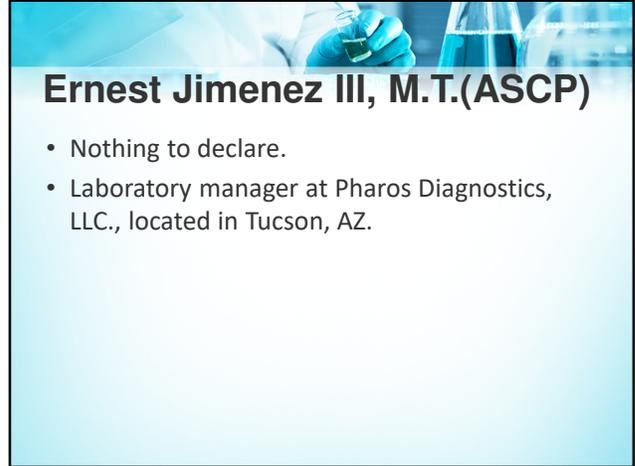




## Pain Management Drug Testing: A Laboratory Perspective

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- Nothing to declare.
- Laboratory manager at Pharos Diagnostics, LLC., located in Tucson, AZ.

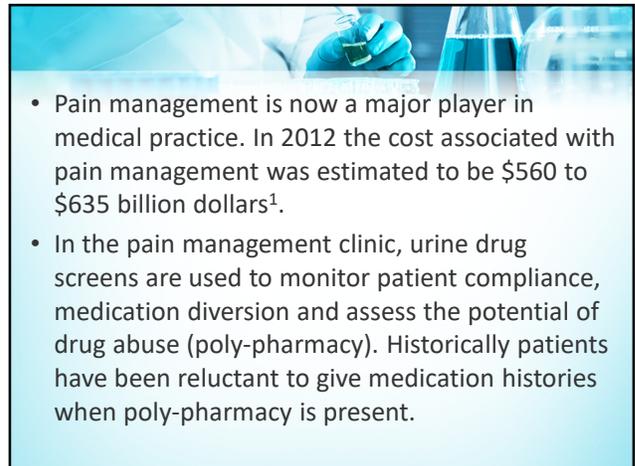
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#### Pain Management Drug Testing: A laboratory perspective:

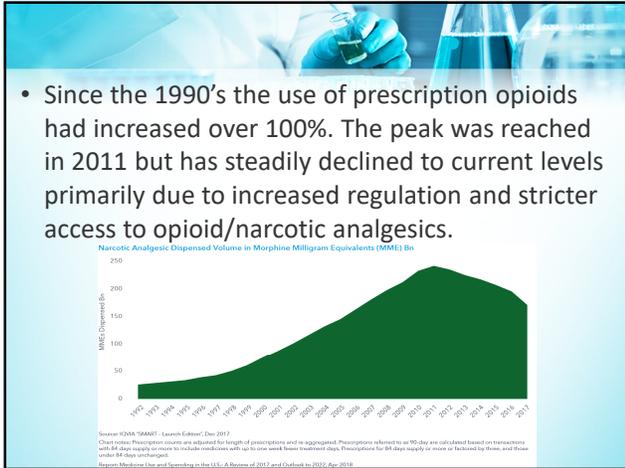
- a. This session will discuss the value of urine drug testing in pain management from the perspective of the clinical laboratory. Focusing on providing accurate and precise data from clinical laboratory studies will assist the pain management clinic to maintain excellent patient care.
- b. The limitations associated with routine urine drug screening and confirmations will be discussed
- c. Careful planning by the clinical laboratory and pain management clinic can provide a successful partnership

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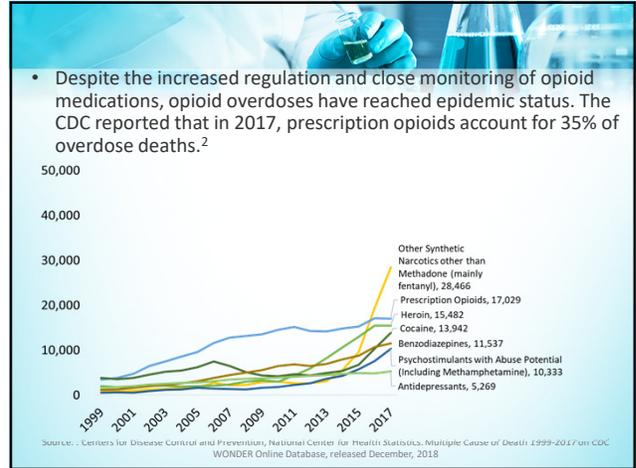


- Pain management is now a major player in medical practice. In 2012 the cost associated with pain management was estimated to be \$560 to \$635 billion dollars<sup>1</sup>.
- In the pain management clinic, urine drug screens are used to monitor patient compliance, medication diversion and assess the potential of drug abuse (poly-pharmacy). Historically patients have been reluctant to give medication histories when poly-pharmacy is present.

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- Given the complex nature of pain and its management, how can the clinical laboratory assist in providing excellent patient care and ultimately respond to the current opioid healthcare crisis?
  - Partner with pain clinics to provide UDT (urine drug testing) services for “risk mitigation” in the care of the chronic pain patient.
  - Provide consultation services on the collection of specimens, testing limitations of UDT and interpretation of UDT results.

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- Traditionally, laboratories have followed a “forensic model” when testing for drugs. Pain management drug testing does not follow this model. Testing tends to be highly tailored to meet client/patient needs.
- Urine drug testing in the pain management sphere focuses primarily on the detection of drugs as part of patient care. Focus is on the need to detect or not detect the prescribed drug and whether the patient is using any other drug that has not been prescribed by the clinician (this could include illicit drugs).

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- Testing track:
  1. Urine is collected, then sent to the laboratory. The laboratory accesses the specimen and proceeds to the analysis.
  2. The specimen is screened by an immunoassay and all positive findings are confirmed by GC/MS or LC-MS. In some cases negative results will need to be confirmed for non-compliance.
  3. Results are generated and reported.
  4. Easy??? Not really...

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- The Laboratory's Role:
  1. Provide diagnostic services, e.g., specimen validity testing, immunoassays, mass spectrometry, technical consultation
  2. Specimen validity testing should include: specific gravity, creatinine levels, pH
  3. Immunoassays (IA) – used to screen classes of drugs
    - a. EMIT
    - b. KIMS
    - c. CEDIA
    - d. ELISA
  3. Mass spectrometry – used to confirm IA results
    - a. GC/MS (gas chromatography with mass spectrometry)
    - b. LC-MS/MS (HPLC with tandem mass spectrometry)
  4. Provide guidance in designing drug testing panels.

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- How should laboratories establish testing services when there are literally hundreds of drugs available for patients? Focus on key drugs and drug classes.
- Drug or drug classes analyzed: amphetamines, barbiturates, benzodiazepines, cocaine, THC, opiates for screens. Followed by targeted analysis on the mass spectrometer for prescribed or non-prescribed medications.
- Following the three tiered system of panel testing as recommended by the ACC's Academy Laboratory Medicine Practice Guidelines, "Using Clinical Laboratory Test to Monitor Drug Therapy in Pain Management Patients"<sup>3</sup>.

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### Three Tiered System of Drug Testing

- Tier I : routine monitoring for amphetamines, barbiturates, benzodiazepines, Cannabinoids, Cocaine and Opiates/Opioids
- Tier II: High Risk Patients with known history of drug abuse. Include Tier I drugs plus alcohol, anticonvulsants, antidepressants, synthetic cathinones, dissociative anesthetics, hallucinogens, muscle relaxants.
- Tier III: only as clinically indicated. All of Tier I and II drugs plus "OTC" analgesics, antihistamines, antipsychotics and synthetic cannabinoids.

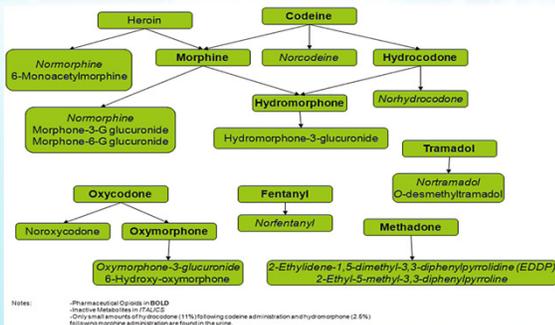
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### Immunoassays: Pros and Cons

- Readily available for any clinical chemistry analyzer
- Qualitative or semi-quantitative results. Should be reported as "detected" or "not detected". Positive vs. Negative can give a false sense of security.
- Improved detection limits, by validating at lower cut-off values than normally used in regular toxicology screens. If modified it must be validated
- Limited in the substances detected. General rule is the immunoassay will detect classes of drugs not specific drugs. Interference can occur, resulting in false positive and false negative results
- If possible leave the POCT devices in the clinic.

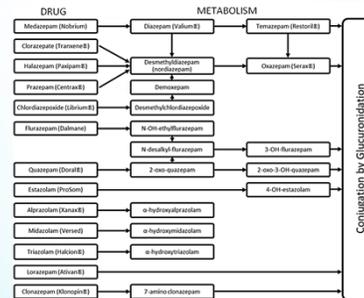
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#### Opiate and Opioid Metabolic pathways



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#### Benzodiazepine Metabolism Chart



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### Targeted or Confirmatory Testing

- Methodologies: Gas Chromatography/Mass Spectrometry (GC/MS) and Liquid Chromatography with Mass Spectrometry (LC/MS)
- Very specific and sensitive methodologies. With the caveat that the methods are highly variable and all considered laboratory developed test (LDT)
- Can be very expensive to purchase, operate and maintain. Require highly skilled laboratory personnel.
- Confirmation studies include detection/identification and quantitation of parent drug and metabolite(s)

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### Mass Spec Technologies

- Very specific for analyte identification, utilization of chromatography to separate mixtures of compounds, measures mass/charge ( $m/z$ ) of molecules in conjunction with molecular ion production for identification.
- GC/MS is usually single quad technology. Require analyte derivatization for analysis and operate on high temperatures.
- LC-MS/MS will use liquid chromatography in conjunction with triple quad technology to analyze samples. This is now the preferred method of confirmation because of the sensitivity of the instrumentation. Does not require derivatization for analysis. Great for heat labile compounds.

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### Mass Spectrometry: The Good, The Bad and The Ugly

- The Good: very sensitive, can usually detect compounds in the ng/mL or pg/mL levels. Able to use multiplex analysis for numerous compounds in one run to provide a broad spectrum analysis.
- The Bad: expensive equipment, standards, and expensive to operate. Requires highly trained personnel for the analysis to be complete.
- The Ugly: all mass spec analysis are LDT's. There is a lack of uniformity throughout the country. Not fool-proof. Analysis is highly dependent upon correct analysis of data generated

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### Reporting and Interpretation of Results

- Develop professional relationships with pain management clinicians and pharmacologist. Use a team effort for development of testing panels and distribution of results.
- Stick to the facts. Follow national reporting guidelines and recommendations. Provide as much information on the laboratory report as possible without information overload.
- Know the technical limitations of your analysis and clearly state those limits, e.g., cut-offs are clearly documented, list drugs detected by class in immunoassays, document whether or not the drug was confirmed, state whether or not the analysis utilizes hydrolysis for the detection of drugs

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- Require that patients who are being monitored for compliance submit a medication list with the requisition.
- Compare the drug list with the findings of your analysis. If the results are consistent with the medication list, the testing is complete. If there is a discrepancy document it on the report. Use factual data statements only.
- Understand basic pharmacogenomics when interpreting results that appear discordant. Take into consideration that the FDA does allow for some impurities to exist in narcotic formulations. Have specimen validity checks passed. Is there any possibility sample tampering?

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- Common pitfalls:
  - Too much information, followed by not enough information. Report format should be carefully coordinate with the provider to be meaningful
  - Not understanding the limitations of your instrumentation and technology
  - Not avoiding the “It’s easy to fire up a toxicology service” pep talk
  - Be prepared to have a relatively slow ROI. Not understanding the economics of developing a pain management service. Billing and compliance problems are major factors contributing to unsuccessful services.
  - Infrastructure, infrastructure, infrastructure. There exist the possibility that enormous amounts of data will be generated from the drug testing panel. Be prepared to make adjustments to the LIMS, EHR, and other patient/healthcare IT.

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### References and Resources:

1. IOM (Institute of Medicine). 2011. Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research. Washington, DC: The National Academies Press
2. National Vital Statistics Reports, Vol. 67, No. 9, December 12, 2018.
3. AACC Academy: Laboratory Medicine Practice Guidelines. 2017. *Using Clinical Laboratory Tests to Monitor Drug Therapy in Pain Management Patients*.
4. CLSI. Laboratory Support for Pain Management Programs. 1<sup>st</sup> ed. CLSI guideline C63. Wayne, PA: Clinical and Laboratory Standards Institute; 2018

**Resources:**

1. The Journal of Applied Laboratory Medicine. January 2018; volume 2, issue 4
2. <https://www.aruplab.com/pain-management>
3. [https://www.labce.com/toxicology\\_laboratory\\_pain\\_management.aspx](https://www.labce.com/toxicology_laboratory_pain_management.aspx)
4. <https://www.drugabuse.gov/sites/default/files/files/UrineDrugTesting.pdf>
5. <https://www.aacc.org/science-and-practice/practice-guidelines/using-clinical-laboratory-tests-to-monitor-drug-therapy-in-pain-management-patients>

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