

Overview

Useful For

Monitoring fentanyl therapy

Method Name

Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS)

NY State Available

Yes

Specimen

Specimen Type

Serum Red

Specimen Required

**Supplies:** Sarstedt Aliquot Tube, 5 mL (T914)

**Collection Container/Tube:** Red top (Serum gel/SST are **not acceptable**)

**Submission Container/Tube:** Plastic vial

**Specimen Volume:** 2.3 mL

**Collection Instructions:** Within 2 hours of collection, centrifuge and aliquot serum into a plastic vial.

Forms

If not ordering electronically, complete, print, and send a [Therapeutics Test Request](#) (T831) with the specimen.

Specimen Minimum Volume

1.25 mL

Reject Due To

Gross hemolysis	OK
Gross lipemia	OK
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum Red	Frozen (preferred)	28 days	
	Ambient	72 hours	

	Refrigerated	14 days	
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Clinical & Interpretive

Clinical Information

Fentanyl is an extremely fast-acting synthetic opioid related to the phenylpiperidines.(1,2) It is available in injectable as well as transdermal formulations.(1) The analgesic effects of fentanyl are similar to those of morphine and other opioids(1), as it interacts predominantly with the opioid mu-receptor. These mu-binding sites are discretely distributed in the human brain, spinal cord, and other tissues.(1,3)

Fentanyl is approximately 80% to 85% protein bound.(1) Fentanyl plasma protein-binding capacity decreases with increasing ionization of the drug. Alterations in pH may affect its distribution between plasma and the central nervous system (CNS). The average volume of distribution for fentanyl is 6 L/kg (range 3-8).(3,4)

In humans, the drug appears to be metabolized primarily by oxidative N-dealkylation to norfentanyl and other inactive metabolites that do not contribute materially to the observed activity of the drug. Within 72 hours of intravenous (IV) administration, approximately 75% of the dose is excreted in urine, mostly as metabolites with less than 10% representing unchanged drug.(3,4)

- The mean elimination half-life is:(1-3)
- IV: 2 to 4 hours
  - Iontophoretic transdermal system (Ionsys), terminal half-life: 16 hours
  - Transdermal patch: 17 hours (range 13-22 hours, half-life is influenced by absorption rate)
  - Transmucosal:
    - Lozenge: 7 hours
    - Buccal tablet
      - 100 to 200 mcg: 3 to 4 hours
      - 400 to 800 mcg: 11 to 12 hours

In clinical settings, fentanyl exerts its principal pharmacologic effects on the CNS. In addition to analgesia, alterations in mood (euphoria, dysphoria) and drowsiness commonly occur.(1,3) Because the biological effects of fentanyl are similar to those of heroin and other opioids, fentanyl has become a popular drug of abuse.

Reference Values

Fentanyl:

Average serum fentanyl concentrations 24 hours after application of transdermal patch:

25 mcg/hour: 0.3-1.2 ng/mL

50 mcg/hour: 0.6-1.8 ng/mL

75 mcg/hour: 1.1-2.6 ng/mL

100 mcg/hour: 1.9-3.8 ng/mL

(Baselt RC. Disposition of Toxic Drugs and Chemical in Man. 12th ed. Biomedical Publications; 2020)

Norfentanyl:

Reference range: Not established

Cutoff concentrations by liquid chromatography tandem mass spectrometry:

Fentanyl: 0.05 ng/mL

Norfentanyl: 0.25 ng/mL

### Interpretation

Both fentanyl and norfentanyl are reported.

Tolerant individuals may require many-fold increases in dose to achieve the same level of analgesia, which can greatly complicate interpretation of therapeutic drug monitoring results and establishment of a therapeutic window.

Concentration at which toxicity occurs varies and should be interpreted in light of clinical situation.

### Cautions

Specimens collected in serum gel tubes are not acceptable because the drug can absorb on the gel and lead to falsely decreased concentrations.

### Clinical Reference

1. Gutstein HB, Akil H. Opioid analgesics. In: Brunton LL, Lazo JS, Parker KL, eds. Goodman and Gilman's: The Pharmacological Basis of Therapeutics. 11th ed. McGraw-Hill Companies; 2006:chap 21
2. Kerrigan S, Goldberger BA. Opioids. In: Levine B, eds. Principles of Forensic Toxicology. 2nd ed. AACC Press; 2003:187-205
3. DURAGESIC (fentanyl transdermal system). Package insert: Janssen Pharmaceutica Products, LP; 2006
4. Baselt RC. Disposition of Toxic Drugs and Chemicals in Man. 12th ed. Biomedical Publications; 2020
5. Yaksh T, Wallace M. Opioids, Analgesia, and Pain Management. In: Brunton LL, Hilal-Dandan R, Knollmann BC, eds. Goodman and Gilman's: The Pharmacological Basis of Therapeutics, 13th ed. McGraw-Hill Education; 2017
6. Langman LJ, Bechtel LK, Holstege CP. Clinical toxicology. In: Rifai N, Chiu RWK, Young I, Burnham CAD, Wittwer CT, eds. Tietz Textbook of Laboratory Medicine. 7th ed. Elsevier; 2023:chap 43
7. Fentanyl. In: Merative Micromedex (electronic version). Merative US 2024. Accessed April 7, 2025. Available at [www.micromedexsolutions.com](http://www.micromedexsolutions.com)

## Performance

### Method Description

Fentanyl is isolated from serum using a liquid/liquid extraction. The solvent is dried, and the analytes are reconstituted with mobile phase. Analysis is performed by liquid chromatography tandem mass spectrometry using selected ion monitoring. (Unpublished Mayo method)

### PDF Report

No

### Day(s) Performed

Tuesday, Thursday

Report Available

2 to 7 days

Specimen Retention Time

14 days

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Superior Drive

Fees & Codes

Fees

- Authorized users can sign in to [Test Prices](#) for detailed fee information.
- Clients without access to Test Prices can contact [Customer Service](#) 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact [Customer Service](#).

Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

G0480  
80354 (if appropriate for select payers)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
FENTS	Fentanyl and Metabolites, S	81275-0

Result ID	Test Result Name	Result LOINC® Value
31829	Norfentanyl	11074-2
31830	Fentanyl	3636-8
31832	Chain of Custody	77202-0