONTENT	Contents of kit
→	Volume after reconstitution or mixing
GTIN	Global Trade Item Number

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Roche Diagnostics warrants that this product will meet the specifications stated in the labeling when used in accordance with such labeling and will be free from defects in material and workmanship until the expiration date printed on the label. THIS LIMITED WARRANTY IS IN LIEU OF ANY OTHER WARRANTY, EXPRESS OR IMPLIED, INCLUDING ANY IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR PARTICULAR PURPOSE. IN NO EVENT SHALL ROCHE DIAGNOSTICS BE LIABLE FOR INCIDENTAL, INDIRECT, SPECIAL OR CONSEQUENTIAL DAMAGES.

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