Drug Testing to Support Pain Management Clinics

June 21, 2011

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University of Utah, ARUP Laboratories
Outline

- Provide an overview of “pain management”, and discuss concerns relative to use and availability of opioid drugs
- Describe the role of drug testing to support pain management clinicians, and patients
- Discuss approaches to drug testing
- Review considerations for interpretation of test results
  - Unexpected negative results
  - Unexpected positive results
  - Drug adherence versus dose and dosing adherence
Pain is a major health and social issue

Pain is the #1 reason people seek medical care

Prevalence of chronic non-cancer pain (>3 months) in the U.S. is estimated at 20-60%, over a lifetime

Chronic non-cancer pain is expensive

- Leading cause of health-related absenteeism
- Increased risk of depressive and anxiety disorders
- Estimated medical costs in the U.S. >$100 billion/yr
Pain management is a medical specialty (American Board of Pain Medicine)

Treatment approach is multi-disciplinary

Commonly used medications include opioids, benzodiazepines, antidepressants, anticonvulsants, THC, and muscle relaxants
Drugs in “Top 200” U.S. scripts (2009)

• Opioid analgesics
  – Hydrocodone (#1, 3, 66)
  – Oxycodone (#33, 57, 126, 160, 175)
  – Tramadol (#47, 138)
  – Codeine (#73)
  – Propoxyphene (#79, 163)
  – Buprenorphine (#189)

• Non-opioid analgesics
  – Ibuprofen (#27, 171)
  – Naproxen (#135, 195)

• Benzodiazepines
  – Alprazolam (#39, 58, 83, 122)
  – Clonazepam (#46)
  – Lorazepam (#86, 144)
  – Diazepam (#111)

• Other medications
  – Gabapentin (#70, 186)
  – Pregabalin (#71)
  – Carisoprodol (#112)
  – Antidepressants (#11, 95, 116, 134)

Rank #s from www.pharmacytimes.com
Pain relievers are misused

- Pain relievers are the #1 new illicit drug in the U.S.  
  *National Survey on Drug Use in Health (NSDUH), 2009*

- 13% of 12th graders reported nonmedical use of hydrocodone or oxycodone  
  *NSDUH, 2009*

- 60% of people who use pain relievers for nonmedical reasons obtain the drug from a friend or relative  
  *SAMHSA, 2006*
Motive for drug diversion may be $34

<table>
<thead>
<tr>
<th>Drug</th>
<th>“Street” Price (per pill)</th>
<th>Retail Price Estimate (per pill)</th>
<th>Potential “Profit” (per pill)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxycodone</td>
<td>$12 - 40</td>
<td>$6</td>
<td>$34</td>
</tr>
<tr>
<td>Oxycontin®</td>
<td>$50 - 80</td>
<td></td>
<td>$74</td>
</tr>
<tr>
<td>Percocet®</td>
<td>$10 - $15</td>
<td></td>
<td>$9</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>$5 - 20</td>
<td>$1.50</td>
<td>$18.50</td>
</tr>
<tr>
<td>Vicodin®</td>
<td>$5 - $25</td>
<td></td>
<td>$23.50</td>
</tr>
</tbody>
</table>

CNN Money; June 1, 2011
Unintentional U.S. deaths, drug-related

www.cdc.gov/HomeandRecreationalSafety/Poisoning/brief.htm
“REMS” requirements by the FDA

REMS = Risk Evaluation and Mitigation Strategies intended to “protect patients from serious harm”


Opioid drug sponsors/manufacturers of select formulations (primarily ER) will be required to provide educational programs and materials, for both prescribers and patients, as part of “new safety information” requirements – discussions currently ongoing

Drugs selected for REMS include fentanyl, morphine, buprenorphine, methadone, oxycodone, oxymorphone, and hydromorphone
Objectives of drug testing

1. Detect drug use
   • Verify adherence to drugs prescribed
   • Identify use of undisclosed drugs

2. Discourage drug misuse

*Drug testing is a tool, intended to supplement self-reporting, as well as behavioral and clinical monitoring*
Drug testing approaches

Pre-therapeutic comprehensive testing:

*selected illicit and prescription drugs*

Periodic testing (during therapy):

*random testing, to detect selected illicit and prescription drugs, every 1-12 months, tailored to patient scenario*
Specimen selection

Average time of drug detection

Concentration

Hours  Days  Weeks  Months

Blood

Oral Fluid

Urine

Hair

Actual pharmacokinetics (PK) varies

- Absorption and Distribution
  - Formulation
  - Route of administration
- Metabolism
  - First pass
  - Phase I enzymes (e.g. cytochrome P450 isozymes)
  - Phase II enzymes (e.g. UDP-glucuronosyltransferase)
  - Drug/drug or food/drug interactions
  - Hepatic function
- Elimination
  - Renal function

Consider specific prescribed medications, patient clinical status, genetics, history, etc.
Urine drug testing (UDT) results


- Expected drugs: 26%
- Illicits: 11%
- Unexpected prescription drugs: 29%
- Missing drugs: 38%
Another example of UDT results

- Retrospective study of 470 pain clinic patients
- Urine drug testing results confirmed by GC-MS
- All results reviewed/verified vs. patient charts for appropriateness of test results

- Expected opioid 55% (vs. 22%)
- Missing opioid 10% (vs. 38%)
- Unexpected opioid 15% (vs. 29%)
- Illicit substances 20% (vs. 11%)

Lab definitions

• **Screen**: a qualitative (positive/negative) test; usually designed to detect many drugs or drug classes; confidence in results may be poor, but depends on the assay. Commonly based on immunoassay; may be accomplished with “point of care tests” (POCT).

• **Confirmation**: a test designed to provide a high degree of confidence in identification of individual drugs/compounds; may be qualitative or quantitative (reports the amount of drug present). Commonly based on a combination of chromatography and mass spectrometry.
Selecting the best drug test

Drug testing for pain management purposes should **NOT mirror traditional drugs of abuse testing**

- Objective(s) of testing?
- Define testing needs
  - Time to result
  - Specimen(s)
  - Specific drug(s) of interest
  - Qualitative or quantitative
  - Sensitivity
  - Specificity
• **Sensitivity:** the minimum concentration that is reliably detected. May be defined by the limit of quantification (LOQ) of an assay or the “cutoff,” which is the concentration used to distinguish between a positive and a negative result. Cutoff concentration is defined by the assay manufacturer, or by the laboratory.
## Example cutoffs: SAMHSA vs ARUP (ng/mL)

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Forensic Screen</th>
<th>Medical Screen</th>
<th>Drug</th>
<th>Forensic Confirm</th>
<th>Medical Confirm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amps</td>
<td>500</td>
<td>300</td>
<td>Amphetamine, Methamphetamine, MDMA, MEA, MDA</td>
<td>250</td>
<td>200</td>
</tr>
<tr>
<td>THC</td>
<td>50</td>
<td>20</td>
<td>THC-COOH</td>
<td>15</td>
<td>4</td>
</tr>
<tr>
<td>Cocaine</td>
<td>300</td>
<td>150</td>
<td>Benzoylecgonine</td>
<td>100</td>
<td>50</td>
</tr>
<tr>
<td>Opiates*</td>
<td>2000</td>
<td>300</td>
<td>Morphine</td>
<td>2000</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Codeine</td>
<td>2000</td>
<td>5</td>
</tr>
<tr>
<td>PCP</td>
<td>25</td>
<td>25</td>
<td>PCP</td>
<td>25</td>
<td>10</td>
</tr>
</tbody>
</table>

* New for 2010, guidelines mandate screening for 6-monoacetylmorphine at 10 ng/mL
• **Specificity**: accuracy. Ability of a test to detect and distinguish between individual drugs/compounds. Poor specificity could lead to false positive or false negative results. Consult the cross-reactivity profile (~affinity of the antibody) for immunoassays.
Specificity and immunoassay results

**SPECIFICITY**

- Poor = FALSE negative
- Good (but wrong drug) = FALSE positive

Defined by:
- Antibody
- Cutoff
- Calibrator

TRUE negative/positive
Substances with poor cross-reactivity

<table>
<thead>
<tr>
<th>Drug class</th>
<th>Compounds not detected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marijuana</td>
<td>Spice, K2</td>
</tr>
<tr>
<td>Amphetamines</td>
<td>Methylphenidate</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>Clonazepam, Zolpidem</td>
</tr>
<tr>
<td>Methadone</td>
<td>EDDP</td>
</tr>
<tr>
<td>Opiates</td>
<td>Oxycodone, Fentanyl, Tramadol, Buprenorphine</td>
</tr>
</tbody>
</table>

Possible FALSE negative

Tenore *J of Addictive Diseases* 2010; 29:436-48
### Substances with good cross-reactivity

<table>
<thead>
<tr>
<th>Drug class</th>
<th>Compounds detected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cannabinoids</td>
<td>NSAIDs, Pantoprazole</td>
</tr>
<tr>
<td>Opioids</td>
<td>Chlorpromazine, Fluoroquinolones</td>
</tr>
<tr>
<td>Benzodiazepine</td>
<td>Oxaprozin, Sertraline</td>
</tr>
<tr>
<td>Methadone</td>
<td>Propoxyphene, Seroquel</td>
</tr>
<tr>
<td>PCP</td>
<td>Dextromethorphan, Meperidine</td>
</tr>
<tr>
<td>Amphetamines</td>
<td>Vicks, Desipramine, Trazodone</td>
</tr>
</tbody>
</table>

*Possible FALSE positive*

Christoi et al. *Pain Physician* 2011;14:123-43
Tenore *J of Addictive Diseases* 2010; 29:436-48
Most likely approach

• Random urine

• Multi-drug qualitative screen
  – POCT common
    • Rapid turnaround time
    • Ease/convenience of use
    • Some tests have been granted “waived” status under CLIA
    • Detects most drugs of interest for monitoring in pain management settings
  – Discuss results with patient, real-time

• Targeted testing for drugs of interest, or when confirmation testing is indicated
When to “confirm” a result

1. Screen does not detect drugs of interest
2. Screen results are inconsistent with clinical expectations
3. Quantitative results are necessary for interpretation

Mass spectrometry: GC-MS, LC-MS/MS, LC-MS/TOF
# POCT in pain patients

<table>
<thead>
<tr>
<th>Drug/Drug Class</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Agreement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine, Codeine, Hydrocodone, Hydromorphone</td>
<td>92.2%</td>
<td>93.1%</td>
<td>92.5%</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>75.4%</td>
<td>92.3%</td>
<td>90.0%</td>
</tr>
<tr>
<td>Methadone</td>
<td>96.1%</td>
<td>98.8%</td>
<td>98.7%</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>74.7%</td>
<td>98.0%</td>
<td>87.4%</td>
</tr>
<tr>
<td>Marijuana</td>
<td>90.9%</td>
<td>98.0%</td>
<td>97.8%</td>
</tr>
<tr>
<td>Cocaine</td>
<td>25.0%</td>
<td>100%</td>
<td>99.4%</td>
</tr>
<tr>
<td>Methamphetamine</td>
<td>40.0%</td>
<td>98.8%</td>
<td>98.5%</td>
</tr>
<tr>
<td>Amphetamine</td>
<td>47.0%</td>
<td>99.1%</td>
<td>98.2%</td>
</tr>
</tbody>
</table>

Possible UDT algorithm

UDT

- Results appropriate
- Results not appropriate

No further action, if patient is low risk

Confirm results

- Results appropriate
- Results not appropriate

Confirmation testing was required for ~35% of POCT results in the Manchikanti 2011 studies
Interpretation consideration:

Unexpected negative results
Reasons for a negative result

Drug was not taken
Drug was taken incorrectly (less than prescribed or less frequently than prescribed)
Drug was not absorbed
Accelerated metabolism/elimination
Drug delivery was variable
~1000 outpatients prescribed transdermal fentanyl patches for pain management

~50% needed more analgesia before the end of the standard 72 hour dose period

Average pain control was ~63 hrs

Kim et al Support Care Cancer 19(2):297-301, 2010

Suggests variation in actual drug delivery and/or patient pharmacokinetics
Reasons for a negative result

Drug was not taken
Drug was taken incorrectly (less than prescribed or less frequently than prescribed)
Drug was not absorbed
Accelerated metabolism/elimination
Drug delivery was variable
Specimen was collected too late after use
Specimen was dilute, or adulterated
Detection limits reflect

Assay method and cutoff
Drug and formulation
Patient pharmacokinetics
Sample
  – Type
  – Timing of collection
  – Quality of specimen (e.g. dilution)
Example: effect of urine dilution on drug screen

Assume opiate cutoff of 300 ng/mL
Samples contain 428 ng morphine/mg creatinine

Sample 1: positive
- morphine: 856 ng/mL
- creatinine: 200 mg/dL

Sample 2: negative
- morphine: 214 ng/mL
- creatinine: 50 mg/dL

\[
\frac{\text{Drug} \times 100}{\text{Creatinine}} = \text{ng drug/mg creatinine}
\]
<table>
<thead>
<tr>
<th>Sample</th>
<th>Sample Check (%) Microgenics, CEDIA</th>
<th>Creatinine (mg/dL) Syva (Dade), EMIT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human urine</td>
<td>80-100</td>
<td>&gt; 5 (DOT)</td>
</tr>
<tr>
<td>Dog urine (n=7)</td>
<td>52 - 85</td>
<td>87 - 284</td>
</tr>
<tr>
<td>Horse urine (n=1)</td>
<td>92</td>
<td>104</td>
</tr>
<tr>
<td>Energy drinks (n=44)</td>
<td>72-103</td>
<td>0-63</td>
</tr>
<tr>
<td>Margarita mix (n=2)</td>
<td>73-74</td>
<td>71-76</td>
</tr>
<tr>
<td>Fruit juice (n=8)</td>
<td>39-81</td>
<td>0-62</td>
</tr>
</tbody>
</table>

Reasons for a negative result

Drug was not taken
Drug was taken incorrectly (less than prescribed or less frequently than prescribed)
Drug was not absorbed
Accelerated metabolism/elimination
Drug delivery was variable
Specimen was collected too late after use
Specimen was dilute, or adulterated
Clinic or lab mixup
Test performed is not designed to detect drug
“False” negatives for oxycodone common

<table>
<thead>
<tr>
<th>Drug (ng/mL)</th>
<th>Abbott FPIA</th>
<th>Dade Behring (Syva) EMIT II</th>
<th>Roche CEDIA DAU</th>
<th>BIOSITE Triage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>300</td>
<td>300</td>
<td>300</td>
<td>300</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>100</td>
<td>300</td>
<td>364</td>
<td>300</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>1000</td>
<td>5,388</td>
<td>10,000</td>
<td>20,000</td>
</tr>
</tbody>
</table>

The Clinical Toxicology Laboratory, AACC Press, 2003, pp. 491-2
Summary Point 1:

Failure to detect an expected drug should stimulate investigation of the test, the drug, the patient, and the sample.
Interpretation consideration:

Unexpected positive results
Reasons for a positive result

Appropriate drug was taken
Appropriate drug was added directly to the urine
Distribution of free buprenorphine

n=885
February 2010 – 2011

~90% < 32 ng/mL

Was drug added directly to the urine?
Adulteration possible?

- 2 mg buprenorphine (tablet):

\[
\frac{2,000,000 \text{ ng}}{100 \text{ mL}} = 20,000 \text{ ng/mL buprenorphine}
\]

- 0.5 mg naloxone companion (Suboxone):

\[
\frac{500,000 \text{ ng}}{100 \text{ mL}} = 5,000 \text{ ng/mL naloxone}
\]
Patient results suggest adulteration

<table>
<thead>
<tr>
<th></th>
<th>BUP (ng/mL)</th>
<th>NORBUP (ng/mL)</th>
<th>Naloxone (ng/mL)</th>
<th>BUP:Naloxone Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>39,400</td>
<td>24</td>
<td>6,690</td>
<td>5.9</td>
</tr>
<tr>
<td>2</td>
<td>39,200</td>
<td>36</td>
<td>9,560</td>
<td>4.1</td>
</tr>
<tr>
<td>3</td>
<td>31,100</td>
<td>20</td>
<td>8,500</td>
<td>3.7</td>
</tr>
<tr>
<td>4</td>
<td>20,200</td>
<td>23</td>
<td>5,160</td>
<td>3.9</td>
</tr>
<tr>
<td>5</td>
<td>19,300</td>
<td>11</td>
<td>4,470</td>
<td>4.3</td>
</tr>
<tr>
<td>6</td>
<td>18,800</td>
<td>31</td>
<td>4,430</td>
<td>4.2</td>
</tr>
<tr>
<td>7</td>
<td>15,000</td>
<td>7</td>
<td>2,300</td>
<td>6.5</td>
</tr>
<tr>
<td>8</td>
<td>12,100</td>
<td>14</td>
<td>3,110</td>
<td>3.9</td>
</tr>
<tr>
<td>9</td>
<td>11,100</td>
<td>12</td>
<td>2,920</td>
<td>3.8</td>
</tr>
<tr>
<td>10</td>
<td>10,900</td>
<td>7</td>
<td>3,010</td>
<td>3.6</td>
</tr>
</tbody>
</table>

NOTES:

Glucuronides were < 20 ng/mL

Expected ratio of BUP:Naloxone for Suboxone® = 4

Average ratio of BUP:Naloxone for these patients: 4.4
Reasons for a positive result

Appropriate drug was taken
Appropriate drug was added directly to the urine
Inappropriate use of unprescribed drug
Past prescription and time since drug discontinuation insufficient for elimination
Prescription obtained from another clinic
Incorrect prescription was filled
Clinic or lab mixup
Test performed has poor specificity (false positive)
Drug detected is a metabolite of prescribed drug
Simplified opioid metabolism

- Codeine → Morphine → 6-Monoacetyl morphine (6-AM)
- Hydrocodone → Hydromorphone

*Poppy seeds* not specifically detected by most assays

*Heroin* not specifically detected by most assays
Interpreting concentrations

**Patient results**

- 2033 ng/mL Morphine
- 15 ng/mL Hydromorphone

**Metabolic ratios**

Hydromorphone: Morphine

- Morphine is metabolized to hydromorphone (minor pathway); usually <3%
- Thresholds for independent use of hydromorphone are not well established, but >1:1 is very suggestive

Simplified benzodiazepine metabolism

- demoxepam
- halazepam
- chlorazepate
- prazepam
- chlordiazepoxide

- ketazolam
- medazepam

- nordiazepam
- diazepam

- oxazepam
- temazepam
Reasons for a positive result

Appropriate drug was taken
Appropriate drug was added directly to the urine
Inappropriate use of unprescribed drug
Past prescription and time since drug discontinuation insufficient for elimination
Prescription obtained from another clinic
Incorrect prescription was filled
Clinic or lab mixup
Test performed has poor specificity (false positive)
Drug detected is a metabolite of prescribed drug
Drug detected represents a process impurity
### Patient results

- 2033 ng/mL Morphine
- 15 ng/mL Hydromorphone
- 5 ng/mL Codeine

### Process Impurity?

- Codeine is not a metabolite of morphine or hydromorphone
- Codeine can be an impurity in some morphine preparations; up to 0.5% is allowed

*West et al, TDM 31(6):776-8, 2009*
### Opioid process impurities

<table>
<thead>
<tr>
<th>Active pharmaceutical compound</th>
<th>Process impurities</th>
<th>Allowable pharmaceutical impurity limit (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Codeine</td>
<td>Morphine</td>
<td>0.15</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>Codeine</td>
<td>0.15</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>Morphine, Hydrocodone</td>
<td>0.15, 0.1</td>
</tr>
<tr>
<td>Morphine</td>
<td>Codeine</td>
<td>0.5</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>Hydrocodone</td>
<td>1.0</td>
</tr>
<tr>
<td>Oxymorphone</td>
<td>Hydromorphone, Oxycodone</td>
<td>0.15, 0.5</td>
</tr>
</tbody>
</table>

MRO Alert XXI, No. 3, 2010
Summary Point 2:
Detection of an unexpected drug should stimulate investigation of the test, the drug, the patient, and the sample
Interpretation consideration:

Drug adherence versus dose and dosing adherence
UDT cannot reliably evaluate dosing

- Dose delivery may vary with formulation
- Pharmacokinetics will vary by patient
- Time of specimen collection vs drug dosing is usually NA
  - Drug administration may or may not be timed
  - UDT specimens are not usually timed (prior + collected void)
- Urine varies based on hydration status, other medications, renal function, urine pH, etc.
- Not all drug is eliminated in urine
- UDT is based primarily on measurement of drug metabolites which can arise from more than one drug
- Routine/chronic administration of a drug affects the amount of drug and drug metabolites observed in the urine
- Laboratory methods vary
Free vs Total: laboratory tests differ

- Free drug concentrations reflect the concentrations observed of non-glucuronidated compound.
- Total drug concentrations in urine reflect the concentrations observed after cleaving glucuronide conjugates through hydrolysis:
  - Enzymatic
  - Chemical

- Patient variation in proportion of metabolites is known.
- Changes in proportion of metabolites occurs over time.
- Glucuronide metabolites may not be stable in vitro.
- Efficiency of hydrolysis reactions varies.
### Expected urine findings

<table>
<thead>
<tr>
<th>Parent drug</th>
<th>% of a dose eliminated in the urine within 72 hrs</th>
<th>% of a dose eliminated as FREE parent drug</th>
<th>% of a dose eliminated as glucuronide conjugate of parent drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>~87%</td>
<td>~10%</td>
<td>~75%</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>~26%</td>
<td>~12%</td>
<td>NA</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>~50%</td>
<td>~6%</td>
<td>~30%</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>~72%</td>
<td>~5%</td>
<td>NA</td>
</tr>
<tr>
<td>Oxymorphone</td>
<td>~49%</td>
<td>~2%</td>
<td>~44%</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>~27%</td>
<td>~1%</td>
<td>~9.4%</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>~85%</td>
<td>~6%</td>
<td>NA</td>
</tr>
</tbody>
</table>

Baselt RC, *Disposition of Toxic Drugs and Chemicals in Man*, 8th Ed, 2008
### Hydrolysis efficiency for morphine

<table>
<thead>
<tr>
<th>Morphine Metabolite</th>
<th>Chemical (acid)</th>
<th>Enzyme (P. vulgata, 2 hrs)</th>
<th>Enzyme (H. pomatia, 16 hrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine-3-glucuronide</td>
<td>100 ± 4</td>
<td>94 ± 2</td>
<td>50 ± 13</td>
</tr>
<tr>
<td>Morphine-6-glucuronide</td>
<td>98 ± 5</td>
<td>12 ± 1</td>
<td>0 ± 0</td>
</tr>
<tr>
<td>Patient urine</td>
<td>100 ± 0</td>
<td>64 ± 19</td>
<td>35 ± 20</td>
</tr>
</tbody>
</table>

Percent (%) recovery of opioids using different hydrolysis methods

### Urine concentrations with Duragesic®

<table>
<thead>
<tr>
<th></th>
<th>25 µg/h</th>
<th>50 µg/h</th>
<th>75 µg/h</th>
<th>100 µg/h</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fentanyl</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (ng/mL)</td>
<td>32</td>
<td>58</td>
<td>95</td>
<td>79</td>
</tr>
<tr>
<td>Range of central 90%</td>
<td>0-167</td>
<td>0-250</td>
<td>4-444</td>
<td>0-350</td>
</tr>
<tr>
<td><strong>Norfentanyl</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (ng/mL)</td>
<td>173</td>
<td>251</td>
<td>285</td>
<td>327</td>
</tr>
<tr>
<td>Range of central 90%</td>
<td>0-980</td>
<td>0-860</td>
<td>4-1330</td>
<td>0-1670</td>
</tr>
<tr>
<td>Number of samples</td>
<td>142</td>
<td>184</td>
<td>85</td>
<td>135</td>
</tr>
</tbody>
</table>

Poklis and Backer, JAT 28:422-5, 2004
Timed blood testing may help

- **Fentanyl pharmacokinetic highlights**
  - Absorption varies with application site, body temperature, etc
  - Drug delivery rate varies with product
  - Time to peak (Cmax), 24-72 hrs after administration
  - Half-life, 13-22 hrs
  - CYP3A4 substrate

- **Blood is the preferred specimen for dose assessments and pharmacokinetic studies**

http://www.rxlist.com/duragesic-drug.htm
Summary Point 3:

UDT cannot reliably determine the dose taken, or the frequency at which a dose was taken
Conclusions

- UDT offers many useful opportunities to identify and evaluate patient drug use
- Testing technologies and frequency of testing should be aligned with clinical needs/expectations
- Results should be interpreted in the context of the test, drug(s), patient, and sample(s) tested
- Unexpected positive or negative results should be discussed with the patient, and confirmed if needed
- Dose and dosing of a drug cannot be reliably determined by UDT
- Testing alternative specimens may be appropriate