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ADVIA Centaur® XP
ADVIA Centaur® XPT
Immunoassay Systems

Cyclosporine (CsA)

Current revision and date [a]	Rev. N, 2020-08	
Product Name	ADVIA Centaur® Cyclosporine assay	**REF** 04564446
Systems	ADVIA Centaur XP system ADVIA Centaur XPT system	
Materials Required but Not Provided	ADVIA Centaur CsA Pretreatment Reagent ADVIA Centaur CsA Calibrator ADVIA Centaur Wash 1 (2 x 1500 mL) ADVIA Centaur Wash 1 (2 x 2500 mL)	**REF** 04567127 **REF** 04567682 **REF** 01137199 **REF** 03773025
Specimen Types	EDTA Whole blood	
Assay Range	30–1500 ng/mL (25–1247 nmol/L)	
Reagent Storage	2–8°C	
Reagent On-System Stability	42 days	

a In Rev. B or later, a vertical bar in the margin indicates a technical update to the previous version.

Intended Use

The ADVIA Centaur® Cyclosporine (CsA) assay is an *in vitro* diagnostic immunoassay for the quantitative determination of cyclosporine in human whole blood using the ADVIA Centaur® XP and ADVIA Centaur® XPT systems. This assay is intended for use as an aid in the management of cyclosporine therapy in kidney, heart, and liver transplant patients.

Summary and Explanation

Cyclosporine is a hydrophobic cyclic oligopeptide of fungal origin that suppresses the immune system. Although the mechanism of action is not entirely understood, cyclosporine is thought to inhibit T-cell mediated responses, as well as the production and release of lymphokines. During the last 20 years, cyclosporine has substantially improved patient and graft survival in patients receiving heart, kidney, liver, pancreas, or lung transplants.[1–6]

Monitoring cyclosporine concentrations is recommended[7] in conjunction with other clinical tests and examinations to help optimize immunosuppression and reduce adverse events in organ transplant recipients. Whole blood is the recommended sample type since cyclosporine is rapidly distributed into the red blood cells.

Principles of the Procedure

The ADVIA Centaur Cyclosporine assay is a competitive immunoassay using direct chemiluminescent technology. Cyclosporine in the patient sample competes with acridinium ester-labeled cyclosporine in the Lite Reagent for a limited amount of biotin-labeled monoclonal mouse anti-cyclosporine antibody. Biotin-labeled anti-cyclosporine binds to streptavidin that is covalently coupled to paramagnetic particles in the Solid Phase. In the ADVIA Centaur Cyclosporine assay, the sample is manually pretreated to lyse the cells and solubilize the cyclosporine.

Reagents

Reagent	Description	Storage	Reagent Stability
ADVIA Centaur CsA ReadyPack® primary reagent pack; Lite Reagent	5.0 mL/reagent pack cyclosporine (~6 ng/mL) labeled with acridinium ester in phosphate buffer with bovine serum albumin, surfactant, and preservatives	2–8°C	**Unopened:** Stable until the expiration date on the carton **On-system:** 42 days
ADVIA Centaur CsA ReadyPack primary reagent pack; Solid Phase Reagent	12.5 mL/reagent pack streptavidin coupled to paramagnetic particles (~160 µg/mL) in phosphate buffered saline with bovine serum albumin, mouse gamma globulin, surfactant, and preservatives	2–8°C	**Unopened:** Stable until the expiration date on the carton **On-system:** 42 days
ADVIA Centaur CsA ReadyPack primary reagent pack; Ancillary Reagent	5.0 mL/ reagent pack biotinylated monoclonal mouse anti-cyclosporine antibody (100 ng/mL) in phosphate buffered saline with bovine serum albumin, mouse gamma globulin, surfactant, and preservatives	2–8°C	**Unopened:** Stable until the expiration date on the carton **On-system:** 42 days
ADVIA Centaur CsA Reagent vial; Pretreatment Reagent [a] PRE	26.0 mL/vial detergents, glycerol, anti-foam and preservatives	2–8°C	**Unopened:** Stable until the expiration date on the vial **On-system:** 21 consecutive weeks after accessing the vial
ADVIA Centaur CsA Calibrator [a]	2.0 mL/vial human serum with detergents, glycerol, anti-foam and preservatives	2–8°C	**Unopened:** Stable until the expiration date on the vial **On-system:** 4 hours **Opened:** 21 consecutive weeks after accessing the vial
ADVIA Centaur Wash 1[a] WASH 1	1500 mL/pack phosphate-buffered saline with sodium azide (< 0.1%) and surfactant	2–25°C	**Unopened:** Stable until the expiration date on the pack **On-system:** 1 month
ADVIA Centaur Wash 1[a] WASH 1	2500 mL/pack phosphate-buffered saline with sodium azide (< 0.1%) and surfactant	2–25°C	**Unopened:** Stable until the expiration date on the pack **On-system:** 1 month
ADVIA Centaur Multi-Diluent 12[b] M-DIL 12	20.0 mL/vial human serum with detergents, glycerol, anti-foam and preservatives	2–8°C	**Unopened:** Stable until the expiration date on the vial **On-system:** 21 consecutive weeks after accessing the vial

a See *Materials Required but Not Provided*

b See *Optional Materials*

Warnings and Precautions

Safety data sheets (MSDS/SDS) available on www.siemens.com/diagnostics.

CAUTION

This device contains material of animal origin and should be handled as a potential carrier and transmitter of disease.

Contains sodium azide as a preservative. Sodium azide can react with copper or lead plumbing to form explosive metal azides. On disposal, flush reagents with a large volume of water to prevent buildup of azides. Disposal into drain systems must be in compliance with prevailing regulatory requirements.

H412	Harmful to aquatic life with long lasting effects.
P273, P501	Avoid release to the environment. Dispose of contents and container in accordance with all local, regional, and national regulations. **Contains:** Microprotect; ADVIA Centaur CsA ReadyPack

Dispose of hazardous or biologically contaminated materials according to the practices of your institution. Discard all materials in a safe and acceptable manner and in compliance with prevailing regulatory requirements.

For *in vitro* diagnostic use.

Preparing Reagents

All reagents are liquid and ready to use.

Mix all primary reagent packs by hand before loading them onto the system. Visually inspect the bottom of the reagent pack to ensure that all particles are dispersed and resuspended. For detailed information about preparing the reagents for use, refer to the system operating instructions.

Note

- Discard the primary reagent packs at the end of the on-system stability interval.
- Do not use reagents beyond the expiration date.

Storing and Stability

Store the reagents upright at 2–8°C.

Protect reagent packs from all heat and light sources. Reagent packs loaded on the system are protected from light. Store unused reagent packs at 2–8°C away from heat and light sources.

All reagents are stable at 2–8°C until the expiration date on the packaging.

Specimen Collection and Handling

Whole Blood

Whole blood is the recommended sample type for this assay. EDTA is recommended as the anticoagulant of choice for assaying cyclosporine in whole blood samples. Heparinized samples are not recommended because they may form clots during storage.[8]

The following recommendations for handling and storing blood samples are furnished by the Clinical and Laboratory Standards Institute (CLSI):[9]

- Collect all blood samples observing universal precautions for venipuncture.
- Keep tubes stoppered and upright at all times.
- Test samples as soon as possible after collecting. Do not use samples stored at room temperature for longer than 6 hours.

- Tightly cap and refrigerate specimens at 2–8°C if the assay is not completed within 8 hours. You can store samples at 2–8°C for up to 7 days.
- If longer storage is necessary, freeze samples at or below -20°C up to 1 month in non frost-free freezers.
- Freeze samples only once, and mix thoroughly after thawing.

Whole Blood Hemolysate

- Do not keep pretreated samples at room temperature for longer than 4 hours.
- Keep pretreated samples up to 24 hours at 2–8°C.
- Do not freeze pretreated samples.

The purpose of handling and storage information is to provide guidance to users. It is the responsibility of the individual laboratory to use all available references and/or its own studies when establishing alternate stability criteria to meet specific needs.

Procedure

Materials Provided

The following materials are provided:

REF	Contents	Number of Tests
04564446	1 ReadyPack primary reagent pack containing ADVIA Centaur Cyclosporine Lite Reagent, Solid Phase and Ancillary Reagent ADVIA Centaur Cyclosporine Master Curve card	50

Materials Required but Not Provided

The following materials are required to perform this assay, but are not provided:

Item	Description	
REF 04567127	ADVIA Centaur CsA Pretreatment reagent PRE	2 x 26 mL/vial
REF 04567682	ADVIA Centaur CsA Calibrator	2 vials of low calibrator CAL L 2 vials of high calibrator CAL H Barcode labels for the calibrators ADVIA Centaur CsA Calibrator Assigned Value card
REF 01137199 (112351)	ADVIA Centaur Wash 1 WASH 1	2 x 1500 mL/pack
REF 03773025	ADVIA Centaur Wash 1[a] WASH 1	2 x 2500 mL/pack

a For use with systems with 2500 mL capacity

Optional Materials

The following materials may be used to perform this assay, but are not provided:

Item	Description	
REF 04786546	ADVIA Centaur Multi-Diluent 12 M-DIL 12	20.0 mL/vial
REF 03685177	ADVIA Centaur CsA Master Curve Material	5 x 1 mL

Assay Procedure

For detailed instructions on performing the procedure, refer to the system operating instructions.

The system automatically performs the following steps:

1. Dispenses 30 µL of pretreated sample into a cuvette.
2. Dispenses 100 µL of Ancillary Reagent and incubates for 2.5 minutes at 37°C.
3. Dispenses 100 µL of Lite Reagent and incubates for 2.5 minutes at 37°C.
4. Dispenses 250 µL of Solid Phase and incubates for 2.5 minutes at 37°C.
5. Separates, aspirates, and washes the cuvettes with Wash 1.
6. Dispenses 300 µL each of Acid Reagent and Base Reagent to initiate the chemiluminescent reaction.
7. Reports results according to the selected option, as described in the system operating instructions.

An inverse relationship exists between the amount of cyclosporine present in the patient sample and the amount of relative light units (RLUs) detected by the system.

Preparing the System

Ensure that the system has sufficient primary and ancillary reagent packs. For detailed information about preparing the system, refer to the system operating instructions.

Load the ReadyPack reagent packs in the primary reagent area using the arrows as a placement guide. The system automatically mixes the primary reagent packs to maintain homogeneous suspension of the reagents. For detailed information about loading reagents, refer to the system operating instructions.

Preparing the Samples

This assay requires 30 µL of pretreated sample for a single determination. This volume does not include the unusable volume in the sample container or the additional volume required when performing duplicates or other tests on the same sample. For detailed information about determining the minimum required volume, see the system operating instructions.

Preparing the Whole Blood Hemolysate

Note Do not pretreat Calibrators and Master Curve Materials.

- Dispense exactly 400 µL of of the ADVIA Centaur CsA Pretreatment Reagent into a sample cup or test tube.
- Thoroughly mix the stoppered sample by gentle inversion to ensure homogeneity of the sample.
- Pipet exactly 100 µL of blood into the sample cup. Use a new pipet tip for each sample, and carefully wipe the outside of the tip with a lint-free tissue before transfer to the sample cup. Avoid pipeting insoluble materials that may form when samples are frozen.
- Cover the sample cup and vortex individually for 10 seconds. Examine each sample cup to ensure a homogeneous solution. Additional vortex may be required.
- Place sample cup or test tube on the instrument.

Before placing samples on the system, ensure that samples have the following characteristics:

- Samples are free of fibrin or other particulate matter.
- Samples are free of bubbles.

On-System Stability

The ADVIA Centaur CsA assay reagents are stable unopened until the expiration date on the carton or onboard the system for 42 days.

Performing Calibration

For calibration of the ADVIA Centaur CsA assay, use the ADVIA Centaur CsA Calibrator. Perform the calibration as described in the calibrator instructions for use.

Calibration Frequency

Calibrate the assay at the end of the 28-day calibration interval.

Additionally, the ADVIA Centaur Cyclosporine assay requires a two-point calibration:

- When changing lot numbers of primary reagent packs.
- When replacing system components.
- When quality control results are repeatedly out of range.

Performing Master Curve Calibration

The ADVIA Centaur Cyclosporine assay requires a Master Curve calibration when using a new lot number of Lite Reagent and Solid Phase, and Ancillary Reagent. For each new lot number of Lite Reagent, Solid Phase, and Ancillary Reagent, use the barcode reader or keyboard to enter the Master Curve values on the system. The Master Curve card contains the Master Curve values. For detailed information about entering calibration values, refer to the system operating instructions.

Performing Quality Control

Follow government regulations or accreditation requirements for quality control frequency.

For detailed information about entering quality control values, refer to the system operating instructions.

To monitor system performance and chart trends, as a minimum requirement, assay 2 levels of quality control material on each day that samples are analyzed. Assay quality control samples when performing a 2-point calibration. Treat all quality control samples the same as patient samples.

For quality control of the ADVIA Centaur Cyclosporine assay, use Bio-Rad Lyphochek Whole Blood Control and Bio-Rad Lyphochek Elevated Immunosuppressant Control or an equivalent whole blood quality control material. Refer to the quality control product insert for the suggested Expected Values. Users should follow federal, state, and local guidelines for quality control.

Taking Corrective Action

If the quality control results do not fall within the Expected Values or within the laboratory's established values, do not report results. Take the following actions:

- Verify that the materials are not expired.
- Verify that required maintenance was performed.
- Verify that the assay was performed according to the instructions for use.
- Rerun the assay with fresh quality control samples.
- If necessary, contact your local technical support provider or distributor for assistance.

Results

Calculation of Results

For detailed information about how the system calculates results, refer to the system operating instructions.

The system reports cyclosporine results in ng/mL (common units) or nmol/L (SI units), depending on the units defined when setting up the assay. The conversion formula is 1 ng/mL = 0.8315 nmol/L.

Dilutions

The following information pertains to dilutions:

- Manually dilute the pretreated patient samples 1:5 when cyclosporine levels exceed 1500 ng/mL (1247 nmol/L), or when laboratory protocol requires manual dilution.
- Use Multi-Diluent 12 to manually dilute pretreated patient samples, and then load the diluted sample in the sample rack, replacing the undiluted sample.
- Ensure that results are mathematically corrected for dilution. If a dilution factor is entered when scheduling the test, the system automatically calculates the result.

Interpretation of Results

Results of this assay should always be interpreted in conjunction with patient's medical history, clinical presentation and other findings.

Limitations

This assay has not been evaluated in a pediatric population.

Always use measurements of CsA in conjunction with other diagnostic procedures, including information from the patient’s clinical evaluation.

Patients with impaired liver function, elevated bilirubin levels, unexpectedly high drug values, or increased time post-therapy can show falsely increased values in cyclosporine immunoassays because of accumulation of CsA metabolites. For these patients, results of cyclosporine immunoassays may be supported by an HPLC-MS method which is highly specific for the parent drug.[10]

Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays.[11] Routine exposure to animals or animal serum products can cause interference and anomalous values. Diagnosis may require additional information.

High levels of triglycerides and cholesterol may result in low quantitation in lipemic samples.

Do not use in patients taking biotin supplements.

Clearance of biotin could be different in patients that are not apparently healthy, for example patients with impaired renal function may have higher concentrations of biotin in whole blood.

Expected Values

No firm therapeutic range exists for cyclosporine in whole blood. The complexity of the clinical state, individual differences in sensitivity to immunosuppressive and nephrotoxic effects of cyclosporine, coadministration of other immunosuppressants, type of transplant, time post-transplant, and a number of other factors will cause different requirements for optimal blood levels of cyclosporine. Each clinician should establish a range based on clinical experience, and evaluate each patient before treatment adjustments are made. In addition, ranges will vary according to the commercial *in vitro* diagnostic test used. Do not use conversion factors between commercial assays to predict values for individual patients. Consistent use of one assay for an individual patient is recommended because of varying patterns of cross-reactivity with metabolites.[10]

Measurements of CsA should be used in conjunction with other diagnostic procedures and clinical evaluation. Do not base changes in the cyclosporine treatment regimen on individual cyclosporine values.

Performance Characteristics

Analytical Measuring Range

The ADVIA Centaur CsA assay measures cyclosporine concentrations from 30–1500 ng/mL (25–1247 nmol/L).

Specificity

Whole blood samples containing 200 ng/mL of cyclosporine were spiked with 1000 ng/mL of metabolites AM1, AM1c, AM4N, AM9 and AM19. The calculated cross-reactivity is shown below:

Metabolite	Tested Concentration (ng/mL)	% Cross-Reactivity
AM1	1000	< 5%
AM1c	1000	< 5%
AM4N	1000	< 5%
AM19	1000	< 5%
AM9	1000	15.0

Sensitivity

The ADVIA Centaur Cyclosporine assay measures cyclosporine concentrations up to 1500 ng/mL (1247 nmol/L) with a lower limit of 30 ng/mL (25 nmol/L).

The functional sensitivity is defined as the lowest cyclosporine concentration determined at a coefficient of variation of 20%. The ADVIA Centaur Cyclosporine assay functional sensitivity is 30 ng/mL (25 nmol/L).

Precision

Five controls and 3 patient pools were assayed for 5 days at 3 clinical trial sites using 2 reagent lots and 2 calibrator lots (n = 150 for each sample).

Sample	Mean (ng/mL)	Within-run % CV	Total % CV
Control 1	84	7.1	7.5
Control 2	177	5.1	5.6
Control 3	348	5.4	5.5
Control 4	615	6.1	6.7
Control 5	1138	5.9	7.7
Pool 1	171	4.5	5.3
Pool 2	291	5.4	5.8
Pool 3	482	4.9	5.7

Precision was also evaluated according to CLSI protocol EP5-A2.[12] Five control products were assayed in 3 replicates twice a day for 20 days (n = 120 for each sample) using 1 reagent lot on 2 ADVIA Centaur systems.

Sample	Mean (ng/mL)	Within-run % CV	Total % CV
Control 1	85	3.8	5.7
Control 2	181	2.9	4.1
Control 3	372	2.8	5.5
Control 4	639	4.1	6.7
Control 5	1023	4.6	9.0

Precision was also conducted by assaying 2 samples in 5 replicates in 2 runs over 5 days on 1 ADVIA Centaur system using 1 reagent lot.

Sample	Mean (ng/mL)	Within-run % CV	Total % CV
Sample 1	1490.03	1.8	5.1
Sample 2	1385.23	1.1	4.8

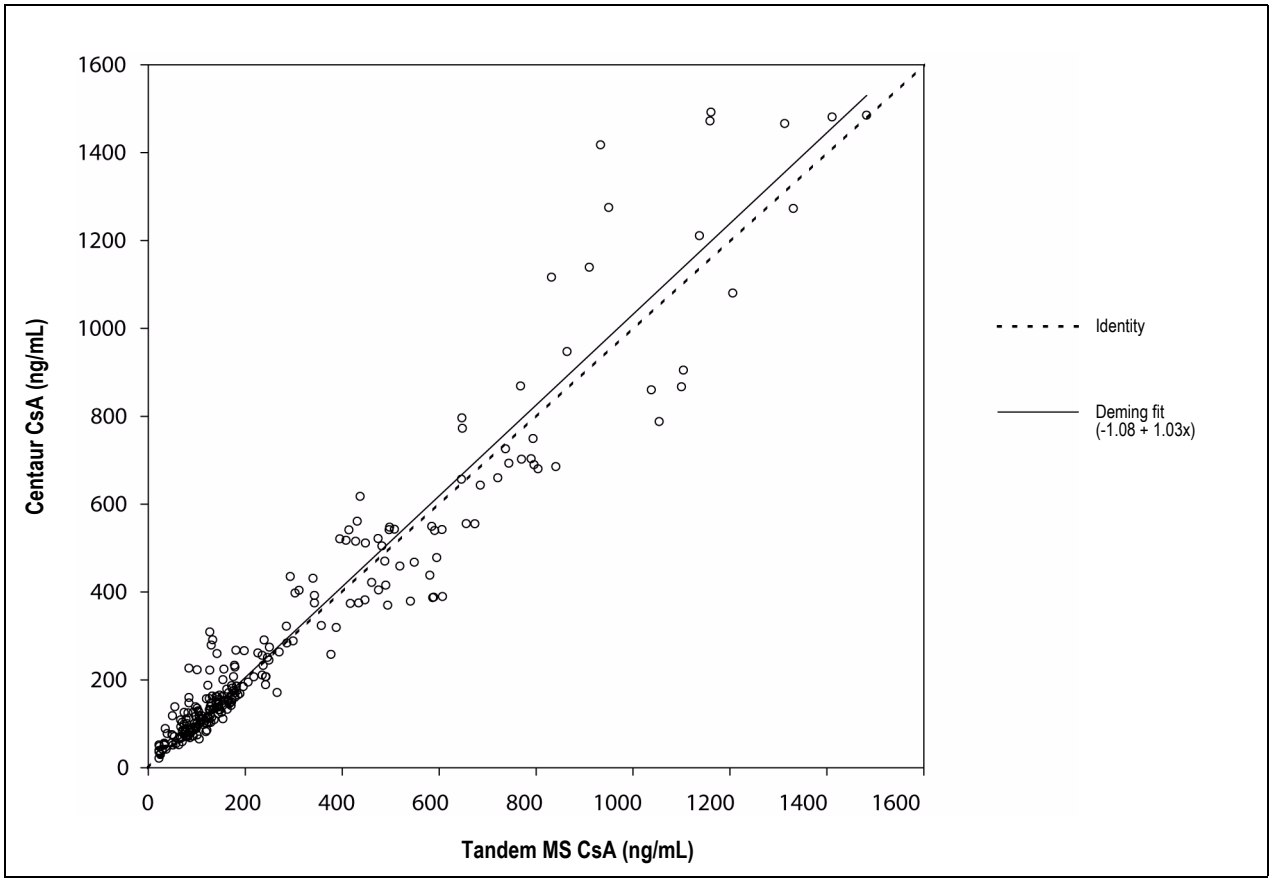
Accuracy / Method Comparison

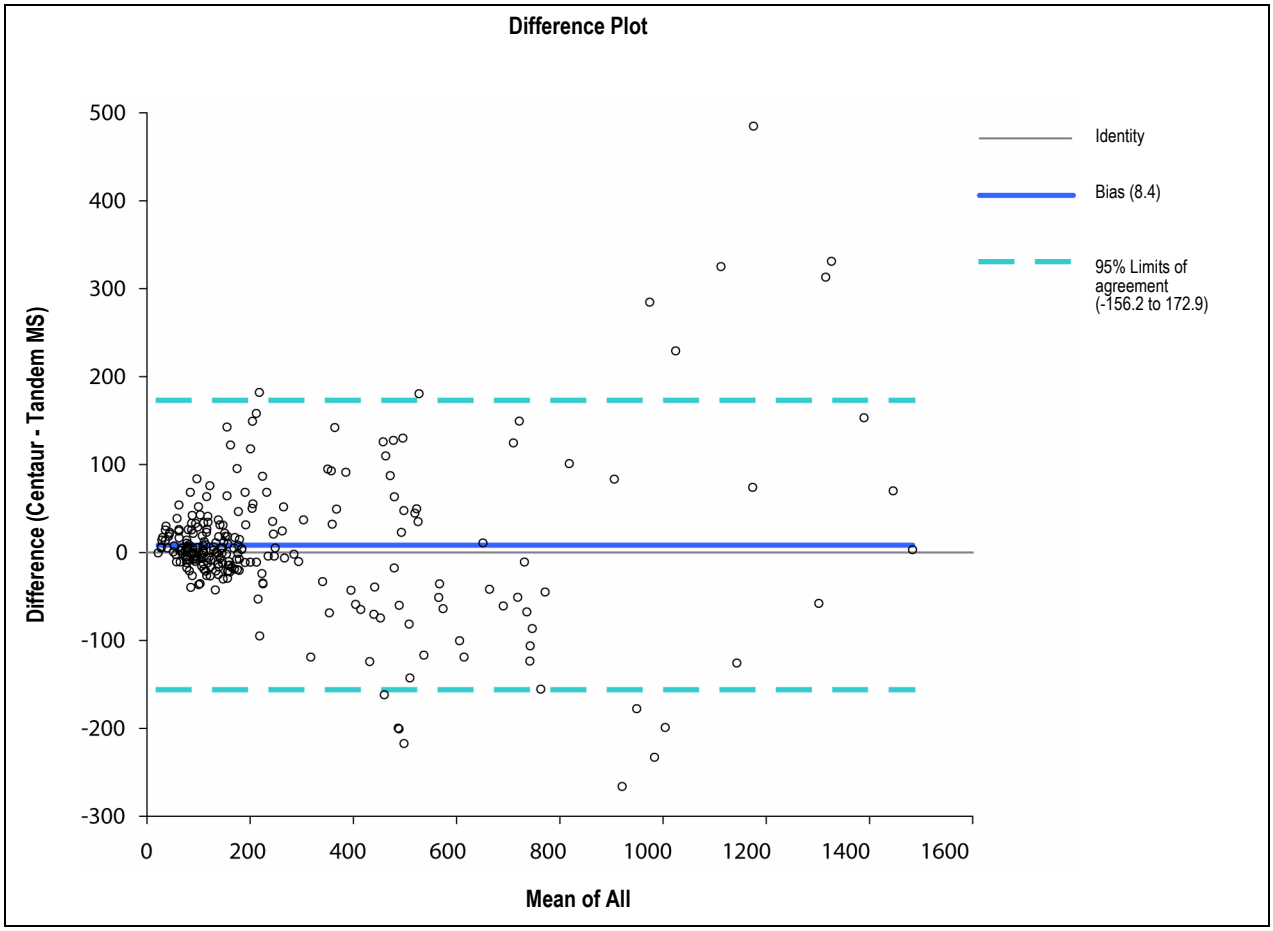
The relationship between the ADVIA Centaur Cyclosporine assay and Tandem-MS was established by testing whole blood samples from transplant patients on cyclosporine therapy at 3 clinical trial sites. Testing was also performed at 3 sites with the Abbott TDx assay and at 1 site with the Abbott AxSYM assay. These relationships, as determined by Deming Regression, are described in the following tables:

Alternate Method	Transplant Type	Number of Patient Samples	Slope	Intercept	Correlation Coefficient
Tandem-MS	kidney	108	1.11	-8	0.962
	liver	75	1.04	-5	0.967
	heart	67	0.89	20	0.966
	all	250	1.03	-1	0.963

Alternate Method	Site	Number of Patient Samples	Slope	Intercept	Correlation Coefficient
Tandem-MS	site 1	97	0.88	14	0.963
	site 2	105	1.05	-15	0.978
	site 3	48	1.14	35	0.958
	all	250	1.03	-1	0.963
Abbott TDx	site 1	97	0.76	10	0.967
	site 2	97	0.67	-2	0.987
	site 3	48	0.73	9	0.968
	all	242	0.72	4	0.970
Abbott AxSYM	site 1	219	0.68	18	0.960

Alternate Method	Peak/Trough Samples	Number of Patient Samples	Slope	Intercept	Correlation Coefficient
Tandem-MS	trough	182	1.02	8	0.909
	peak	68	1.15	-104	0.898
	all	250	1.03	-1	0.963


Centaur CsA (ng/mL)
Tandem MS CsA (ng/mL)
0
200
400
600
800
1000
1200
1400
1600
Identity
Deming fit
(-1.08 + 1.03x)


Difference Plot
Difference (Centaur - Tandem MS)
Mean of All
500
400
300
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100
0
-100
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200
400
600
800
1000
1200
1400
1600
Identity
Bias (8.4)
95% Limits of
agreement
(-156.2 to 172.9)

Interferences

Whole blood specimens that are . . .	Demonstrate ≤ 10% change in results up to . . .
icteric	60 mg/dL conjugated bilirubin
icteric	40 mg/dL unconjugated bilirubin
lipemic	900 mg/dL triglycerides
lipemic	300 mg/dL cholesterol
uremic	20 mg/dL uric acid
hyperproteinemic	8 g/dL albumin
hyperproteinemic	12 g/dL gamma globulin
hematocrit range	12.3 to 58.6%

Analyte Concentration (ng/mL)	Biotin Test Level (ng/mL)					
	9	19	38	75	150	600
	% Bias					
581	1	2	8	30	116	> AR[a]
765	-1	3	5	18	126	> AR

a AR = Assay range

Specimens that contain biotin at a concentration of 38 ng/mL demonstrate a less than or equal to 10% change in results. Biotin concentrations greater than this may lead to falsely elevated results for patient samples.

The recommended adult daily dietary intake for biotin is 30 µg/day. Over the counter dietary supplements promoted for use in hair, skin and nail health may contain 5–100 mg of biotin, with recommendations to take multiple pills per day. Pharmacokinetic studies in healthy adults have shown that, in subjects ingesting 5 mg, 10 mg, and 20 mg of biotin, serum concentrations of biotin can reach up to 73 ng/mL, 141 ng/mL, and 355 ng/mL, respectively.[13] Subjects who take up to 300 mg of biotin per day may have plasma biotin levels as high as 1160 ng/mL.[14]

Whole blood samples containing 200 ng/mL of cyclosporine were spiked with the compounds listed below to concentrations as shown. ADVIA Centaur Cyclosporine assay results from the spiked samples were compared with those of unspiked control samples. These compounds caused less than 10% bias in the ADVIA Centaur Cyclosporine measurements.

Compound	Amount Added (µg/mL)	Compound	Amount Added (µg/mL)
Tacrolimus (FK506)	100	Lidocaine	100
Mycophenolic acid	100	Lincomycin	100
Mycophenolic acid glucuronide	1000	Methotrexate	100
Rapamycin (Sirolimus)	5	Methylprednisolone	100
N-Acetylprocainamide	100	Neomycin sulfate	100
Acetaminophen	200	Oxytocin	100
Amikacin	100	Penicillin-G (sodium salt)	100

Compound	Amount Added (µg/mL)	Compound	Amount Added (µg/mL)
Amikacin sulfate	100	Penicillin V	100
Ampicillin	100	Phenobarbital	150
Apresoline	100	Phenytoin	100
Azathioprine	100	Prazosin	100
Carbamazepine	120	Prednisolone	100
Cefaclor (Cephalosporin)	230	Prednisone	100
Chloramphenicol	250	Primidone	100
Cimetidine	100	Procainamide	100
Digitoxin	100	Propranolol	100
Digoxin	100	Quinidine sulfate	100
Dipyridamole	100	Rifampicin	100
Disopyramide	100	Salicylic acid	500
EDTA	2924	Spectinomycin	100
Erythromycin	200	Theophylline	250
Ethosuximide	100	Tobramycin	100
Furosemide	100	Triamterene	100
Gentamicin	120	Valproic acid	500
Kanamycin	100	Vancomycin	630
Kanamycin sulfate B	100	Verapamil	100
Ketoconazole	100		

Interferences were determined according to CLSI Document EP7-A2.[15]

Dilution Recovery

Five human whole blood samples in the range of 191 to 1478 ng/mL (159 to 1229 nmol/L) of cyclosporine were diluted 1:2, 1:4, and 1:8 with Multi-Diluent 12 and assayed for recovery and parallelism. The recoveries ranged 90.7 to 108.5% with a mean of 97.4%.

Sample	Dilution	Observed (ng/mL)	Expected (ng/mL)	Observed (nmol/L)	Expected (nmol/L)	Recovery %
1	—	1478		1229		
	1:2	678	739	564	614	91.8
	1:4	341	370	284	308	92.4
	1:8	176	185	146	154	95.0
	Mean					93.1
2	—	728		605		
	1:2	377	364	313	303	103.7
	1:4	193	182	160	151	105.9
	1:8	84	91	70	76	92.6
	Mean					100.7
3	—	635		528		
	1:2	339	317	282	264	106.8
	1:4	172	159	143	132	108.5
	1:8	72	79	60	66	90.7
	Mean					102.0
4	—	198		165		
	1:2	96	99	80	83	97.0
	1:4	47	50	40	41	94.0
	1:8	24	25	20	21	96.0
	Mean					95.7
5	—	191		159		
	1:2	94	95	78	79	98.9
	1:4	44	48	37	40	91.7
	1:8	23	24	19	20	95.8
	Mean					95.5
Mean						**97.4**

Spiking Recovery

Varying amounts of cyclosporine were added to 2 cyclosporine-free normal whole blood samples and 2 samples from patients taking cyclosporine. The recoveries ranged from 91 to 108% with a mean of 96.5%.

Sample	Amount Added (ng/mL)	Expected (ng/mL)	Observed (ng/mL)	Amount added (nmol/L)	Expected (nmol/L)	Observed (nmol/L)	% Recovery
1	—						
	100	100	97	83	83	81	97.0
	400	400	400	333	333	332	99.9
	800	800	787	665	665	654	98.3
	1500	1500	1624	1247	1247	1350	108.2
	Mean						100.9
2	—						
	100	100	96	83	83	80	95.8
	400	400	389	333	333	324	97.3
	800	800	739	665	665	614	92.3
	1500	1500	1367	1247	1247	1136	91.1
	Mean						94.1
3	-	175.1	175				
	400	575.1	526	333	478	437	91.4
	800	975.1	938	665	811	780	96.2
	Mean						93.8
4		318.4	318				
	400	718.4	667	333	597	554	92.8
	800	1118.4	1098	665	930	913	98.2
	Mean						95.5
Mean							**96.5**

Standardization

The ADVIA Centaur Cyclosporine assay is traceable to an internal standard manufactured using highly purified cyclosporine (USP grade). Assigned values of calibrators and ranges of controls are traceable to this standardization.

Technical Assistance

For customer support, please contact your local technical support provider or distributor.

www.siemens.com/diagnostics

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Definition of Symbols

The following symbols may appear on the product labeling:

Symbol	Definition	Symbol	Definition
IVD	*In vitro* diagnostic medical device	REF REF	Catalog number
	Legal manufacturer	EC REP	Authorized Representative in the European Community
CE	CE Mark	CE 0088	CE Mark with identification number of notified body
	Consult instructions for use		Biological risk
0°C	Do not freeze (> 0°C)		Temperature limitation
	Lower limit of temperature		Upper limit of temperature
	Keep away from sunlight and heat	UP	Up
	Use by	Σ (n)	Contains sufficient for (n) tests
LOT	Batch code		Shake the reagent pack vigorously. Refer to *Preparing Reagents* in the assay-specific ADVIA Centaur product instructions for detailed information.
YYYY-MM-DD	Date format (year-month-day)	Rev.	Revision
MC DEF	Master Curve Definition	CHECKSUM	Variable hexadecimal number that ensures the Master Curve and Calibrator definition values entered are valid.
LOT DTL	Lot Details	DER GRÜNE PUNKT	Green dot
	Recycle	PRINTED WITH SOY INK	Printed with soy ink

Trademarks

US Pats 5,609,822; 5,788,928; 6,664,043

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