

All the Right Technology in All the Right Places:

The Necessary Evolution of Urine Drug Testing

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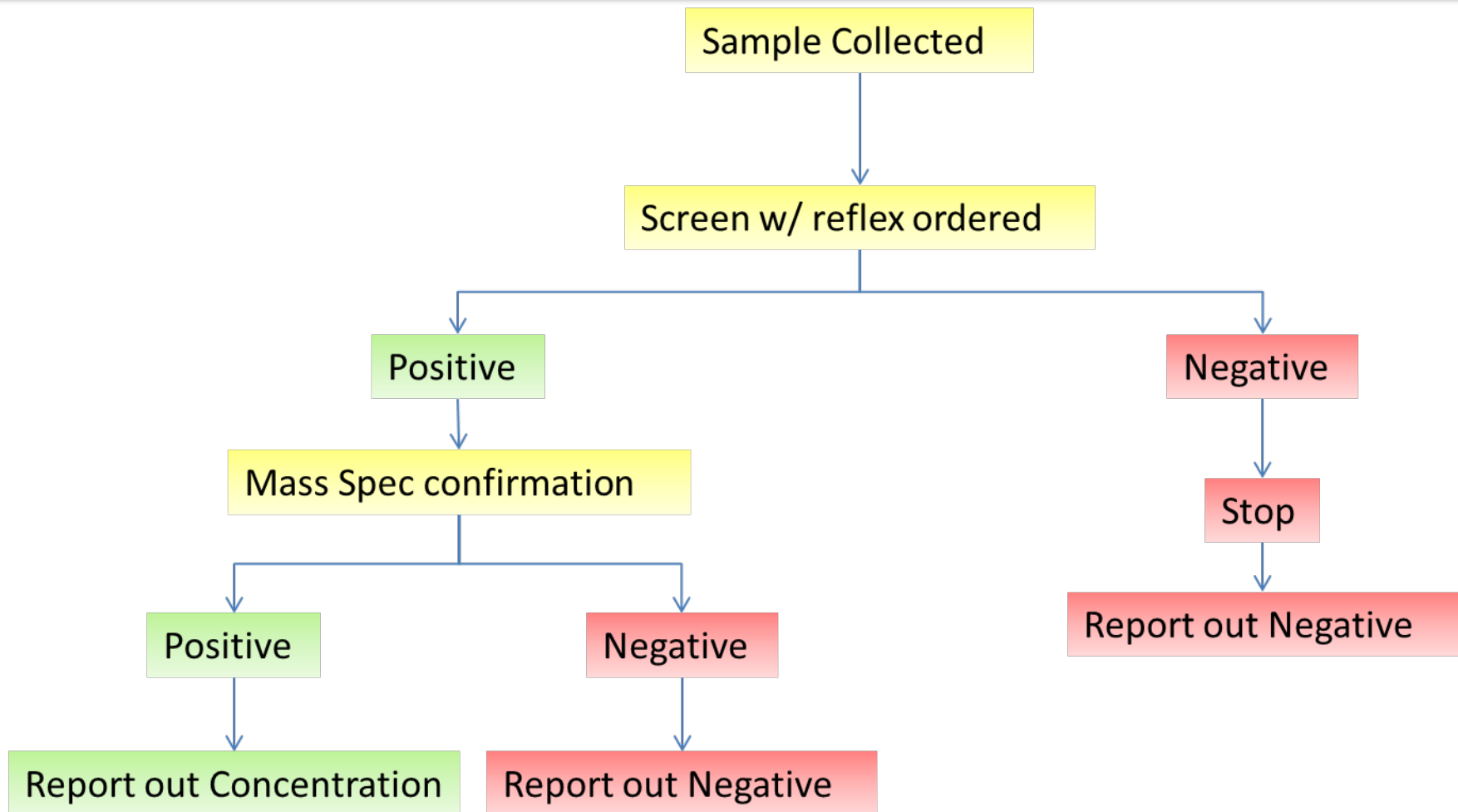
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AACC Annual Meeting (August 2nd, 2016)

Current State of Urine Toxicology Testing

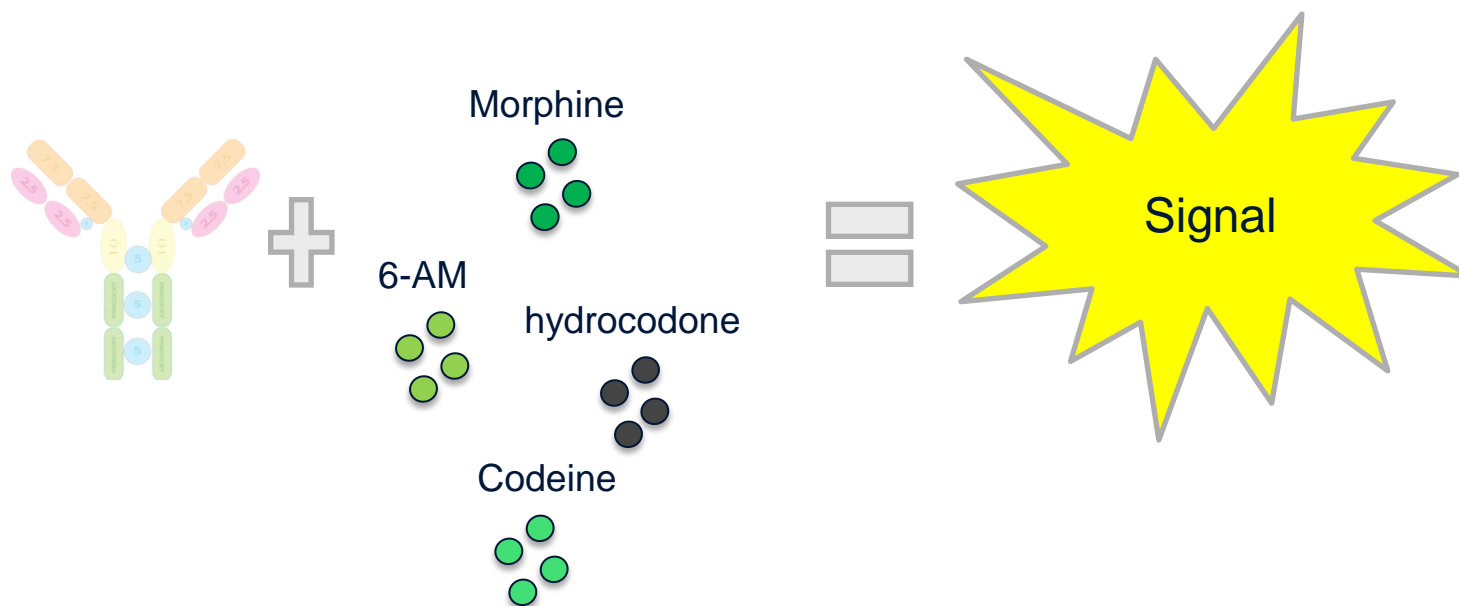
- Immunoassay screen only
 - Immunoassay screen with reflex to confirmation by LC/GC MS
 - Direct to GC/LC-MS
 - Hybrid (IA + LC-MS without “confirmation”)
-
- Immunoassays
 - Quadrupole
 - Time-of-Flight
 - Quadrupole + Time-of-Flight

Tried and True Workflow



Challenges with (some) IA Screens

- Presumptive screening method used
 - e.g., immunoassay for opiates



Interpretation:

Morphine only?

6-AM?

All of them?

None of them?

“You need this reflexed to confirmation.”

More Problems with Immunoassays

Table IV. Summary Results from Immunoassay Screens and Confirmatory Testing

	Immunoassay screens			Confirmation (tested when screen POS)				Confirmed POS Specimens			
	Total tested (#)	Pos (#)	Pos (%)	Confirm pos (#)	Confirm neg (#)	True pos (%)	False pos (%)	Males (#)	Females (#)	Males (%)	Females (%)
AMPH ^a	8,825	705	8.0	608	97	86.2	13.8	263	345	43.3	56.7
BARB	8,825	163	1.9	159	4	97.5	2.5	54	105	34.0	66.0
BENZO	8,825	1,130	12.8	1,125	5	99.6	0.4	480 ^b	653 ^b	42.4	57.6
COC	8,825	237	2.7	237	0	100.0	0.0	140	97	59.1	40.9
ETOH	2,296	35	1.5	35	0	100.0	0.0	16	19	45.7	54.3
MDMA ^a	8,825	174	2.0	0	174	0.0	100	0	0	–	–
MTD	8,825	262	3.0	262	0	100.0	0.0	98	164	37.4	62.6
OPI ^c	8,825	2,642	29.9	1,744	898	66.0	34.0	820	924	47.0	53.0
OXY ^c	8,825	1,215	13.8	1,192	23	98.1	1.9	601 ^c	684 ^c	46.8	53.2
PCP	8,825	4	0.05	0	4	0.0	100	0	0	–	–
PPXY	8,825	4	0.05	3	1	75.0	25.0	2	1	66.7	33.3
THC	8,825	1,793	20.3	1,777	16	99.1	0.9	906	871	51.0	49.0
Totals	99,371	8,364	8.4%	7,142	1,222	85.4%	14.6%	3,380	3,863		

Johnson-Davis et al. (2016). *Journal of Analytical Toxicology* **40**(2), 97-107.

Panels – One Size Doesn't Fit All

Panel 1

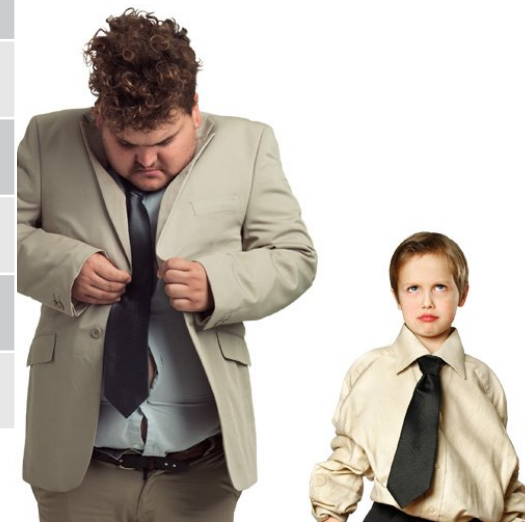
Marijuana
Cocaine
Opiates
Oxycodone
Phencyclidine
Amphetamines
MDMA (Ecstasy)
Barbiturates
Benzodiazepines
Methadone
Propoxyphene

Panel 2

Marijuana
Cocaine
Opiates
Ethanol
Phencyclidine
Amphetamines
Barbiturates
Benzodiazepines

Panel 3

Marijuana
Cocaine
Opiates
Phencyclidine
Amphetamines
MDMA (Ecstasy)
Barbiturates
Benzodiazepines
Methadone
Propoxyphene



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The Expanded Screen

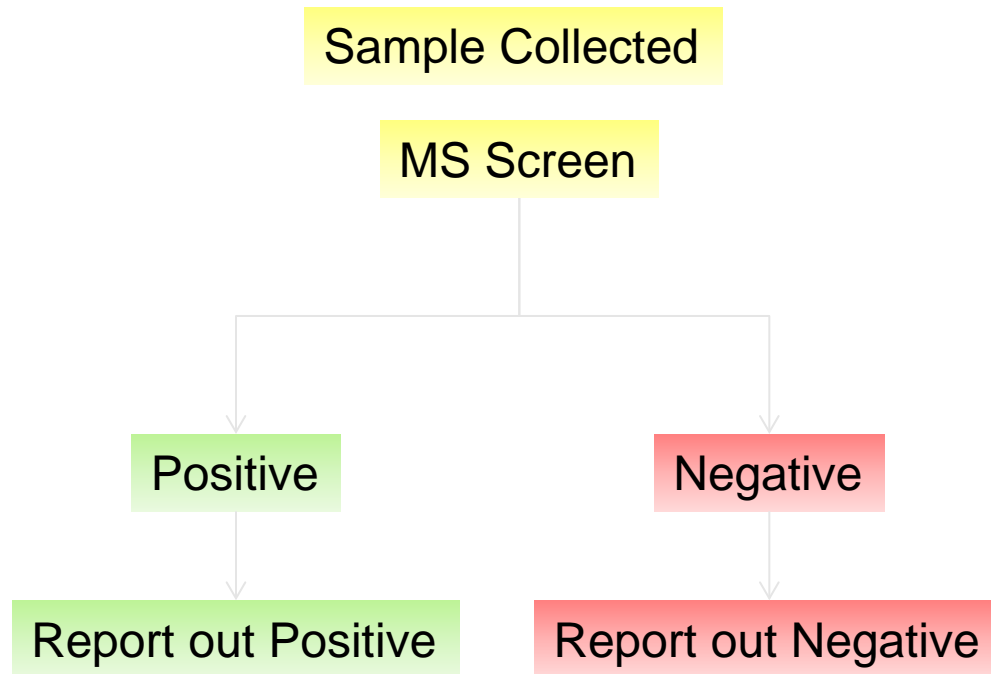
Something is (always) Missing

Drugs/Drug Classes
Amphetamines
Barbiturates
Benzodiazepines
Buprenorphine
Carisoprodol
Cocaine
Ethyl Glucuronide
Fentanyl
MDMA (Ecstasy)
Meperidine
Methadone
Opiates
Oxycodone
Phencyclidine
Propoxyphene
Tapentadol
Tramadol
THC (Cannabinoids)
Zolpidem

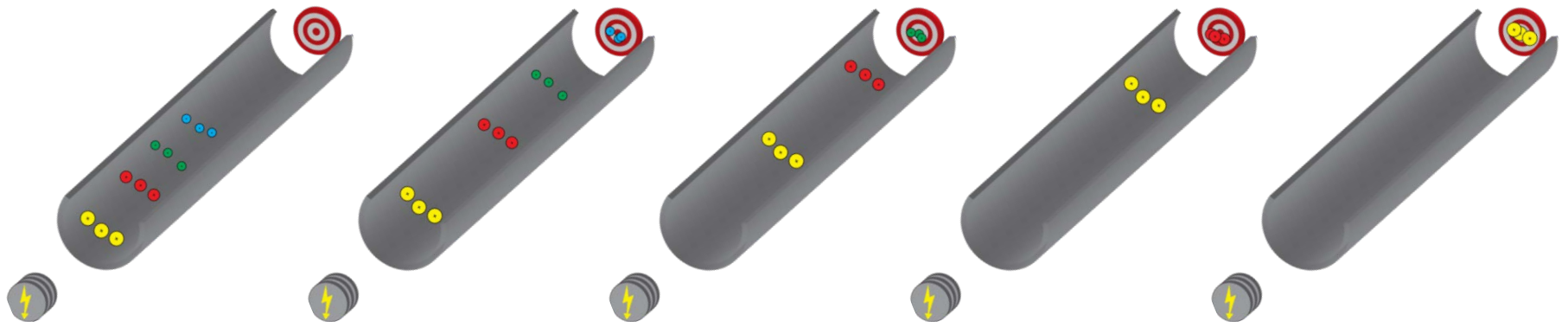
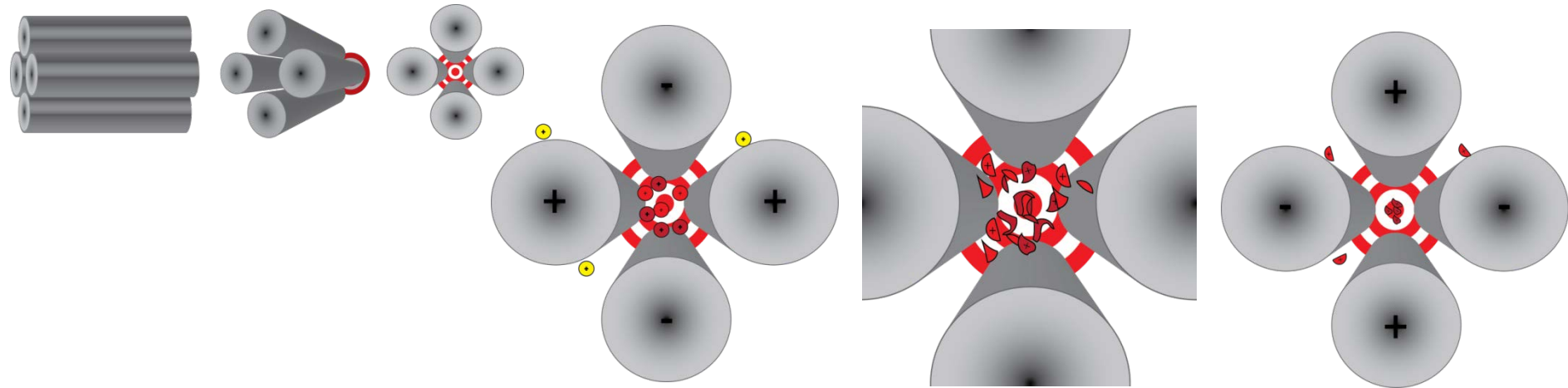


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Mass Spec-based Screen



MS: Quadrupoles and Flight Tubes



Benefits of a MS Screen

- Sensitivity & Specificity on par with classic “confirmatory” methods
- Individual compound/metabolite identification
- Elimination of cross-reactivity complications
- Drug/metabolite pairs for interpretations
- Drug abuse testing conducted concurrently for high risk populations
- Relatively easy integration of new targets
- If qualitative “Reflex to Quantitation” still possible when needed



[Pain Med.](#) 2016 Jul 17. pii: pnw165. [Epub ahead of print]

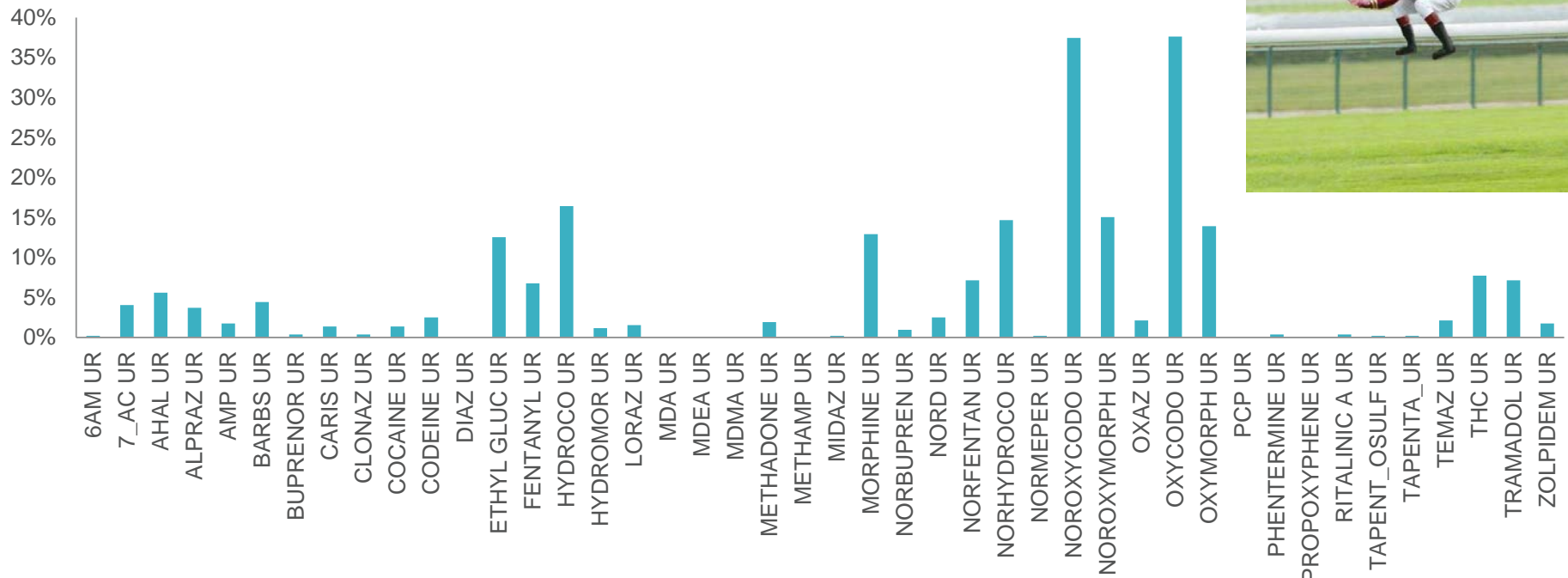
Cost and Efficacy Assessment of an Alternative Medication Compliance Urine Drug Testing Strategy.

[Doyle K¹](#), [Strathmann FG²](#).

[Author information](#)

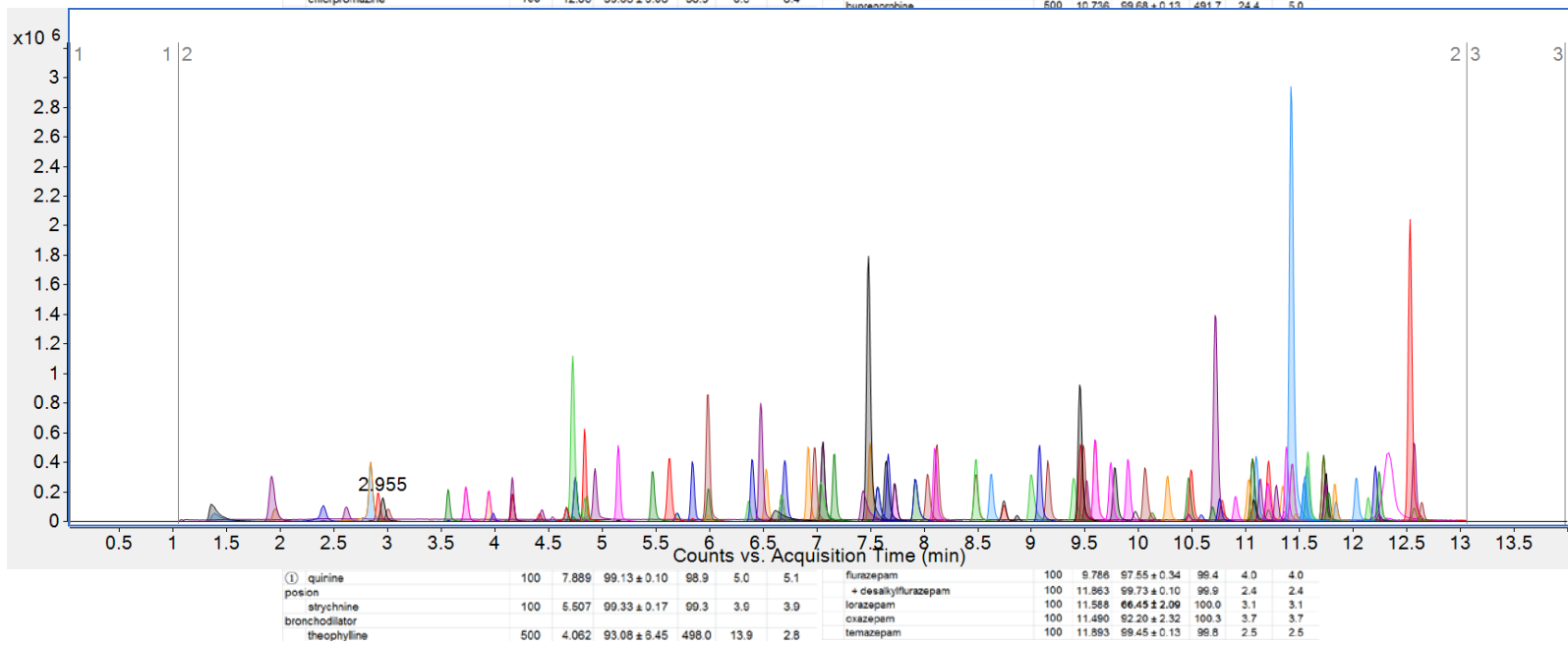
Panels – One Size Doesn't Fit All

Positivity Rate



One Size Fits All. Not the Right Answer.

Drug Name + metabolite(s) / Isobaric pairs	Cutoff (ng/ml)	RT (min)	Mass Match Score Cal (N = 4)	Inter-assay Precision 5 Days, 4 Replicates Cal (N = 20)	Mean ± SD	Mean ± SD	%CV
antidepressant							
amitriptyline	100	11.466	99.43 ± 0.05	99.0	4.7	4.8	
bupropion	100	8.078	98.83 ± 0.10	100.1	2.4	2.4	
citalopram	100	9.513	98.28 ± 0.40	100.0	1.6	1.6	
clomipramine	100	12.269	99.18 ± 0.28	98.9	7.3	7.4	
desipramine	100	11.257	99.43 ± 0.10	99.2	2.1	2.1	
doxepin (cis/trans)	100	9.837	99.60 ± 0.08	99.9	2.0	2.0	
+ nortdoxepin	100	9.958	98.50 ± 0.18	100.0	2.4	2.4	
duloxetine	500	11.390	98.93 ± 0.41	496.7	15.4	3.1	
fluoxetine (prozac)	100	11.857	99.15 ± 0.21	99.1	3.2	3.2	
+ norfluoxetine	500	11.879	98.23 ± 0.42	497.9	14.2	2.8	
imipramine	100	11.106	99.33 ± 0.15	99.3	3.5	3.6	
nortriptyline	100	7.644	99.35 ± 0.06	99.7	2.7	2.7	
nortriptyline	100	11.605	99.28 ± 0.22	98.9	3.1	3.1	
paroxetine	100	10.955	98.85 ± 0.45	98.5	5.1	5.2	
sertraline	100	12.170	99.10 ± 0.28	99.6	4.6	4.6	
trazodone	100	8.524	99.28 ± 0.17	100.5	3.5	3.5	
trimipramine	100	11.614	99.48 ± 0.22	99.2	4.4	4.4	
+ nortrimipramine	100	11.780	99.33 ± 0.17	99.3	2.6	2.6	
anti-psychotic							
chlorpromazine	100	12.06	99.65 ± 0.06	98.9	8.3	8.4	
Drug Name + metabolite(s) / Isobaric pairs							
Art-arrhythmic							
siltazem	100	10.535	98.63 ± 0.17	98.3	6.9	7.1	
lidocane	100	8.869	99.63 ± 0.10	100.1	1.8	1.8	
metoprolol	100	7.212	99.50 ± 0.36	99.9	1.6	1.6	
propranolol	100	9.216	99.35 ± 0.17	100.5	4.0	4.0	
quinidine	100	7.525	99.18 ± 0.25	99.0	4.3	4.4	
verapamil	100	10.801	92.33 ± 0.41	92.4	37.1	40.2	
+ norverapamil	100	10.742	91.73 ± 4.43	93.2	31.1	33.4	
Art-convulsant							
carbamazepine	100	10.811	98.28 ± 0.15	98.6	2.1	2.1	
+ carbamazepine-10, 11-epoxide	100	8.873	92.93 ± 0.29	100.7	5.4	5.4	
lamotrigine	100	6.768	99.68 ± 0.10	100.1	2.0	2.0	
phenytoin	500	3.077	86.08 ± 0.32	500.9	18.7	3.7	
valproic acid	500	3.907	99.73 ± 0.05	499.6	17.7	3.5	
Barbiturate							
butabital	500	2.938	98.63 ± 0.44	500.0	17.1	3.4	
phenobarbital	500	2.338	99.50 ± 0.22	500.6	17.5	3.5	
Opiate/opioids							
buprenorphine	500	10.736	99.68 ± 0.13	491.7	24.4	5.0	



What are we looking for from a workflow?

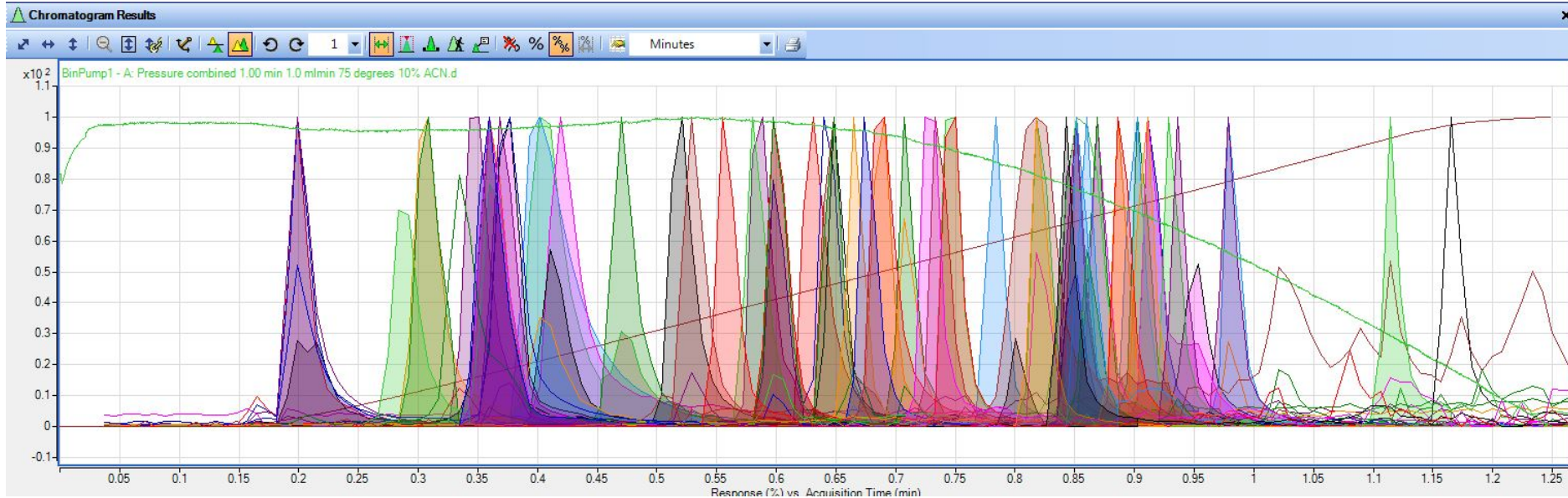
- Qualitative screen to rule out
 - Allows broad panel
 - Detect illicit drugs
 - Detect abuse
 - Sensitive/Specific
 - Cheap
 - Fast
 - Comprehensive
 - Easy (for the lab!)
- Quantitative confirmation
 - Sensitive/Specific
 - Metabolite ratios
 - Pharmaceutical impurities
 - D/L Ratios



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One Exciting New Possibility

LC-TOF Rapid Screen

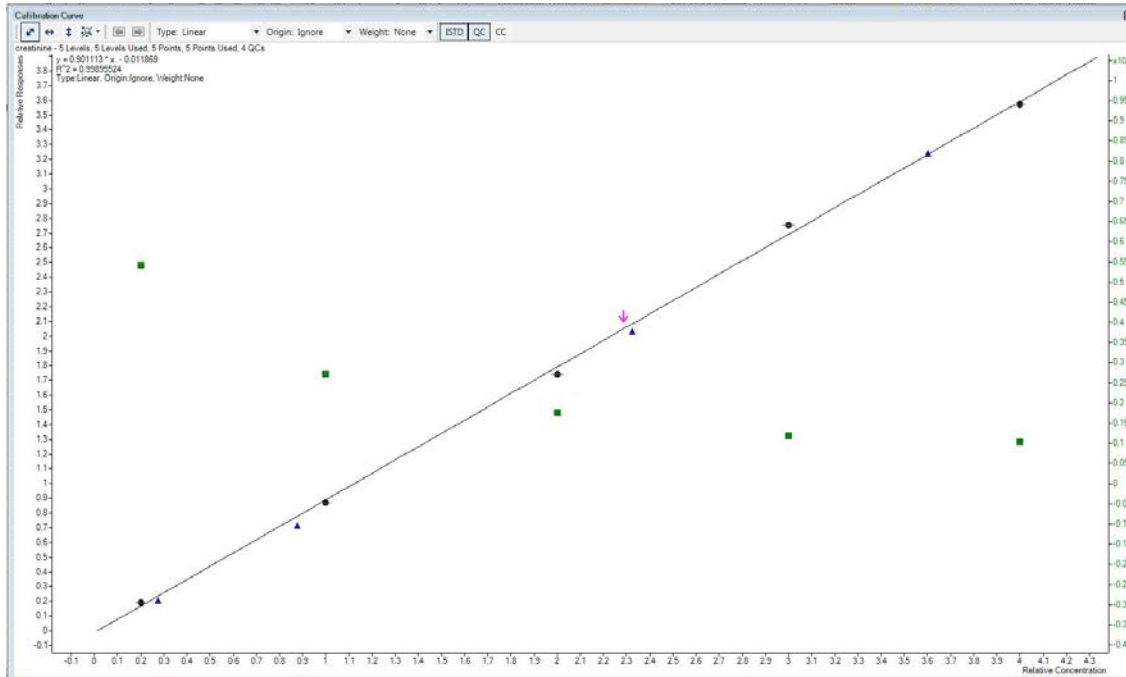


- < 1.2 minutes to cover ALL currently offered immunoassays
- Cost equivocal to a routine 9 compound immunoassay panel
- Includes enzymatic hydrolysis for added sensitivity

Analytical Performance

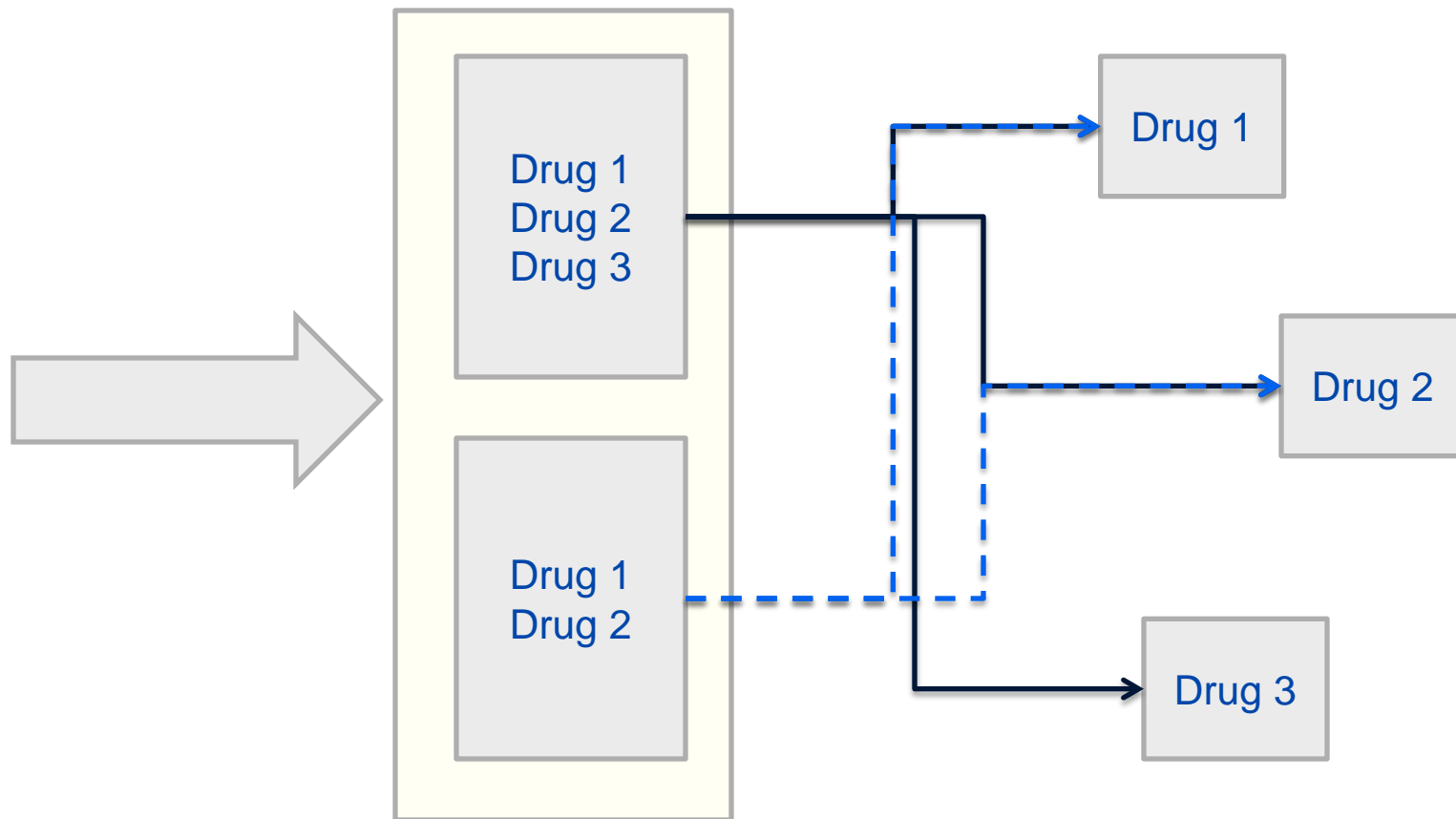
Substance	HEIA	TOF-MS	pos	neg
Amp	HEIA	TOF-MS	14	0
Barb	HEIA	TOF-MS	4	1
Benzo	HEIA	TOF-MS	0	88
Cariso	HEIA	TOF-MS	4	1
Cocaine	HEIA	TOF-MS	5	0
Fentanyl	HEIA	TOF-MS	8	0
MDMA	HEIA	TOF-MS	1	5
Mtd	HEIA	TOF-MS	6	0
Opiates	HEIA	TOF-MS	46	0
PCP	HEIA	TOF-MS	0	0
Tap	HEIA	TOF-MS	4	1
THC	HEIA	TOF-MS	14	2
Tram	HEIA	TOF-MS	27	1
Zolp	HEIA	TOF-MS	2	0
Bup	HEIA	TOF-MS	5	0
Ethanol	HEIA	TOF-MS	10	1
Meper	HEIA	TOF-MS	0	88
Oxy	HEIA	TOF-MS	0	0
Ppxy	HEIA	TOF-MS	0	0
MDMA	HEIA	TOF-MS	0	86
MDMA	HEIA	TOF-MS	0	81

Quantitative Creatinine Result Included



- Imprecision
 - 3% @ 87 mg/dL
 - 2% @ 230 mg/dL
- Accuracy
 - 8% bias throughout AMR (20-400 mg/dL)

Custom Panels with Confirmation



Summary & Key Points

- MKAE THE CMLOPEX SIMPLE
- Design Testing with the Patient and Physician in Mind, not Reimbursement.
- Find the Right Technology for the Right Job.
- The Future is in Intelligently Designed Custom Panels Using Advanced Screening Capabilities with Tried and True Confirmatory Methods.

Contact Information

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