



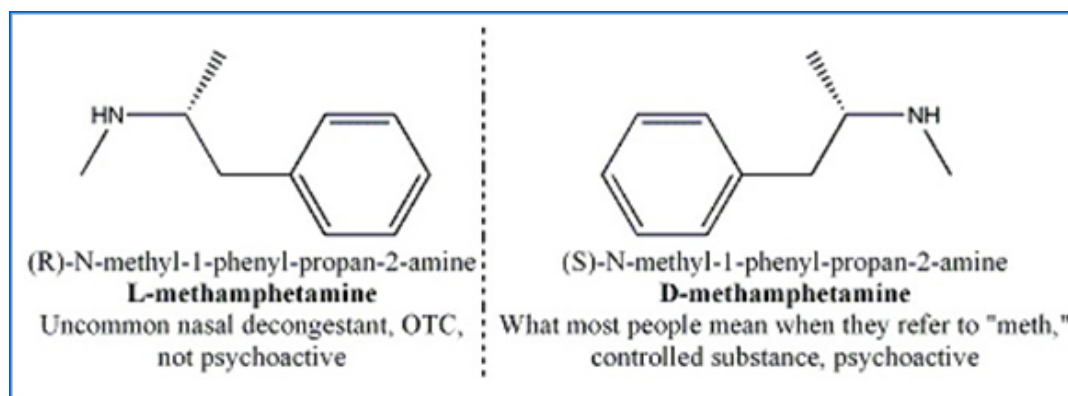
## Clinical Update: July 2019

### What did my patient actually take? An Overview of Methamphetamine Results

#### Methamphetamine D/L Isomer

Methamphetamine is a well-known central nervous system (CNS) stimulant that is abused recreationally and, infrequently, prescribed as a stimulant or appetite suppressant. Methamphetamine exists in two different forms known as enantiomers: levo-methamphetamine (*l*-methamphetamine) and dextro-methamphetamine (*d*-methamphetamine). Each has the same chemical formula, but a different arrangement of atoms in the molecule making them mirror images of each other (see Figure 1). The slight variation in chemical structure produces different properties for each enantiomer, or isomer. *d*-methamphetamine is more stimulating and psychoactive and, therefore, has a higher abuse potential, while *l*-methamphetamine is less CNS-active, vasoconstrictive, and has a lower abuse potential. The D/L isomer test offered by Aegis helps narrow down the potential source(s) of a methamphetamine positive result. Following exposure, methamphetamine is detectable in urine for up to 5 days, up to 48 hours in oral fluid, and up to 24 hours in blood.

Figure 1:



<https://scienceblogs.com/moleculeoftheday/2006/10/27/lmethamphetamine-would-you-bel>

At Aegis, we report out the results of the D/L isomer test according to the concentration/quantification of methamphetamine in nanograms per milliliter (ng/mL) and the percentage of the detected amount that is the *d*-isomer (0-100%). If D/L Isomer testing is ordered through one of our testing profiles, **there will be two "Medication Compliance" result interpretations for methamphetamine:** 1) concentration of methamphetamine in ng/mL and 2) percentage of *d*-methamphetamine. See Figures 2, 3, and 4 for example reports with both methamphetamine "Medication Compliance" result interpretations. Side note: Methamphetamine metabolizes to amphetamine and we will occasionally see amphetamine present as a metabolite of methamphetamine. The vice versa is not true – amphetamine does not metabolize to methamphetamine.<sup>1</sup>

#### 95-100% *d*-methamphetamine results

If the reported *d*- percentage is between 95 and 100%, potential sources would be prescription methamphetamine (brand name Desoxyn®), prescription benzphetamine, and illicit methamphetamine. Desoxyn® is a schedule II controlled substance prescribed for attention deficit disorder with hyperactivity and for short-term treatment of obesity. Benzphetamine is a Schedule III controlled substance prescribed for the treatment of obesity and metabolizes to *d*-methamphetamine. Prescription verification and/or assessment of Prescription Drug Monitoring Program (PDMP)

records are important to rule out legitimate prescription use before considering illicit methamphetamine as a potential source. See Figure 2 for an example of how 95-100% *d*-methamphetamine results are displayed on an Aegis report.

**Figure 2:**

<b>Medication(s) Prescribed</b>			
None Indicated			
<b>Test(s) Requested</b>			
00199U - PainComp All Tests Requested		04440 - Marijuana	00156 - Synthetic Cannabinoids
<b>Medication Compliance</b>			
Drug and/or Metabolites	Result Interpretation	Result	Comment
Methamphetamine	PRESENT	290 ng/mL	Test result indicates ingestion within 5 days of the urine collection.
d-Methamphetamine	PRESENT	100 %	Stimulant form of methamphetamine present; for additional information please consult clinical scientists at 1-877-552-3232.

**0-5% *d*-methamphetamine results (otherwise known as 95-100% *l*-methamphetamine)**

If the reported *d*- percentage is between 0 and 5%, the potential sources would be predominantly *l*-methamphetamine products. Selegiline, known by brand names Eldepryl®, EMSAM®, and Zelapar®, is prescribed for the treatment of Parkinson’s disease and major depression, and metabolizes to levmetamfetamine (*l*-methamphetamine). Also, some over the counter (OTC) nasal decongestant vapor inhalers contain predominantly levmetamfetamine as the active ingredient. After controlled administration of an OTC nasal decongestant vapor inhaler containing levmetamfetamine in a study, the maximum concentrations of *l*-methamphetamine in urine and oral fluid were 1,440ng/mL and 380ng/mL, respectively.<sup>2,3</sup> There have been case reports of illicit methamphetamine composed of predominantly *l*-methamphetamine; however, illicit methamphetamine would be expected to be predominantly *d*-methamphetamine given the desire for stimulant effects with illicit use.<sup>4,5</sup> See Figure 3 for an example of how 0-5% *d*-methamphetamine (otherwise known as 95-100% *l*-methamphetamine) results are displayed on an Aegis report.

**Figure 3:**

<b>Medication(s) Prescribed</b>			
None Indicated			
<b>Test(s) Requested</b>			
00197iU - QMP Plus D/L		00021 - Drug-Drug Interaction (DDI)	
04420 - Barbiturates		04440 - Marijuana	
<b>Medication Compliance</b>			
Drug and/or Metabolites	Result Interpretation	Result	Comment
Benzodiazepine Metabolites	PRESENT	3,600 ng/mL	A prescription drug, not indicated as prescribed on the requisition form, was detected.
Buprenorphine	PRESENT	1,730 ng/mL	A prescription drug, not indicated as prescribed on the requisition form, was detected.
Hydrocodone	PRESENT	150 ng/mL	A prescription drug, not indicated as prescribed on the requisition form, was detected.
Methamphetamine	PRESENT	269 ng/mL	Test result indicates ingestion within 5 days of the urine collection.
d-Methamphetamine	NOT PRESENT	0 %	Non-stimulant form of methamphetamine present; for additional information please consult clinical scientists at 1-877-552-3232.



**Mixed *d*- and *l*-methamphetamine results**

Illicit methamphetamine can be any percentage of *d*-, given it is manufactured illicitly and the contents are not controlled. If the *d*- percentage is between 5 and 95 % (a mixture of isomers), the most likely source is illicit methamphetamine. However, combining a predominantly *l*-product with a predominantly *d*-product may result in such a finding as well. In this case, the patient would need to provide proof of having a valid prescription for both a *d*- and *l*- product, or a prescription for a *d*-product and report using an OTC nasal decongestant vapor inhaler containing levmetamfetamine. For the most accurate interpretation, prescription verification and/or assessment of the PDMP are important in determining the potential source(s) of the D/L isomer test results and to rule out illicit methamphetamine use. See Figure 4 for an example of how mixed *d*- and *l*-methamphetamine results are displayed on an Aegis report.

**Figure 4:**

Test(s) Requested		
00184i - Amphetamines + d/l MethAmp	04469co - Fentanyl	04460co - Opiates
04420 - Barbiturates	04462co - Heroin	00115 - Specimen Validity Tests (SVT)
04430co - Benzodiazepines	04003co - Meperidine	04125co - Tramadol
04496 - Buprenorphine	04458co - Methadone	
04450 - Cocaine	01640U - Naloxone	

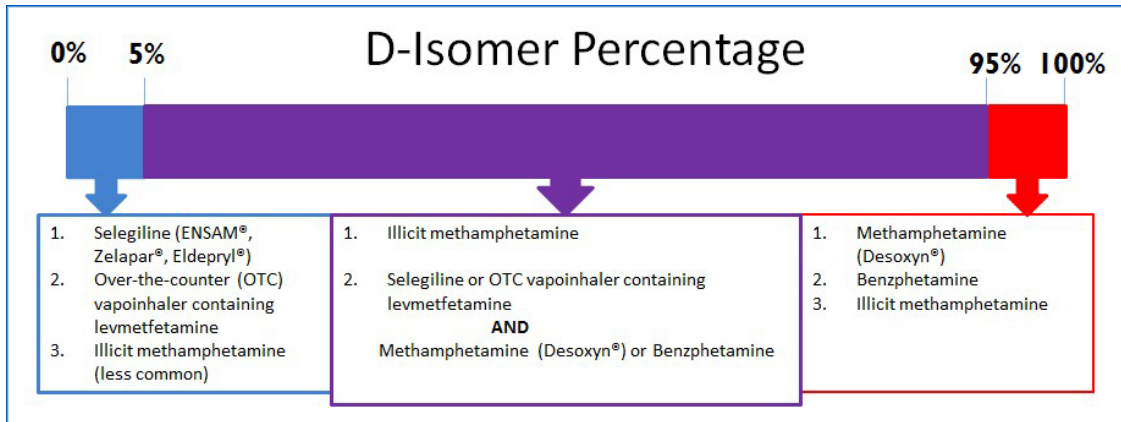
Medication Compliance			
Drug and/or Metabolites	Result Interpretation	Result	Comment
Naloxone	PRESENT	947 ng/mL	A prescription drug, not indicated as prescribed on the requisition form, was detected.
Methamphetamine	PRESENT	83,200 ng/mL	Test result indicates ingestion within 5 days of the urine collection.
d-Methamphetamine	PRESENT	12 %	Stimulant form of methamphetamine present; for additional information please consult clinical scientists at 1-877-552-3232.

Please see Table 1 and Figure 5 for a summarization of methamphetamine result interpretation.

**Table 1:**

Drugs potentially responsible for 95-100% d-methamphetamine results:
<ul style="list-style-type: none"> <li>• Methamphetamine (Desoxy<sup>®</sup>)</li> <li>• Benzphetamine</li> <li>• Illicit methamphetamine</li> </ul>
Drugs potentially responsible for 0-5% d-methamphetamine/ 95-100% l-methamphetamine results:
<ul style="list-style-type: none"> <li>• Selegiline (Eldepryl<sup>®</sup>, EMSAM<sup>®</sup>, Zelapar<sup>®</sup>)</li> <li>• Over-the-counter (OTC) vapor inhaler containing levmetfetamine</li> <li>• Illicit methamphetamine (less common)</li> </ul>
Drugs <u>NOT</u> responsible for any positive methamphetamine results:
<ul style="list-style-type: none"> <li>• Pseudoephedrine (Sudafed<sup>®</sup>) products</li> <li>• Amphetamine/ Dextroamphetamine products (Adderall<sup>®</sup>, Dexedrine<sup>®</sup>, Vyvanse<sup>®</sup>)</li> <li>• Phentermine (Adipex-P<sup>®</sup>, Lomaira<sup>®</sup>, Qsymia<sup>®</sup>)</li> <li>• Methylphenidate products (Concerta<sup>®</sup>, Ritalin<sup>®</sup>)</li> <li>• Other OTC or prescription products</li> </ul>

Figure 5:



Please call our clinical team at 1-877-552-3232 if you require additional information.

NOTICE: The information above is intended as a resource for health care providers. Providers should use their independent medical judgment based on the clinical needs of the patient when making determinations of who to test, what medications to test, testing frequency, and the type of testing to conduct.

**References:**

1. Baselt RC. *Disposition of toxic drugs and chemicals in man*. 11<sup>th</sup> ed. Seal Beach, CA: Biomedical Publications; 2017.
2. Smith M, Nichols D, Underwood P, et al. Methamphetamine and amphetamine isomer concentrations in human urine following controlled Vicks Vapoinhaler administration. *J Anal Toxicol*. 2014;38(8):524-7.
3. Newmeyer MN, Concheiro M, da Costa J, Flegel R, Gorelick DA, Huestis MA. Oral Fluid with three modes of collection and plasma methamphetamine and amphetamine enantiomer concentrations after controlled intranasal l-methamphetamine administration. *Drug Test Anal*. 2105;7(10):877-83.
4. The Drug Enforcement Administration, Office of Forensic Sciences, Unusual l-methamphetamine clandestine laboratory in Los Angeles, California. *Microgram Bulletin*. 2004;37(6):65-6.
5. Mendelson J, Uemura N, Jones R, et al. Human pharmacology of the methamphetamine stereoisomers. *Clin Pharm Ther*. 2006;80(4):403-20.