Laboratory Perspective on Additional Drug Testing and Associated Costs

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This presentation was modified from its original format for 508 compliancy.

MEDTOX

- MEDTOX is a clinical and forensic reference laboratory in St. Paul, MN
- Provides drugs of abuse testing services for regulated and non-regulated workplaces, medical professionals, pain clinics and criminal justice clients

Scope of Testing

- How testing is performed within the laboratory varies depending on the scope of the panel requested
- Test panels range from discrete 5 – 10 panel immunoassays with chromatographic confirmation to comprehensive screens utilizing multiple methodologies to incorporate a wide range of prescription and non-prescription compounds

Approaches to Testing for Additional Compounds

- Non-regulated workplace
  - Standard homogeneous immunoassay tests: barbiturates, benzodiazepines, opiates, oxycodone, methadone, propoxyphene
  - GCMS and/or LCMSMS confirmations
  - Confirmation components vary; may ‘expand’ to include additional compounds
  - Added costs primarily due to instrument overhead (both cost and usage)

Instrument Utilization/Overhead

- THC, BE, Amphetamines, Opiate 2000, PCP cycle times:
  - 5 - 8 min/sample
  - GCMS instrumentation
- Barbiturates, Benzodiazepines, Expanded Amphetamines cycle times:
  - 25 – 50% longer
  - Benzos confirmed by LCMSMS
- Expanded opiates
  - GCMS – 2 – 3x longer
  - LCMSMS – reduced run time, added equipment cost

Approaches to Testing for Additional Compounds

- Professional Panels, Pain Management
  - Screens include standard IA tests, expanded confirms by GCMS and LCMSMS
  - Additional esoteric compounds; many require ELISA or chromatographic screens
  - Additional costs incurred in instrument overhead, labor and reagent costs
- Tiered approach for pricing
  - Tier 1: homogeneous immunoassays
  - Tier 2: Tier one plus ELISAs (cost/test 5 – 10x depending on reagent)
  - Tier 3: Tiers 1 and 2 plus chromatographic screen ($$$$)

Additional Considerations

- Many of the ELISAS available for screening are not FDA-cleared
  - Home brew validations; additional laboratory workload
- Newer homogeneous tests tend to be more expensive than standard tests
- Comprehensive chromatographic screens have extended run times and data review is labor-intensive

Laboratory strategies to integrate esoteric panels into routine workflow

- Utilize homogeneous immunoassays with applications on automated analyzers when available
- Automate ELISAS
- Combine discrete assays into larger panels when possible (+/-)

Laboratory strategies to integrate esoteric panels into routine workflow

- Utilize more advanced instrumentation to minimize sample preparation, reduce run times
  - Many compounds are amenable to LCMSMS analysis
    - Instruments are costly
  - Newer HPLC technology (UPLC) can significantly reduce run times
    - Columns are expensive
    - Not as straightforward for operators

MEDTOX Workplace Testing Demographics

- 30% regulated; 70% non-regulated
- Of the non-regulated customer group, 50 - 60% test for compounds beyond the standard 5 panel
- Barbiturates, Benzodiazepines, Methadone, Propoxyphene: 0.5 – 1% positive rate

Distribution of Barbiturate and Benzodiazepine Positives

- Benzodiazepines detected 2007-2008

Drug	% of Total
Alprazolam	11.4
α-Hydroxyalprozolam	21.2
Lorazepam	2.1
Oxazepam	27.7
Temazepam	23.5
Desmethyldiazepam	14.1
Clonazepam	0
Dealkylfluazepam	0
Diazepam	0.02

- Barbiturates detected 2007-2008

Drug	% of Total
Amobarbital	0.2
Butabarbital	0.2
Butalbital	70.2
Pentobarbital	0.1
Phenobarbital	29.0
Secobarbital	0.5

Results of Non-Regulated Drug Screens

- Opiates
  - 65% of non-regulated screens mimic the DHHS panel (screen @ 2000, confirm for codeine/morphine/6-AM)
    - 0.4% positive rate
  - 35% of non-regulated screens include expanded panel
    - 1.6% positive rate
  - 10% of non-regulated screens include directed oxycodone screen
    - 1.7% positive rate

Opiate Incidence – Opiate Screen with Expanded Confirmation

- Opiates detected (expanded)

Drug	**% of Total**
Hydrocodone	32.8
Hydromorphone	26.3
Morphine	21.2
Codeine	11.9
Oxymorphone	3.3
Oxycodone	2.5
6-Acetylmorphine	2.0

Screening Medical Professionals

- Distribution of Positives

Drug	**% of Total**
Amphetamines	7.2%
Barbiturates	9.6%
Benzodiazepines	19.2%
Cocaine	0.6%
Narcotic Analgesics	55.7%
Marijuana	7.8%

Distribution of Narcotic Analgesic Positives

- Medical Professionals: narcotic analgesic positives

Drug	**% of Total**
Hydrocodone	26.3
Propoxyphene	21.2
Hydromorphone	17.8
Oxymorphone	9.3
Morphine	6.8
Oxycodone	6.8
Tramadol	5.9
Codeine	2.5
Methadone	2.5
Buprenorphine	0.8

Pain Management

- Additional nuances in testing requirements
  - Physicians are interested in both what patients are taking and what they are not taking
  - Comprehensive screens can identify several hundred prescription and non-prescription compounds
  - Methodology includes IA, GCMS, LCMSMS

Comprehensive Screening for Pain Management

- Pain Clinic Positives

Drug	% of Total
Oxycodone/oxymorphone	11.8
Benzodiazepines	11.3
Acetaminophen	10.9
Hydrocodone	6.2
THC metabolite	5.7
Morphine	4.1
Hydromorphone	3.5
Diphenhydramine	3.2
Methadone	2.4
Citalopram	2.2
Tramadol and metabolite	2.2
Propoxyphene	2.0

Drug	% of Total
Venlafaxine and metabolite	1.7
Metoprolol	1.4
Naproxen	1.4
Fentanyl	1.2
Carisoprodol/meprobamate	1.2
Bupropion and metabolite	1.2
Salicylate	1.2
Nortriptyline	1.2
Ethyl alcohol	1.1
Cabapentin	1.1
Cycobenzaprine	1.0
Sertraline	1.0

Criminal Justice Supplemental Comprehensive Screen

- Included categories:
  - Narcotics/Opiates
  - Muscle Relaxants
  - Sedatives/Hypnotic
  - Antihistamines
  - Stimulants
  - Antidepressants
  - Anticholinergics
  - Anticonvulsants
- Methodology
  - Comprehensive chromatographic drug screen (ion trap)
  - Various confirmation methodologies (ELISA, GCMS, LCMSMS)

Supplemental Screen Results

- Narcotics/Opiates
  - Butorphanol
  - Dextromethorphan
  - Fentanyl
  - Levorphanol
  - Meperidine
  - Pentazocine
  - Propoxyphene
  - Tramadol**
- Muscle Relaxants
  - Carisoprodol
  - Cyclobenzaprine
- Sedatives/Hypnotics
  - Butalbital
  - Eszopiclone
  - Ketamine
  - Scoplamine
  - Zaleplon
  - Zolpidem

Supplemental Screen Results

- Antihistamines
  - Brompheniramine
  - Chlorpheniramine
  - Diphenhydramine*
  - Hydroxyzine
  - Promethazine
  - Pyrilamine
- Stimulants
  - Caffeine
  - Methylphenidate
- Antidepressants
  - Buproprion
  - Isocarboxazid
- Anticholinergics
  - Atropine
- Anticonvulsants
  - Gabapentin

Summary

- Additional compounds add complexity to the testing process
- A variety of methodologies are required to screen and confirm more esoteric compounds
- Laboratories incur added costs in reagent and instrumentation costs, instrument overhead and labor

Summary

- Laboratories with limited resources may not perform these tests
- Expanded panels have different detection profiles (if you build it, they will come)
- MRO interpretation key