



ARCHITECT

SYSTEM

en

*i*Gentamicin

REF 1P31

49-5763/R1


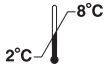


B1P310

*i*Gentamicin

Customer Service: Contact your local representative or find country specific contact information on www.abbottdiagnostics.com

Package insert instructions must be carefully followed. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.

Key to symbols used

REF	List Number	REACTION VESSELS	Reaction Vessels
IVD	<i>In Vitro</i> Diagnostic Medical Device	SAMPLE CUPS	Sample Cups
LOT	Lot Number	REPLACEMENT CAPS	Replacement Caps
	Expiration Date	REAGENT LOT	Reagent Lot
SN	Serial Number	CONTROL NO.	Control Number
	Store at 2-8°C	SEPTUMS	Septums
	Consult instructions for use	WARNING: SENSITIZER	Warning: May cause an allergic reaction
	Manufacturer	CONTAINS: AZIDE	Contains Sodium Azide. Contact with acids liberates very toxic gas.

See **REAGENTS** section for a full explanation of symbols used in reagent component naming.

NAME

ARCHITECT *i*Gentamicin

INTENDED USE

The ARCHITECT *i*Gentamicin assay is an *in vitro* chemiluminescent microparticle immunoassay (CMIA) for the quantitative determination of gentamicin, an antibiotic drug, in human serum or plasma on the ARCHITECT *i* System with *STAT* protocol capability. The measurements obtained are used in the diagnosis and treatment of gentamicin overdose and in monitoring levels of gentamicin to help ensure appropriate therapy.

SUMMARY AND EXPLANATION OF TEST

Gentamicin is an aminoglycoside antibiotic which exhibits high potency and a broad spectrum bacterial action against both gram-negative and gram-positive organisms. It exhibits a narrow therapeutic index which makes its use hazardous, especially in patients with impaired renal function. In addition, the dose-serum level profile curve of gentamicin is unpredictable, both in terms of peak-serum levels and elimination half-life from plasma.¹

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

The ARCHITECT *i*Gentamicin assay is a one-step immunoassay for the quantitative determination of gentamicin in human serum or plasma using CMIA technology with flexible assay protocols, referred to as Chemiflex.

In the ARCHITECT *i*Gentamicin assay, sample, anti-gentamicin coated paramagnetic microparticles, and gentamicin acridinium-labeled conjugate are combined to create a reaction mixture. The anti-gentamicin coated microparticles bind to the gentamicin present in the sample and to the acridinium-labeled conjugate. After washing, pre-trigger and trigger solutions are added to the reaction mixture. The resulting chemiluminescent reaction is measured as relative light units (RLUs). An indirect relationship exists between the amount of gentamicin in the sample and the RLUs detected by the ARCHITECT *i* System optics.

For additional information on system and assay technology, refer to the ARCHITECT System Operations Manual, Section 3.

REAGENTS

Reagent Kit, 100 Tests

ARCHITECT *i*Gentamicin Reagent Kit (1P31)

- **MICROPARTICLES** 1 Bottle (7.11 mL) Anti-gentamicin (mouse, monoclonal) coated microparticles in TRIS buffer with protein (bovine) stabilizers. Minimum concentration: 0.16% solids. Preservatives: ProClin 950 and sodium azide.
- **CONJUGATE** 1 Bottle (11.75 mL) Gentamicin acridinium-labeled conjugate in MES buffer. Minimum concentration: 3 nM. Preservative: ProClin 300.

Assay Diluent

ARCHITECT *i* Multi-Assay Manual Diluent (7D82-50)

- **MULTI-ASSAY MANUAL DILUENT** 1 Bottle (100 mL) ARCHITECT *i* Multi-Assay Manual Diluent containing phosphate buffered saline solution. Preservative: antimicrobial agent.

Other Reagents

ARCHITECT *i* Pre-Trigger Solution

- **PRE-TRIGGER SOLUTION** Pre-Trigger Solution containing 1.32% (w/v) hydrogen peroxide.

ARCHITECT *i* Trigger Solution

- **TRIGGER SOLUTION** Trigger Solution containing 0.35 N sodium hydroxide.

ARCHITECT *i* Wash Buffer

- **WASH BUFFER** Wash Buffer containing phosphate buffered saline solution. Preservatives: antimicrobial agents.

WARNINGS AND PRECAUTIONS

- **IVD**
- For *In Vitro* Diagnostic Use.
- Package insert instructions must be carefully followed. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.

Safety Precautions

- **CAUTION:** This product requires the handling of human specimens. It is recommended that all human sourced materials be considered potentially infectious and be handled in accordance with the OSHA Standard on Bloodborne Pathogens.² Biosafety Level 2³ or other appropriate biosafety practices^{4,5} should be used for materials that contain or are suspected of containing infectious agents.
- This product contains sodium azide; for a specific listing, refer to the **REAGENTS** section. Contact with acids liberates very toxic gas. This material and its container must be disposed of in a safe way.
- The following warnings and precautions apply to these components:
 - Microparticles
 - Conjugate



WARNING: Contains methylothiazolones
H317 May cause an allergic skin reaction.

Prevention

P261 Avoid breathing mist/vapours/spray.
P272 Contaminated work clothing should not be allowed out of the workplace.
P280 Wear protective gloves/protective clothing/eye protection.

Response


P302+P352 IF ON SKIN: Wash with plenty of water.
P333+P313 If skin irritation or rash occurs: Get medical advice/attention.
P363 Wash contaminated clothing before use.

- This material and its container must be disposed of in a safe way.
- For information on the safe disposal of sodium azide and a detailed discussion of safety precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 8.

Handling Precautions

- Do not use reagent kits beyond the expiration date.
- Do not freeze ARCHITECT *i*Gentamicin reagents.
- **Do not pool reagents within a reagent kit or between reagent kits.**
- Before loading the ARCHITECT *i*Gentamicin Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that may have settled during shipment. For microparticle mixing instructions, refer to the **PROCEDURE, Assay Procedure** section of this package insert.
- **Septums MUST be used to prevent reagent evaporation and contamination and to ensure reagent integrity. Reliability of assay results cannot be guaranteed if septums are not used according to the instructions in this package insert.**
- To avoid contamination, wear clean gloves when placing a septum on an uncapped reagent bottle.
 - Once a septum has been placed on the reagent bottle, **do not invert the bottle** as this will result in reagent leakage and may compromise assay results.
 - Over time, residual liquids may dry on the septum surface. These are typically dried salts, and have no effect on assay efficacy.
- For a detailed discussion of handling precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 7.

Storage Instructions

-  The ARCHITECT *i*Gentamicin Reagent Kit must be stored at 2-8°C in an upright position and may be used immediately after removal from 2-8°C storage.
- When stored and handled as directed, the reagents are stable until the expiration date.
- The ARCHITECT *i*Gentamicin Reagent Kit may be stored on board the ARCHITECT *i* System with *STAT* protocol capability for a maximum of 30 days. After 30 days, the reagent kit must be discarded. Recalibration may be required to obtain maximum onboard reagent stability. For information on tracking onboard time, refer to the ARCHITECT System Operations Manual, Section 5.

- Reagents may be stored on or off the ARCHITECT *i* System. If reagents are removed from the system, store them at 2-8°C (with septums and replacement caps) in an upright position. For reagents stored off the system, it is recommended that they be stored in their original trays and boxes to ensure they remain upright. **If the microparticle bottle does not remain upright (with a septum installed) while in refrigerated storage off the system, the reagent kit must be discarded.** For information on unloading reagents, refer to the ARCHITECT System Operations Manual, Section 5.

Indications of Reagent Deterioration

When a control value is out of the specified range, it may indicate deterioration of the reagents or errors in technique. Associated test results are invalid and samples must be retested. Assay recalibration may be necessary. For troubleshooting information, refer to the ARCHITECT System Operations Manual, Section 10.

INSTRUMENT PROCEDURE

- The ARCHITECT *i*Gentamicin assay is designed for use on the ARCHITECT *i* System with *STAT* protocol capability equipped with ARCHITECT System Software version 7.00 or higher.
- The ARCHITECT *i*Gentamicin assay file must be installed on the ARCHITECT *i* System with *STAT* protocol capability from the ARCHITECT *i* System Assay CD-ROM before performing the assay. For detailed information on assay file installation and viewing and editing assay parameters, refer to the ARCHITECT System Operations Manual, Section 2.
- ARCHITECT *i*Gentamicin samples analyzed in the presence of some ARCHITECT hepatitis assays may generate Error Code *1700 Unable to process test, due to interference from Assay number (x) (x = Assay number)*. Refer to the **RESULTS, Flags** section of this package insert.
- For information on printing assay parameters, refer to the ARCHITECT System Operations Manual, Section 5.
- For a detailed description of system procedures, refer to the ARCHITECT System Operations Manual.
- The default result unit for the ARCHITECT *i*Gentamicin assay is µg/mL. An alternate result unit, µmol/L, may be selected for reporting results by editing assay parameter "Result concentration units" to µmol/L.
 - Conversion Formula: (concentration in µg/mL) x (2.09) = µmol/L.

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Types

The specimen collection tubes listed below were verified for use with the ARCHITECT *i*Gentamicin assay. Other specimen collection tubes have not been tested with this assay.

Glass	Plastic
<ul style="list-style-type: none"> Serum Sodium EDTA 	<ul style="list-style-type: none"> Serum Lithium heparin Sodium heparin Dipotassium EDTA

- The ARCHITECT *i* System does not provide the capability to verify specimen type. It is the responsibility of the operator to verify that the correct specimen types are used in the ARCHITECT *i*Gentamicin assay.

Specimen Conditions

- Do not use specimens with the following conditions:
 - heat-inactivated
 - pooled
 - grossly hemolyzed
 - obvious microbial contamination
- Performance has not been established for the use of cadaveric specimens or body fluids other than human serum and plasma.
- For accurate results, serum and plasma specimens should be free of fibrin, red blood cells, and other particulate matter.** Serum specimens from patients receiving anticoagulant or thrombolytic therapy may contain fibrin due to incomplete clot formation.

- Use caution when handling patient specimens to prevent cross contamination. Use of disposable pipettes or pipette tips is recommended.
- For optimal results, inspect all specimens for bubbles. Remove bubbles with an applicator stick before analysis. Use a new applicator stick for each specimen to prevent cross contamination.

Preparation for Analysis

- Follow the tube manufacturer's processing instructions for serum and plasma collection tubes. Gravity separation is not sufficient for specimen preparation.
- Mix thawed specimens thoroughly by low speed vortexing or by inverting 10 times. Visually inspect the specimens. If layering or stratification is observed, continue mixing until specimens are visibly homogeneous.
- To ensure consistency in results, specimens must be transferred to a centrifuge tube and centrifuged at >10,000 RCF (Relative Centrifugal Force) for 10 minutes before testing if
 - they contain fibrin, red blood cells, or other particulate matter or
 - they were frozen and thawed.
- Centrifuged specimens with a lipid layer on the top must be transferred to a sample cup or secondary tube. Care must be taken to transfer only the clarified specimen without the lipemic material.
- Transfer clarified specimen to a sample cup or secondary tube for testing.

Storage

- Specimens may be stored on or off the clot or red blood cells for
 - up to 24 hours at room temperature (15-30°C) or
 - up to 7 days at 2-8°C.
- If testing will be delayed more than 7 days, remove serum or plasma from the clot or red blood cells and store at -20°C or colder.
- Avoid more than three freeze/thaw cycles.
- Samples containing β-lactam antibiotics should be stored frozen if a delay in analysis of more than 8 hours is anticipated. Failure to freeze samples containing these antibiotics may result in falsely low gentamicin levels due to *in vitro* inactivation.⁶⁻⁹

Shipping

- Before shipping specimens, it is recommended that specimens be removed from the clot or red blood cells.
- When shipping specimens, package and label specimens in compliance with applicable state, federal, and international regulations covering the transport of clinical specimens and infectious substances.
- Specimens may be shipped ambient, at 2-8°C (wet ice), or frozen (dry ice). Do not exceed the storage time limitations listed above.

PROCEDURE

Materials Provided

- 1P31 ARCHITECT *i*Gentamicin Reagent Kit

Materials Required but not Provided

- ARCHITECT *i* System with *STAT* protocol capability equipped with ARCHITECT System Software 7.00 or higher (all systems) and Maintenance and Diagnostics Procedure 6445, version 7.00 or higher (ARCHITECT *i* 1000_{SR} only)
- ARCHITECT *i* System **ASSAY CD-ROM**
- 1P31-01 ARCHITECT *i*Gentamicin Calibrators
- Commercially available control material containing gentamicin
- 7D82-50 ARCHITECT *i* **MULTI-ASSAY MANUAL DILUENT**
- ARCHITECT *i* **PRE-TRIGGER SOLUTION**
- ARCHITECT *i* **TRIGGER SOLUTION**
- ARCHITECT *i* **WASH BUFFER**
- ARCHITECT *i* **REACTION VESSELS**
- ARCHITECT *i* **SAMPLE CUPS**
- ARCHITECT *i* **SEPTUM**
- ARCHITECT *i* **REPLACEMENT CAPS**
- Pipettes or pipette tips (optional) to deliver the volumes specified on the patient or control order screen.

For information on materials required for maintenance procedures, refer to the ARCHITECT System Operations Manual, Section 9.

Assay Procedure

- Before loading the ARCHITECT *i*Gentamicin Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that may have settled during shipment. After the first time the microparticles have been loaded, no further mixing is required.
 - **Invert the microparticle bottle 30 times.**
 - Visually inspect the bottle to ensure microparticles are resuspended. If microparticles are still adhered to the bottle, continue to invert the bottle until the microparticles have been completely resuspended.
 - **If the microparticles do not resuspend, DO NOT USE. Contact your local Abbott representative.**
 - Once the microparticles have been resuspended, place a septum on the bottle. For instructions about placing septums on bottles, refer to the **Handling Precautions** section of this package insert.
- Load the ARCHITECT *i*Gentamicin Reagent Kit on the ARCHITECT *i* System with *STAT* protocol capability.
 - Verify that all necessary reagents are present.
 - Ensure that septums are present on all reagent bottles.
- Order calibration, if necessary.
 - For information on ordering calibrations, refer to the ARCHITECT System Operations Manual, Section 6.
- Order tests.
 - For information on ordering patient specimens and controls and for general operating procedures, refer to the ARCHITECT System Operations Manual, Section 5.
 - NOTE: ARCHITECT *i*Gentamicin samples analyzed in the presence of some ARCHITECT hepatitis assays may generate Error Code *1700 Unable to process test, due to interference from Assay number (x)* (*x* = Assay number). Refer to the **RESULTS, Flags** section of this package insert.
- The minimum sample cup volume is calculated by the system and is printed on the Orderlist report. No more than 10 replicates may be sampled from the same sample cup. To minimize the effects of evaporation, verify adequate sample cup volume is present before running the test.
 - Priority: 35 μ L for the first *i*Gentamicin test plus 25 μ L for each additional *i*Gentamicin test from the same sample cup.
 - \leq 3 hours on-board: 150 μ L for the first *i*Gentamicin test plus 25 μ L for each additional *i*Gentamicin test from the same sample cup.
 - $>$ 3 hours on-board: replace with a fresh sample (patient specimens, controls, and calibrators).
 - If using primary or aliquot tubes, use the sample gauge to ensure sufficient patient specimen is present.
- Prepare calibrators and controls.
 - Mix the ARCHITECT *i*Gentamicin Calibrators by gentle inversion before use.
 - To obtain the recommended volume requirements for the ARCHITECT *i*Gentamicin Calibrators, hold the bottles **vertically**, and dispense a minimum of 5 drops of each calibrator into each respective sample cup.
 - Follow the manufacturer's instructions for preparation of commercially available control material.
- Load samples
 - For information on loading samples, refer to the ARCHITECT System Operations Manual, Section 5.
- Press RUN.
- For additional information on principles of operation, refer to the ARCHITECT System Operations Manual, Section 3.
- For optimal performance, it is important to perform routine maintenance as described in the ARCHITECT System Operations Manual, Section 9. Perform maintenance more frequently when required by laboratory procedures.

Specimen Dilution Procedure

Specimens with gentamicin concentrations of $>$ 10.00 μ g/mL will be flagged as " $>$ 10.00 μ g/mL" and may be diluted using the Manual Dilution Procedure.

- Manual dilutions should be performed as follows:
 - The suggested dilution for the ARCHITECT *i*Gentamicin assay is 1:5.
 - Add 50 μ L of the patient specimen to 200 μ L of the ARCHITECT *i*Gentamicin Calibrator A or ARCHITECT *i* Multi-Assay Manual Diluent.
 - The operator must enter the dilution factor in the Patient or Control order screen. The system will use this dilution factor to automatically calculate the concentration of the sample before dilution and report the result. The result should be greater than 0.3 μ g/mL before the dilution factor is applied.
- For detailed information on ordering dilutions, refer to the ARCHITECT System Operations Manual, Section 5.

Calibration

- To perform an ARCHITECT *i*Gentamicin calibration, test the calibrators in duplicate. The calibrators should be priority loaded.
- Calibration Range: 0.0 - 10.0 μ g/mL.
- To evaluate the calibration of the ARCHITECT *i*Gentamicin assay using commercially available controls, a single sample of all levels of controls must be tested.
 - Order controls as described in the **Assay Procedure** section.
 - Ensure that assay control values are within the established ranges.
- Once an ARCHITECT *i*Gentamicin calibration is accepted and stored, all subsequent samples may be tested without further calibration unless:
 - A reagent kit with a new lot number is used.
 - Controls are out of range.
- For detailed information on how to perform an assay calibration, refer to the ARCHITECT System Operations Manual, Section 6.

QUALITY CONTROL PROCEDURES

The recommended control requirement for the ARCHITECT *i*Gentamicin assay is that a single sample of each control be tested once every 24 hours each day of use. If your laboratory quality control procedures require more frequent use of controls to verify test results, follow those procedures. Additional controls may be tested in conformance with local, state, and/or federal regulations or accreditation requirements and your laboratory's quality control policy.

Each laboratory should establish control ranges to monitor the acceptable performance of the assay. If a control is out of its specified range, the associated test results are invalid and samples must be retested. Recalibration may be indicated.

When using commercially available controls, each laboratory should establish its own concentration ranges for new control lots at each clinically relevant control level. This can be accomplished by assaying a minimum of 20 replicates over several (3-5) days. Sources of variation that can be expected should be included in this study in order to be representative of future system performance. These may include:

- Multiple stored calibrations
- Multiple reagent lots
- Multiple calibrator lots
- Multiple processing modules
- Data points collected at different times of the day

These results should be applied to your laboratory's quality control practices. In addition, the laboratory must ensure that the matrix of the control material is suitable for use in the assay per the assay package insert.

Unless specified, target values and ranges provided with the commercial control product insert are guidelines only and should not be used for quality control purposes.

Refer to Clinical and Laboratory Standards Institute (CLSI) Document C24-A3¹⁰ or other published guidelines for general quality control recommendations.

Verification of Assay Claims

For protocols to verify package insert claims, refer to the ARCHITECT System Operations Manual, Appendix B. The ARCHITECT *i*Gentamicin assay belongs to method group 1.

RESULTS

The ARCHITECT *i*Gentamicin assay uses a 4 Parameter Logistic Curve fit (4PLC, Y-weighted) data reduction method to generate a calibration curve.

Flags

Some results may contain information in the Flags field. For a description of the flags that may appear in this field, refer to the ARCHITECT System Operations Manual, Section 5.

Exception: Error Code 1700 (For ARCHITECT Systems running hepatitis assay(s) only)

- The ARCHITECT assays that contain gentamicin as a preservative are listed in the table below. ARCHITECT *i*Gentamicin samples analyzed in the presence of any of the assays listed in the table below may generate an exception, Error Code 1700 *Unable to process test, due to interference from Assay number (x) (x = Assay number)*.
- If a sample generates Error Code 1700 the first time, do the following:
 - Reorder and run the ARCHITECT *i*Gentamicin test.
 - Reorder and run any remaining tests for the sample.
- **NOTE: DO NOT** reorder the ARCHITECT *i*Gentamicin test with any of the assays listed below.
- In the event that the **RETESTED** sample described above generates Error Code 1700, do the following:
 - Perform the ARCHITECT maintenance procedure below **two times**:
 - For ARCHITECT *i* 2000_{SR}, perform *2130 Flush Fluids*.
 - For ARCHITECT *i* 1000_{SR}, perform *2137 Flush Fluids*.
 - Reorder and run the ARCHITECT *i*Gentamicin test.
- Refer to ARCHITECT System Operations Manual, Section 9.

Gentamicin-Containing Assays		
Assay Name	List Number ^a	Assay Number
ARCHITECT AUSAB	1L82	872
ARCHITECT Anti-HBs	7C18	131
ARCHITECT HBsAg	1L80	873
	6C36	701
ARCHITECT HBsAg Qualitative	1P97	149
ARCHITECT HBsAg Confirmatory	1L81	874
ARCHITECT HBsAg Qualitative Confirmatory	1P98	159/160
ARCHITECT HBsAg Confirmatory V.1	9C94	151
ARCHITECT HBe Antigen	6C32	301
ARCHITECT Anti-HCV	1L79	871
	6C37	161
ARCHITECT HCV Antigen	6L47	801

^a Some list numbers are not available in all countries.

Measuring Interval (Reportable Range)

The measuring interval of the ARCHITECT *i*Gentamicin assay is 0.3 µg/mL to 10.0 µg/mL. Refer to the **SPECIFIC PERFORMANCE CHARACTERISTICS, Measuring Interval** section of this package insert. When using the manual dilution procedure, the assay can report values up to 50.0 µg/mL.

LIMITATIONS OF THE PROCEDURE

- If the gentamicin results are inconsistent with clinical evidence, additional testing is suggested to confirm the result.
- For diagnostic purposes, results should be used in conjunction with other data, e.g., symptoms, results of other tests, clinical impressions, etc.
- Samples containing β-lactam antibiotics should be stored frozen if a delay in analysis of more than 8 hours is anticipated. Failure to freeze samples containing these antibiotics may result in falsely low gentamicin levels due to *in vitro* inactivation.⁶⁻⁹
- Patient samples which contain the drugs cephalixin, netilmicin, sisomicin, and sagamicin¹¹ will yield falsely elevated values for gentamicin. Refer to the **SPECIFIC PERFORMANCE CHARACTERISTICS, Interference** section for further explanation. However, these drugs are not usually coadministered with gentamicin. High concentration of penicillins or cephalosporins have been shown to inactivate gentamicin *in vitro*. The degree of inactivation is dependent on the particular aminoglycoside being measured, the type and concentration of the penicillin or cephalosporin that is also present and the storage conditions of the sample.⁷⁻⁹ Samples from patients receiving additional antibiotics of these types should be assayed immediately or stored frozen.
- Specimens from patients who have received preparations of mouse monoclonal antibodies for diagnosis or therapy may contain human anti-mouse antibodies (HAMA).^{12,13} Specimens containing HAMA may produce anomalous values when tested with assay kits such as ARCHITECT *i*Gentamicin that employ mouse monoclonal antibodies.¹²
- Heterophilic antibodies in human specimens can react with reagent immunoglobulins, interfering with *in vitro* immunoassays.¹⁴ Patients routinely exposed to animals or to animal serum products can be prone to this interference and anomalous values may be observed. Additional information may be required for diagnosis.
- Refer to the **SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS** section of this package insert for specimen limitations.

EXPECTED VALUES

Strong correlations have been shown between serum levels and both therapeutic effect and toxicity in specific patient types. Peak serum levels of gentamicin in the range of 5 to 10 µg/mL are suggested for optimal therapeutic effectiveness. Persistently elevated peak concentrations (10 µg/mL) have been shown to cause renal and eighth cranial nerve toxicity.^{15,16} Nephrotoxicity takes the form of damage to the proximal renal tubules, and is associated with impaired renal function. Central nervous system toxicity is most often manifested as damage to the vestibular and auditory branches of the eighth cranial nerve.^{15,16} Trough levels offer a more discrete indication of impending toxicity since they more closely correspond to tissue levels and are less affected by sampling errors.¹⁷ Slowly rising trough levels have been shown to correspond to tissue accumulation of the drug, and trough levels greater than 2 µg/mL have been associated with renal failure in some patients.¹⁵⁻¹⁸ Refer to the drug manufacturer's package insert or the Physicians' Desk Reference (PDR) for proper drug dosage and for gentamicin measurement sampling times.

SPECIFIC PERFORMANCE CHARACTERISTICS

Data in the **SPECIFIC PERFORMANCE CHARACTERISTICS** section were generated using the ARCHITECT *i* 2000_{SR} System.

Assay results obtained in individual laboratories may vary from data presented.

Precision

The ARCHITECT *i*Gentamicin assay is designed to have an imprecision of ≤ 8% total CV for samples with gentamicin concentrations ranging from 2 µg/mL to 10 µg/mL.

Within-Laboratory Precision

A study was performed based on guidance from the National Committee for Clinical Laboratory Standards (NCCLS) document EP5-A2.¹⁹ Testing was conducted at Abbott Laboratories using two lots of ARCHITECT *i*Gentamicin Reagent Kits, one lot of ARCHITECT *i*Gentamicin Calibrators, one lot of commercially available controls (Bio-Rad Liquichek Therapeutic Drug Monitoring Controls), and two instruments. Three levels of controls and four levels of human serum panels were assayed in a minimum of two replicates at two separate times per day for 20 different days. Each reagent lot used a single calibration curve throughout the study. The data are summarized in the following table.

Sample	Instrument	Reagent Lot	n	Mean (µg/mL)	Within Run		Total	
					SD	%CV	SD	%CV
Control Level 1	1	1	120	1.2	0.03	2.3	0.03	2.4
		2	120	1.2	0.03	2.3	0.03	2.4
	2	1	120	1.3	0.03	2.0	0.03	2.3
		2	120	1.3	0.03	2.2	0.03	2.4
Control Level 2	1	1	120	3.7	0.08	2.3	0.10	2.7
		2	120	3.7	0.11	2.9	0.12	3.2
	2	1	120	3.8	0.12	3.1	0.12	3.1
		2	120	3.9	0.11	2.9	0.12	3.1
Control Level 3	1	1	120	6.5	0.20	3.1	0.23	3.5
		2	120	6.8	0.28	4.1	0.36	5.3
	2	1	120	6.9	0.25	3.7	0.29	4.2
		2	120	6.8	0.26	3.8	0.27	4.0
Panel 1	1	1	120	0.2	0.01	2.7	0.01	4.3
		2	120	0.2	0.01	2.7	0.01	4.4
	2	1	120	0.3	0.01	2.8	0.01	3.1
		2	120	0.3	0.01	2.8	0.01	3.1
Panel 2	1	1	120	1.0	0.03	2.8	0.03	3.5
		2	120	1.0	0.02	2.0	0.03	3.2
	2	1	120	1.0	0.02	1.9	0.02	2.0
		2	120	1.0	0.02	2.5	0.03	2.8
Panel 3	1	1	119	3.6	0.10	2.9	0.14	3.9
		2	120	3.6	0.13	3.6	0.14	3.9
	2	1	120	3.8	0.10	2.6	0.11	2.9
		2	120	3.7	0.10	2.6	0.11	3.1
Panel 4	1	1	120	8.2	0.31	3.7	0.35	4.3
		2	120	8.4	0.37	4.4	0.44	5.2
	2	1	120	8.6	0.31	3.6	0.33	3.8
		2	120	8.3	0.38	4.5	0.42	5.0

Recovery

The ARCHITECT *i*Gentamicin assay is designed to have a mean percent recovery of 91 to 109 for samples with gentamicin concentrations ranging from 2 µg/mL to 10 µg/mL.

A study was performed with 12 specimens containing no gentamicin or low levels of gentamicin. The specimens were spiked with additional gentamicin to create test samples at concentrations of 2.5, 4.0, 6.0, and 8.0 µg/mL. The samples were tested using the ARCHITECT *i*Gentamicin assay on one instrument, and the resulting percent recovery was calculated. The individual percent recovery ranged from 91.1 to 99.2, and the mean percent recovery was 95.7.

Sensitivity

Limit of Quantitation

The ARCHITECT *i*Gentamicin assay is designed to have a Limit of Quantitation (LoQ) of ≤ 0.3 µg/mL.

Based on guidance from the NCCLS document EP17-A,²⁰ a study was performed with five zero-level samples and six samples with gentamicin concentrations of approximately 0.025, 0.05, 0.075, 0.1, 0.2 and 0.3 µg/mL. These samples were tested in five separate runs over a minimum of 3 days using two reagent lots and two instruments. The LoQ for the ARCHITECT *i*Gentamicin assay was 0.20 µg/mL.

Limit of Blank and Limit of Detection

In the same study, the Limit of Blank (LoB) and Limit of Detection (LoD) were determined. The LoB was 0.00 µg/mL and the LoD was 0.05 µg/mL.

Linear Range

Based on guidance from the NCCLS document EP6-A,²¹ a study was performed to establish the linear range of the ARCHITECT *i*Gentamicin assay. Eleven samples were prepared by mixing a high gentamicin sample (> 10.0 µg/mL) in specific ratios with a low gentamicin sample (< 0.3 µg/mL) and tested using the ARCHITECT *i*Gentamicin assay.

Using an absolute deviation from linearity of ≤ 9% for samples with concentrations ≥ 1 µg/mL and ≤ 18% for samples with gentamicin concentrations < 1 µg/mL, a linear range of 0.11 to 11.16 µg/mL was established for the ARCHITECT *i*Gentamicin assay.

Measuring Interval

Measuring Interval is defined as the range of values in µg/mL which meets the limits of acceptable performance for both imprecision and bias for an undiluted sample. For the verification studies described in this package insert, the range was 0.3 µg/mL to 10.0 µg/mL.

Interference

Potentially Interfering Endogenous Substances

Based on guidance from the CLSI document EP7-A2,²² potentially interfering endogenous substances were evaluated to determine whether gentamicin concentrations were affected when using the ARCHITECT *i*Gentamicin assay. The endogenous substances listed below were spiked into samples with different levels of gentamicin (approximately 2.5 and 7.0 µg/mL). The samples were assayed, and the gentamicin concentrations of the spiked samples were compared to the control samples. The data are summarized in the following table.

Potentially Interfering Endogenous Substance	Minimum Interferent Concentration	% Interference ^a	
		2.5 µg/mL	7.0 µg/mL
Bilirubin	20 mg/dL	-0.6	0.7
Hemoglobin	500 mg/dL	2.7	3.4
Total Protein	12 g/dL	0.9	4.8
Triglycerides	3000 mg/dL	-1.6	0.4

$$^a \text{ \% Interference} = \frac{\text{Test Result} - \text{Control Result}}{\text{Control Result}} \times 100$$

Potentially Interfering Clinical Conditions

Potentially interfering clinical conditions were evaluated to determine whether gentamicin concentrations were affected when using the ARCHITECT *i*Gentamicin assay. A normal human serum pool and samples containing the clinical conditions listed below were spiked at two levels of gentamicin (approximately 2.5 and 7.0 µg/mL). The samples were assayed, and the gentamicin concentrations of the spiked samples were compared to the samples without gentamicin. The data are summarized in the following table.

Potentially Interfering Clinical Condition	n	% Recovery Range ^a (Individual)	
		2.5 µg/mL	7.0 µg/mL
Human Anti-Mouse Antibodies (HAMA)	12	99.4 - 107.1	91.2 - 103.7
Heterophilic Antibodies	12	97.6 - 107.9	87.6 - 105.2
Rheumatoid Factor	12	95.8 - 105.6	93.2 - 101.5

$$^a \text{ \% Recovery} = \frac{\text{Post-Spike Result} - \text{Pre-Spike Result}}{\text{Result of Spiked Normal Serum Samples}} \times 100$$

Potentially Interfering Drugs

Based on guidance from the CLSI document EP7-A2,²² potentially interfering drugs were evaluated to determine whether gentamicin concentrations were affected when using the ARCHITECT *i*Gentamicin assay. The compounds listed below were spiked into samples in the absence of gentamicin (0.0 µg/mL) and into samples with different levels of gentamicin (approximately 2.5 and 7.0 µg/mL). The samples were assayed, and the gentamicin concentrations of the spiked samples were compared to the control samples. The data are summarized in the following table.

Test Compound	Test Compound Concentration (µg/mL)	Gentamicin Concentration (µg/mL)				
		0.0	2.5		7.0	
		Conc. Diff. ^a	Conc. Diff. ^a	% Cross-React. ^b	Conc. Diff. ^a	% Cross-React. ^b
Acetaminophen	200	0.00	0.03	0.0	0.08	0.0
Acetylcysteine	1,000	0.00	-0.01	0.0	0.01	0.0
Acetylsalicylic acid	300	0.00	-0.01	0.0	-0.34	-0.1
Amikacin	300	0.00	0.08	0.0	0.32	0.1
Amphotericin B	100	0.00	0.00	0.0	0.11	0.1
Ampicillin	50	0.00	-0.02	0.0	-0.36	-0.6
Ascorbic acid	30	0.00	-0.01	0.0	-0.03	-0.1
Carbenicillin	2,500	0.00	-0.33	0.0	-0.83	0.0
Cefamandole	250	0.00	-0.05	0.0	-0.08	0.0
Cefoxitin	1,000	0.00	-0.05	0.0	-0.21	0.0
Cephalexin	320	0.01	0.91	0.3	2.34	0.7
Cephalosporin C	1,000	0.00	0.02	0.0	0.06	0.0
Cephalothin	1,000	0.00	0.02	0.0	0.18	0.0
Chloramphenicol	250	0.00	-0.04	0.0	0.03	0.0
Clindamycin	2,000	0.00	0.00	0.0	0.00	0.0
Cyclosporine	6,000	0.00	0.10	0.0	0.59	0.0
Erythromycin	500	0.00	-0.12	0.0	0.24	0.0
Ethacrynic acid	400	0.00	0.04	0.0	-0.28	-0.1
5-Fluorocytosine	30	0.00	-0.01	0.0	-0.01	0.0
Furosemide	100	0.00	0.03	0.0	-0.40	-0.3
Fusidic acid	1,000	0.00	-0.04	0.0	-0.01	0.0
Ibuprofen	7,000	0.00	-0.01	0.0	-0.34	0.0
Kanamycin A	400	0.00	0.13	0.0	0.45	0.1
Kanamycin B	400	0.00	0.22	0.1	0.87	0.2
Levodopa	1,000	0.00	0.02	0.0	-0.03	0.0
Lincomycin	2,000	0.00	0.01	0.0	-0.02	0.0
Methicillin	200	0.00	-0.03	0.0	-0.15	-0.1
Methotrexate	50	0.00	-0.01	0.0	-0.10	-0.2
Methylprednisolone	200	0.00	-0.02	0.0	-0.03	0.0
Metronidazole	1,000	0.00	0.00	0.0	0.19	0.0
Neomycin	100	0.00	0.15	0.1	1.01	0.9
Netilmicin	10	4.41	4.58	45.8	4.93	49.3
Oxytetracycline	2,000	0.00	0.04	0.0	0.02	0.0
Penicillin V	10	0.00	0.00	0.0	0.08	0.7
Phenylbutazone	1,000	0.00	0.00	0.0	-0.06	0.0
Prednisolone	12	0.00	0.03	0.2	-0.04	-0.3
Rifampin	50	0.00	0.01	0.0	0.00	0.0
Sagamycin ^c	N/A	N/A	N/A	N/A	N/A	N/A
Sisomicin	10	3.29	3.29	27.4	3.78	31.5
Spectinomycin	100	0.00	-0.09	-0.1	-0.23	-0.2
Streptomycin	400	0.03	0.03	0.0	0.21	0.0
Sulfadiazine	1,000	0.00	-0.03	0.0	-0.02	0.0
Sulfamethoxazole	400	0.00	-0.01	0.0	0.20	0.0
Tetracycline	2,000	0.00	0.10	0.0	0.59	0.0
Theophylline	200	0.00	0.01	0.0	0.14	0.1
Ticarcillin	100	0.00	-0.20	-0.2	-0.09	-0.1
Tobramycin	100	0.00	0.28	0.2	0.84	0.7
Trimethoprim	20	0.00	0.01	0.0	-0.09	-0.4
Vancomycin	400	0.00	0.03	0.0	-0.06	0.0

^a Conc. Diff. = Concentration Difference

^b % Cross-React. = % Cross-Reactivity = $\frac{\text{Concentration Difference}}{\text{Test Compound Concentration}} \times 100$

^c Not available for testing.

Method Comparison

The ARCHITECT *i*Gentamicin assay is designed to have a slope of 1.0 ± 0.1 and a correlation coefficient (*r*) of ≥ 0.95 for samples with gentamicin concentrations ranging from 0.3 µg/mL to 10 µg/mL when compared to AxSYM Gentamicin. A correlation study was performed based on guidance from the NCCLS Document EP9-A2²³ using the Passing-Bablok regression method to compare the ARCHITECT *i*Gentamicin assay to the AxSYM Gentamicin assay using serum specimens (*n* = 146). The data are summarized in the following table.

Correlation of ARCHITECT *i*Gentamicin to AxSYM Gentamicin

Concentration Range (µg/mL)		Correlation Coefficient (<i>r</i>)		Intercept (µg/mL)	95% CI ^b	Slope	95% CI ^b
ARCHITECT	AxSYM	<i>r</i>	95% CL ^a				
0.31 - 8.82	0.46 - 9.23	0.993	0.990	-0.04	(-0.08, 0.00)	0.96	(0.94, 0.97)

^a 95% CL = Confidence Limit (Lower, One-sided)

^b CI = Confidence Interval

BIBLIOGRAPHY

- Chambers, HF. Chapter 45: Aminoglycosides. In: Brunton LL, Lazo JS, Parker KL, editors. *Goodman and Gilman's The Pharmacological Basis of Therapeutics*. 11th ed. McGraw-Hill, 2006. <http://online.statref.com/document.aspx?fxid=75&docid=430>. Accessed June 22, 2010.
- US Department of Labor, Occupational Safety and Health Administration, 29 CFR Part 1910.1030, Bloodborne Pathogens.
- US Department of Health and Human Services. *Biosafety in Microbiological and Biomedical Laboratories*. 5th ed. Washington, DC: US Government Printing Office; January 2007.
- World Health Organization. *Laboratory Biosafety Manual*. 3rd ed. Geneva: World Health Organization; 2004.
- Clinical and Laboratory Standards Institute. *Protection of Laboratory Workers from Occupationally Acquired Infections: Approved Guideline—Third Edition*. CLSI Document M29-A3. Wayne, PA: Clinical and Laboratory Standards Institute; 2005.
- Glew RH, Pavuk RA. Stability of gentamicin, tobramycin, and amikacin in combination with four β-lactam antibiotics. *Antimicrob Agents Chemother* 1983;24(4):474-7.
- Tindula RJ, Ambrose PJ, Harralson AF. Aminoglycoside inactivation by penicillins and cephalosporins and its impact on drug-level monitoring. *Drug Intell Clin Pharm* 1983;17:906-8.
- Pickering LK, Rutherford I. Effect of concentration and time upon inactivation of tobramycin, gentamicin, netilmicin and amikacin by azlocillin, carbenicillin, mecillinam, mezlocillin and piperacillin. *J Pharmacol Exp Ther* 1981;217(2):345-9.
- Pickering LK, Gearhart P. Effect of time and concentration upon interaction between gentamicin, tobramycin, netilmicin, or amikacin and carbenicillin or ticarcillin. *Antimicrob Agents Chemother* 1979;15(4):592-6.
- Clinical and Laboratory Standards Institute (CLSI). *Statistical Quality Control for Quantitative Measurement Procedures: Principles and Definitions; Approved Guideline - Third Edition*. CLSI Document C24-A3. Wayne, PA: Clinical and Laboratory Standards Institute; 2006.
- Micronomicin Sulfate In: Sweetman, SC. editor. *Martindale - The Complete Drug Reference* 36th ed. Pharmaceutical Press, 2009: p 736. <http://csi.micromedex.com/hcsdata/mt/mtm736%2Dp.htm> Accessed June 29, 2010.
- Primus FJ, Kelley EA, Hansen HJ, et al. "Sandwich" type immunoassay of carcinoembryonic antigen in patients receiving murine monoclonal antibodies for diagnosis and therapy. *Clin Chem* 1988;34(2):261-4.
- Schroff RW, Foon KA, Beatty SM, et al. Human anti-murine immunoglobulin responses in patients receiving monoclonal antibody therapy. *Cancer Res* 1985;45:879-85.
- Boscato LM, Stuart MC. Heterophilic antibodies: a problem for all immunoassays. *Clin Chem* 1988;34(1):27-33.

15. Nordström L, Banck G, Belfrage S, *et al.* Prospective study of the ototoxicity of gentamicin. *Acta Path Microbiol Scand* (Section B. 81) (Supp 241) 1973;58-61.
16. Dayal VS, Smith EL, McCain WG. Cochlear and vestibular gentamicin toxicity. A clinical study of systemic and topical usage. *Arch Otolaryngol* 1974;100:338-40.
17. Mangione A, Schentag JJ. Therapeutic monitoring of aminoglycoside antibiotics: An approach. *Ther Drug Monit* 1980;2(2):159-67.
18. Barza M, Lauermann M. Why monitor serum levels of gentamicin? *Clin Pharmacokinet* 1978;3:202-15.
19. National Committee for Clinical Laboratory Standards (NCCLS). *Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline-Second Edition*. NCCLS Document EP5-A2. Wayne, PA: NCCLS; 2004.
20. National Committee for Clinical Laboratory Standards (NCCLS). *Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline*. NCCLS Document EP17-A. Wayne, PA: NCCLS; 2004.
21. National Committee for Clinical Laboratory Standards (NCCLS). *Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline*. NCCLS document EP6-A. Wayne, PA: NCCLS; 2003.
22. Clinical and Laboratory Standards Institute (CLSI). *Interference Testing in Clinical Chemistry; Approved Guideline-Second Edition*. CLSI Document EP7-A2. Wayne, PA: CLSI; 2005.
23. National Committee for Clinical Laboratory Standards. (NCCLS). *Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline-Second Edition*. NCCLS document EP9-A2. Wayne, PA: NCCLS; 2002.

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