BECKMAN COULTER CE

SYNCHRON System(s)
Chemistry Information Sheet

THC
Cannabinoid 100 ng

REF 445990

For *In Vitro* Diagnostic Use

Rx Only

ANNUAL REVIEW

Reviewed by	Date	Reviewed by	Date

PRINCIPLE

INTENDED USE

THC reagent, when used in conjunction with UniCel® DxC 600/800 System(s) and SYNCHRON® Systems THC Urine Calibrators, is intended for qualitative determination of cannabinoids concentration in human urine.

This assay provides a rapid screening procedure for determining the presence of cannabinoids in urine, using a 100 ng/mL cutoff value. This test provides only a preliminary analytical result; a positive result by this assay should be confirmed by another generally accepted non-immunological method such as thin layer chromatography (TLC), gas chromatography (GC), or gas chromatography/mass spectrometry (GC/MS). GC/MS is the preferred confirmatory method.[1,2]

Clinical consideration and professional judgement should be applied to any drug of abuse test result, particularly when preliminary positive results are used.

CLINICAL SIGNIFICANCE

Cannabinoid hallucinogenic compounds include delta-9-tetrahydrocannabinol, cannabidiol and cannabinol. Measurements of cannabinoids are used in the diagnosis and treatment of cannabinoid use or abuse, and in monitoring the presence of cannabinoids during clinical investigational use.

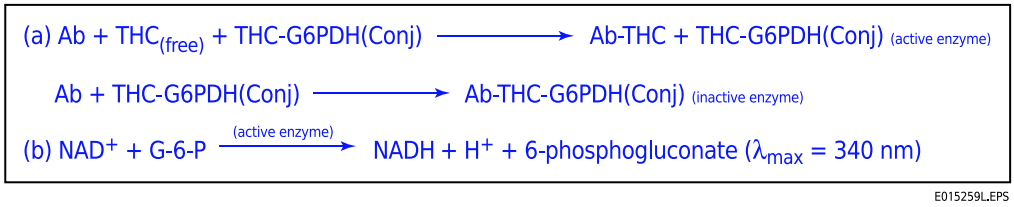
METHODOLOGY

The THC assay utilizes a homogenous enzyme immunoassay method.[3] The THC reagent is comprised of specific antibodies which can detect cannabinoid metabolite in urine. A drug-labeled glucose-6-phosphate dehydrogenase (G6PDH) conjugate competes with any free drug from the urine sample for a fixed amount of specific antibody binding sites. In the absence of free drug from the sample, the drug-labeled G6PDH conjugate is bound by the specific antibody and enzyme activity is inhibited. This reaction creates a direct relationship between drug concentration and

enzyme activity. The G6PDH enzyme activity is determined spectrophotometrically by measuring its ability to convert nicotinamide adenine dinucleotide (NAD) to NADH (reduced form).

The SYNCHRON System(s) automatically proportions the appropriate sample and reagent volumes into the cuvette. The ratio for THC is one part sample to 12.5 parts reagent. The system monitors the change in absorbance at 340 nanometers to calculate and express a reaction rate. A qualitative result is reported based on a comparison of the sample rate to the calibrated cutoff rate.

CHEMICAL REACTION SCHEME



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GENERAL DISCUSSION

The major psychoactive agent in marijuana and hashish is delta-9-tetrahydrocannabinoid (THC). THC is rapidly metabolized and distributed to body tissues, so that none is excreted in urine unchanged. 11-nor-delta-9-THC-9-carboxylic acid, the principle metabolite, becomes detectable in plasma, feces and urine within hours after exposure.[4] In chronic users, THC may accumulate in fatty tissue faster than it can be excreted, leading to longer detection times in urine for chronic users than for occasional users. Passive inhalation of marijuana smoke can result in an elevation of urine THC concentration as high as 10 to 40 ng/mL.[5,6]

SPECIMEN

TYPE OF SPECIMEN

Freshly collected urine samples should be used for testing. Collect urine samples in glass or plastic (i.e., polypropylene, polycarbonate, polyethylene) containers. Some plastics absorb drugs.[7,8] Urine samples should be collected in the manner routinely used for drug screening analysis.[9] Samples should be at room temperature for testing.[10]

SPECIMEN STORAGE AND STABILITY

If the sample cannot be analyzed immediately, it may be stored at +2°C to +8°C for up to 7 days.[2,9] If longer storage is required or when a split sample collection method is used, samples should be stored frozen at -20°C or less.[9]

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:

One THC Reagent Cartridge (1 x 150 tests)

VOLUMES PER TEST

Sample Volume	20 µL	
Total Reagent Volume	250 µL	
Cartridge Volumes		
A	200 µL	Antibody/Substrate Reagent
B	50 µL	Enzyme Conjugate Reagent
C	– –	

REACTIVE INGREDIENTS

REAGENT CONSTITUENTS

Antibody/Substrate Reagent: 41 mL

Monoclonal anti-▲^{9}-THC antibodies (mouse)

Glucose-6-phosphate (G6P)

REAGENT CONSTITUENTS

Nicotinamide adenine dinucleotide (NAD)

Tris buffer

Enzyme Conjugate Reagent: 10 mL

Glucose-6-phosphate dehydrogenase (G6PDH) labeled with ▲^{9}-THC

Tris buffer

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 DAT Negative Urine Calibrator (0 ng/mL 11-nor-▲^{9}-THC-9-carboxylic acid)
SYNCHRON Systems 100 ng/mL THC Urine Calibrator (100 ng/mL 11-nor-▲^{9}-THC-9-carboxylic acid)
SYNCHRON Systems 200 ng/mL THC Urine Calibrator (200 ng/mL 11-nor-▲^{9}-THC-9-carboxylic acid)
SYNCHRON Systems 75 ng/mL THC Urine Control (75 ng/mL 11-nor-▲^{9}-THC-9-carboxylic acid)
SYNCHRON Systems 125 ng/mL THC Urine Control (125 ng/mL 11-nor-▲^{9}-THC-9-carboxylic acid)

REAGENT PREPARATION

No preparation is required.

ACCEPTABLE REAGENT PERFORMANCE

The acceptability of a reagent is determined by successful calibration and by ensuring that quality control results are within acceptance criteria. Refer to the Quality Control section of this chemistry information sheet for Substance Abuse and Mental Health Services Administration (SAMHSA) guidelines.

REAGENT STORAGE AND STABILITY

THC reagent when stored unopened at +2°C to +8°C, will obtain the shelf-life indicated on the cartridge label. Once opened, the reagent is stable for 60 days at +2°C to +8°C unless the expiration date is exceeded. DO NOT FREEZE.

Reagent storage location:

CALIBRATION

CALIBRATOR REQUIRED

SYNCHRON Systems DAT Negative Urine Calibrator (0 ng/mL 11-nor-▲^{9}-THC-9-carboxylic acid)
SYNCHRON Systems 100 ng/mL (cutoff) THC Urine Calibrator (100 ng/mL 11-nor-▲^{9}-THC-9-carboxylic acid)
SYNCHRON Systems 200 ng/mL THC Urine Calibrator (200 ng/mL 11-nor-▲^{9}-THC-9-carboxylic acid)

CALIBRATOR PREPARATION

No preparation is required.

CALIBRATOR STORAGE AND STABILITY

SYNCHRON® Systems THC Urine Calibrators are stable until the expiration date printed on the calibrator bottles if stored capped in the original containers at +2°C to +8°C.

⚠ CAUTION

Urine is not known to transmit infectious disease such as Hepatitis or HIV. However, because this product contains material of human origin, it should be handled as though capable of transmitting infectious diseases. The United States Food and Drug Administration recommends such samples be handled as specified in the Centers for Disease Control's Biosafety Level 2 guidelines.[11]

Calibrator storage location:

CALIBRATION INFORMATION

1. The DAT assays require three levels of calibrators. The calibration measures the separation between calibrators to ensure reagent integrity.

NOTICE

The calibration factor generated is non-functional for sample result calculation.

2. The system must have a valid calibrator cutoff value in memory before controls or patient samples can be run. The cutoff value for each DAT chemistry represents the mean reaction rate of the Low Calibrator, and is reported in mA/min units on patient and control reports. Cutoff values are stored in memory until the next successful calibration.
3. Under typical operating conditions the THC 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.
4. For detailed calibration instructions, refer to the UniCel DxC 600/800 System *Instructions For Use* (IFU) manual.
5. 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

Good laboratory practices suggest the use of control specimens to ensure proper assay performance. Each analytical run should include controls with levels 25% above and 25% below the cutoff threshold of each drug, as well as negative specimens certified to contain no drug.[12] In addition, these controls should be run with each new calibration, 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.

RESULTS INTERPRETATION

The system performs all calculations internally to produce the final qualitative result, reported as POSITIVE or NEGATIVE. The qualitative result is based on a comparison of the sample rate to the calibrated cutoff rate; a sample rate greater than or equal to the cutoff rate is reported as POSITIVE. A POSITIVE result (≥100 ng/mL) from this assay indicates only the presence of cannabinoids and does not necessarily correlate with the extent of physiological and psychological effects. A NEGATIVE test result indicates that cannabinoids are either not present, or are present at levels below the cutoff threshold of the test.

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.

Additional reporting information as designated by this laboratory:

PROCEDURAL NOTES

LIMITATIONS

1. The test is designed for use with human urine only.
2. Do not dilute the urine samples since this is a qualitative assay. Dilution of samples may produce erroneous results.
3. Interference has been demonstrated from mefenamic acid, a nonopioid analgesic.[13]
4. Adulteration of the urine sample may cause erroneous results. Alteration of a urine specimen may be detected by checking the appearance, temperature, pH specific gravity, and creatinine levels of a sample.[9] If adulteration is suspected, obtain another sample and forward both specimens to the laboratory for testing.
5. An effort should be made to keep pipetted samples free from gross debris. It is recommended that highly turbid specimens be centrifuged before analysis.

PERFORMANCE CHARACTERISTICS

RELATIVE SENSITIVITY AND SPECIFICITY

Eighty clinical urine specimens were collected and tested. One hundred percent agreement was obtained between the SYNCHRON LX System and the SYNCHRON CX7 DELTA. The cutoff value of the SYNCHRON Systems cannabinoid 100 ng assay is 100 ng/mL.

Table 2.0 SYNCHRON LX vs. SYNCHRON CX7 DELTA[14]

THC		SYNCHRON LX		
		Positive	**Negative**	**Total**
SYNCHRON CX7 DELTA	Positive	37	0	37
	Negative	0	43	43
Total		37	43	80

Relative Sensitivity: 100%

Relative Specificity: 100%

Overall Agreement: 100%

CROSS REACTIVITY

Various THC metabolites and potential interfering substances in a human urine matrix were tested for cross-reactivity with the SYNCHRON Systems THC assay. The following table summarizes the results obtained at the concentrations tested for each potential cross-reactant.

Table 3.0 Cross Reactivity[a]

COMPOUND	CONCENTRATION (µg/mL)	EFFECT
l-11-Nor-▲^{9}-THC-9-COOH (cutoff)[b]	0.1	Positive
Cannabinol	0.5	Positive
8-β-11-Dihydroxy-▲^{9}-THC	0.15	Positive
8-β-Hydroxy-▲^{9}-THC	0.25	Positive
11-Hydroxy-▲^{9}-THC	0.25	Positive
l-11-Nor-▲^{8}-THC-9-COOH	0.15	Positive
▲^{9}-THC	0.15	Positive
Acetaminophen	1000	Negative
Acetylsalicylic Acid	1000	Negative
Albuterol	1000	Negative
Amobarbital	1000	Negative
d-amphetamine	1000	Negative
Benzoylecgonine	1000	Negative
Caffeine	100	Negative
Cannabidiol	10	Negative
Cocaine	200	Negative
Codeine	1000	Negative
Dextromethorphan	1000	Negative
Ibuprofen	1000	Negative
Meperidine	1000	Negative
Methadone	1000	Negative
d-Methamphetamine	1000	Negative
Morphine	200	Negative
d-11-Nor-▲^{9}-THC-9-COOH[c]	0.1	Negative
Oxazepam	500	Negative
Phencyclidine	1000	Negative
Phenobarbital	1000	Negative
Propoxyphene	1000	Negative
Secobarbital	1000	Negative

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 Natural urine metabolite of ▲^{9}-THC.
c Synthetic isomer of ▲^{9}-THC metabolite.

PRECISION

The following estimates of within-run imprecision were obtained when 20 replicates of the Negative Calibrator, 75 ng/mL THC Control, 100 ng/mL (cutoff) THC Calibrator, 125 ng/mL THC Control, and 200 ng/mL THC Calibrator were assayed on a properly operated and maintained SYNCHRON LX System.

Table 4.0 Typical Within-Run Imprecision

SAMPLE	MEAN RATE (mA/min)	1 SD (mA/min)	% CV
Negative Cal	399	2.4	0.6
75 ng/mL THC Control	461	3.5	0.8
100 ng/mL THC (cutoff) Cal	536	2.4	0.4
125 ng/mL THC Control	517	4.4	0.8
200 ng/mL THC Cal	482	4.1	0.8

Each laboratory should characterize their own instrument performance for comparison purposes. Instruments operated and maintained according to manufacturer‘s instructions should exhibit a within-run coefficient of variation of ≤ 2.0% for all sample levels.

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

Corrected Intended Use statement from quantitative to qualitative in the English version only.

Revision AG

Updated corporate address.

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

FOOTNOTES

It is possible that other substances and/or factors (e.g. technical or procedural) not listed above may interfere with the test and cause false results.

REFERENCES

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