SIEMENS

CE

ADVIA® 1800
ADVIA® 2400
Chemistry Systems

Cannabinoid_2 (THC_2)

Current Revision and Date[a]	Rev. E, 2019-11	
Product Name	ADVIA® Chemistry Cannabinoid_2 (THC_2) Reagents	REF 10378766
Systems	ADVIA 1800 Chemistry System ADVIA 2400 Chemistry System	
Materials Required but Not Provided	Emit® Calibrators/Controls Level 0 (0 ng/mL) Level 2 (20 ng/mL) Level 3 (50 ng/mL) Level 4 (100 ng/mL) Level 5 (200 ng/mL) Reagent container adapters Commercially available controls	 REF 9A509UL REF 9A549UL REF 9A569UL REF 9A589UL REF 9A609UL
Specimen Types	Urine	
Assay Principle	Enzyme multiplied immunoassay technique (EMIT)	
Assay Range	**Cutoff**	**Range**
	20 ng/mL 50 ng/mL 100 ng/mL	11–55 ng/mL 15–180 ng/mL 20–180 ng/mL
Reagent Storage	2–8°C	
Reagent On-System Stability	30 days	
Reagent Code	74832	

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

Intended Use

For *in vitro* diagnostic use in the qualitative and semiquantitative determination of cannabinoids in human urine on ADVIA® Chemistry systems.

The ADVIA Chemistry Cannabinoid_2 (THC_2) assay provides only a preliminary analytical test result. A more specific alternative chemical method must be used to obtain a confirmed analytical result.[1] Gas chromatography/mass spectrometry (GC/MS) is the preferred confirmatory method.[2] Other chemical confirmation methods are available. Clinical consideration and professional judgement should be applied to any drug-of-abuse test result, particularly when preliminary positive results are used.

Summary and Explanation

Marijuana is a mixture of dried leaves and flowering tops of the plant *Cannabis sativa L*. The agents that produce the hallucinogenic and other biological effects of marijuana are called cannabinoids.

The cannabinoid Δ^9-tetrahydrocannabinol (Δ^9-THC) is the principle psychoactive ingredient in marijuana and hashish. The compound Δ^9-THC is quickly and effectively absorbed by inhalation or from the gastrointestinal tract,[3] and is almost completely metabolized by the liver.[4] Peak plasma levels of Δ^9-THC occur within 10 minutes of inhalation and approximately 1 hour after ingestion.[3] Approximately 30% of a dose of THC is excreted as urinary metabolites within 72 hours after exposure.[3] Concentration depends on the total amount of THC absorbed, the frequency of abuse, the rate of release from fatty tissue, and the time of specimen collection with respect to use. In chronic users, THC may accumulate in fatty tissue faster than it can be eliminated. This accumulation leads to longer detection times in urinalysis for chronic users than for occasional users.[5]

The ADVIA Chemistry THC_2 assay detects the major metabolite of Δ^9-THC, 11-nor-Δ^9-THC-9-carboxylic acid in human urine. It also detects other Δ^9-THC metabolites. The cutoff level for distinguishing positive from negative specimens is 20 ng/mL, 50 ng/mL, or 100 ng/mL. Passive inhalation of marijuana smoke may produce positive results with low cutoff cannabinoid assays. Urine specimens from nonsmokers can test positive for cannabinoid metabolites, but only after exposure to high concentrations of marijuana smoke in a small, unventilated area. Such extreme exposure conditions clearly are not typical of usual social situations.[6] Positive results for specimens containing other compounds structurally unrelated to cannabinoids have not been observed.

Assays historically used to detect cannabinoids in biological fluids include radioimmunoassay, gas chromatography, and enzyme immunoassay.[3,4]

While confirmation techniques other than GC/MS may be adequate for some drugs of abuse, GC/MS is generally accepted as a rigorous confirmation technique for all drugs because it provides the best level of confidence in the result.[2]

Principles of the Procedure

The ADVIA Chemistry THC_2 assay is a homogeneous immunoassay that is used for the qualitative or semiquantitative analysis of cannabinoids in human urine.[4] The ADVIA Chemistry THC_2 assay uses the Syva® Emit® II Plus Cannabinoid reagents in ADVIA Chemistry containers.

This assay is based on competition between drug in the specimen and drug labeled with the enzyme glucose-6-phosphate dehydrogenase (G6PDH) for antibody binding sites. Enzyme activity decreases upon binding to the antibody, so the drug concentration in the specimen can be measured in terms of enzyme activity. In the presence of glucose 6-phosphate (G6P), active enzyme converts nicotinamide adenine dinucleotide (NAD) to reduced nicotinamide adenine dinucleotide (NADH), resulting in an absorbance change that is measured spectrophotometrically at 340/410 nm. Endogenous G6PDH does not interfere because the coenzyme NAD functions only with the bacterial (*Leuconostoc mesenteroides*) enzyme employed in this assay.

Reagents

Reagent	Description	Storage	Reagent Stability
REF 10378766	**ADVIA Chemistry Cannabinoid_2 (THC_2) Reagents**		
Cannabinoid_2 Reagent 1 THC_2 R1	20.0 mL in 20-mL containers Mouse monoclonal antibodies to Δ^9-tetrahydrocannabinol (Δ^9-THC) (1.2 µg/mL)[a] Glucose-6-phosphate (G6P) (5.5 mM) Nicotinamide Adenine Dinucleotide (NAD) (3.5 mM) Bovine serum albumin Preservatives and stabilizers	2–8°C	**Unopened:** Stable until the expiration date on product. **On-system:** 30 days
Cannabinoid_2 Reagent 2 THC_2 R2	10.5 mL in 20-mL containers Δ^9-tetrahydrocannabinol (Δ^9-THC) labeled with bacterial Glucose-6-phosphate dehydrogenase (G6PDH) (0.4 U/mL)[A] Tris/HEPES buffer Bovine serum albumin Preservatives and stabilizers	2–8°C	**Unopened:** Stable until the expiration date on product. **On-system:** 30 days

[a] The antibody titer and enzyme conjugate activity may vary from lot to lot.

Warnings and Precautions

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

Caution

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

H317
P280, P272, P302+P352, P333+P313, P501

Warning!
May cause an allergic skin reaction.
Wear protective gloves/protective clothing/eye protection/face protection. Contaminated work clothing should not be allowed out of the workplace. IF ON SKIN: Wash with plenty of soap and water. If skin irritation or rash occurs: Get medical advice/attention. Dispose of contents and container in accordance with all local, regional, and national regulations.
Contains: 5-chloro-2-methyl-4-isothiazolin-3-one w/ 2-methyl-2H-isothiazol-3-one; ADVIA Chemistry Cannabinoid_2 Reagent 1 and ADVIA Chemistry Cannabinoid_2 Reagent 2

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.

Caution: Federal (USA) law restricts this device to sale by or on the order of a licensed healthcare professional.

For *in vitro* diagnostic use.

Preparing Reagents

All reagents are liquid and ready to use.

Before use, gently invert the capped reagent to disrupt bubbles and ensure homogeneity. If bubbles still exist or foam is present, use a clean transfer pipette to aspirate them from the reagent container prior to use.

Storing and Stability

Unopened reagents are stable until the expiration date printed on the product label when stored at 2–8°C. Do not freeze reagents.

Specimen Collection and Handling

Siemens Healthcare Diagnostics has validated urine for the ADVIA Chemistry THC_2 assay.

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.

Collecting the Specimen

Follow these guidelines for specimens used for this assay:

- Urine specimens may be collected in plastic (such as polypropylene, polycarbonate, or polyethylene) or glass containers. Some plastics can adsorb certain drugs.
- Due to the adsorptive nature of THC, sample cups, if used, must be filled consistently with 1.0 mL of sample, control, or calibrator using an automatic pipette.

  Note Plastic transfer pipettes should not be used.

  This helps to maintain a constant cup-surface-to-sample volume ratio and minimizes drug loss from the sample due to adherence of drugs to the cup surface.
- Specimens with high turbidity should be centrifuged before analysis.
- The recommended pH range for urine specimens is 4.5 to 8.0.
- Adulteration of the urine specimen may cause erroneous results. If adulteration is suspected, obtain another specimen.
- Human urine specimens should be handled and treated as if they are potentially infectious.
- Baby wash/shampoo may contaminate the urine specimen taken from a neonate, causing an erroneous cannabinoid test result. Using a copious amount of water, thoroughly rinse such products from the neonate's body before collecting the specimen.
- Frozen specimens must be thawed and mixed thoroughly prior to analysis.

Storing the Specimen

Follow these guidelines for specimens used for this assay:

- Internal testing has shown that, if not analyzed immediately, specimens may be stored unrefrigerated for up to 7 days. Specimens may be stored refrigerated for 30 days before analysis.
- After 7 days unrefrigerated or 30 days refrigerated, samples should be stored frozen.

Procedure

Materials Provided

The following materials are provided:

Item	Contents	Number of Tests
REF 10378766	Reagent 1: 4 × 20-mL containers Reagent 2: 4 × 20-mL containers	4 × 190

Materials Required but Not Provided

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

Item	Description
REF 9A509UL	Emit Calibrators/Controls Level 0 (0 ng/mL)
REF 9A549UL	Emit Calibrators/Controls Level 2 (20 ng/mL)
REF 9A569UL	Emit Calibrators/Controls Level 3 (50 ng/mL)
REF 9A589UL	Emit Calibrators/Controls Level 4 (100 ng/mL)
REF 9A609UL	Emit Calibrators/Controls Level 5 (200 ng/mL)
REF 02404085	20-mL reagent container adapter for 40-mL slot (ADVIA 1800)
REF 00771668	20-mL reagent container adapter for 70-mL slot (ADVIA 2400)
	Commercially available control materials

Assay Procedure

Sampling, reagent delivery, mixing, and processing are automatically performed by the ADVIA Chemistry system.

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

Preparing the System

For detailed information on preparing the system, refer to the system operating instructions.

Preparing the Samples

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

- Samples are free of particulate matter.
- Samples are free of bubbles.

On-System Stability

The ADVIA Chemistry THC_2 reagents are stable on the system for 30 days.

Do not use reagents beyond the expiration date.

Performing Calibration

To calibrate the ADVIA Chemistry THC_2 assay, use the Emit Calibrators/Controls:

- Level 0 (REF 9A509UL)
- Level 2 (REF 9A549UL)
- Level 3 (REF 9A569UL)
- Level 4 (REF 9A589UL)
- Level 5 (REF 9A609UL)

For both qualitative and semiquantitative analyses, a calibrator is used either as a calibrator or as a control for any individual cutoff level. When a calibrator/control is used as a calibrator for an individual cutoff level, the other levels of calibrators/controls above and below it (as listed in Table 1) are used as controls.

Calibration Frequency

Calibrate the assay every 30 days.

Calibrate the assay after the following events:

- When the reagent lot number changes
- When a reagent pack is replaced by a new reagent pack with the same lot number, and the previous reagent pack was recalibrated during use
- After replacing critical optical or hydraulic components
- When indicated by quality control procedures

Individual laboratory quality control programs and procedures may require more frequent calibration.

Reagent Blank (RBL) Frequency

The ADVIA Chemistry system measures the RBL during assay calibration.

Run an additional RBL on the same reagent pack every day.

Note Use Emit Calibrator/Control - Level 0 as the sample for the RBL in the ADVIA Chemistry THC_2 assay.

For more information on running daily reagent blanks for multiple standard methods on the ADVIA Chemistry systems, refer to the Customer Bulletin entitled: *Performing Reagent Blank (RBL) on Multi Standard (MSTD) Assays* (PN 073D0483, latest revision).

Qualitative Analysis

For qualitative analysis, run the appropriate Emit Calibrators/Controls in duplicate for the 20 ng/mL, 50 ng/mL, or 100 ng/mL cutoff listed in Table 1. Validate the calibration by assaying controls. Recalibrate as indicated by the quality control results.

Semiquantitative Analysis

To calibrate the assay for semiquantitative analysis, run the appropriate Emit Calibrators/Controls listed in Table 1. Validate the calibration by assaying controls. Recalibrate as indicated by the quality control results.

Table 1: Emit Calibrators/Controls for Use in Qualitative or Semiquantitative Analysis

Desired Cutoff Level (ng/mL)	Required Calibrators/Controls for Qualitative Analysis (ng/mL)	Required Calibrators/Controls for Semiquantitative Analysis (ng/mL)
20	Level 0 (0) Level 2 (20) Level 5 (200)	Level 0 (0) Level 2 (20) Level 3 (50) Level 4 (100)
50	Level 0 (0) Level 3 (50) Level 5 (200)	Level 0 (0) Level 2 (20) Level 3 (50) Level 4 (100) Level 5 (200)
100	Level 0 (0) Level 4 (100) Level 5 (200)	Level 0 (0) Level 3 (50) Level 4 (100) Level 5 (200)

Refer to the package insert supplied with the Emit Calibrators/Controls for handling instructions and values, or to the *Calibration* chapter of the operator's guide for more information.

Test Definitions (TDEFs)

Adjust the test definition (TDEF) parameter settings to run the ADVIA Chemistry THC_2 assay as a qualitative or semiquantitative assay, and to change the drug cutoff level.

The TDEF parameters for the ADVIA Chemistry THC_2 assay that are installed in your ADVIA Chemistry system contain the correct settings to run the ADVIA Chemistry THC_2 assay in qualitative mode at the 50 ng/mL cutoff level. To run a test in semiquantitative mode, or to change the cutoff level, adjust the TDEF parameters as listed in Table 2.

For more information on adjusting the parameters to run in the Semiquantitative Mode on the ADVIA Chemistry systems, refer to the Customer Bulletin entitled: *ADVIA Chemistry System EMIT Drugs of Abuse, Customizing the Software for Qualitative and Semiquantitative DAU Testing* (PN 073D0484, latest revision).

The following table provides settings to configure the assay type and cutoff level.

Table 2: ADVIA Chemistry THC_2 Assay TDEF Parameters for Available Assay Modes

		Qualitative			Semiquantitative		
Setting	**TDEF Parameter**	**THC20**	**THC50**	**THC100**	**THC20**	**THC50**	**THC100**
Sub Analytical Conditions	Name	THC20	THC50	THC100	THC20	THC50	THC100
Analytical Conditions	Serum reac s. vol.	25	13	9.5	25	13	9.5
	Urine reac. s. vol.	25	13	9.5	25	13	9.5
Sub Param. #1	Calc. method	STD	STD	STD	MSTD	MSTD	MSTD
	Qualit. judge	Do	Do	Do	Not Do	Not Do	Not Do
One-Point Cal Setting	FV	20	50	100	[a]	[a]	[a]

		Qualitative			Semiquantitative		
Setting	**TDEF Parameter**	**THC20**	**THC50**	**THC100**	**THC20**	**THC50**	**THC100**
Multipoint Cal Setting	Formula	[a]		[a]	Logit Log 2	Logit Log 3	Logit Log 2
	Points	[a]		[a]	4	5	4
	FV2	[a]		[a]	20	20	50
	FV3	[a]		[a]	50	50	100
	FV4	[a]		[a]	100	100	200
	FV5	[a]		[a]	0.0	200	0.0
Qualitative Judgement Set	Urine setting range	20, 99999	50, 99999	100, 99999	[a]		[a]
Standards Setting	Abnml (serum) H	[a]		[a]	55	180	180
	Abnml (serum) L	[a]		[a]	11	15	20
	Abnml (urine) H	[a]		[a]	55	180	180
	Abnml (urine) L	[a]		[a]	11	15	20
	FV	[a]		[a]	20	50	100

[a] Setting values are ignored by the system for these cases.

Performing Quality Control

Follow government regulations or accreditation requirements for quality control frequency.

At least once each day of use, analyze 2 levels (low and high) of quality control (QC) material with known cannabinoids concentrations.

Follow your laboratory internal QC procedures if the results obtained are outside acceptable limits.

The actual frequency of control in a laboratory is based on many factors, such as workflow, system experience, and government regulation. Each laboratory should evaluate the controls based on the frequency established by their laboratory guidelines.

Also, assay controls under the following conditions:

- Whenever you use a new reagent lot
- Following any system maintenance, cleaning, or troubleshooting procedure
- After performing a new calibration or an additional reagent blank

Qualitative Analysis

Ensure that the result from Emit Calibrator/Control Level 0 (0 ng/mL) or the Emit Calibrator/Control Level 5 (200 ng/mL) relates appropriately to the result from the cutoff calibrator chosen from column 1 in Table 1.

If the Emit Calibrator/Control Level 0 (0 ng/mL) was run, ensure that the result is negative relative to the selected cutoff calibrator level.

If Emit Calibrator/Control Level 5 (200 ng/mL) was run, ensure that the result is positive relative to the selected cutoff calibrator level.

Once the calibration is validated, run urine specimens.

Semiquantitative Analysis

Validate the calibration curve by assaying commercial controls. Ensure that control results fall within acceptable limits as defined by your laboratory.

Once the calibration curve is validated, run urine specimens.

Taking Corrective Action

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

1. Determine and correct the cause of the unacceptable control results:
    a. Verify that the assay was performed according to the instructions for use.
    b. Verify that the materials are not expired.
    c. Verify that required maintenance was performed.
    d. Rerun the assay with fresh quality control samples, and confirm that quality control results are within acceptable limits before running patient samples.
    e. If the quality control results are not within acceptable limits, recalibrate the assay, and repeat the prior step.
    f. If necessary, contact your local technical support provider or distributor for assistance.
2. After corrective action is complete, repeat required testing of patient samples before reporting results.

Perform corrective actions in accordance with your established laboratory protocol.

Results

Calculation of Results

The system calculates and reports results based on the absorbance measurements of the test sample during the test, and of the calibrator(s) from calibration.

The instrument provides qualitative analysis results as positive (+) or negative (-), and semiquantitative analysis results in ng/mL (common units or SI units).

Qualitative Analysis

Refer to Table 1 for the appropriate cutoff Emit Calibrator/Control. Table 1 contains the cannabinoid concentration present in the Emit Calibrator/Control selected as a cutoff, used to distinguish positive from negative specimens.

Positive Results: A specimen that gives a change in rate value greater than or equal to the Emit Calibrator/Control cutoff rate value is interpreted as positive (the specimen contains cannabinoids).

Negative Results: A specimen that gives a change in rate value less than the Emit Calibrator/Control cutoff rate value is interpreted as negative. Either the specimen does not contain cannabinoids or they are present in concentrations below the cutoff level for this assay.

Semiquantitative Analysis

The semiquantitation of positive results enables the laboratory to determine an appropriate dilution of the specimen for confirmation by GC/MS. Semiquantitation also permits the laboratory to establish quality control procedures and assess control performance. Refer to the *Analytical Measuring Range* section for the semiquantitative range.

Using the ADVIA Chemistry THC_2 assay, it is possible to make semiquantitative determinations of cannabinoids. Refer to Table 1 for requirements.

Limitations

The ADVIA Chemistry THC_2 procedure has the following limitations:

- The assay is designed for use with human urine only.
- A positive result from the assay indicates the presence of cannabinoids, but does not indicate or measure intoxication.
- Boric acid is not recommended as a preservative for urine.
- This assay does not detect synthetic cannabinoids, such as JWH-018, JWH-073, etc.
- There is a possibility that substances and/or factors not listed (such as technical or procedural errors) may interfere with the test and cause false results.
- Interpretation of results must take into account that urine concentrations can vary extensively with fluid intake and other biological variables.
- Immunoassays that produce a single result in the presence of a drug and its metabolites cannot fully quantitate the concentration of individual components.

A number of substances cause physiological changes in urine analyte concentrations. A comprehensive discussion of possible interfering substances, their urine concentrations, and their possible physiological involvements is beyond the scope of this document. Consult the listed reference for specific details on known potential interfering substances.[7]

As with any chemical reaction, you must be alert to the possible effect on results of unknown interferences from medications or endogenous substances. The laboratory and physician must evaluate all patient results in light of the total clinical status of the patient.

Siemens has determined that there is a possibility for certain reagents to interact with the ADVIA Chemistry THC_2 assay when run on the same system. To mitigate these carryover events, the ADVIA Chemistry system software provides a Contamination Avoidance process. For further information and instructions to establish this process on your systems, refer to the Customer Bulletin entitled: *Consolidated Directory of Contamination Avoidance Settings for ADVIA Chemistry Systems* (PN 073D0354, latest revision).

Expected Values

When the ADVIA Chemistry THC_2 assay is used as a qualitative method, the amount of drugs and metabolites detected by the assay in any given specimen cannot be estimated. The assay results distinguish between positive and negative specimens. Positive-indicating specimens contain cannabinoids.

When run as a semiquantitative method, the ADVIA Chemistry THC_2 assay yields approximate, cumulative concentrations of cannabinoids (refer to the *Results* section).

Performance Characteristics

Analytical Measuring Range

When run as a semiquantitative method, the ADVIA Chemistry THC_2 assay measures the Δ^9-THC concentration in urine ranging from the Limit of Detection (LoD) to the Δ^9-THC concentrations in the following table:

Cutoff	Range
20 ng/mL	11–55 ng/mL
50 ng/mL	15–180 ng/mL
100 ng/mL	20–180 ng/mL

Specificity

The ADVIA Chemistry THC_2 assay detects the major metabolite of Δ^9-THC.

The specificity of the assay was evaluated by assaying compounds whose chemical structure or concurrent usage could potentially interfere with the ADVIA Chemistry THC_2 assay. These data were collected on an automated chemistry system using method parameters equivalent to those used on the ADVIA Chemistry system.[8]

Table 3 lists the concentrations of compounds that this assay detects and the levels at which the compounds give a response approximately equivalent to the Emit Calibrator/Control Level Level 2 (20 ng/mL), Level 3 (50 ng/mL), and Level 4 (100 ng/mL).

These concentrations are within the range of levels found in urine following the use of the drug, or in the case of metabolites, the parent compound. Each concentration represents the reactivity level for the stated compound when it is added to a negative urine sample. If a specimen contains more than one compound detected by the method, lower concentrations than those listed in Table 3 may combine to produce a rate approximately equivalent to or greater than that of the cutoff calibrator.

Table 3: Concentrations of Cannabinoids that Produce a Result Approximately Equivalent to the 20 ng/mL, 50 ng/mL, and 100 ng/mL 11-nor-Δ^9-THC-9-COOH Cutoffs

	Concentration Tested (ng/mL) at		
Compound	**20 ng/mL Cutoff**	**50 ng/mL Cutoff**	**100 ng/mL Cutoff**
8-ß-11-Dihydroxy-Δ^9-THC	24	58	109
8-ß-Hydroxy-Δ^9-THC	26	68	146
11-Hydroxy-Δ^8-THC	43	67	129
11-Hydroxy-Δ^9-THC	42	77	124
9-Carboxy-11-nor-Δ^9-THC-glucuronide	79	95	328
Δ^8-THC	79	220	660
Δ^9-THC	78	220	620

Table 4 lists the concentrations of compounds that were tested and found to produce a negative result by the ADVIA Chemistry THC_2 assay. Positive results for specimens that contain other compounds structurally unrelated to cannabinoids have not been observed.

Table 4: Concentrations of Compounds that Produce a Negative Response at the 20 ng/mL, 50 ng/mL, and 100 ng/mL Cutoffs

Compound	**Concentration Tested at 20 ng/mL 50 ng/mL, and 100 ng/mL Cutoffs (µg/mL)**
Acetaminophen	1000
α-Acetyl-*N*,*N*-dinormethadol (dinor LAAM)	25
l-α-Acetylmethadol (LAAM)	25
N-Acetylprocainamide (NAPA)	400
Acetylsalicylic Acid	1000
Amitriptyline	1000

Compound	Concentration Tested at 20 ng/mL 50 ng/mL, and 100 ng/mL Cutoffs (µg/mL)
D-Amphetamine	1000
Benzoylecgonine	1000
Buprenorphine	1000
Caffeine	1000
Cimetidine	1000
Clomipramine	2.5
Clonidine	1000
Codeine	500
Cotinine	100
Cyclobenzaprine	1000
Desipramine	800
Diphenhydramine	1000
Doxepin	1000
2-Ethylidene-1,5-dimethyl-3,3- diphenylpyrrolidine (EDDP)	1000
Fluoxetine	1000
Glutethimide	[a]
Ibuprofen	1000
Ketamine	100
Ketorolac Tromethamine	1000
Lormetazepam	1
LSD	0.01
Meperidine	1000
D-Methamphetamine	35
Methaqualone	1500
Morphine	1000
Naproxen	1000
Nortriptyline	1000
Oxazepam	300
Phencyclidine	1000
Phenytoin (DPH)	1000
Promethazine	1000
Propoxyphene	1000

Compound	Concentration Tested at 20 ng/mL 50 ng/mL, and 100 ng/mL Cutoffs (µg/mL)
Ranitidine	1000
Scopolamine	500
Secobarbital	1000
Thioridazine	100
Tramadol	1000
Tyramine	100
Zidovudine (AZT)	2000
Zolpidem	100

[a] 500 µg/mL at the 20 ng/mL and 100 ng/mL cutoffs. 300 µg/mL at the 50 ng/mL cutoff.

Precision

The precision of the ADVIA Chemistry THC_2 assay was analyzed as described in CLSI protocol EP05-A2.[9] Each sample was assayed 2 times per run, 1 or 2 runs per day, for at least 10 days.

Qualitative Analysis: 20 ng/mL Cutoff

ADVIA 1650/1800

11-nor-Δ⁹-THC-9-COOH Concentration in Urine	Mean (mA/min)	Within-Run SD[a] (mA/min)	Within-Run CV[b] (%)	Total SD (mA/min)	Total CV (%)
15 ng/mL	239	3.8	1.6	4.1	1.7
20 ng/mL	254	2.1	0.8	2.9	1.1
25 ng/mL	270	3.5	1.3	4.2	1.5

[a] SD = standard deviation
[b] CV = coefficient of variation

ADVIA 2400

11-nor-Δ⁹-THC-9-COOH Concentration in Urine	Mean (mA/min)	Within-Run SD[a] (mA/min)	Within-Run CV[b] (%)	Total SD (mA/min)	Total CV (%)
15 ng/mL	224	2.6	1.2	3.5	1.6
20 ng/mL	239	1.8	0.8	2.0	0.9
25 ng/mL	254	3.6	1.4	4.5	1.8

[a] SD = standard deviation
[b] CV = coefficient of variation

Qualitative Analysis: 50 ng/mL Cutoff

ADVIA 1650/1800

11-nor-Δ^9-THC-9-COOH Concentration in Urine	Mean (mA/min)	Within-Run SD[a] (mA/min)	Within-Run CV[b] (%)	Total SD (mA/min)	Total CV (%)
37.5 ng/mL	277	3.1	1.1	3.7	1.3
50.0 ng/mL	298	2.1	0.7	3.1	1.0
62.5 ng/mL	320	4.6	1.4	7.6	2.4

[a] SD = standard deviation
[b] CV = coefficient of variation

ADVIA 2400

11-nor-Δ^9-THC-9-COOH Concentration in Urine	Mean (mA/min)	Within-Run SD[a] (mA/min)	Within-Run CV[b] (%)	Total SD (mA/min)	Total CV (%)
37.5 ng/mL	259	3.4	1.3	4.2	1.6
50.0 ng/mL	279	2.9	1.0	3.1	1.1
62.5 ng/mL	299	3.1	1.0	6.0	2.0

[a] SD = standard deviation
[b] CV = coefficient of variation

Qualitative Analysis: 100 ng/mL Cutoff

ADVIA 1650/1800

11-nor-Δ^9-THC-9-COOH Concentration in Urine	Mean (mA/min)	Within-Run SD[a] (mA/min)	Within-Run CV[b] (%)	Total SD (mA/min)	Total CV (%)
75 ng/mL	316	1.7	0.5	3.2	1.0
100 ng/mL	354	2.9	0.8	4.4	1.2
125 ng/mL	392	3.5	0.9	4.3	1.1

[a] SD = standard deviation
[b] CV = coefficient of variation

ADVIA 2400

11-nor-Δ^9-THC-9-COOH Concentration in Urine	Mean (mA/min)	Within-Run SD[a] (mA/min)	Within-Run CV[b] (%)	Total SD (mA/min)	Total CV (%)
75 ng/mL	296	2.3	0.8	3.2	1.1
100 ng/mL	333	2.7	0.8	3.9	1.2
125 ng/mL	370	3.7	1.0	5.6	1.5

[a] SD = standard deviation
[b] CV = coefficient of variation

Semiquantitative Analysis: 20 ng/mL Cutoff

ADVIA 1650/1800

11-nor-Δ^9-THC-9-COOH Concentration in Urine	Mean (mA/min)	Within-Run SD[a] (mA/min)	Within-Run CV[b] (%)	Total SD (mA/min)	Total CV (%)
15 ng/mL	17	0.8	4.9	0.9	5.4
20 ng/mL	20	0.4	2.0	0.6	2.9
25 ng/mL	23	0.7	3.1	0.9	3.6

[a] SD = standard deviation
[b] CV = coefficient of variation

ADVIA 2400

11-nor-Δ^9-THC-9-COOH Concentration in Urine	Mean (mA/min)	Within-Run SD[a] (mA/min)	Within-Run CV[b] (%)	Total SD (mA/min)	Total CV (%)
15 ng/mL	17	0.7	4.1	0.9	5.6
20 ng/mL	20	0.4	2.1	0.5	2.3
25 ng/mL	24	0.9	3.6	1.1	4.4

[a] SD = standard deviation
[b] CV = coefficient of variation

Semiquantitative Analysis: 50 ng/mL Cutoff

ADVIA 1650/1800

11-nor-Δ^9-THC-9-COOH Concentration in Urine	Mean (mA/min)	Within-Run SD[a] (mA/min)	Within-Run CV[b] (%)	Total SD (mA/min)	Total CV (%)
37.5 ng/mL	39	1.7	4.2	2.0	5.1
50.0 ng/mL	50	1.0	2.0	1.4	2.9
62.5 ng/mL	60	2.1	3.5	3.5	5.8

[a] SD = standard deviation
[b] CV = coefficient of variation

ADVIA 2400

11-nor-Δ^9-THC-9-COOH Concentration in Urine	Mean (mA/min)	Within-Run SD[a] (mA/min)	Within-Run CV[b] (%)	Total SD (mA/min)	Total CV (%)
37.5 ng/mL	40	2.2	5.6	2.8	7.0
50.0 ng/mL	52	1.6	3.0	1.7	3.3
62.5 ng/mL	62	1.5	2.5	3.1	4.9

[a] SD = standard deviation
[b] CV = coefficient of variation

Semiquantitative Analysis: 100 ng/mL Cutoff

ADVIA 1650/1800

11-nor-Δ^9-THC-9-COOH Concentration in Urine	Mean (mA/min)	Within-Run SD[a] (mA/min)	Within-Run CV[b] (%)	Total SD (mA/min)	Total CV (%)
75 ng/mL	73	1.2	1.6	2.2	3.0
100 ng/mL	101	2.3	2.3	3.4	3.4
125 ng/mL	134	3.9	2.9	4.7	3.5

[a] SD = standard deviation
[b] CV = coefficient of variation

ADVIA 2400

11-nor-Δ^9-THC-9-COOH Concentration in Urine	Mean (mA/min)	Within-Run SD[a] (mA/min)	Within-Run CV[b] (%)	Total SD (mA/min)	Total CV (%)
75 ng/mL	72	1.7	2.4	2.4	3.4
100 ng/mL	101	2.2	2.2	3.2	3.2
125 ng/mL	136	3.9	2.9	6.0	4.4

[a] SD = standard deviation
[b] CV = coefficient of variation

Actual results will vary depending on the study design, and on the sample and sample population used. Results obtained at individual laboratories may vary from the data provided.

Accuracy / Method Comparison

Qualitative Analysis: 20 ng/mL cutoff

Siemens used 176 samples to compare the ADVIA Chemistry THC_2 method (run on the ADVIA 1650/1800 and 2400 Chemistry systems), to the Emit II Plus assay run on the SYVA®-30R Biochemical System.

On all ADVIA Chemistry platforms, both methods showed positive results for 117 samples, and negative results for 58 samples. One sample tested positive on all ADVIA Chemistry platforms and negative in SYVA-30R testing.

The ADVIA Chemistry rate for the discrepant sample was within 6% of the cutoff rate.

Table 5: Qualitative Results for the 20 ng/mL Cutoff for the ADVIA 1650/1800 Chemistry System

		ADVIA 1650/1800 (n = 176) +	ADVIA 1650/1800 (n = 176) -
Reference Method SYVA-30R	+	117	0
	-	1	58

Table 6: Qualitative Results for the 20 ng/mL Cutoff for the ADVIA 2400 Chemistry System

		ADVIA 2400 (n = 176)	
		+	-
Reference Method SYVA-30R	+	117	0
	-	1	58

Qualitative Analysis: 50 ng/mL cutoff

Siemens used 140 samples to compare the ADVIA Chemistry THC_2 method (run on the ADVIA 1650/1800 and 2400 Chemistry systems), to the Emit II Plus assay on the SYVA-30R Biochemical System.

On all ADVIA Chemistry platforms, both methods showed positive results for 84 samples, and negative results for 55 samples. One sample tested positive on all ADVIA Chemistry platforms and negative in SYVA-30R testing.

The ADVIA Chemistry rate for the discrepant sample was within 7.5% of the cutoff rate.

Table 7: Qualitative Results for the 50 ng/mL Cutoff for the ADVIA 1650/1800 Chemistry System

		ADVIA 1650/1800 (n = 140)	
		+	-
Reference Method SYVA-30R	+	84	0
	-	1	55

Table 8: Qualitative Results for the 50 ng/mL Cutoff for the ADVIA 2400 Chemistry System

		ADVIA 2400 (n = 140)	
		+	-
Reference Method SYVA-30R	+	84	0
	-	1	55

Qualitative Analysis: 100 ng/mL cutoff

Siemens used 146 samples to compare the ADVIA Chemistry THC_2 method (run on the ADVIA 1650/1800 and 2400 Chemistry systems), to the Emit II Plus assay on the SYVA-30R Biochemical System.

ADVIA 1650/1800 and 2400: Both methods showed positive results for 58 samples, and negative results for 85 samples. Three samples were positive in ADVIA 1650/1800/2400 testing and negative in SYVA-30R testing.

The ADVIA Chemistry rate for the discrepant sample was within 15% of the cutoff rate.

Table 9: Qualitative Results for the 100 ng/mL Cutoff for the ADVIA 1650/1800 Chemistry System

		ADVIA 1650/1800 (n = 146)	
		+	-
Reference Method SYVA-30R	+	58	0
	-	3	85

Table 10: Qualitative Results for the 100 ng/mL Cutoff for the ADVIA 2400 Chemistry System

		ADVIA 2400 (n = 146)	
		+	-
Reference Method SYVA-30R	+	58	0
	-	3	85

Analytical Recovery

Negative human urine was spiked with concentrations of 11-nor-Δ^9-THC-9-carboxylic acid compounds as outlined in Tables 11–13.

Qualitative Results

In qualitative spike analysis, the ADVIA Chemistry THC_2 assay correctly identified the mean rate from replicate analysis of spiked specimens containing less than the cutoffs listed in Tables 11–13 as negative, and the mean rate from replicate analysis of spiked specimens containing greater than the cutoffs listed in Tables 11–13 as positive.

Semiquantitative Results

For each known drug concentration, drug recovery was calculated using the average concentration obtained from replicate analysis by the ADVIA Chemistry THC_2 assay. Semiquantitative results are shown in Tables 11–13.

Table 11: Analytical Recovery of Semiquantitative Results for 11-nor-Δ^9-THC-9-COOH (20 ng/mL Cutoff)

Nominal 11-nor-Δ^9-THC-9-COOH Concentration (ng/mL)	ADVIA 1650/1800 Average Recovery (ng/mL)	Recovery (%)	ADVIA 2400 Average Recovery (ng/mL)	Recovery (%)
15	16	103	15	97
18	19	106	18	100
22	22	100	22	100
25	27	108	26	104
30	34	112	30	98
55	43	77	42	76

Table 12: Analytical Recovery of Semiquantitative Results for 11-nor-Δ⁹-THC-9-COOH (50 ng/mL Cutoff)

Nominal 11-nor-Δ⁹-THC-9-COOH Concentration (ng/mL)	ADVIA 1650/1800 Average Recovery (ng/mL)	Recovery (%)	ADVIA 2400 Average Recovery (ng/mL)	Recovery (%)
23	26	113	23	102
45	43	94	43	94
68	59	87	63	93
90	80	89	89	98
113	106	94	121	107

Table 13: Analytical Recovery of Semiquantitative Results for 11-nor-Δ⁹-THC-9-COOH (100 ng/mL Cutoff)

Nominal 11-nor-Δ⁹-THC-9-COOH Concentration (ng/mL)	ADVIA 1650/1800 Average Recovery (ng/mL)	Recovery (%)	ADVIA 2400 Average Recovery (ng/mL)	Recovery (%)
50	44	88	46	92
75	68	91	67	89
90	91	101	100	111
100	97	97	110	110
125	128	102	134	107
150	156	104	165	110
180	185	103	182	101

Standardization

Emit Calibrators/Controls are referenced to gravimetrically prepared standards. These standards are qualified by GC/MS from an independent laboratory and must quantitate within ±10% of nominal.

Technical Assistance

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

siemens.com/healthcare

References

1. *Mandatory Guidelines for Federal Workplace Drug Testing Programs.* Federal Register/ Vol 73, No. 228, Effective October 1, 2010:71,858–71,907.
2. Hawks RL, Chiang CN, eds. *Urine Testing for Drugs of Abuse.* Rockville, MD: National Institute on Drug Abuse (NIDA), Department of Health and Human Services; 1986. NIDA research monograph 73.
3. Baselt RC, Cravey RH. *Disposition of Toxic Drugs and Chemicals in Man*. 3rd ed. Chicago, IL: Year Book Medical Publishers Inc; 1990:780–783.
4. Ellenhorn MJ, Barceloux DG. *Medical Toxicology.* New York, NY: Elsevier Science Publishing Company, Inc; 1988:675–682.

5. Wyngaarden JB, Smith LH Jr, eds. *Cecil Textbook of Medicine*. Philadelphia, PA: WB Saunders Co; 1986:52–58.
6. Kwong TC, *et al*. Critical issues in urinalysis of abused substances: report of the substance testing committee. *Clin Chem*. 1988:34/3:605–632.
7. Young DS. *Effects of Drugs on Clinical Laboratory Tests*. 5th ed. Washington, DC: AACC Press; 2000.
8. Syva Emit II Plus Cannabinoid Assay [package insert]. Glasgow, DE: Siemens Healthcare Diagnostics; 2008.
9. Clinical and Laboratory Standards Institute (formerly NCCLS). *Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline—Second Edition*. CLSI document EP05-A2. Wayne, PA: Clinical and Laboratory Standards Institute; 2004.

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
	Keep away from sunlight and heat		Temperature limitation
	Lower limit of temperature		Upper limit of temperature
	Do not freeze (> 0°C)		Up
	Use by	Σ (n)	Contains sufficient for (n) tests
	Recycle	PRINTED WITH SOY INK	Printed with soy ink
Rev.	Revision	**YYYY-MM**	Date format (year-month)
LOT	Batch code	**RxOnly**	Prescription Device (US only)

Trademarks

ADVIA, Syva, and Emit are trademarks of Siemens Healthcare Diagnostics.

Siemens Healthcare Diagnostics Inc.
511 Benedict Avenue
Tarrytown, NY 10591 USA

Global Siemens Headquarters
Siemens AG
Wittelsbacherplatz 2
80333 Muenchen
Germany

Global Siemens Healthcare Headquarters
Siemens AG
Healthcare Sector
Henkestrasse 127
91052 Erlangen
Germany
Phone: +49 9131 84-0
siemens.com/healthcare

Global Division
Siemens Healthcare
Diagnostics Inc.
511 Benedict Avenue
Tarrytown, NY 10591
USA
siemens.com/healthcare