pts Diagnostics

pts detect™ Cotinine

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PROFESSIONAL PERFORMANCE GUIDE

INTENDED USE

The PTS Detect™ cotinine system provides quantitative measurement of the nicotine metabolite cotinine (25 – 200 ng/mL) in capillary (fingerstick) or venous whole blood. The test is for professional use to determine if an individual has been exposed to nicotine.

SUMMARY AND EXPLANATION

Cotinine, the major metabolite of nicotine, indicates exposure to tobacco and other nicotine-containing products. Cotinine has a longer half-life than nicotine, which allows for a more accurate assessment of smoking or exposure status and better monitoring of progress in smoking cessation programs.[1] Because of its longer half-life and relative ease of detection, cotinine is the choice metabolite to assess exposure to nicotine. The amount of cotinine present in the blood is proportional to the amount and recency of nicotine exposure. Point-of-care cotinine testing is typically qualitative, limiting its use in distinguishing between light and heavy nicotine exposure. The PTS Detect cotinine system provides quantitative measurement of cotinine (test reporting range: 25 – 200 ng/mL) in capillary (fingerstick) or venous whole blood.

Cotinine can be measured by a variety of techniques in many sample types, such as hair, saliva, urine, and blood. Laboratory and point-of-care methods exist for the detection of cotinine, with point-of-care assays available for urine and saliva tests. Laboratory methods exist for the detection of cotinine in serum, plasma, urine, and saliva. Point-of-care assays are well suited to environments such as healthcare providers' offices and clinics, as they are generally easy to perform, require minimal sample preparation, require no additional laboratory equipment, and provide rapid turn-around-time from sampling to result.[2]

PRINCIPLE OF THE ASSAY

The PTS Detect cotinine system uses a competitive immunoassay technology to measure the amount of cotinine in whole blood. Upon the addition of the diluted blood sample, blue particles conjugated to anti-cotinine antibodies are released and migrate along the reagent strips. The amount of blue particles captured on the detection zone of the reagent strips is inversely correlated to the amount of cotinine in the sample. The amount of cotinine present in the collected sample is measured and reported in ng/mL.

SPECIMEN COLLECTION AND STORAGE

Fingerstick

The PTS Detect cotinine system requires 40 microliters (µL) of whole blood. Fingerstick blood is obtained by standard techniques with any appropriate lancing system. If alcohol is used for cleansing, be sure the finger is completely dry before lancing.

Venipuncture/Sample Collection for Venous Draw

Venous blood should be collected into heparin tubes (sodium or lithium, "green tops"). Blood samples should be well-mixed and tested at room temperature.

WARNINGS AND PRECAUTIONS

1. For *in vitro* diagnostic use only.
2. Carefully read and follow the product insert(s) to ensure proper test performance.
3. If refrigerated, bring sealed pouches and analyzer to room temperature for one hour prior to use.
4. If any component of the PTS Detect test system is cracked or broken, the broken component should not be used.
5. The test cartridge should not be used if the foil pouch is damaged.
6. Add sample to PTS Detect cotinine test cartridge within 2 minutes after the foil pouch is opened.
7. All components of the PTS Detect cotinine system may be exposed to biohazardous material. Use universal precautions.
8. The dilution buffer in the sampler is a buffered detergent solution containing a preservative. **Do not ingest.** In case of contact with skin or eyes, flush the area with large amounts of water.
9. Do not reuse capillary tubes, test cartridges, or sample dilution kits. **Do not mix analyzers with cartridges and sample dilution kits from different lots.**

KIT STORAGE AND STABILITY

- Pouched test cartridges, PTS Detect cotinine analyzers, capillary tubes, and pouched sample dilution kits may be stored prior to use at room temperature (18 – 28°C) for the time period indicated on the box. Analyzers, test cartridges, and dilution kits stored at room temperature must be thrown away if not used within the time period indicated on the box.
- If the temperature label, placed on the outside of every kit, is exposed to a temperature in excess of 122°F/50°C, the dot on the label will turn red and the product should not be used.
- The capillary tubes, analyzers, test cartridges, and sample dilution kits may be used until the expiration date printed on the box and pouches when stored refrigerated (2 – 8°C). Capillary tubes, analyzers, test cartridges, and sample dilution kits stored in the refrigerator must be thrown away if not used by the expiration date.
- Leave all components in their sealed pouches until use. If refrigerated, ensure pouches are at room temperature before use.
- **Do not mix pouches and analyzers from different lots.**

PACKAGE COMPONENTS

- PTS Detect cotinine analyzer (1)
- PTS Detect cotinine test supplies (40), including cartridges, sample dilution kits, and capillary tubes.
  - Each test cartridge includes the following chemistries: antibody to cotinine conjugated to blue latex particles, antigen conjugate that binds to the antibody, and membranes.
  - Each sample dilution kit includes: sampler (1) containing buffered detergent solution with preservative and piercing cap (1).
- Product insert(s)

MATERIALS REQUIRED BUT NOT SUPPLIED

- **Fingerstick sample**: appropriate sterile and disposable lancet or,
- **Venous sample:** Heparin tubes (sodium or lithium ["green top"]), venous collection supplies
- Alcohol wipes
- Gauze pad or cotton ball
- Bandage

RESULT INTERPRETATION

WHOLE BLOOD COTININE RESULT	APPROXIMATE NUMBER OF CIGARETTES PER DAY	INTERPRETATION
200 or greater ng/mL	10 or more (or equivalent use of alternative tobacco or nicotine products).	• Heavy tobacco user. • Active use of a tobacco product.
41 – 199 ng/mL	1 – 9 cigarettes (or equivalent use of alternative tobacco or nicotine products).	• Light tobacco user. • Low-dose, infrequent or light use of tobacco products.
<40 ng/mL	<1 cigarette (or equivalent use of alternative tobacco or nicotine products).	• Non-tobacco user. • No exposure or passive exposure to tobacco or nicotine products (secondhand smoke). • Usage of nicotine replacement products.

4, 5, 6, 7, 8, 9, 10, 11, 12

TROUBLESHOOTING

See the table below for a description of PTS Detect cotinine system operating and error codes (OR = Out of Range; QC = Quality Control; E = Error).

MESSAGE	DESCRIPTION AND RESOLUTION
OR 5	The analyzer temperature is below 18°C (64°F). Repeat the test at room temperature (18°C – 28°C / 64°F – 82°F).
OR 6	The analyzer temperature is above 28°C (82°F). Repeat the test at room temperature (18°C – 28°C / 64°F – 82°F).
<25	The result is less than 25 ng/mL.
>200	The result is greater than 200 ng/mL.
QC 2	Occurs when you insert a test cartridge that already has the sample added to it. Do not remove and reinsert a test cartridge after adding the sample.*
QC 6	A sample was added to the test cartridge before "SMPL" display. This counts down one test on the analyzer. Remove and discard the test cartridge. To avoid this error, do not add the sample until the "WAIT" prompt clears and "SMPL" appears.
QC 7	The test cartridge remained in the analyzer without a sample addition for 2 minutes after "SMPL" prompt. This counts down one test on the analyzer. Discard the test cartridge and insert a fresh one when you are ready to dispense the sampler.
QC 30 to 33	The analyzer was unable to obtain a valid initial reading. Be sure to remove the sampler within one second after dispensing it into the sample port, and do not disturb the analyzer while the test is running.*
QC 50 to 56	The sample dose was not sufficient. Mix the sampler with a downward motion and be sure to firmly apply the sampler into the sample port.
All other QC codes	The quality control checks did not pass. Call Customer Service toll free at 1-877-870-5610. The test will have to be repeated with another test cartridge, capillary tube, and sample dilution kit.
E1 to E99	The analyzer has a critical error. Call Customer Service toll-free at 1-877-870-5610.

*Carefully repeat the test using a new capillary tube, test cartridge, and a new sample dilution kit.

LIMITATIONS

- The PTS Detect cotinine system is only for use with human whole blood.
- As with any laboratory procedure, a large discrepancy between clinical impression and test results usually warrants investigation. Clinical consideration and professional judgment must be applied to any test result.

PERFORMANCE

Expected Values

The PTS Detect cotinine system reports whole blood cotinine concentrations from 25 to 200 ng/mL. Concentrations less than 25 ng/mL will be displayed as "<25" ng/mL and those greater than 200 ">200" ng/mL.

The expected normal value for serum cotinine for smokers and non-smokers has been established through the literature. Benowitz et. al reported in 2004 in the American Journal of Epidemiology expected serum cotinine levels for smokers and non-smokers in the United States based on smoking status, gender, and ethnicity. The mean serum cotinine value for smokers is 122.37 ng/mL, with 95% confidence limits of 112.04 ng/mL – 132.69 ng/mL. Serum cotinine values for males and females who are smokers are highly similar, with mean values of 122.08 ng/mL and 122.72 ng/mL respectively. Average cotinine values vary based on ethnicity, with non-Hispanic whites, non-Hispanic blacks, and Mexican Americans who are smokers exhibiting mean values of 142.44 ng/mL, 181.65 ng/mL, and 32.10 ng/mL, respectively.[3]

The mean serum cotinine value for nonsmokers is 0.08 ng/mL, with 95% confidence limits of 0.08 ng/mL – 0.09 ng/mL. Serum cotinine values for males and females who are nonsmokers are highly similar, with mean values of 0.09 ng/mL and 0.07 ng/mL respectively. Average cotinine values vary slightly based on ethnicity, with non-Hispanic whites, non-Hispanic blacks, and Mexican Americans who are nonsmokers exhibiting mean values of 0.08 ng/mL, 0.16 ng/mL, and 0.07 ng/mL, respectively.[3]

Each laboratory should determine its own reference ranges to conform to the population being tested.

Linearity

Linearity studies were performed to evaluate the linearity of the PTS Detect cotinine system across its dynamic range. Fifteen samples were prepared and tested in replicates of at least 3 (n=3). The observed results were evaluated by first, second, and third order polynomial fits to determine the linearity of response over the dynamic range of the system as per CLSI EP06. The test is linear for cotinine levels across the dynamic range of 25 ng/mL to 200 ng/mL.

Within the linear range, the PTS Detect cotinine system produces reliable results with hematocrits between 30% and 55% packed cell volume (PCV).

Interference Testing/Specificity

Studies were performed to assess the effect of potential test interferents, including over-the-counter therapeutic agents. The following compounds were tested in accordance with CLSI EP07 and shown to have less than 15% interference when present at the test concentrations listed. See table below.

INTERFERENT	TEST CONCENTRATION
Acetaminophen	1324 µmol/L
Ascorbic acid	170 µmol/L
Aspirin (Acetylsalicylic Acid)	3.62 µmol/L
Caffeine	308 µmol/L
Naproxen	1953 µmol/L
Niacin	800 µmol/L
Tetracycline	34 µmol/L
Primidone	164.7 µmol/L
Atorvastatin	2.16 µmol/L
Vitamin B-12	0.0148 µmol/L
Fish Oil	0.9%
Vitamin D2	7.25 µmol/L
Vitamin D3	7.25 µmol/L
Nicotine	0.031 µmol/L

The studies showed no effect from any of these potential interferents at concentrations up to approximately 3 times or greater their typical levels or therapeutic doses.

Precision

Precision testing was conducted according to CLSI EP05 using plasma at 2 levels of cotinine concentrations, 58.84 and 129.15 ng/mL. The intraday precision was evaluated at 3 sites over 5 days, n=5 for each site per day, yielding a total of 75 results per level. The overall CV was 3.47% at the low level and 2.53% at the high level.

Accuracy

Accuracy studies were conducted according to CLSI EP09 with 98 samples across the range of the PTS Detect cotinine system on 3 lots. Fingerstick sampling was performed on each subject for testing with the PTS Detect cotinine system, and venous blood was collected from each subject for testing on the PTS Detect cotinine system and for comparative testing using a qualified reference method for the determination of the concentration of cotinine from plasma.

Additionally, venous samples were prepared by dilution with compatible cotinine-negative blood. The qualified reference method used was immunoassay. The immunoassay test was qualified according to the College of American Pathologists (CAP) Accreditation Division standards.

The cotinine results ranged from 25 ng/mL to 199 ng/mL (reference results). Data analysis consisted of weighted least squares linear regression (x = reference results). The analysis demonstrated that the PTS Detect cotinine system may be used with either fingerstick (capillary) or venous (heparin-anticoagulated) whole blood samples. The data are provided in the table below.

	Venous versus Reference	Venous versus Capillary
n	98	32
Slope	1.04	1.00
y-intercept	7.01	1.99
"r"	0.90	0.98

Bias

Bias was determined at 50 ng/mL, a significant tobacco-use discrimination cut-point, as compared to an accredited reference laboratory. The average percent bias at 50 ng/mL was 2.9%.

REFERENCES

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INTERNATIONAL SYMBOLS	
	MANUFACTURER
Σ n	CONTAINS SUFFICIENT FOR <N> TESTS
IVD	IN VITRO DIAGNOSTIC MEDICAL DEVICE
EC REP	AUTHORIZED REPRESENTATIVE IN THE EUROPEAN COMMUNITY
2°C 36°F 8°C 46°F	STORE REFRIGERATED (2-8°C, 36-46°F)
REF	CATALOG NUMBER
CE	THIS PRODUCT FULFILS THE REQUIREMENTS OF DIRECTIVE 98/79/EC ON IN VITRO DIAGNOSTIC MEDICAL DEVICES.
	CONSULT INSTRUCTIONS FOR USE
	IMPORTANT
	USE BY
	SEPARATE COLLECTION: BATTERIES MUST BE DISPOSED OF IN ACCORDANCE WITH LAWS IN YOUR COUNTRY. CONTACT YOUR COMPETENT LOCAL ADMINISTRATION FOR INFORMATION ON THE RELEVANT LAWS REGARDING DISPOSAL AND RECYCLING IN YOUR AREA.

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