BECKMAN COULTER CE

SYNCHRON System(s)
Chemistry Information Sheet

GEN
Gentamicin

REF 469137

For *In Vitro* Diagnostic Use

Rx Only

ANNUAL REVIEW

Reviewed by	Date	Reviewed by	Date

PRINCIPLE

INTENDED USE

GEN reagent, when used in conjunction with UniCel® DxC 600/800 System(s) and SYNCHRON® Systems Drug Calibrator 3 Plus, is intended for quantitative determination of gentamicin concentration in human serum or plasma.

CLINICAL SIGNIFICANCE

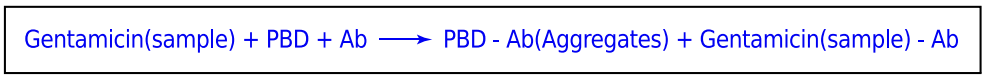
Gentamicin is an antibiotic used to treat serious gram-negative bacterial infections. Gentamicin therapy is monitored for effectiveness of the dose and possible nephrotoxicity.

METHODOLOGY

GEN reagent is used to measure the GEN concentration by a particle enhanced turbidimetric inhibition immunoassay method.[1] A particle-bound drug (PBD) binds to GEN specific antibody (Ab) resulting in the formation of insoluble aggregates causing light scatter. Non-particle-bound GEN in the patient sample competes with the PBD for the antibody binding sites, inhibiting formation of insoluble aggregates. The rate and amount of particle aggregation is inversely proportional to the concentration of GEN in the sample.

The SYNCHRON System(s) automatically proportions the appropriate sample and reagent volumes into a cuvette. The ratio used is one part sample to 105 parts reagent. The system monitors the aggregate formation by measuring the change in absorbance at 380 nanometers. This change in absorbance is inversely proportional to the concentration of gentamicin in the sample and is used by the System to calculate and express the gentamicin concentration based upon a multi-point calibration curve.

CHEMICAL REACTION SCHEME



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SPECIMEN

TYPE OF SPECIMEN

Biological fluid samples should be collected in the same manner routinely used for any laboratory test.[2] Freshly drawn serum or plasma are the preferred specimens. Acceptable anticoagulants are listed in the PROCEDURAL NOTES section of this chemistry information sheet. Whole blood or urine are not recommended for use as a sample.

SPECIMEN STORAGE AND STABILITY

1. Tubes of blood are to be kept closed at all times and in a vertical position. It is recommended that the serum or plasma be physically separated from contact with cells within two hours from the time of collection.[3]
2. Separated serum or plasma should not remain at room temperature longer than 8 hours. If assays are not completed within 8 hours, serum or plasma should be stored at +2°C to +8°C. If assays are not completed within 48 hours, or the separated sample is to be stored beyond 48 hours, samples should be frozen at -15°C to -20°C. Frozen samples should be thawed only once. Analyte deterioration may occur in samples that are repeatedly frozen and thawed.[3]

Additional specimen storage and stability conditions as designated by this laboratory:

SAMPLE VOLUME

The optimum volume, when using a 0.5 mL sample cup, is 0.3 mL of sample. For optimum primary sample tube volumes and minimum volumes, refer to the Primary Tube Sample Template for your system.

CRITERIA FOR UNACCEPTABLE SPECIMENS

Refer to the PROCEDURAL NOTES section of this chemistry information sheet for information on unacceptable specimens.

Criteria for sample rejection as designated by this laboratory:

PATIENT PREPARATION

Special instructions for patient preparation as designated by this laboratory:

SPECIMEN HANDLING

Special instructions for specimen handling as designated by this laboratory:

REAGENTS

CONTENTS

Each kit contains the following items:

Two GEN Reagent Cartridges (2 x 100 tests)

VOLUMES PER TEST

Sample Volume	3 µL
Total Reagent Volume	315 µL
Cartridge Volumes	
A	245 µL
B	40 µL
C	30 µL

REACTIVE INGREDIENTS

REAGENT CONSTITUENTS

Gentamicin Particle Reagent	6.8 mL
Monoclonal anti-Gentamicin Antibodies (mouse)	4.7 mL
Gentamicin Reaction Buffer	110.0 mL

Also non-reactive chemicals necessary for optimal system performance.

⚠ CAUTION

Sodium azide preservative may form explosive compounds in metal drain lines. See NIOSH Bulletin: Explosive Azide Hazard (8/16/76).
To avoid the possible build-up of azide compounds, flush wastepipes with water after the disposal of undiluted reagent. Sodium azide disposal must be in accordance with appropriate local regulations.

GHS HAZARD CLASSIFICATION

Not classified as hazardous

SDS Safety Data Sheet is available at techdocs.beckmancoulter.com

MATERIALS NEEDED BUT NOT SUPPLIED WITH REAGENT KIT

SYNCHRON® Systems Drug Calibrator 3 Plus
At least two levels of control material
Saline

REAGENT PREPARATION

No preparation is required. Do not mix.

ACCEPTABLE REAGENT PERFORMANCE

The acceptability of a reagent is determined by successful calibration and by ensuring that quality control results are within your facility's acceptance criteria.

REAGENT STORAGE AND STABILITY

GEN reagent when stored unopened at +2°C to +8°C, will remain stable until the expiration date printed on the cartridge label. Once opened, the reagent is stable for 42 days at +2°C to +8°C unless the expiration date is exceeded. DO NOT FREEZE. Do not expose reagent to temperatures above +35°C or to direct sunlight.

Reagent storage location:

CALIBRATION

CALIBRATOR REQUIRED

SYNCHRON® Systems Drug Calibrator 3 Plus

CALIBRATOR PREPARATION

No preparation is required.

CALIBRATOR STORAGE AND STABILITY

SYNCHRON® Systems Drug Calibrator 3 Plus is stable until the expiration date printed on the calibrator bottle if stored capped in the original container at +2°C to +8°C.

> ⚠ **CAUTION**
>
> **Because this product is of human origin, it should be handled as though capable of transmitting infectious diseases. Each serum or plasma donor unit used in the preparation of this material was tested by United States Food and Drug Administration (FDA) approved methods and found to be negative for antibodies to HIV and HCV and nonreactive for HbsAg. Because no test method can offer complete assurance that HIV, hepatitis B virus, and hepatitis C virus or other infectious agents are absent, this material should be handled as though capable of transmitting infectious diseases. This product may also contain other human source material for which there is no approved test. The FDA recommends such samples to be handled as specified in Centers for Disease Control's Biosafety Level 2 guidelines.[4]**

Calibrator storage location:

CALIBRATION INFORMATION

1. The system must have a valid calibration curve in memory before control or patient samples can be run.
2. Under typical operating conditions the GEN reagent cartridge must be calibrated every 14 days and also with certain parts replacements or maintenance procedures, as defined in the UniCel DxC 600/800 System *Instructions For Use* (IFU) manual. This assay has within-lot calibration available. Refer to the UniCel DxC 600/800 System *Instructions For Use* (IFU) manual for information on this feature.
3. For detailed calibration instructions, refer to the UniCel DxC 600/800 System *Instructions For Use* (IFU) manual.
4. The system will automatically perform checks on the calibration and produce data at the end of calibration. In the event of a failed calibration, the data will be printed with error codes and the system will alert the operator of the failure. For information on error codes, refer to the UniCel DxC 600/800 System *Instructions For Use* (IFU) manual.

TRACEABILITY

For Traceability information refer to the Calibrator instructions for use.

QUALITY CONTROL

At least two levels of control material should be analyzed daily. In addition, these controls should be run with each new calibration, with each new reagent cartridge, and after specific maintenance or troubleshooting procedures as detailed in the appropriate system manual. More frequent use of controls or the use of additional controls is left to the discretion of the user based on good laboratory practices or laboratory accreditation requirements and applicable laws.

The following controls should be prepared and used in accordance with the package inserts. Discrepant quality control results should be evaluated by your facility.

Table 1.0 Quality Control Material

CONTROL NAME	SAMPLE TYPE	STORAGE

TESTING PROCEDURE(S)

1. If necessary, load the reagent onto the system.
2. After reagent load is completed, calibration may be required.
3. Program samples and controls for analysis.
4. After loading samples and controls onto the system, follow the protocols for system operations.

For detailed testing procedures, refer to the UniCel DxC 600/800 System *Instructions For Use* (IFU) manual.

CALCULATIONS

The SYNCHRON System(s) performs all calculations internally to produce the final reported result. The system will calculate the final result for sample dilutions made by the operator when the dilution factor is entered into the system during sample programming.

REPORTING RESULTS

Equivalency between the SYNCHRON LX and UniCel DxC 600/800 Systems has been established. Chemistry results between these systems are in agreement and data from representative systems may be shown.

REFERENCE INTERVALS

Therapeutic GEN concentrations vary significantly, depending upon the individual. The lower limit for one patient may be ineffective in another, while the upper limit may prove toxic in a third. The physician should determine the appropriate reference interval for each patient. The reference intervals listed below were taken from the literature.[5]

Table 2.0 Reference intervals

INTERVALS	SAMPLE TYPE	DRUG LEVEL	THERAPEUTIC INTERVAL		TOXIC INTERVAL	
			CONVENTIONAL UNITS (µg/mL)	S.I. UNITS (µmol/L)	CONVENTIONAL UNITS (µg/mL)	S.I. UNITS (µmol/L)
Literature	Serum or Plasma	Peak			> 10 - 12	> 21 - 25
		Less severe infection	5 - 8	10.4 - 16.7		
		Severe infection	8 - 10	16.7 - 20.9		
		Trough			> 2 - 4	> 4.2 - 8.4
		Less severe infection	< 1	< 2.1		
		Moderate infection	< 2	< 4.2		
		Severe infection	< 2 - 4	<4.2 - 8.4		

INTERVALS	SAMPLE TYPE	DRUG LEVEL	THERAPEUTIC INTERVAL		TOXIC INTERVAL	
			CONVENTIONAL UNITS (µg/mL)	S.I. UNITS (µmol/L)	CONVENTIONAL UNITS (µg/mL)	S.I. UNITS (µmol/L)
Laboratory	Serum or Plasma	Peak				
		Trough				

Refer to References (6,7,8) for guidelines on establishing laboratory-specific reference intervals.

Additional reporting information as designated by this laboratory:

PROCEDURAL NOTES

ANTICOAGULANT TEST RESULTS

If plasma is the sample of choice, the following anticoagulants were found to be compatible with this method based on a study of 20 healthy volunteers:

Table 3.0 Acceptable Anticoagulants[a]

ANTICOAGULANT	LEVEL TESTED FOR IN VITRO INTERFERENCE	AVERAGE PLASMA-SERUM BIAS (µg/mL)
Lithium Heparin	14 Units/mL	NSI[b]
Sodium Heparin	14 Units/mL	NSI

a Data shown was collected using SYNCHRON CX Systems. Equivalency between SYNCHRON LX Systems has been established by Deming regression analysis to SYNCHRON CX Systems.

b NSI = No Significant Interference (within ± 0.4 µg/mL or 10%).

LIMITATIONS

None identified

INTERFERENCES

1. The following substances were tested for interference with this methodology:

   Table 4.0 Interferences

SUBSTANCE	SOURCE	LEVEL TESTED	OBSERVED EFFECT
Hemoglobin	RBC hemolysate	500 mg/dL	NSI[a]
Bilirubin	Porcine	30 mg/dL	NSI
Rheumatoid Factor	Human	300 IU/mL	NSI
Lipemia	Human	4+	NSI
Paraprotein (IgM)	Human	500 mg/dL	NSI

   a NSI = No Significant Interference (within ± 0.4 µg/mL or 10%).

2. Refer to References (9,10,11) for other interferences caused by drugs, disease and preanalytical variables.

3. For assays employing mouse antibodies, the possibility exists for interference by human anti-mouse antibodies (HAMA) in the sample. Human anti-mouse antibodies may be present in samples from patients who have received immunotherapy or diagnostic procedures utilizing monoclonal antibodies or in individuals who have been regularly exposed to animals.[12,13] Additionally, other heterophile antibodies, such as human anti-goat antibodies may be present in patient samples. Interpretation of results should be done in the context of the overall clinical presentation of the patient, including symptoms, clinical history, data from additional tests and other appropriate information.

SPECIFICITY

1. The following list of substances were added at the concentration listed to separate aliquots of a serum pool containing 6.4 µg/mL gentamicin. In most cases the value shown approximates maximum physiological concentrations. The recovered values were subtracted from the serum pool value. If the results were within ± 2X of the within-run precision specifications there was no significant interference. If the recovered results were more than ± 2X of the within-run precision specifications the difference is listed under observed effect.

Table 5.0 Specificity - Peak Gentamicin level[a]

SUBSTANCE	CONCENTRATION (µg/mL)	OBSERVED RECOVERY (µg/mL)	OBSERVED EFFECT
Amikacin	70	6.5	NSI[b]
Ampicillin	100	6.3	NSI
Carbenicillin	250	7.1	+11%
Cephalothin	500	6.5	NSI
Chloramphenicol	50	6.6	NSI
Clindamycin	100	6.8	NSI
Erythromycin	40	6.5	NSI
Kanamycin	30	6.5	NSI
Lincomycin	100	6.4	NSI
Neomycin	60	6.3	NSI
Netilmicin	20	6.6	NSI
Penicillin G	50	6.5	NSI
Sisomicin	10	8.3	+30%
Streptomycin	60	6.3	NSI
Sulfanilimide	100	6.4	NSI
Tetracycline	500	6.5	NSI
Tobramycin	20	6.5	NSI
Trimethoprin	500	6.5	NSI
Vancomycin	100	6.4	NSI

a Data shown was collected using SYNCHRON CX Systems. Equivalency between SYNCHRON LX Systems has been established by Deming regression analysis to SYNCHRON CX Systems.

b NSI = No Significant Interference (within ± 10%).

2. The following list of substances were added at the concentration listed to separate aliquots of a serum pool containing 2.0 µg/mL gentamicin. In most cases the value shown approximates maximum physiological concentrations. The recovered values were subtracted from the serum pool value. If the results were within ± 2X of the within-run precision specifications there was no significant interference. If the recovered results were more than ± 2X of the within-run precision specifications the difference is listed under observed effect.

Table 6.0 Specificity - Trough Gentamicin level[a]

SUBSTANCE	CONCENTRATION (µg/mL)	OBSERVED RECOVERY (µg/mL)	OBSERVED EFFECT (µg/mL)
Amikacin	70	2.0	NSI[b]
Ampicillin	100	2.0	NSI
Carbenicillin	250	2.0	NSI
Cephalothin	500	2.0	NSI
Chloramphenicol	50	1.9	NSI

Table 6.0 Specificity - Trough Gentamicin level, Continued

SUBSTANCE	CONCENTRATION (µg/mL)	OBSERVED RECOVERY (µg/mL)	OBSERVED EFFECT (µg/mL)
Clindamycin	100	2.0	NSI
Erythromycin	40	2.0	NSI
Kanamycin	30	2.2	NSI
Lincomycin	100	2.1	NSI
Neomycin	60	2.1	NSI
Netilmicin	10	2.1	NSI
Netilmicin	20	2.2	NSI
Penicillin G	50	2.1	NSI
Sisomicin	5	5.2	+3.2
Sisomicin	10	7.9	+5.9
Streptomycin	60	2.2	NSI
Sulfanilimide	100	2.1	NSI
Tetracycline	500	2.1	NSI
Tobramycin	20	2.1	NSI
Trimethoprin	500	2.1	NSI
Vancomycin	100	2.1	NSI

a Data shown was collected using SYNCHRON CX Systems. Equivalency between SYNCHRON LX Systems has been established by Deming regression analysis to SYNCHRON CX Systems.

b NSI = No Significant Interference (within ±0.4 µg/mL).

PERFORMANCE CHARACTERISTICS

ANALYTIC RANGE

The SYNCHRON System(s) method for the determination of this analyte provides the following analytical ranges:

Table 7.0 Analytical Range

SAMPLE TYPE	CONVENTIONAL UNITS	S.I. UNITS
Serum or Plasma	0.5 – 12.0 µg/mL	1.0 – 25.1 µmol/L

Samples with concentrations outside of the analytical range will be reported as "<0.5 µg/mL" ("<1.0 µmol/L") or ">12.0 µg/mL" (">25.1 µmol/L").

Samples reported out as greater than the analytical range may be confirmed by diluting with saline and reanalyzing. The appropriate dilution factor should be applied to the reported result.

The analytical range of this assay is 0.5-12.0 µg/mL (1.0-25.1 µmol/L). Very rarely, a patient sample may contain a nonspecific protein which could cause a false low GEN result. It is recommended that the low limit of the reportable range of this assay be set to the default value of 0.1 µg/mL (0.2 µmol/L). All samples with printed results below 0.1 µg/mL (0.2 µmol/L) will need to be confirmed by dilution. Printed results between 0.1 µg/mL and 0.49 µg/mL (0.2 µmol/L and 0.98 µmol/L) do not need to be confirmed by dilution and can be reported as "<0.5 µg/mL" ("<1.0 µmol/L"). However, if the low reportable range of the assay is set to 0.5 µg/mL (1.0 µmol/L), all printed results which are "<0.5 µg/mL" ("<1.0 µmol/L") need to be confirmed by dilution.

Dilution protocol: Confirm a suspected low GEN sample result by adding one measured volume of test sample to an equal volume of a sample with known GEN concentration. The assayed GEN result of this diluted sample should be approximately half of the value of the known sample. If the assayed result of the diluted sample is not close to half of the known sample value, testing needs to be performed using an alternate method.

REPORTABLE RANGE (AS DETERMINED ON SITE):

Table 8.0 Reportable Range

SAMPLE TYPE	CONVENTIONAL UNITS	S.I. UNITS

SENSITIVITY

Sensitivity is defined as the lowest measurable concentration which can be distinguished from zero with 95% confidence. Sensitivity for GEN determination is 0.5 µg/mL (1.0 µmol/L).

EQUIVALENCY

Equivalency was assessed by Deming regression analysis of patient samples to accepted clinical methods.

Serum or plasma (in the range of 0.5 to 7.9 µg/mL):

Y (SYNCHRON LX Systems)	= 0.990X - 0.06
N	= 75
MEAN (SYNCHRON LX Systems)	= 2.81
MEAN (SYNCHRON CX7 DELTA)	= 2.90
CORRELATION COEFFICIENT (r)	= 0.990

Refer to References (14) for guidelines on performing equivalency testing.

PRECISION

A properly operating SYNCHRON System(s) should exhibit precision values less than or equal to the following:

Table 9.0 Precision Values

TYPE OF PRECISION	SAMPLE TYPE	1 SD		CHANGEOVER VALUE[a]		% CV
		µg/mL	µmol/L	µg/mL	µmol/L	
Within-run	Serum/Plasma	0.2	0.4	4.0	8.0	5.0
Total	Serum/Plasma	0.3	0.6	4.0	8.0	7.5

a When the mean of the test precision data is less than or equal to the changeover value, compare the test SD to the SD guideline given above to determine the acceptability of the precision testing. When the mean of the test precision data is greater than the changeover value, compare the test % CV to the guideline given above to determine acceptability. Changeover value = (SD guideline/CV guideline) x 100.

Comparative performance data for a SYNCHRON LX® System evaluated using the NCCLS Proposed Guideline EP5-T2 appears in the table below.[15] Each laboratory should characterize their own instrument performance for comparison purposes.

Table 10.0 NCCLS EP5-T2 Precision Estimate Method

TYPE OF IMPRECISION	SAMPLE TYPE		No. Systems	No. Data Points[a]	Test Mean Value (µg/mL)	EP5-T2 Calculated Point Estimates	
						SD	%CV
Within-run	Serum	Control 1	1	80	2.2	0.1	5.3
	Serum	Control 2	1	80	6.1	0.1	1.8
	Serum	Control 3	1	80	9.7	0.2	2.0
Total	Serum	Control 1	1	80	2.2	0.2	7.1
	Serum	Control 2	1	80	6.1	0.2	2.5
	Serum	Control 3	1	80	9.7	0.2	2.1

a The point estimate is based on the pooled data from one system, run for twenty days, two runs per day, two observations per run on an instrument operated and maintained according to the manufacturer's instructions.

NOTICE

These degrees of precision and equivalency were obtained in typical testing procedures on a SYNCHRON LX® System and are not intended to represent the performance specifications for this reagent.

ADDITIONAL INFORMATION

For more detailed information on UniCel DxC Systems, refer to the appropriate system manual.

SHIPPING DAMAGE

If damaged product is received, notify your Beckman Coulter Clinical Support Center.

REVISION HISTORY

Revision AF

Added Saline and removed Gentamicin-free serum or plasma from the Material Needed But Not Supplied with Reagent list, and revised Quality Control section.

Revision AG

Updated corporate address; removed EDTA as an Acceptable Anticoagulant claim.

Revision AH

Added Revision History.

Revision AJ

Added new language requirement: Czech, and Korean.

Revision AK

Removed references to CX and LX systems as they are discontinued effective 12/2013.

Added Beckman Coulter trademark statement and disclaimer.

Revision AL

Added GHS Classification information

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