

## Overview

### Useful For

Detection of in utero drug exposure up to 5 months before birth

### Method Name

LiquidChromatography-TandemMassSpectrometry(LC-MS/MS)

### NY State Available

Yes

## Specimen

### Specimen Type

Meconium

### Advisory Information

For chain-of-custody testing, order MAMMX / 6-Monoacetylmorphine (6-MAM) Confirmation, Chain of Custody, Meconium.

### Specimen Required

**Supplies:** Stool container, Small (Random), 4 oz (T288)

**Container/Tube:** Stool container (T288)

**Specimen Volume:** 1 g (approximately 1 teaspoon)

### Collection Instructions:

1. Collect entire random meconium specimen.
2. Send specimen frozen. When refrigerated, a significant percentage of 6-MAM will convert to morphine in less than 24 hours.

### Forms

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

### Specimen Minimum Volume

0.3 g (approximately 1/4 teaspoon)

### Reject Due To

Grossly bloody	Reject
Stool, diapers	Reject

### Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Meconium	Frozen	14 days	

## Clinical and Interpretive

### Clinical Information

Heroin (diacetylmorphine) is a semisynthetic opiate that is closely related to morphine. It is no longer used clinically in the United States, though it is used elsewhere for rapid relief of pain.(1) Like morphine and other opiates, its relaxing and euphoric qualities make heroin a popular drug of abuse. Heroin is commonly injected intravenously, although it can be administered by other means such as snorting, smoking, or inhaling vapors.

Heroin shares the core structure of morphine, with the addition of 2 acetyl groups, which are thought to enhance its permeation into the central nervous system.(2,3) Heroin is metabolized by sequential removal of these acetyl groups; loss of the first acetyl converts heroin into 6-monoacetylmorphine (6-MAM).(2,3) Heroin is rarely found in meconium since only 0.1% of a dose is excreted unchanged. 6-MAM is a unique metabolite of heroin, and its presence is a definitive indication of heroin use. Like heroin, 6-MAM has a very short half-life; however, its detection time in meconium, the first fecal material passed by the neonate, is uncharacterized. 6-MAM is further metabolized into morphine, the dominant metabolite of heroin, and morphine will typically be found in a specimen containing 6-MAM.

Opiates, including heroin, have been shown to readily cross the placenta and distribute widely into many fetal tissues.(4) Opiate use by the mother during pregnancy increased the risk of prematurity and being small for gestational age. Furthermore, heroin-exposed infants exhibit an early onset of withdrawal symptoms compared with methadone-exposed infants. Heroin-exposed infants demonstrate a variety of symptoms including irritability, hypertonia, wakefulness, diarrhea, yawning, sneezing, increased hiccups, excessive sucking, and seizures. Long-term intrauterine drug exposure may lead to abnormal neurocognitive and behavioral development as well as an increased risk of sudden infant death syndrome.(5)

The disposition of drug in meconium is not well understood. The proposed mechanism is that the fetus excretes drug into bile and amniotic fluid. Drug accumulates in meconium either by direct deposit from bile or through swallowing of amniotic fluid.(6) The first evidence of meconium in the fetal intestine appears at approximately the 10th to 12th week of gestation, and slowly moves into the colon by the 16th week of gestation.(7) Therefore, the presence of drugs in meconium has been proposed to be indicative of in utero drug exposure during the final 4 to 5 months of pregnancy, a longer historical measure than is possible by urinalysis.(6)

### Reference Values

Negative

Positives are reported with a quantitative LC-MS/MS result.

Cutoff concentration:

6-MAM by LC-MS/MS: 5 ng/g

### Interpretation

The presence of 6-monoacetylmorphine (6-MAM) in meconium is definitive for heroin use by the mother. However, the absence of 6-MAM does not rule-out heroin use, because of its short half-life.

### Cautions

No significant cautionary statements

The short half-life of 6-monoacetylmorphine (6-MAM) may prevent its detection in heroin users.

6-MAM is metabolized to morphine, but the presence of morphine alone is not sufficient evidence to prove heroin use. 6-MAM is the only definitive metabolite of heroin.

Send frozen if possible. When refrigerated, a significant percentage of 6MAM will convert to morphine in less than 24 hours.

### **Clinical Reference**

1. Giovannelli M, Bedford N, Aitkenhead A: Survey of intrathecal opioid usage in the UK. *Eur J Anaesthesiol* 2008;25:118-122
2. Principles of Forensic Toxicology. Second edition. Washington DC, AACCC Press, 2003 pp 187-205
3. Goodman and Gilman's: The Pharmacological Basis of Therapeutics, 10th edition. New York, McGraw-Hill Professional, 2001 pp 590-592
4. Szeto HH: Kinetics of drug transfer to the fetus. *Clin Obstet Gynecol* 1993;36:246-254
5. Kwong TC, Ryan RM: Detection of intrauterine illicit drug exposure by newborn drug testing. *Clin Chem* 1997;43(1):235-242
6. Ostrea EM Jr, Brady MJ, Parks PM, et al: Drug screening of meconium in infants of drug-dependent mothers: an alternative to urine testing. *J Pediatr* 1989 Sep;115(3):474-477
7. Ahanya SN, Lakshmanan J, Morgan BL, Ross MG: Meconium passage in utero mechanisms, consequences, and management. *Obstet Gynecol Surv* 2005 Jan;60(1):45-56; quiz 73-74

### **Performance**

#### **Method Description**

Meconium is mixed with internal standard and extracted with methanol. The methanolic extract is further processed by solid-phase extraction. The extract is analyzed by HPLC with detection by tandem mass spectrometry.(Unpublished Mayo method)

#### **PDF Report**

No

#### **Day(s) and Time(s) Test Performed**

Monday through Sunday; Varies

#### **Analytic Time**

2 days

#### **Specimen Retention Time**

2 weeks

#### **Performing Laboratory Location**

Rochester

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**Fees and 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 Regional Manager. 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. This test has not been cleared or approved by the U.S. Food and Drug Administration.

**CPT Code Information**

80356

G0480 (if appropriate)

**LOINC® Information**

Test ID	Test Order Name	Order LOINC Value
6MAMM	6-MAM Confirmation, M	29345-6

Result ID	Test Result Name	Result LOINC Value
31874	6-Monoacetylmorphine	29345-6
31875	Interpretation	69050-3