Overview of urine drug screening

Jessica M. Boyd, PhD FCACB DABCC(TC)
Medical Director, Clinical Toxicology

ARUP LABORATORIES

SSM HEALTH
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Disclosures

- None

Learning Objectives

- Review the utility of urine drug screening
- Review the strengths and weaknesses of analytical methodologies commonly used for drug screening
- Discuss common interpretive challenges and how to follow up unexpected positive or negative results

Drug Screen Utility

- Clinical use:
  - » Identification of unknown toxicant
  - » Assessment of compliance for prescribed drugs
  - » Detection of undisclosed drug use

- Out of scope:
  - » Workplace drug testing
  - » Forensic drug testing

Sample Collection

- Urine still preferred sample for most drug screening applications
  - » Non-invasive collection
  - » Large sample volume
  - » High concentration of analytes (usually metabolites)
  - » Longer detection windows than blood
  - » Simple matrix
  - » Many methods available

Image credit: Wikipedia.org

Sample Collection

- Disadvantages of urine
  - » Some patients unable or unwilling to give a urine sample
  - » Sample adulteration is a risk as most collections are not witnessed
    - Substitution
    - Addition
    - Dilution
    - Spiking
  - » Provides no information on drug dose, timing or impairment

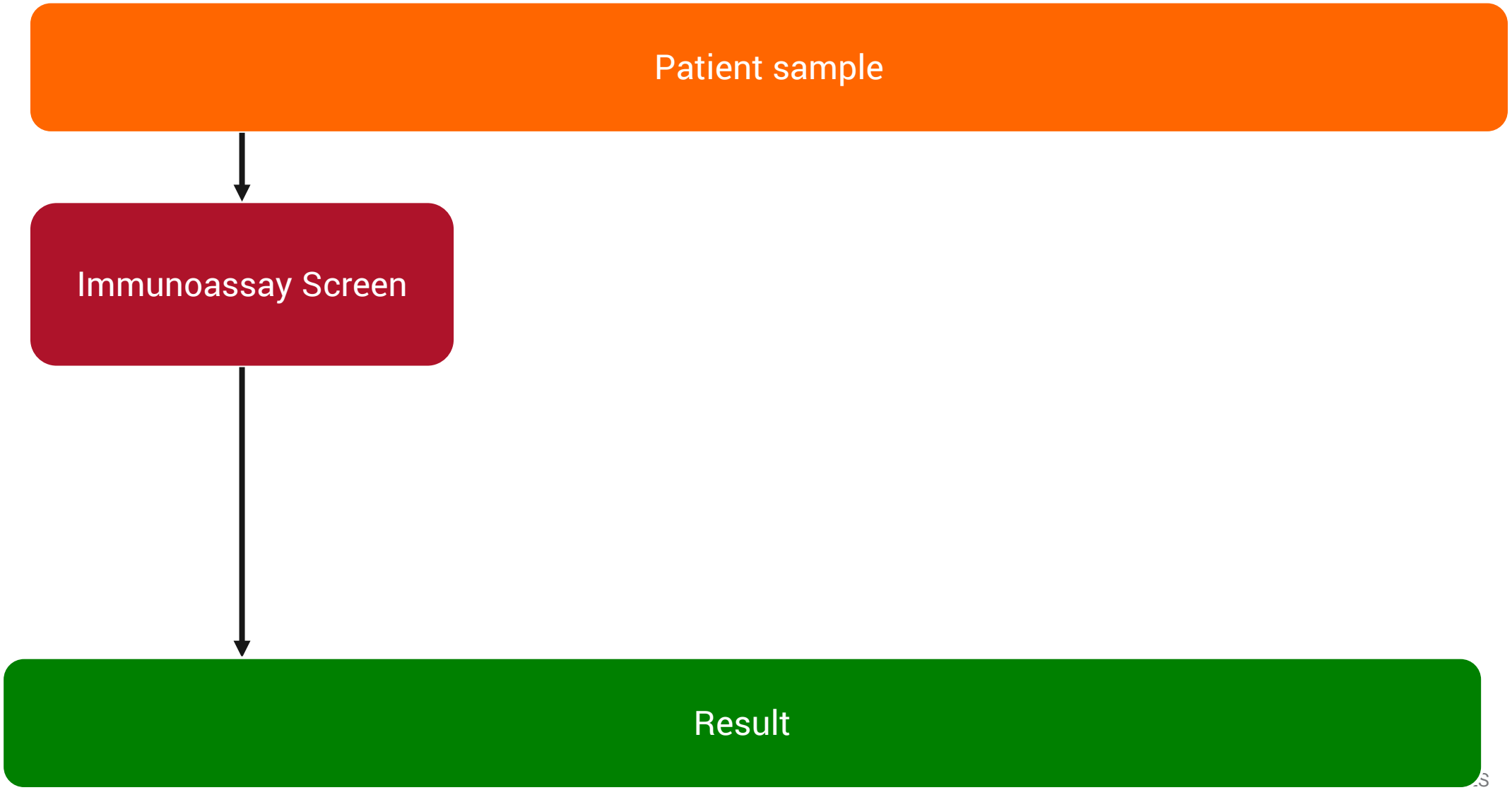
Drug Detection Windows in Urine

Drug	Typical urine detection window
Amphetamine/Methamphetamine	1-5 days
Delta9-THC	1-45 days
Cocaine metabolites	1-2 days
Opiates	1-3 days
Fentanyl	1-3 days
Methadone	3-12 days
Buprenorphine and metabolites	1-14 days
Phencyclidine	1-30 days
Benzodiazepines	1-21 days

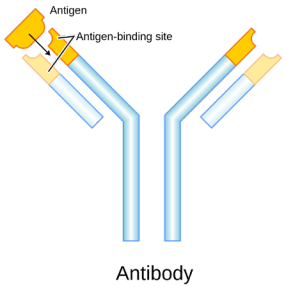
Alternative specimen types

- Blood
  - » Parent drugs tend to be more prevalent – Interpretation is different from urine
  - » Much shorter detection window than urine
  - » Difficult to adulterate
  - » Not commonly performed by laboratories → requires send out
  - » Useful for patients who can't/won't give a urine sample

Drug Screening Options



Screening by immunoassay



- Many advantages
  - » Fast
  - » Screen may be class-based or for an individual analyte (e.g. Opiates vs Methadone)
  - » Many methods available including near patient and automated analyzer options
  - » Results should be considered *presumptive only*

- Typically, positive screens are sent on for mass spectrometry based confirmation

Image credit: Wikipedia.org

Crossreactivity

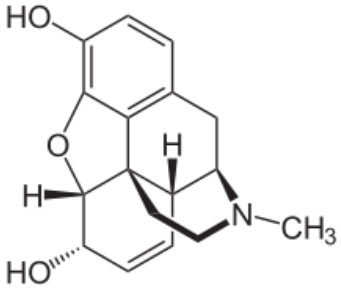
- Class based urine drug screens do not react equally with all drugs within the class.
  - May not react as well
  - May not react at all

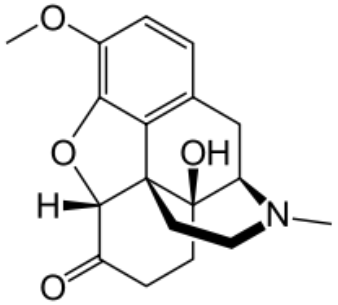
} False Negatives e.g. Opiates, benzodiazepines

Opiates and Opioids

- Opiate and opioid are often used interchangeably, but mean very different things for lab testing

Opioids		
Opiates	**Semi-synthetic Opioids**	**Synthetic Opioids**
Morphine	Hydrocodone	Methadone
Codeine	Hydromorphone	Fentanyl
	Oxycodone	Buprenorphine
	Oxymorphone	Meperidine
		Naloxone





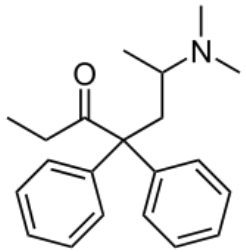


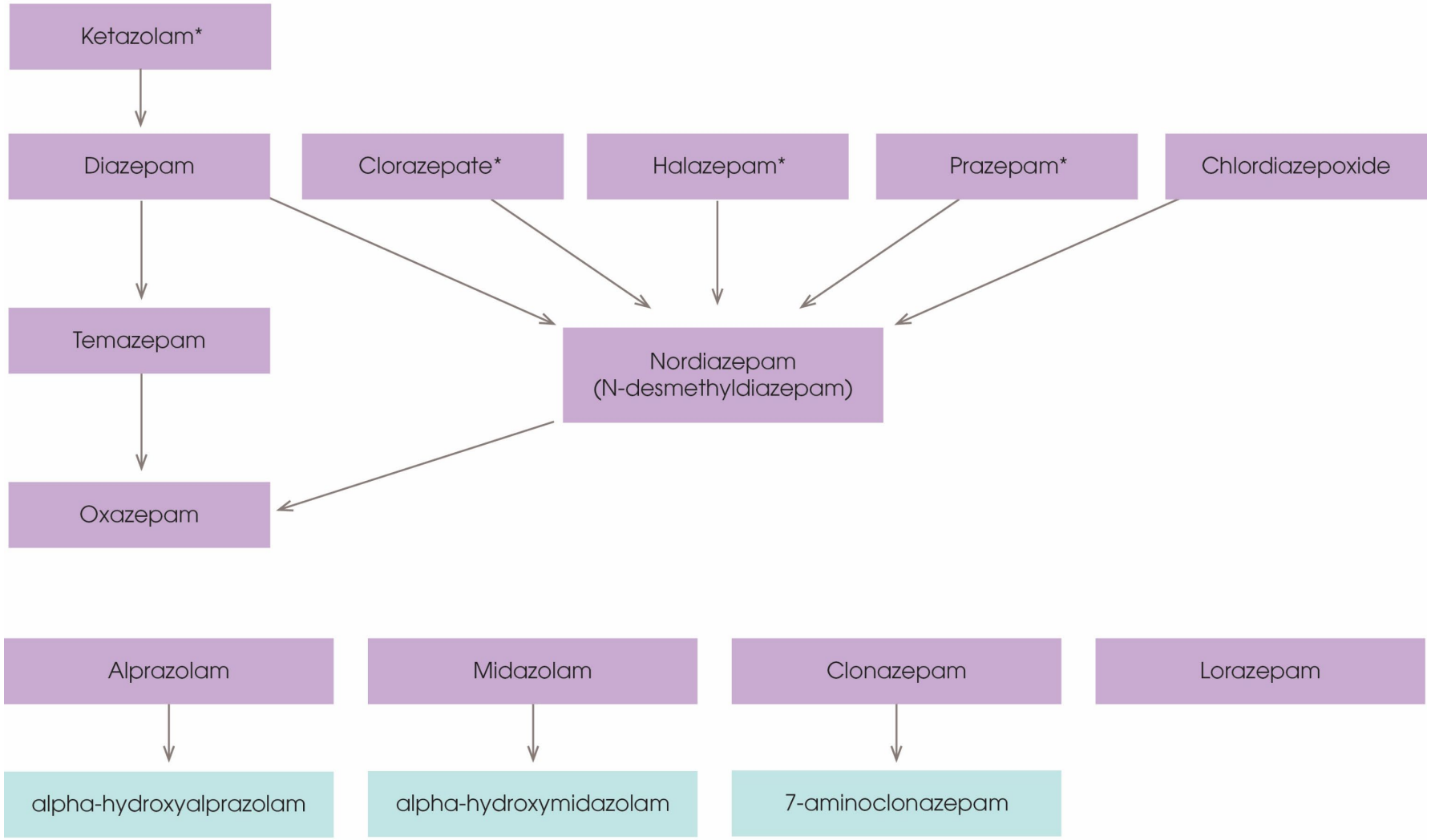
Photo credit: Wikipedia

Opiates and Opioids

- Urine Opiate immunoassays
  - » Detect: Codeine, Morphine
  - » May detect (depending on manufacturer and lab): 6-acetylmorphine, hydrocodone, hydromorphone, oxycodone
  - » Will not detect: fentanyl, buprenorphine, methadone, tramadol and other opioids

- Detection of most opioids requires either drug specific immunoassays or mass spectrometry

Benzodiazepines



Benzodiazepines

- Urine benzodiazepines immunoassays
  - » Common false negatives: alprazolam, lorazepam, clonazepam
    - Mass Spectrometry preferred for these analytes

Crossreactivity

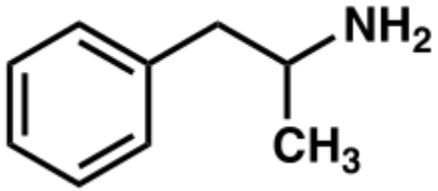
- Class based urine drug screens do not react equally with all drugs within the class.
  - May not react as well
  - May not react at all

} False Negatives e.g. Opiates, benzodiazepines

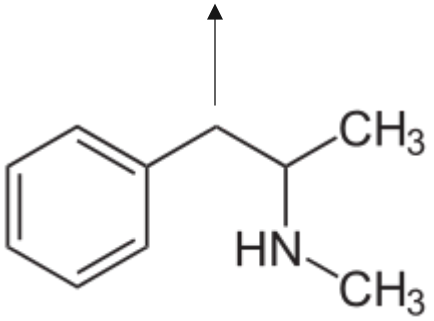
- All immunoassays may react with something that is not the drug of interest
  - » False Positives e.g. Amphetamines

Amphetamines

- Amphetamines immunoassays usually designed to react with amphetamine and methamphetamine. May have crossreactivity with other amphetamines such as MDMA.
- Amphetamines immunoassays are known to have a high rate of false positivity in immunoassay screens (typically 30-40%)
  - » Many OTC drugs known to cross react
    - Labetalol
    - mCPP (Trazodone metabolite)
    - Ranitidine
    - Buproprion
- Confirmation of positive screens by mass spec should be considered (especially if unexpected)



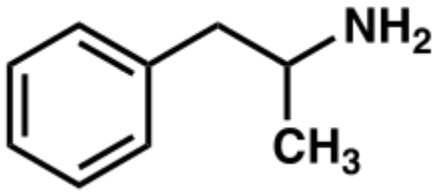
Amphetamine



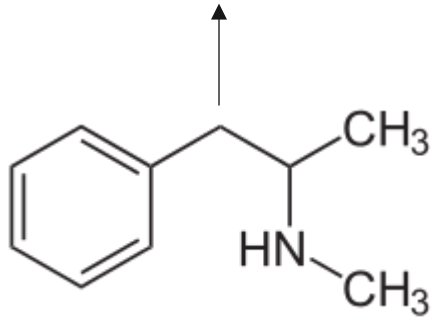
Methamphetamine

Amphetamines

- Medication compliance monitoring for amphetamine containing prescription medications
  - » Examples:
    - Adderall (Amphetamine)
    - Vyvance (metabolizes to amphetamine
  - » Methamphetamine should not be detected from use of these medications
- A small number of prescription medications do contain/metabolize to methamphetamine
  - » Selegiline, Benzphetamine
- Ritalin (Methylphenidate)
  - » Does not metabolize to amphetamine and will test negative in amphetamine targeting immunoassay and MS assays



Amphetamine

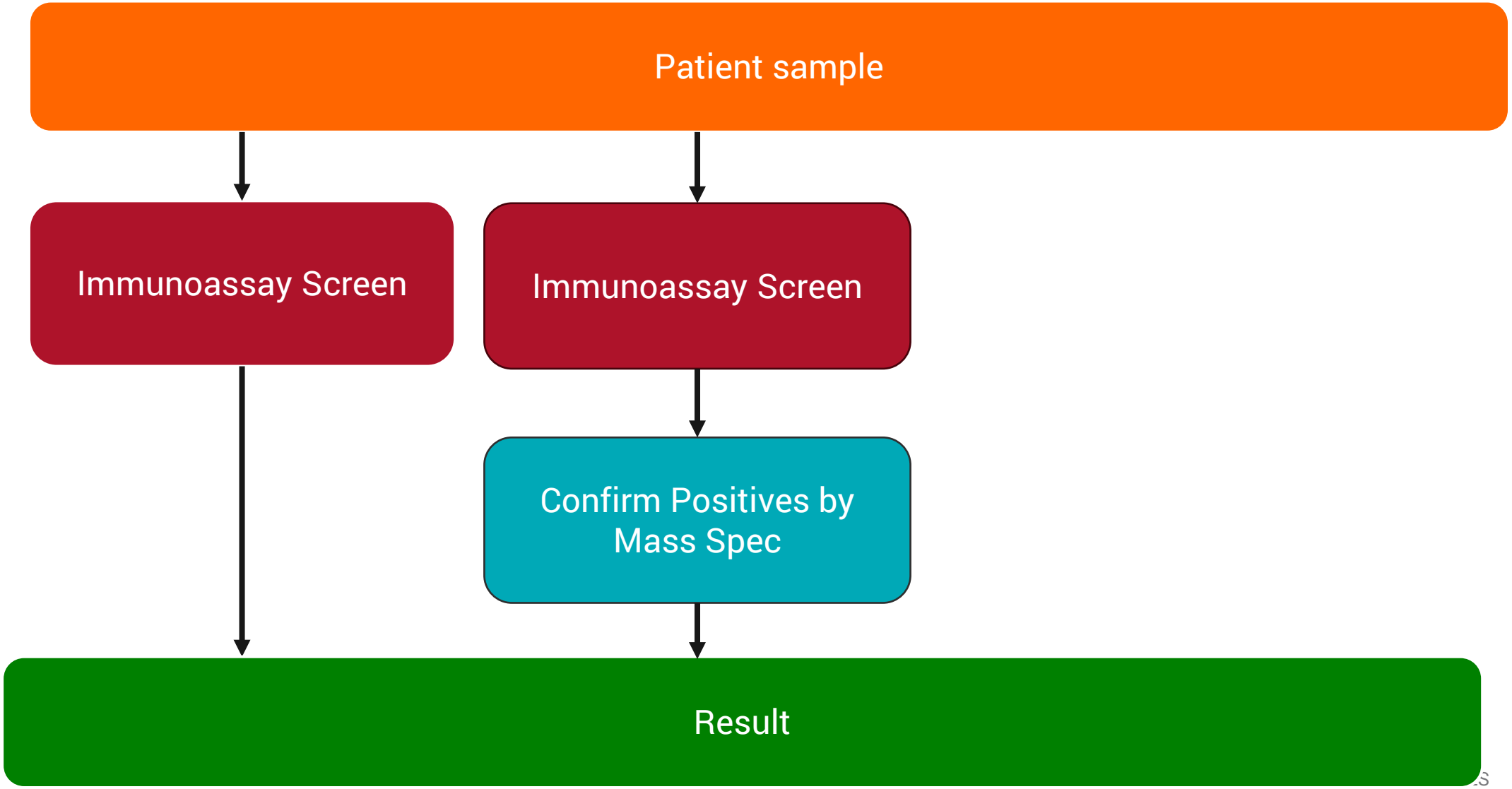


Methamphetamine

Immunoassay Challenges

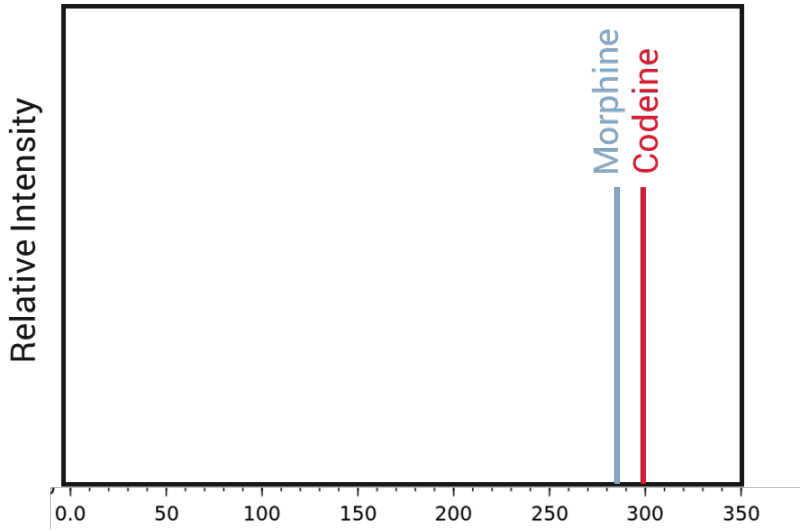
- Crossreactivity differences may result in unexpected positives or negatives
- A presumptive positive result does not provide any information on what caused the positive
- Individual tests required for each drug/drug class

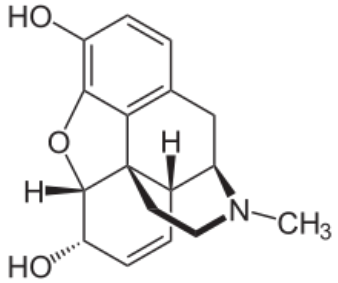
Drug Screening Options



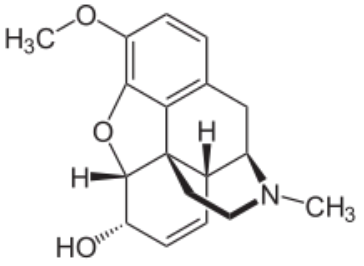
Drug Screen Testing by Mass Spectrometry

- Considered the gold standard method
  - » Looks at the molecular weight of a drug (superior specificity compared to immunoassays
  - » Monitor parent and metabolite(s) separately
  - » Monitor multiple drugs simultaneously within a sample





Morphine
m/z = 286



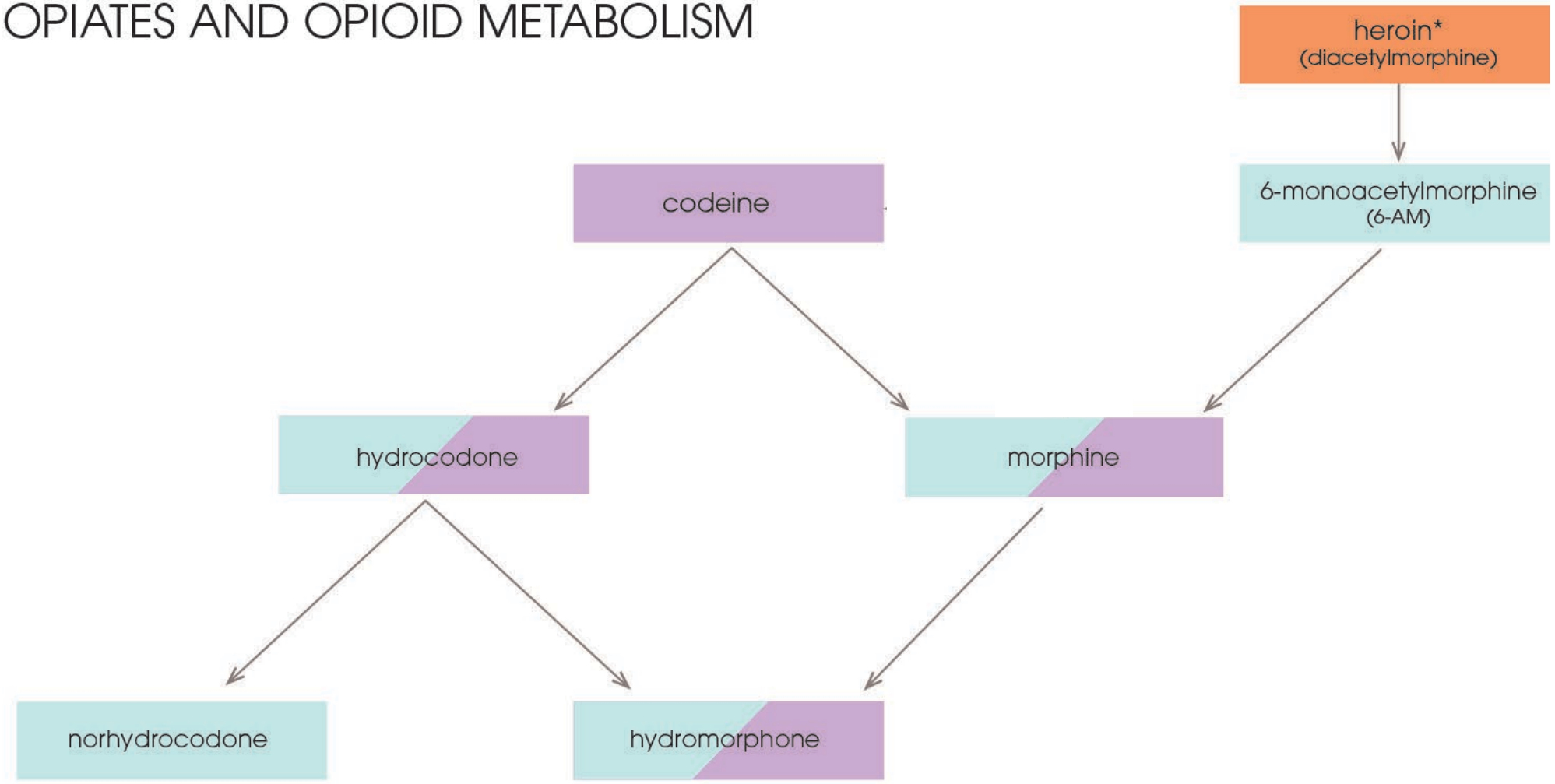
Codeine
m/z = 300

Confirmation mass spectrometry

- Typically used to confirm positive immunoassay results
  - » Will miss false negative immunoassay screens

- May be quantitative
  - » Provides an indication of ‘intensity’ above assay cutoff and relative to metabolites
  - » Does not indicate how much drug taken, when it was taken, or degree of impairment

OPIATES AND OPIOID METABOLISM



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Confirmation of positive opiates screen

Methodology	Test	Scenario 1 – Codeine use	Scenario 2 – Heroin use	Scenario 3 – Possible poppy seed consumption
Immunoassay	Opiates Screen	Presumptive Positive	Presumptive Positive	Presumptive Positive
LC-MS/MS	Codeine	8214	<cutoff	231
	Morphine	6702	7142	170
	6-MAM	<cutoff	521	<cutoff
	Hydrocodone	409	<cutoff	<cutoff
	Hydromorphone	<cutoff	<cutoff	<cutoff
	Oxycodone	<cutoff	<cutoff	<cutoff
	Noroxycodone	<cutoff	<cutoff	<cutoff

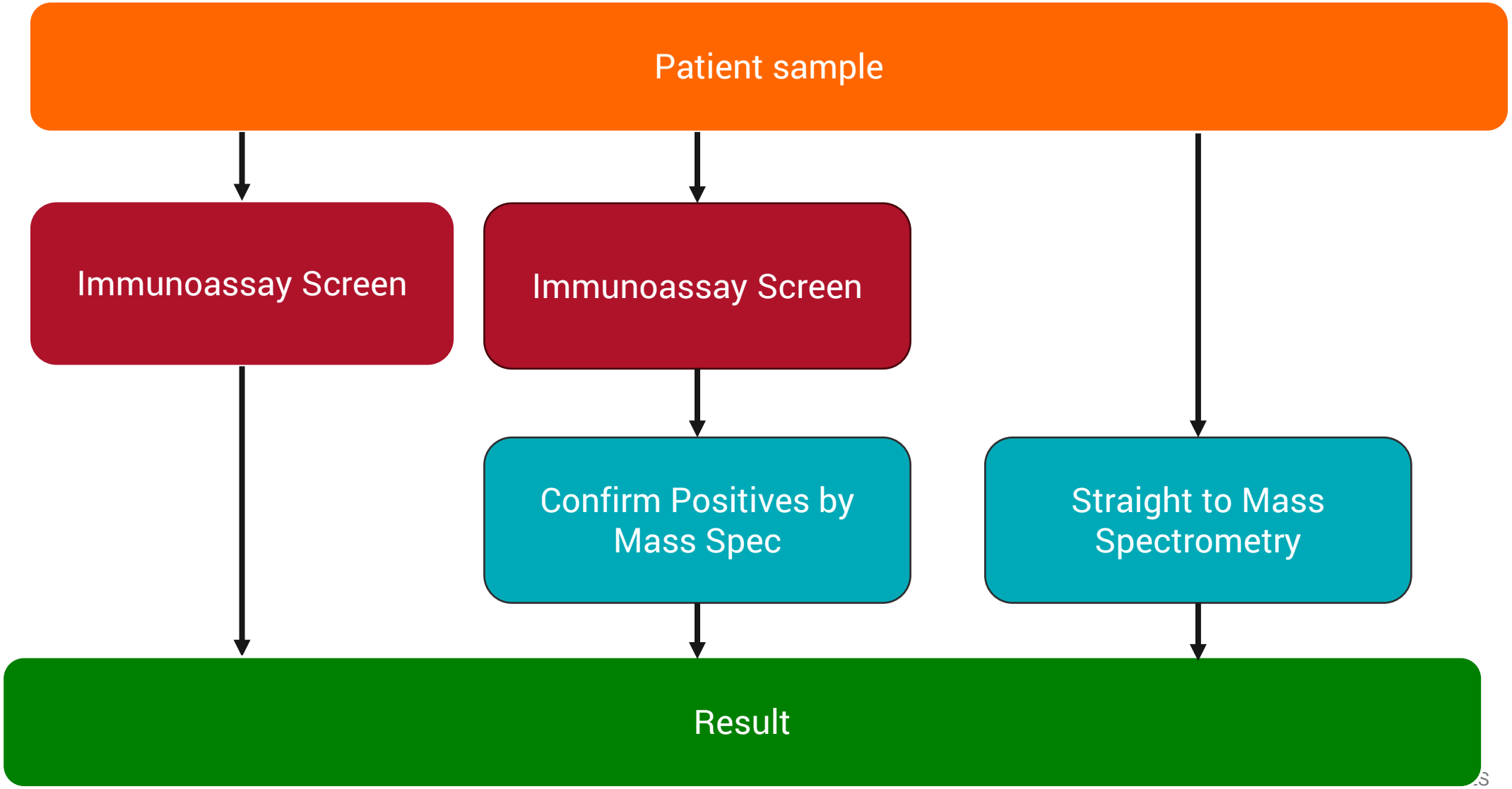
THC

- THC immunoassays and MS assays designed to detect metabolites of Δ9-THC
  - » Usually do not distinguish between other isomers e.g. Δ8, Δ10
  - » Do not detect CBD

- Assays may pick up THC from legal preparations depending on:
  - » Cutoff of the assay (MS cutoffs often much lower than immunoassays)
  - » Urine concentration

- THC is highly lipophilic and partitions into adipose tissue
  - » Regular users often have detectable low concentrations of THC for weeks to months even after discontinuing THC use
  - » Urine THC concentrations normalized to creatinine may be helpful in detecting new use

Drug Screening Options



Straight to mass spectrometry testing

- Two approaches:
  - » Only interested in one drug or drug class → Order confirmation test directly
  - » Want a broader screen to check for compliance and possible use of non-disclosed drugs → Mass Spec panel tests
    - Typically includes major drug classes including opioids, benzodiazepines, amphetamines, cocaine etc.

- Avoids risk of immunoassay false negatives
  - » Particularly helpful for drugs that immunoassays are known to miss
    - Hydrocodone, hydromorphone
    - Lorazepam, alprazolam, clonazepam

ARUP Pain Management Panel

Drugs covered and range of cutoff concentrations.
Note: Some drugs are identified based on the presence of unique drug metabolites not listed below.

Drugs/Drug Classes	Range of Cutoff Concentrations
Barbiturates	200 ng/mL
Benzodiazepine-like: alprazolam, clonazepam, diazepam, lorazepam, midazolam, nordiazepam, oxazepam, temazepam, zolpidem	20 - 60 ng/mL
Cannabinoids (11-nor-9-carboxy-THC)	50 ng/mL
Ethyl Glucuronide	500 ng/mL
Muscle Relaxant(s): carisoprodol, meprobamate	100 ng/mL
Opiates/Opioids: buprenorphine, codeine, fentanyl, heroin, hydrocodone, hydromorphone, meperidine, methadone, morphine, naloxone, oxycodone, oxymorphone, tapentadol, tramadol	2-200 ng/mL
GABA analogues: Gabapentin, pregabalin	3,000 ng/mL
Phencyclidine (PCP)	25 ng/mL
Stimulants: amphetamine, cocaine, methamphetamine, methylphenidate, MDMA (Ecstasy), MDEA (Eve), MDA, phentermine	50-200 ng/mL

Mass Spectrometry challenges

- Can detect USP allowable impurities in prescribed drugs
  - » Eg. Low levels of hydrocodone detectable in patients taking prescription oxycodone
- Glucuronidated metabolites still a challenge
  - » Assays looking for free drugs may report a negative result if drug is fully glucuronidated
    - Hydromorphone, lorazepam
- Longer turnaround time compared to immunoassay

Follow-up of unexpected results

Immunoassay Result

- Was the right screen ordered?
- Is the patient on other medications that could cross react?
- Consider lab consult and mass spectrometry testing

Mass Spectrometry Result

- Are the unexpected drugs metabolites or known impurities?
- Does the method detect glucuronide metabolites?
- Consider lab consult

Urine test codes at SSM Health

Testing Modality	SSM Health Order	Testing performing location	Description
Immunoassay only	Drug Screen Urine Abuse INHOUSE – LAB07796	SSM Lab	Confirmation by mass spectrometry can be added on manually
Screen with reflex to mass spectrometry	Drug Abuse Urine Panel 7A Reflex to Confirm – LAB2438	ARUP	
	Drug Abuse Urine Panel 9A Reflex to Confirm – LAB12438	ARUP	7A Panel plus methadone and propoxyphene
	Drug Profile Urine Screen w/ Reflex to Quant - LAB14163	ARUP	9A Panel plus buprenorphine, carisoprodol, meperidine, Tapentadol, tramadol, zolpidem
Direct to mass spectrometry	Pain Clinic Survey Urine No Reflex - LAB07473	ARUP	Immunoassay testing with no reflex for cocaine, methadone, THC, tramadol, PCP, Ethyl glucuronide, barbiturates, carisoprodol

Other drug screen codes at SSM Health

Specimen Type	Testing Modality	SSM Health Order	Testing performing location
Blood	Screen with reflex to mass spectrometry	Drug Screen Blood Panel 9 with Reflex confirm - LAB04365	ARUP
Miscellaneous - Blood		LAB MISC TEST Blood Only - LAB11146	
Miscellaneous -Not Blood		LAB MISC TEST (NOT BLOOD) - LAB04393	

Resources

- ARUP Consult (https://arupconsult.com/content/drug-testing)
  - » Metabolic patterns for opiates and benzodiazepines
  - » Urine and Serum drug windows of detection
  - » Discussion of common drug testing interpretation questions

- ARUP Pathologist on Call Service (1-800-533-2787)
  - » Available Weekdays 8 am – 6 pm
  - » Provide assistance with interpretation questions and investigation of unexpected results

Questions?

- jessica.boyd@aruplab.com

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