ITS NOT ABOUT THE NUMBER

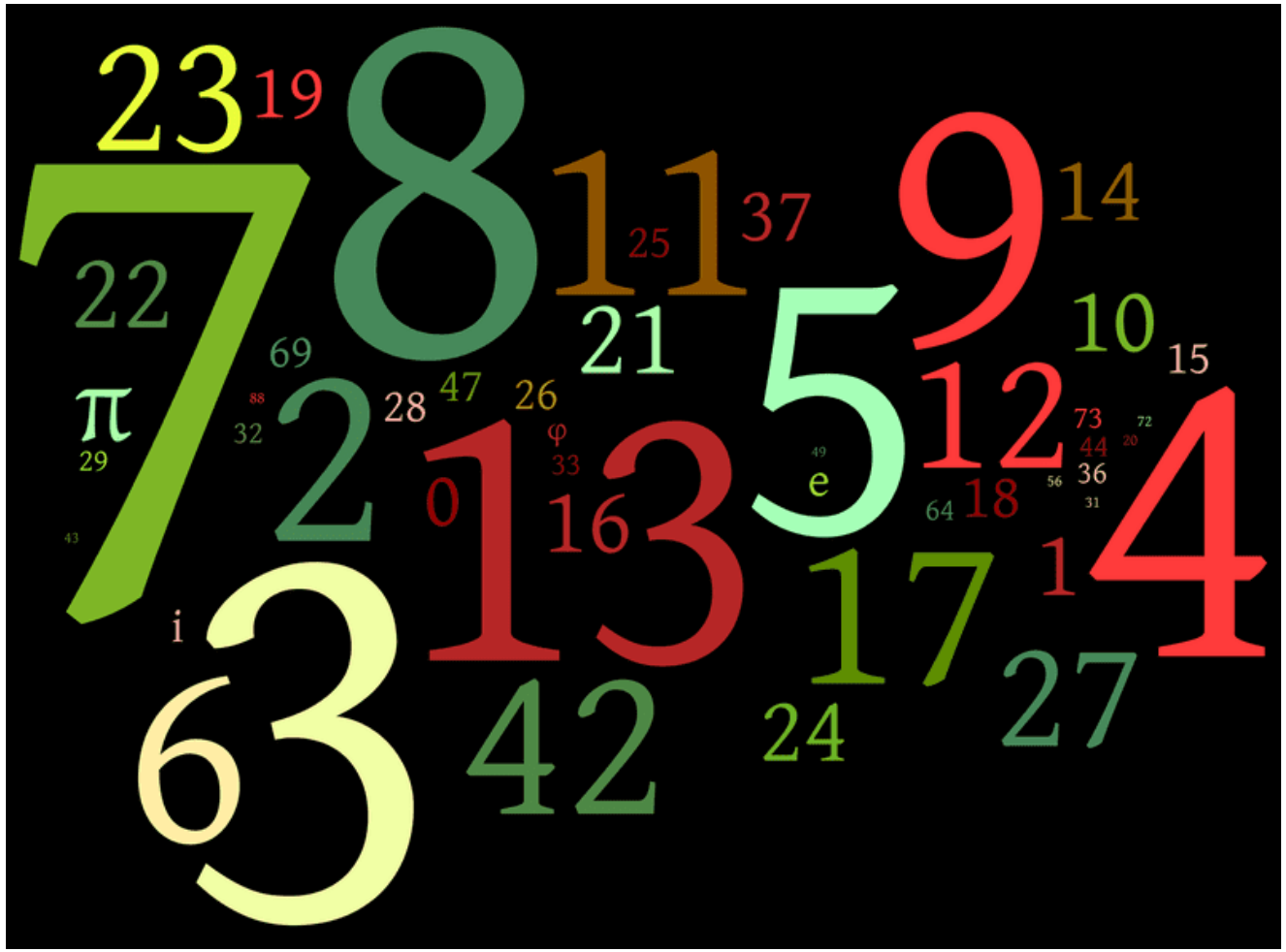
Human Performance Toxicology

Oklahoma Summer Judicial Conference 2026

CHRIS HEARTSILL
REGIONAL
TOXICOLOGY LIAISON

MID-SOUTH US

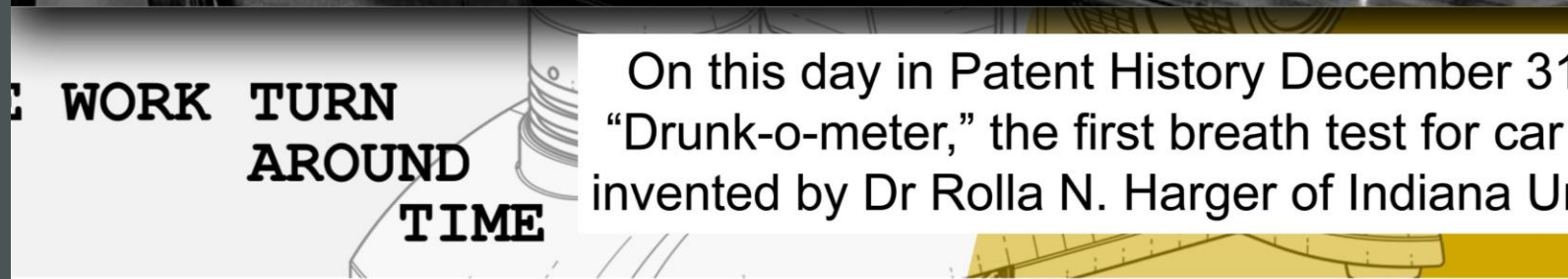
ITS NOT ABOUT THE NUMBER!!!



BUT WE HAVE A NUMBER!!!

BRIEF HISTORY OF PER SE (ALCOHOL)

- 1910 – New York adopts laws against driving while intoxicated
  - California and other states followed
- 1936 – Harger develops the Drunkometer
- 1938 – AMA and NSC studied the issue – recommend 0.15%
- 1953 – Borkenstein develops the Breathalyzer



BRIEF HISTORY OF PER SE (ALCOHOL)

- 1960s – NHTSA worked to demonstrate the dangers of drunk driving
- Some states dropped their permissible BAC to 0.10% or 0.12%
- 1972 – states began passing per se laws
- 2000 – President Clinton requires states to move to 0.08%
  - 2004 – all states had complied
- 2018 – Utah goes 0.05% Per Se

#100

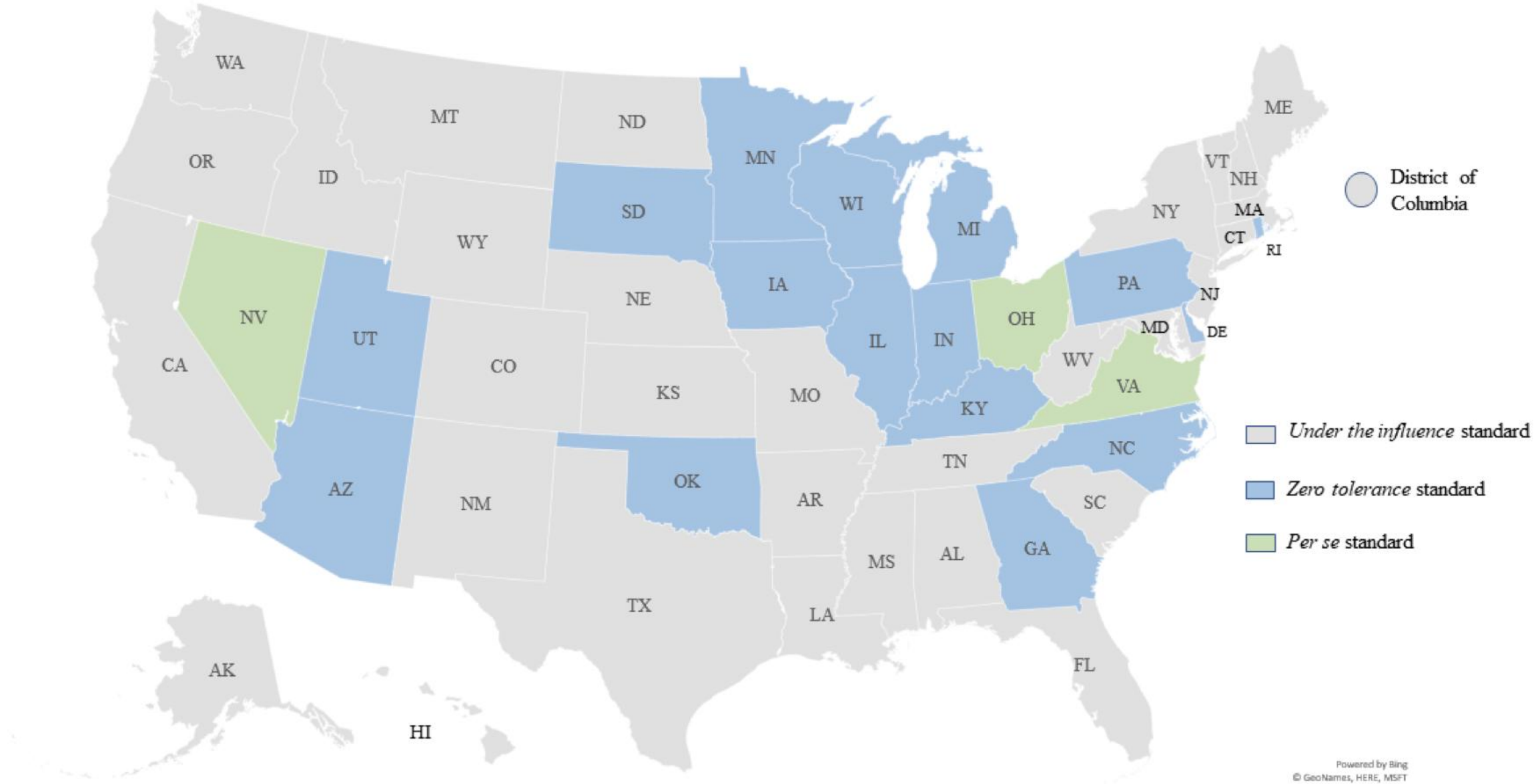
National Safety Council

Position/Policy Statement

Alcohol Impairment Concentrations

Every person, regardless of that person's experience with alcohol beverage consumption, is impaired in driving performance if that person's alcohol concentration is 0.08 or more. Research indicates that the ability of many individuals is impaired for driving and driving-related tasks at alcohol blood or breath concentrations below 0.08, and that for some individuals, impairment occurs at alcohol concentrations below 0.05. Therefore, at alcohol concentrations below 0.05, no statutory presumption regarding the presence or absence of alcohol influences should be made.

Drugged Driving Laws (Other Schedule I Substances)



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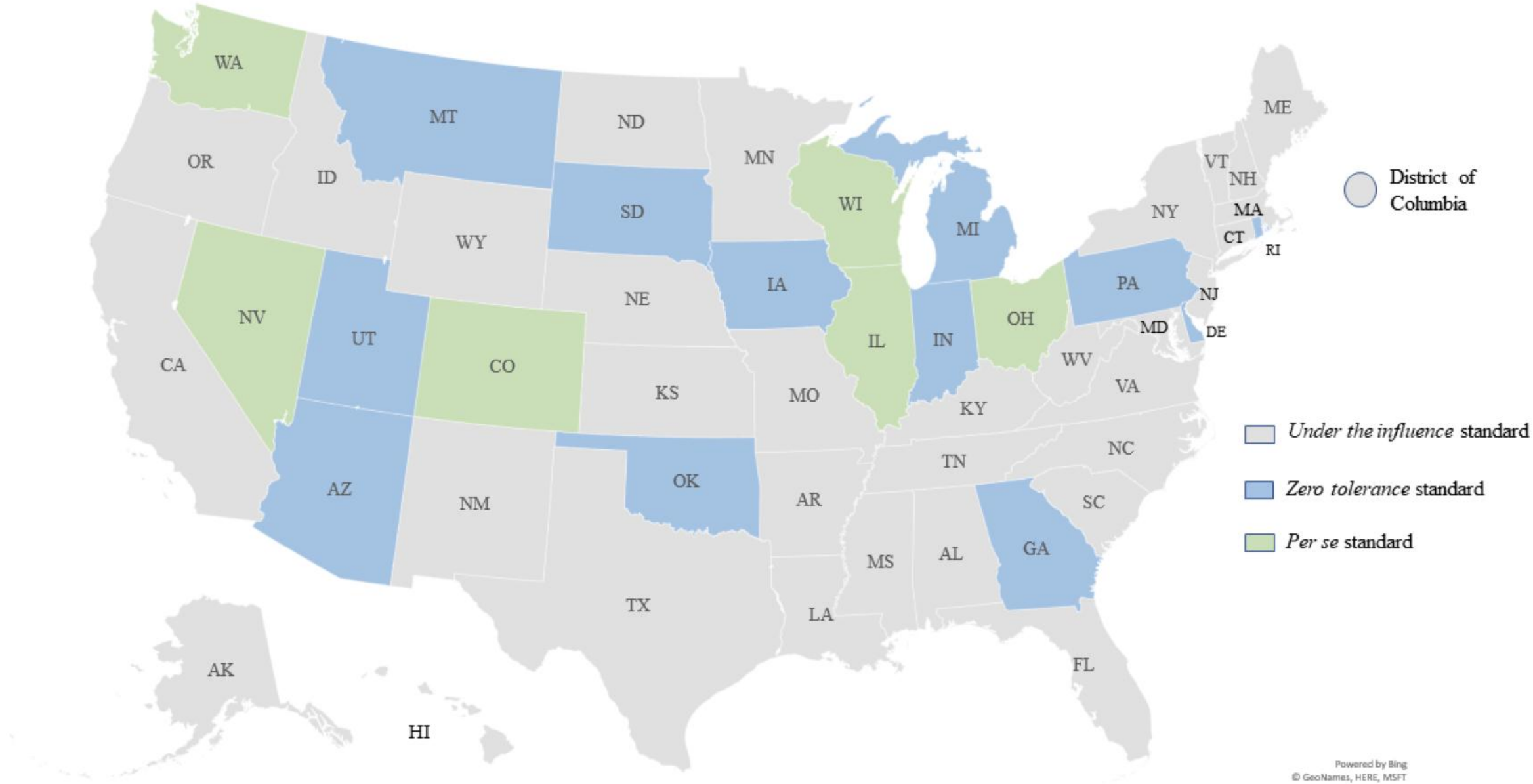
Drugged Driving Laws (Cannabis/THC)



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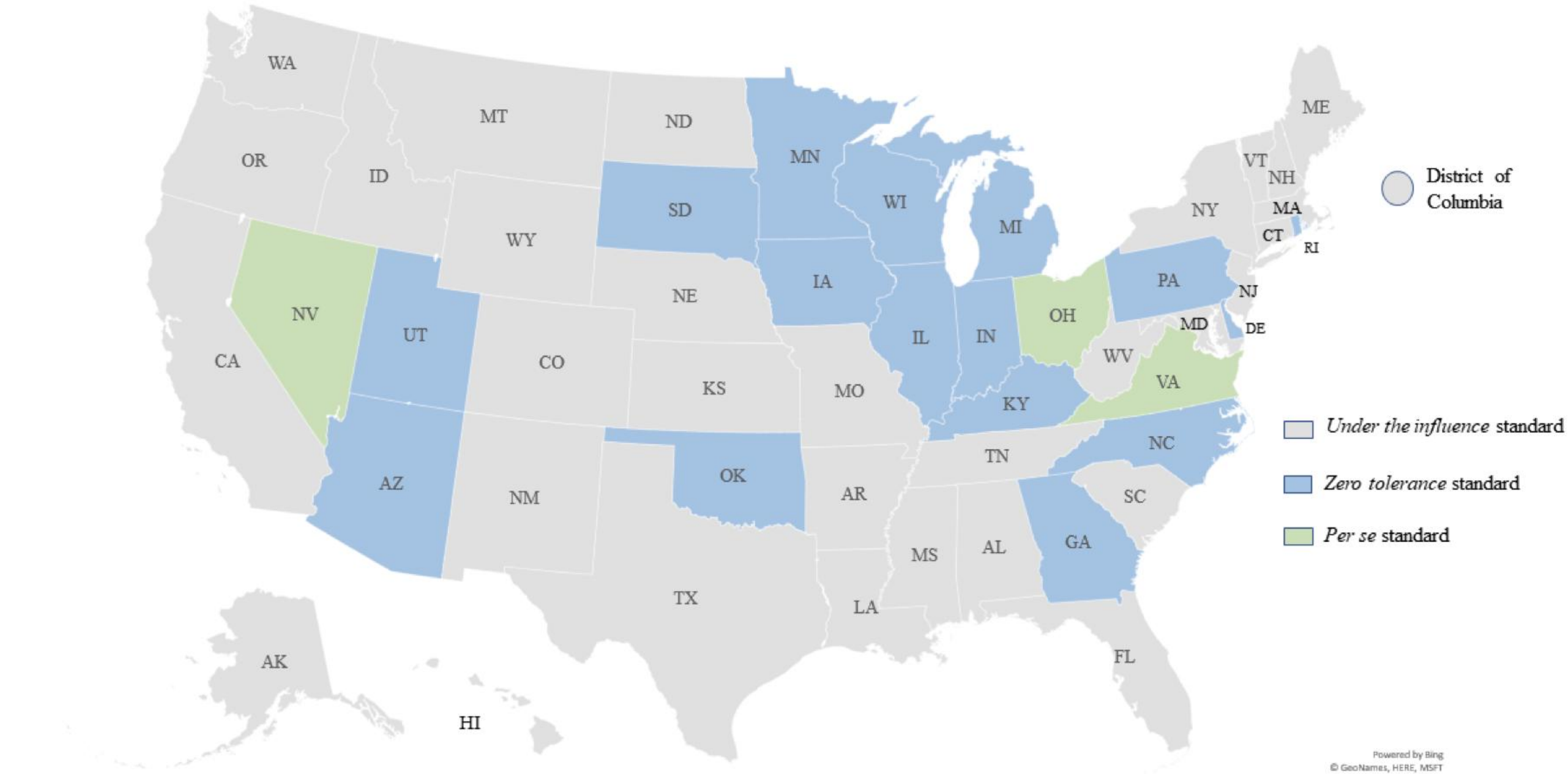
NV
UT
CA

Does the DUID statute have a *per se* standard for other substances?	Yes. It is unlawful to operate a motor vehicle with any of a list of prohibited substances in one's urine or blood at or above certain amounts, given in nanograms per milliliter. These substances and amounts are amphetamine (500 ng/ml urine, 100 ng/ml blood), cocaine (150/50), cocaine metabolite (150/50), heroin (2,000/50), heroin metabolite—morphine (10/10), heroin metabolite—6-monoacetyl morphine (10/10), LSD (25/10), marijuana (10/2), marijuana metabolite (15/5), methamphetamine (500/100), and phencyclidine (25/10).[155]

Does the DUID statute have a zero-tolerance standard for other substances?	Yes. It is unlawful to operate a motor vehicle "upon the ways of this state open to the public while the person's delta-9-tetrahydrocannabinol level, excluding metabolites, as shown by analysis of the person's blood, is 5 ng/ml or more."[146]

Drugged Driving Laws (Other Schedule I Substances)



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CO
KS
MO
OK
M
AR

	arrest of such person.
Does the DUID statute have a zero-tolerance standard for other substances?	Yes. A person may not operate a motor vehicle with "any amount of a Schedule I chemical or controlled substance, as defined in Section 2-204 of Title 63 of the Oklahoma Statutes, or one of its metabolites or analogs in the person's blood, saliva, urine or any other bodily fluid at the time of a test of such person's blood, saliva, urine or any other bodily fluid administered within two (2) hours after the arrest of such person."[191]
[illegible]	[illegible]

Does this jurisdiction have a Driving Under the Influence (DUI/DUID) statute?	Yes. In Texas, it is unlawful to operate a motor vehicle while "intoxicated,"[221] defined as "not having the normal use of mental or physical faculties by reason of the introduction of alcohol, a controlled substance, a drug, a dangerous drug, a combination of two or more of those substances, or any other substance into the body."[222]

PER SE

Means – by itself

LE does not have to provide other evidence of intoxication if per se is met.

PER SE

A safe level?

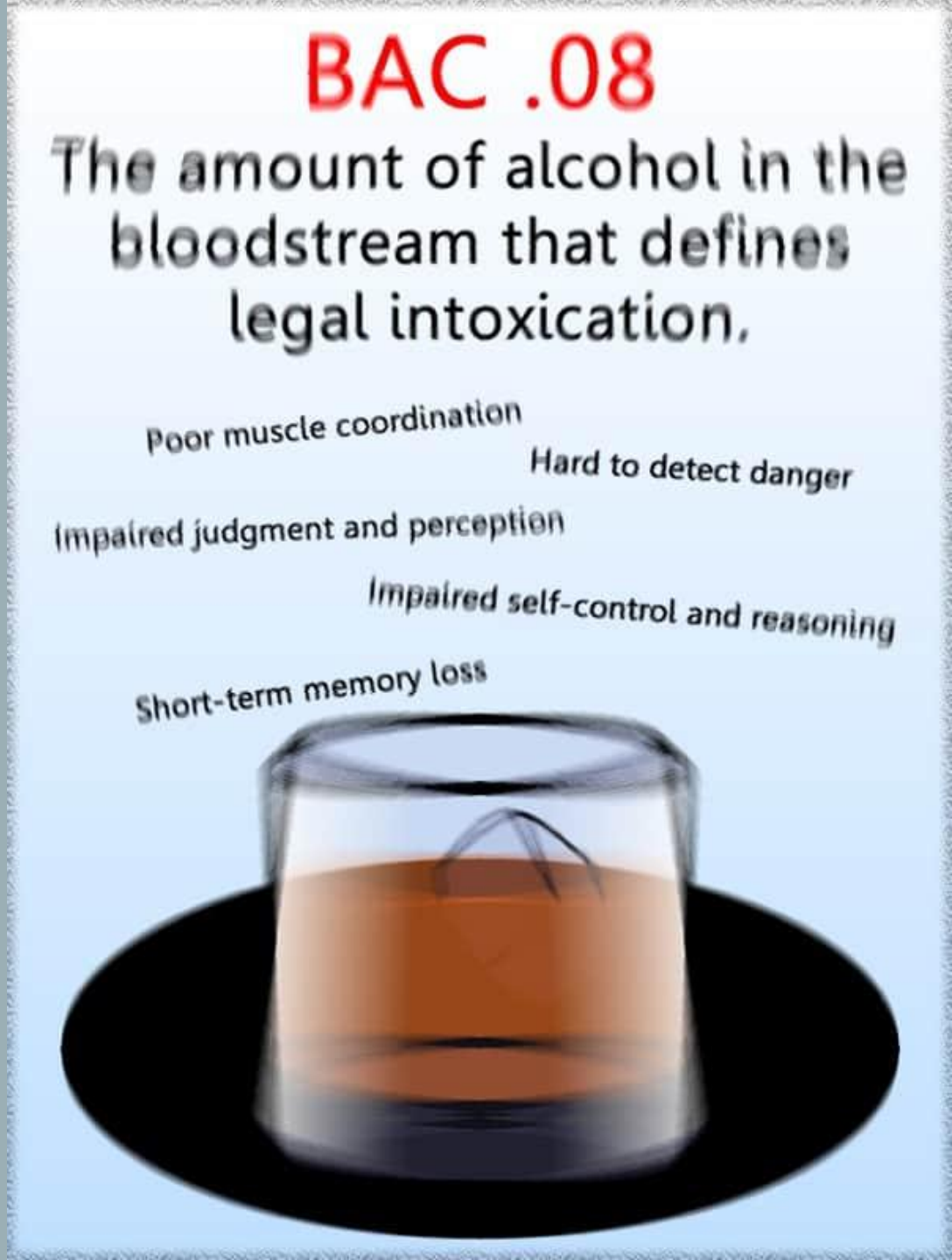
Intoxication does not care about a number

EtOH +
0.043 g%

- Amphetamine 17 ng/mL
- Methamphetamine 240 ng/mL
- Fentanyl 6.3 ng/mL
- NorFentanyl 7.1 ng/mL
- Clonazolam 13 ng/mL
- Gabapentin 17,360 ng/mL
- Buprenorphine 1.2 ng/mL
- Norbuprenorphine 2.6 ng/mL
- Tramadol 66 ng/mL
- Acetone + 0.022 g%

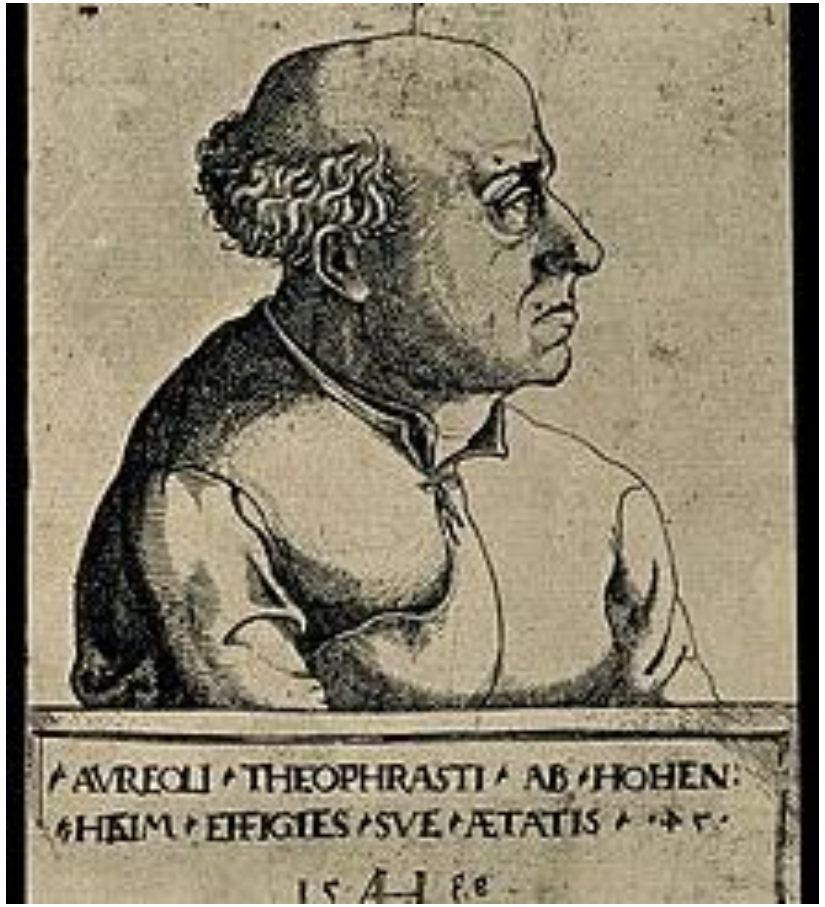
THE AGE-OLD QUESTION

How does this drug concentration compare to a 0.08 Alcohol?




The Dose Makes the Poison

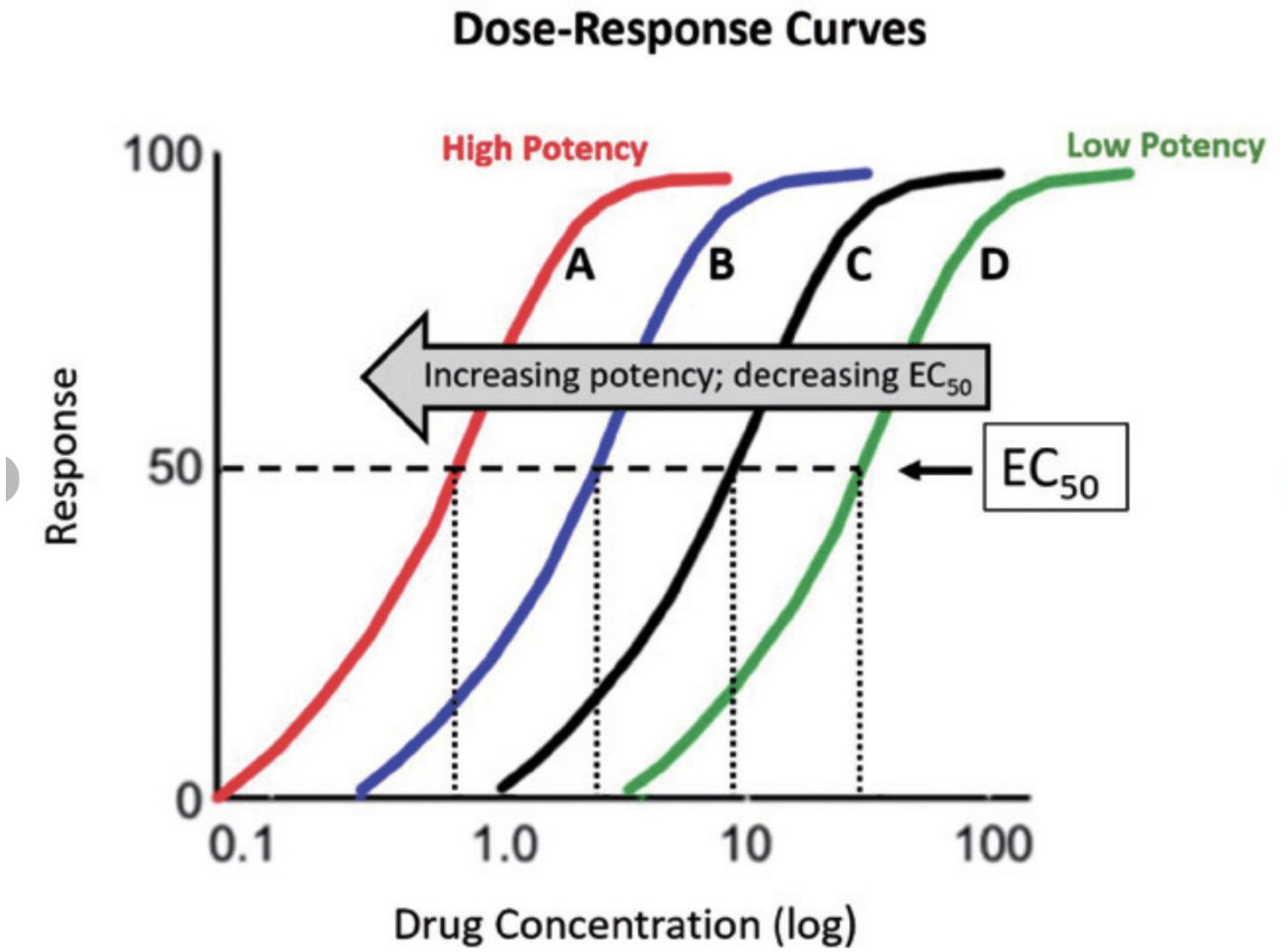
All things are poison, and nothing is without poison; the dosage alone makes it so a thing is not a poison



DEFINITIONS

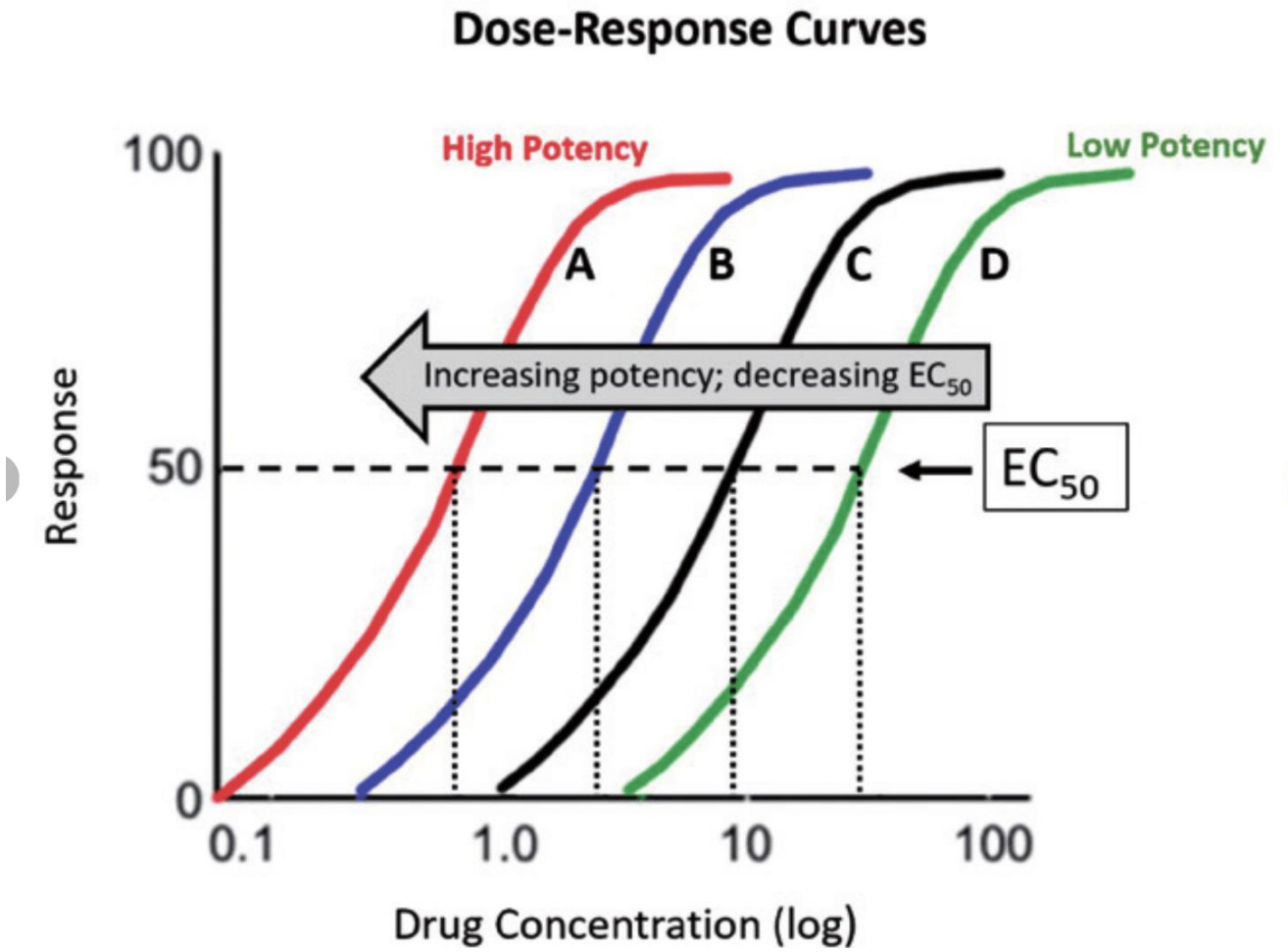
Dose – a specific amount of drug taken at one specific time

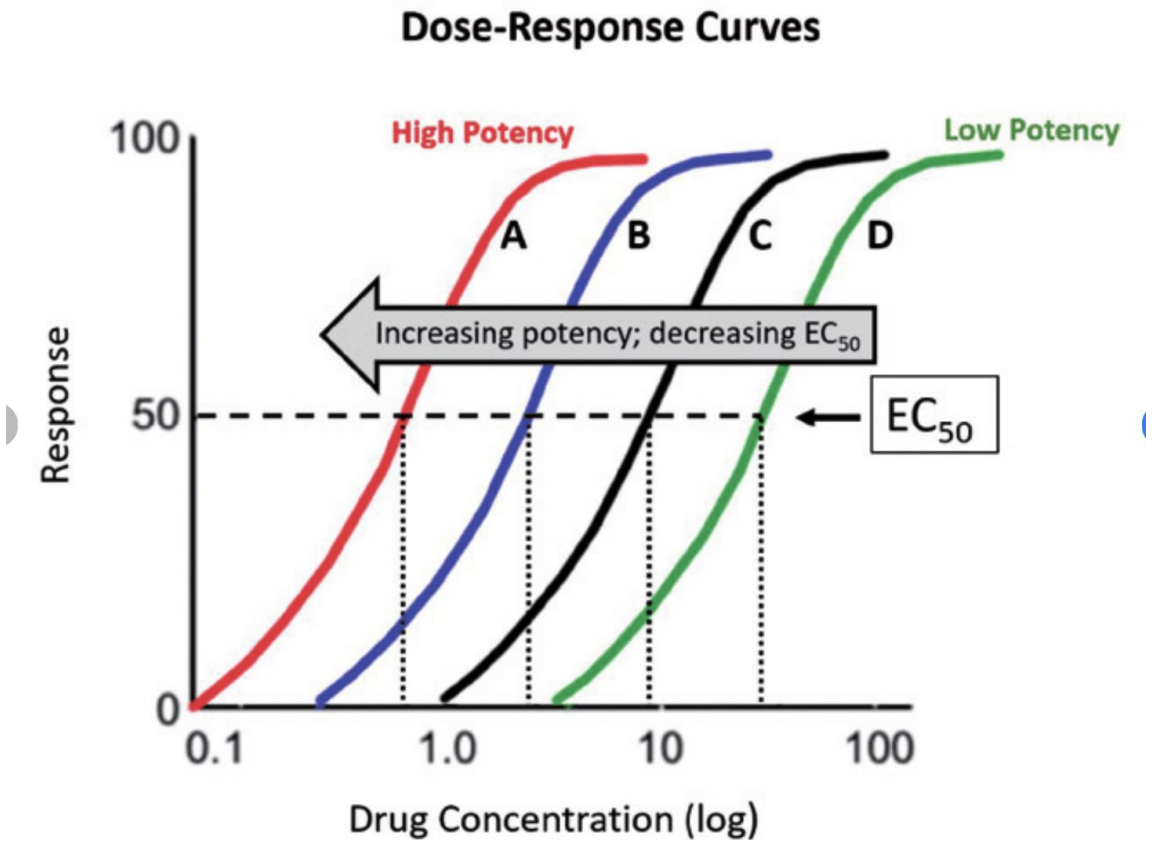
Dosage – how to take medication (includes doses over time)

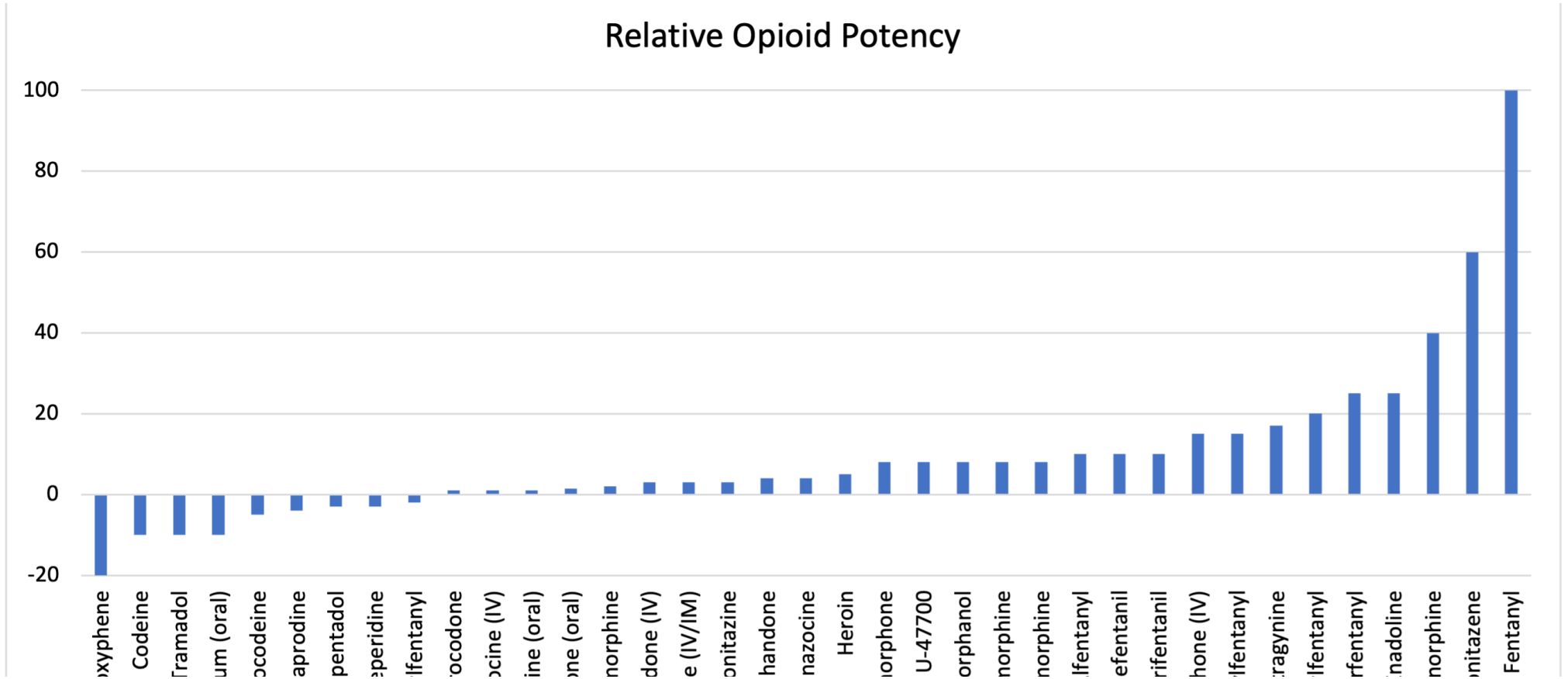


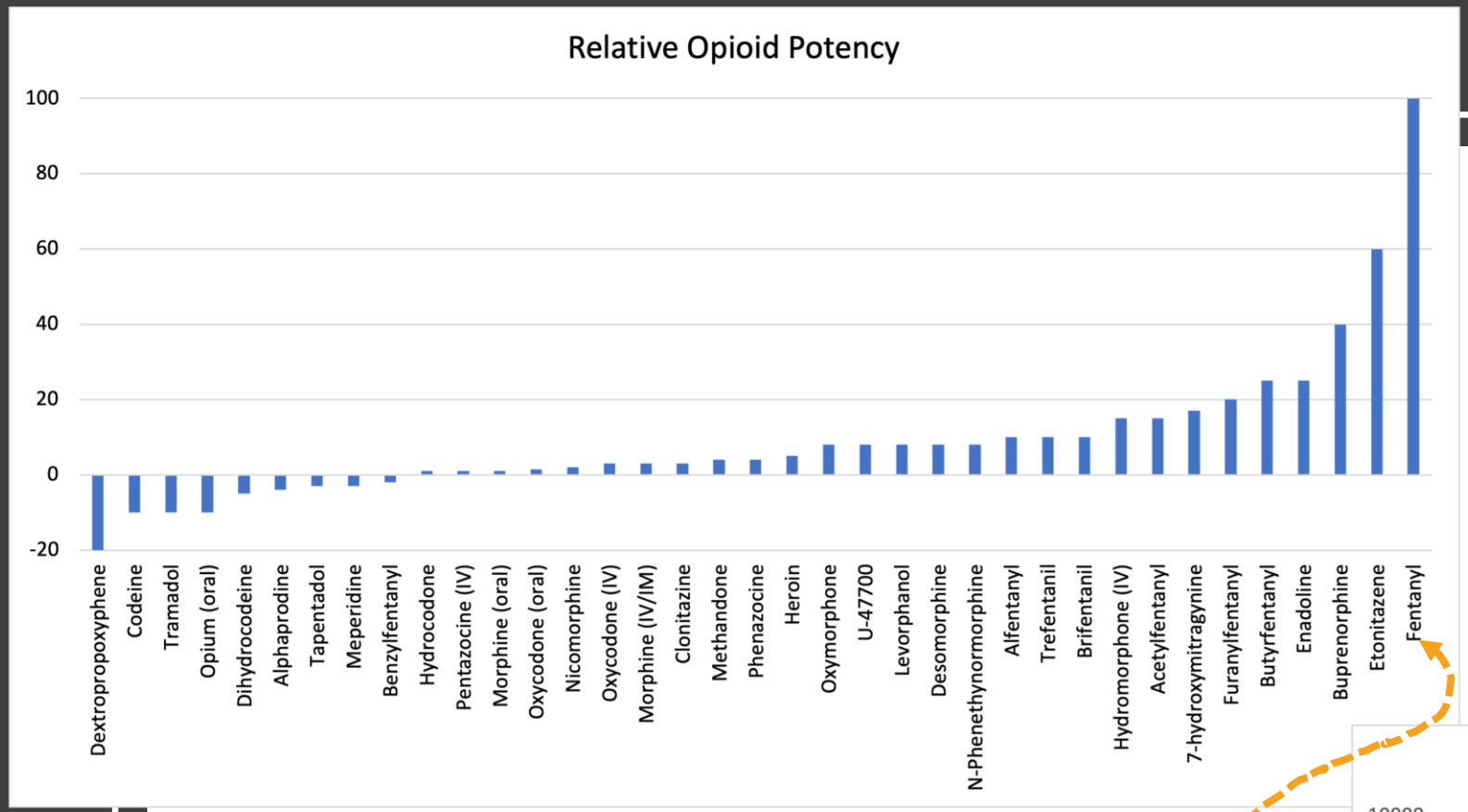
DEFINITIONS

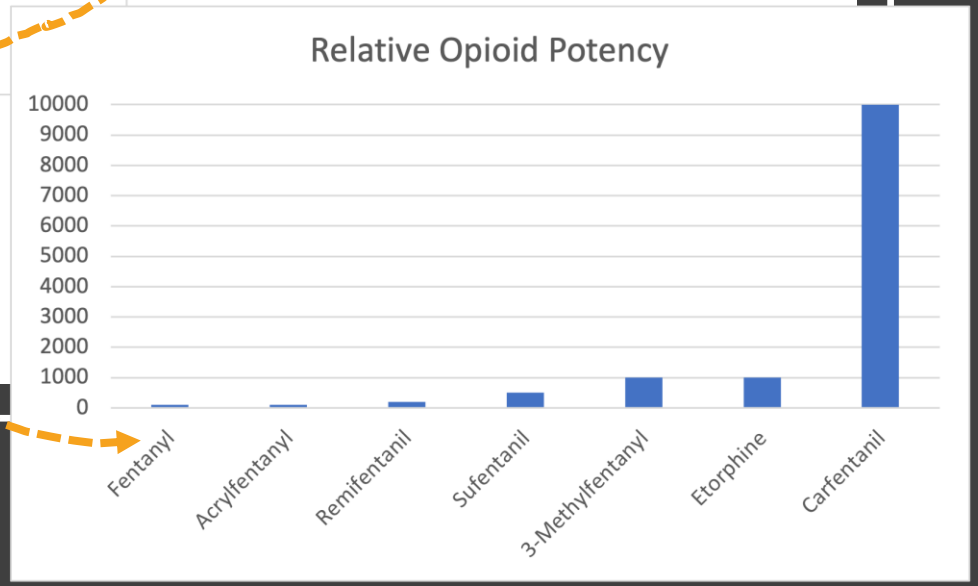
Potency – a measure of a drugs biological activity in terms of the dose required to produce a pharmacological effect of a given intensity

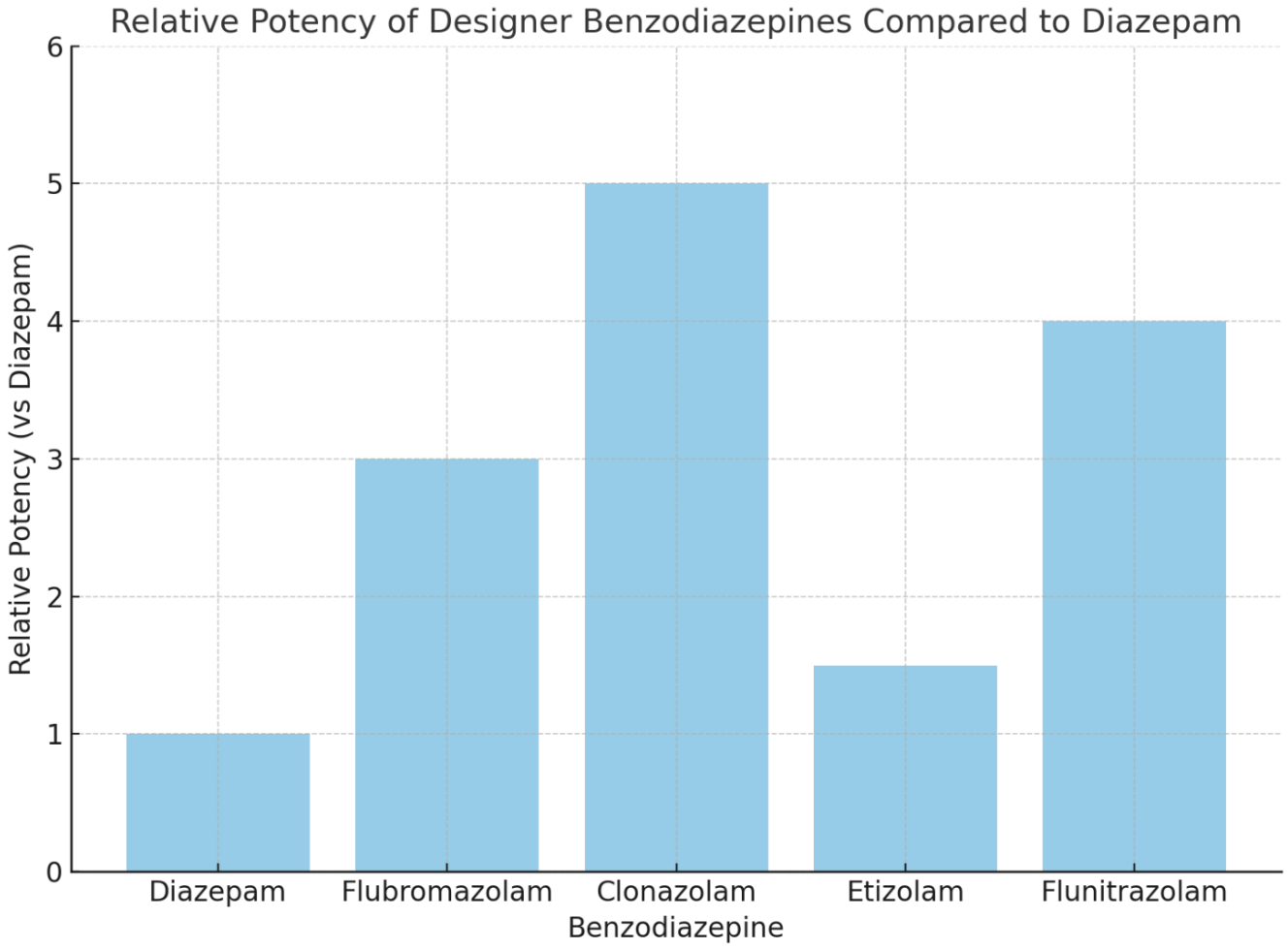



Dose-Response Curves
High Potency
Low Potency
A
B
C
D
Increasing potency; decreasing EC50
EC50
100
50
0
Response
0.1
1.0
10
100
Drug Concentration (log)


Relative Opioid Potency
100
80
60
40
20
0
-20
Codeine
Heroin
Fentanyl


Relative Opioid Potency
100
80
60
40
20
0
-20
Dextropropoxyphene
Codeine
Tramadol
Opium (oral)
Dihydrocodeine
Alphaprodine
Tapentadol
Meperidine
Benzylfentanyl
Hydrocodone
Pentazocine (IV)
Morphine (oral)
Oxycodone (oral)
Nicomorphine
Oxycodone (IV)
Morphine (IV/IM)
Clonitazine
Methandone
Phenazocine
Heroin
Oxymorphone
U-47700
Levorphanol
Desomorphine
N-Phenethynormorphine
Alfentanyl
Trefentanil
Brifentanil
Hydromorphone (IV)
Acetylfentanyl
7-hydroxymitragynine
Furanylfentanyl
Butyrfentanyl
Enadoline
Buprenorphine
Etonitazene
Fentanyl


Relative Opioid Potency
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
Fentanyl
Acrylfentanyl
Remifentanil
Sufentanil
3-Methylfentanyl
Etorphine
Carfentanil


Relative Potency of Designer Benzodiazepines Compared to Diazepam
Relative Potency (vs Diazepam)
0
1
2
3
4
5
6
Diazepam
Flubromazolam
Clonazolam
Etizolam
Flunitrazolam
Benzodiazepine

DOSE

Alcohol (ethanol) – 14

Gabapentin – up to 3600

Marijuana – 10

Fentanyl – 12 – 100

DOSE

Alcohol – 14 G/drink

Gabapentin – up to 3600 mg/day

Marijuana – 10 mg in edibles

Fentanyl – 12 – 100 ug for pain

DOSE

Alcohol – 14 G/drink

Gabapentin – up to 3600 mg/day

Marijuana – 10 mg in edibles

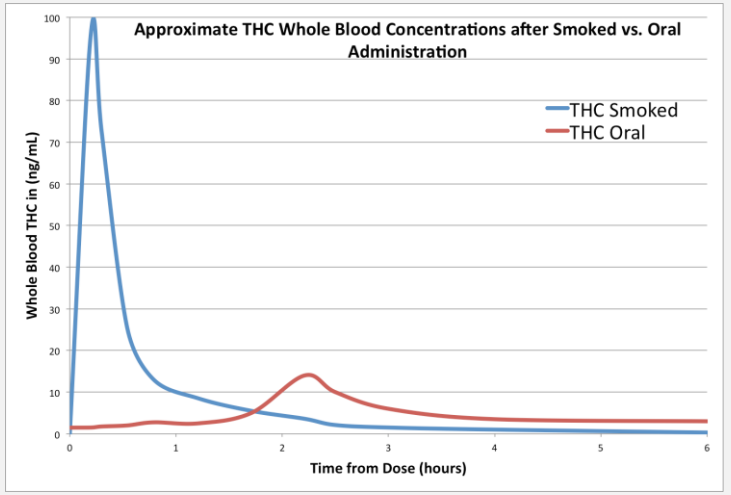
Fentanyl – 12 – 100 ug for pain

1 G = 1000 mg

1 mg = 1000 ug

ROUTE OF ADMINISTRATION

- Oral
- IV
- Smoked
- All the others



Inhaled versus Oral

	INHALED	ORALLY INGESTED
Peak Blood Levels (min)	3-10	60-120
Bioavailability (%)	10-40	<15
Time to peak psychoactive activity (min)	20	120-240

Indicators Consistent with Drug Categories

	CNS Depressants	CNS Stimulants	Hallucinogens	Dissociative Anesthetics	Narcotic Analgesics	Inhalants	Cannabis
HGN	Present	None	None	Present	None	Present	None
Vertical Gaze Nystagmus	Present (High Dose)	None	None	Present	None	Present (High Dose)	None
Lack of Convergence	Present	None	None	Present	None	Present	Present
Pupil Size	Normal (1)	Dilated	Dilated	Normal	Constricted	Normal (4)	Dilated (6)
Reaction to Light	Slow	Slow	Normal (3)	Normal	Little or None Visible	Slow	Normal
Pulse Rate	Down (2)	Up	Up	Up	Down	Up	Up
Blood Pressure	Down	Up	Up	Up	Down	Up/Down (5)	Up
Body Temperature	Normal	Up	Up	Up	Down	Up/Down/ Normal	Normal
Muscle Tone	Flaccid	Rigid	Rigid	Rigid	Flaccid	Normal or Flaccid	Normal
General Indicators	Disorientation Droopy eyelids Drowsiness Drunk-like behavior Slow, sluggish reactions Thick, slurred speech Uncoordinated Unsteady walk	Anxiety Body tremors Dry mouth Euphoria Exaggerated reflexes Excited Eyelid tremors Grinding teeth Increased alertness Insomnia Irritability Redness to the nasal area Restlessness Runny nose Talkative	Body tremors Dazed appearance Difficulty with speech Flashbacks Hallucinations Memory loss Nausea Paranoia Perspiring Poor perception of time and distance Synesthesia Uncoordinated NOTE: With LSD, Piloerection may be observed (goose bumps, hair standing on end)	Blank stare Confusion Chemical odor (PCP) Cyclic behavior Difficulty with speech Disoriented Early HGN Onset Hallucinations Incomplete verbal responses Increased pain threshold "Moon Walking" Non-communicative Perspiring (PCP) Possibly violent Sensory distortions Slow, slurred speech Slowed responses Warm to touch (PCP)	Depressed reflexes Droopy eyelids Drowsiness Dry mouth Euphoria Facial itching Inability to concentrate Nausea "On the Nod" Puncture marks Slow, low, raspy speech Slow breathing Slow deliberate movements NOTE: Tolerant users exhibit relatively little psychomotor impairment.	Bloodshot eyes Confusion Disoriented Flushed face Intense headaches Lack of muscle control Non-communicative Odor of substance Possible nausea Residue of substance Slow, thick, slurred speech Watery eyes	Altered time/distance perception Alteration in thought formation Body tremors Bloodshot eyes Disoriented Drowsiness Eyelid tremors Euphoria Impaired memory Increased appetite Lack of concentration Mood changes Odor of Marijuana Rebound Dilation Relaxed inhibitions Sedation
Duration of Effects	Ultra-Short: A few minutes Short: Up to 5 hours Intermediate: 6-8 hours Long: 8-14 hours	Cocaine: 5-90 minutes Methamphetamine: Up to 12 hours	Duration varies widely from one hallucinogen to another: LSD: 10-12 hours Psilocybin: 2-3 hours	PCP Onset: 1-5 minutes Peak Effects: 15-30 minutes Exhibits effects up to 4-6 hours DXM: Onset 15-30 min. Effects 3-6 hours	Heroin: 4-6 hours Methadone: Up to 24 hours Others: Vary	6-8 hours for most volatile solvents Anesthetic gases and aerosols – very short duration	2-3 hours – exhibit and feel effects (Impairment may last up to 24 hours, without awareness of effects)
Usual Methods of Administration	Injected (occasionally) Insufflation Oral	Insufflation Injected Oral Smoked	Insufflation Oral Smoked Transdermal	Injected Insufflation Oral Smoked Transdermal	Injected Insufflation Oral Smoked Transdermal	Inhalation	Oral Smoked Transdermal
Overdose Signs	Clammy skin Coma Rapid, weak pulse Shallow breathing	Agitation Hallucinations	Intense bad "trip" Hyperthermia Convulsions	Deep coma Seizures and convulsions	Cold, clammy skin Coma Convulsions Slow, shallow breathing	Cardiac arrhythmia Possible psychosis Respiration ceases Severe nausea/vomiting Risk of death	Excessive vomiting Fatigue Acute anxiety attacks Paranoia Possible psychosis

FOOTNOTE: These indicators are the most consistent with the category, keep in mind that there may be variations due to individual reaction, dose taken and drug interactions.

1) Soma, Quaaludes and some antidepressants usually dilate pupils
2) Quaaludes, ETOH and some antidepressants may elevate
3) Certain psychedelic amphetamines may cause slowing
4) Normal, but may be dilated
5) Down with anesthetic gases, up with volatile solvents and aerosols
6) Pupil size possibly normal

Indicators Consistent with Drug Categories

	CNS Depressants	CNS Stimulants	Hallucinogens	Dissociative Anesthetics	Narcotic Analgesics	Inhalants	Cannabis
HGN	Present	None	None	Present	None	Present	None
Vertical Gaze Nystagmus	Present (High Dose)	None	None	Present	None	Present (High Dose)	None
Lack of Convergence	Present	None	None	Present	None	Present	Present
Pupil Size	Normal (1)	Dilated	Dilated	Normal	Constricted	Normal (4)	Dilated (6)
Reaction to Light	Slow	Slow	Normal (3)	Normal	Little or None Visible	Slow	Normal
Pulse Rate	Down (2)	Up	Up	Up	Down	Up	Up
Blood Pressure	Down	Up	Up	Up	Down	Up/Down (5)	Up
Body Temperature	Normal	Up	Up	Up	Down	Up/Down/ Normal	Normal
Muscle Tone	Flaccid	Rigid	Rigid	Rigid	Flaccid	Normal or Flaccid	Normal

General Indicators	Disorientation Droopy eyelids Drowsiness Drunk-like behavior Slow, sluggish reactions Thick, slurred speech Uncoordinated Unsteady walk	Anxiety Body tremors Dry mouth Euphoria Exaggerated reflexes Excited Eyelid tremors Grinding teeth Increased alertness Insomnia Irritability Redness to the nasal area Restlessness Runny nose Talkative	Body tremors Dazed appearance Difficulty with speech Flashbacks Hallucinations Memory loss Nausea Paranoia Perspiring Poor perception of time and distance Synesthesia Uncoordinated NOTE: With LSD, Piloerection may be observed (goose bumps, hair standing on end)	Blank stare Confusion Chemical odor (PCP) Cyclic behavior Difficulty with speech Disoriented Early HGN Onset Hallucinations Incomplete verbal responses Increased pain threshold "Moon Walking" Non-communicative Perspiring (PCP) Possibly violent Sensory distortions Slow, slurred speech Slowed responses Warm to touch (PCP)	Depressed reflexes Droopy eyelids Drowsiness Dry mouth Euphoria Facial itching Inability to concentrate Nausea "On the Nod" Puncture marks Slow, low, raspy speech Slow breathing Slow deliberate movements NOTE: Tolerant users exhibit relatively little psychomotor impairment.	Bloodshot eyes Confusion Disoriented Flushed face Intense headaches Lack of muscle control Non-communicative Odor of substance Possible nausea Residue of substance Slow, thick, slurred speech Watery eyes	Altered time/distance perception Alteration in thought formation Body tremors Bloodshot eyes Disoriented Drowsiness Eyelid tremors Euphoria Impaired memory Increased appetite Lack of concentration Mood changes Odor of Marijuana Rebound Dilation Relaxed inhibitions Sedation
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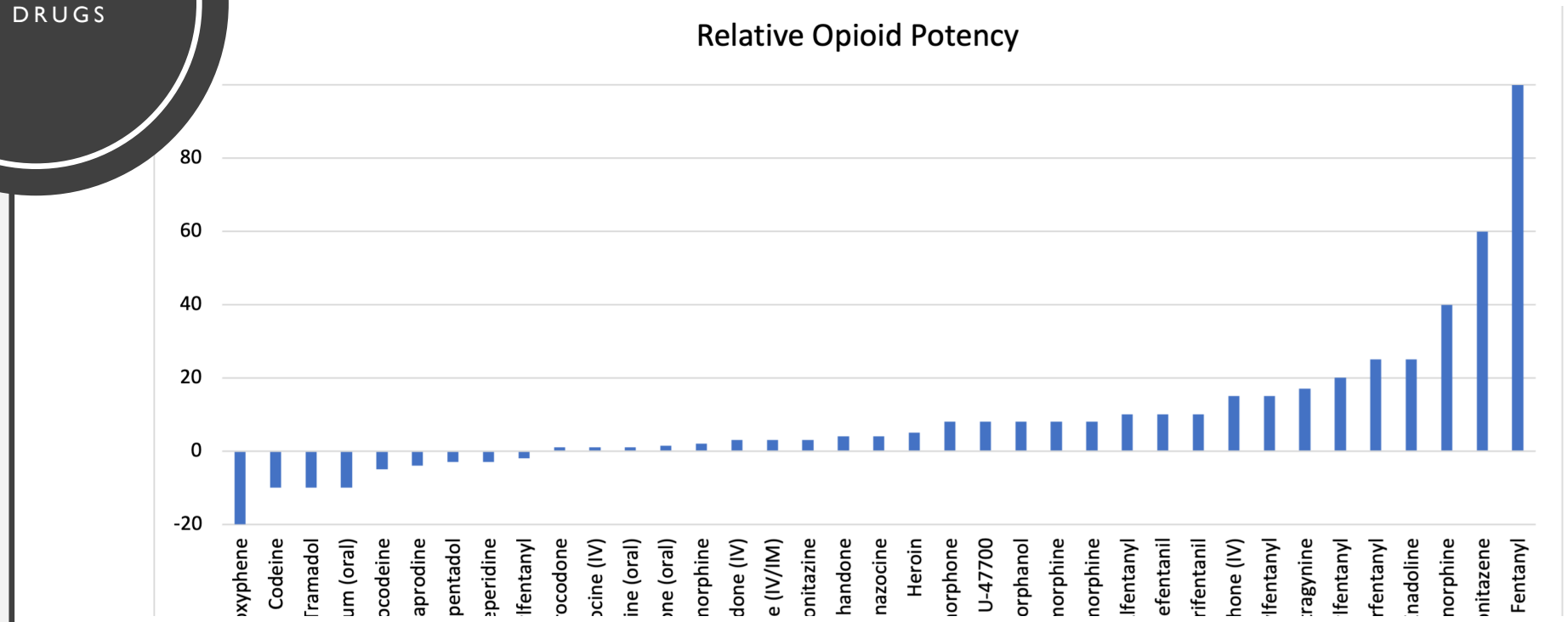
Usual Methods of Administration	Injected (occasionally) Insufflation Oral	Insufflation Injected Oral Smoked	Insufflation Oral Smoked Transdermal	Injected Insufflation Oral Smoked	Injected Insufflation Oral Smoked	Inhalation	Oral Smoked Transdermal

SO NOW I KNOW THAT I CAN'T COMPARE TO A 0.08 ALCOHOL

But why can't we have a per se for each drug or a category?

CATEGORY OF DRUGS



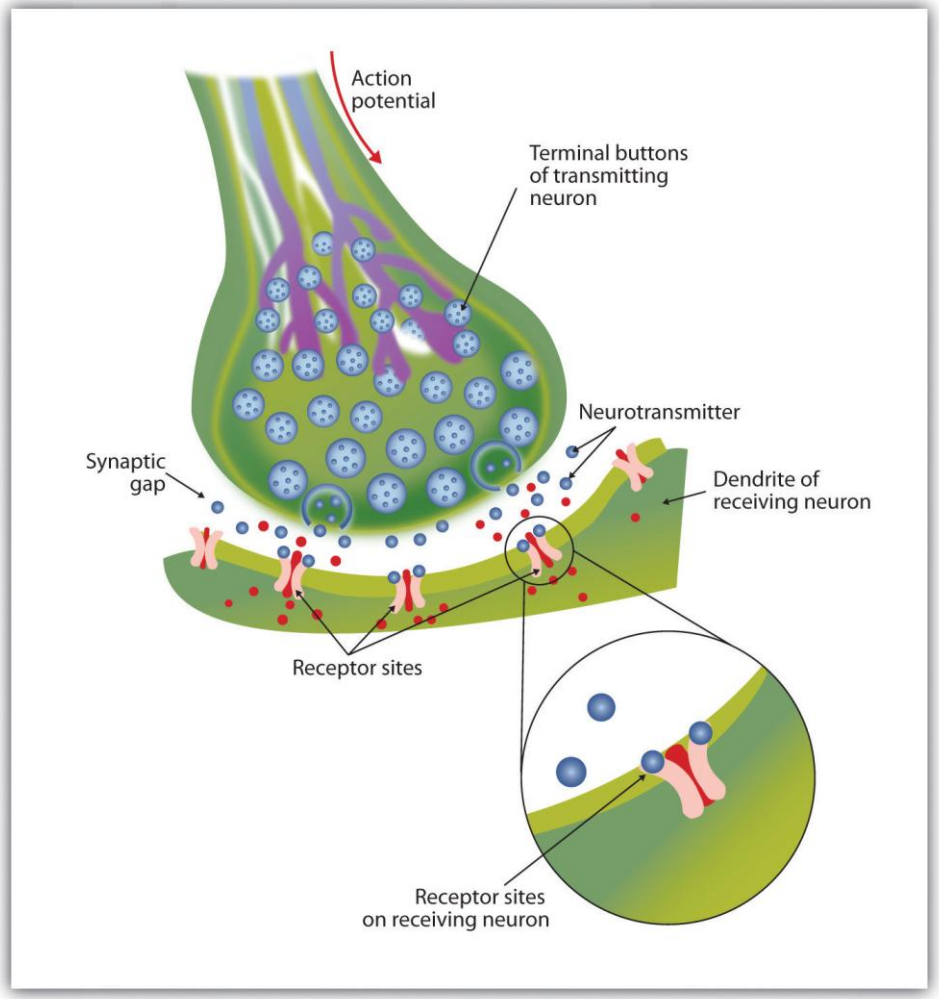
TOLERANCE

- A person's diminished response to a drug, which occurs when the drug is used repeatedly and the body adapts to the continued presence of the drug.
  - Tolerance does not mean abuse or addiction
  - However, abuse and addiction lead to tolerance.

TOLERANCE

- Receptor desensitization
- Reduction in receptor density
- Changes in action potential firing rate
- Alterations in protein transcription

- Adaptations in behavior
  - Learning to actively overcome drug-induced impairment through practice



TOLERANCE

- Opioids – start with hydrocodone and work up with chronic pain
- Fentanyl - wow
  - Therapeutic is 1-3 ng/ml
  - Death around 5-6 ng/ml
- Societal Tolerance

4-Year Assessment of Concentration Data

- Number of meth positives nearly doubled from 1,541 to 2,998

- Number of fentanyl positive cases climbed to 2,122 in 2020 from 330 in 2017

Drug	Year	Median (ng/mL)	Max (ng/mL)
THC	2017	4.0	140
	2018	4.4	100
	2019	4.4	230
	2020	4.5	160

4-Year Assessment of Concentration Data

- Number of meth positives nearly doubled from 1,541 to 2,998

- Number of fentanyl positive cases climbed to 2,122 in 2020 from 330 in 2017

Drug	Year	Median (ng/mL)	Max (ng/mL)
Methamphetamine	2017	180	5,500
	2018	230	8,800
	2019	240	8,200
	2020	240	13,000

4-Year Assessment of Concentration Data

- Number of meth positives nearly doubled from 1,541 to 2,998

- Number of fentanyl positive cases climbed to 2,122 in 2020 from 330 in 2017

Drug	Year	Median (ng/mL)	Max (ng/mL)
Fentanyl	2017	4.2	56
	2018	3.4	83
	2019	4.6	140
	2020	5.4	310
Amphetamine	2017	36	1,400
	2018	39	4,100
	2019	39	5,400
	2020	37	2,700

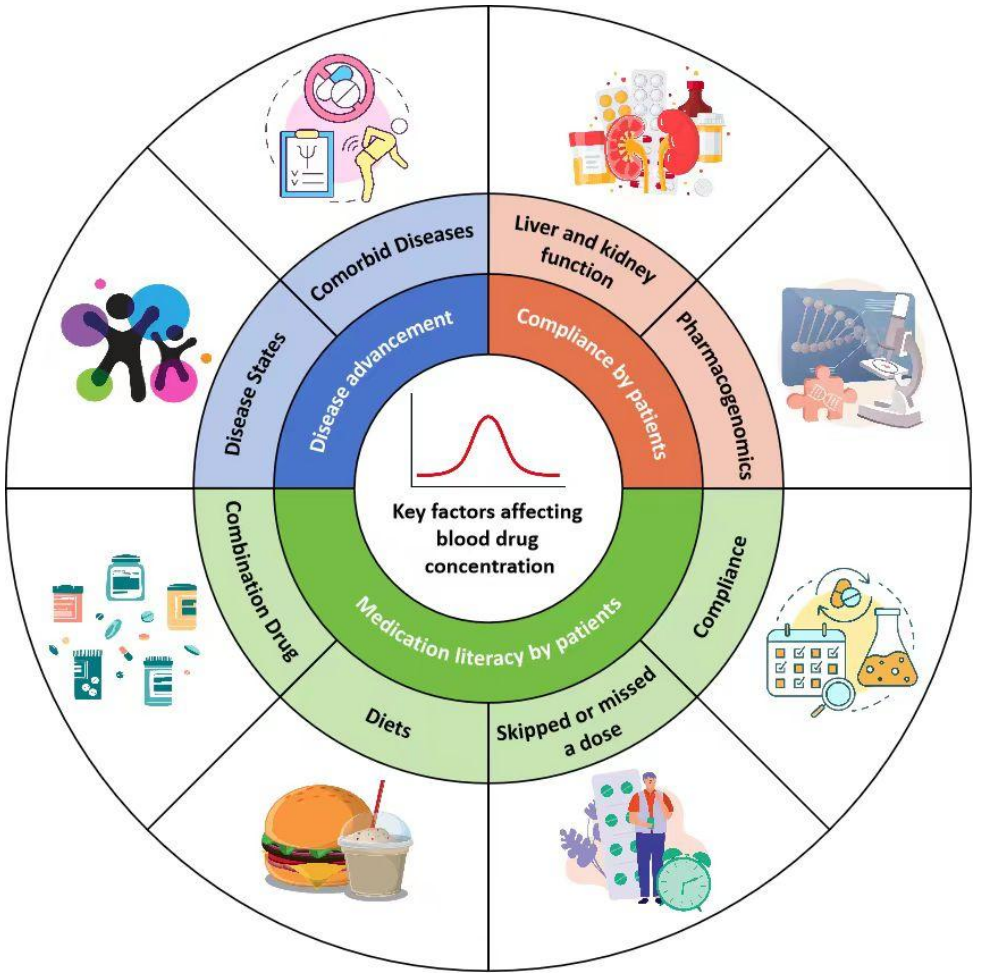
4-Year Assessment of Concentration Data

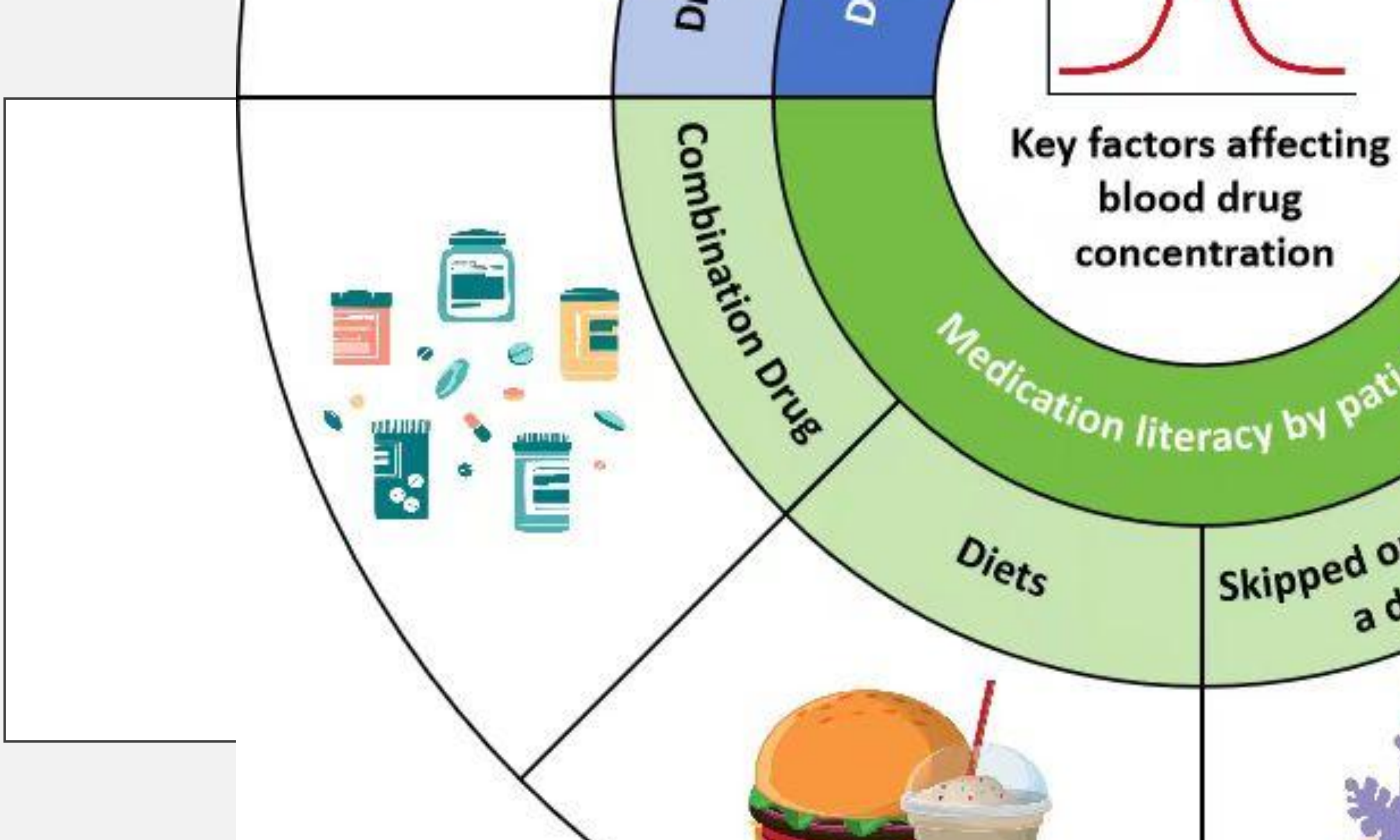
- Number of alprazolam cases steadily declined from 1,951 in 2017 to 46 in 2020

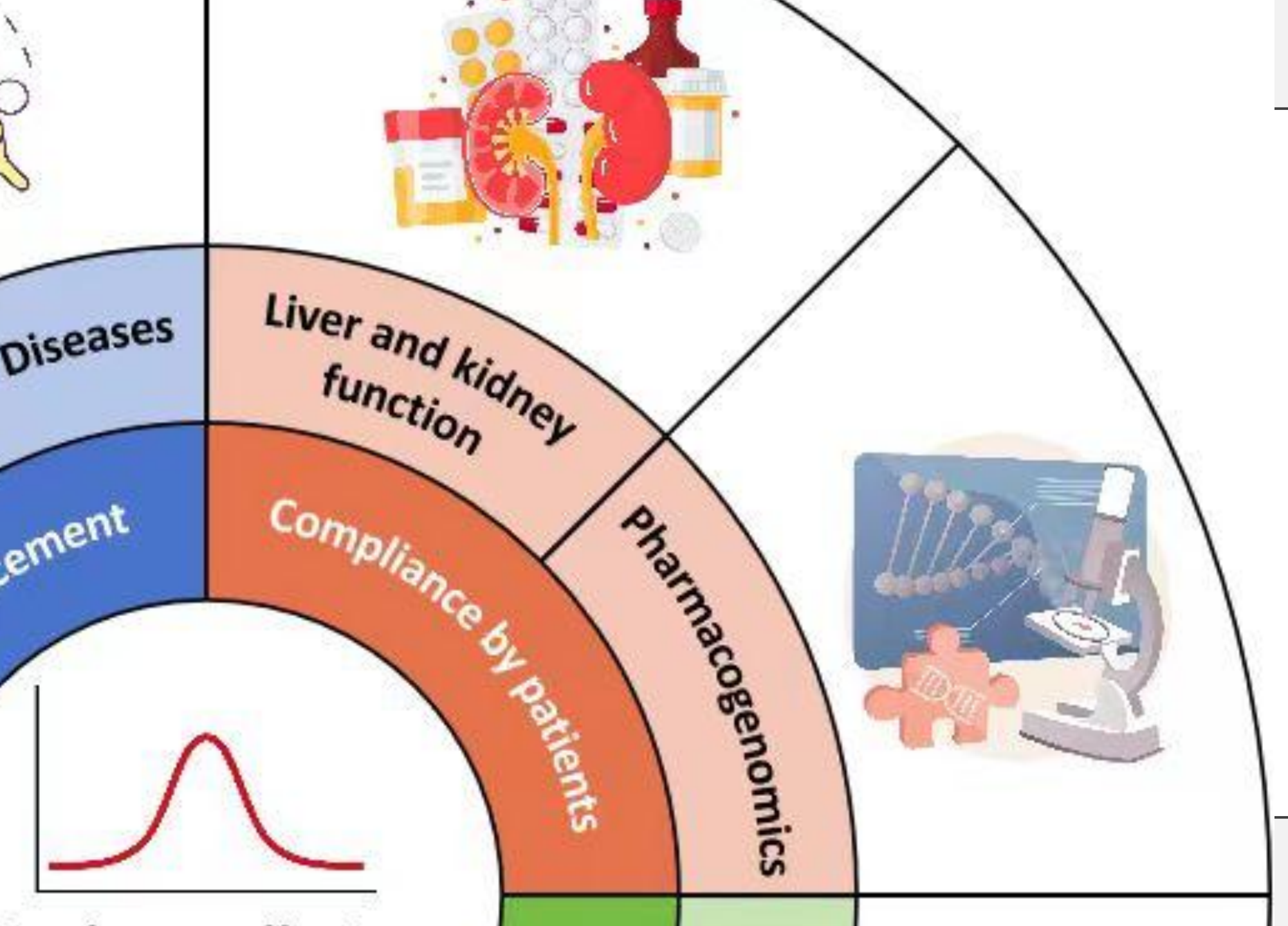
Drug	Year	Median (ng/mL)	Max (ng/mL)
Cocaine	2017	65	7,000
	2018	66	2,300
	2019	67	7,000
	2020	56	1,400
Alprazolam	2017	44	1,300
	2018	40	1,200
	2019	34	390
	2020	32	1,400
Methadone	2017	190	1,200
	2018	215	1,000
	2019	230	1,100
	2020	210	1,200
7-aminoclonazepam	2017	24	340
	2018	25	290
	2019	35	380
	2020	30	180

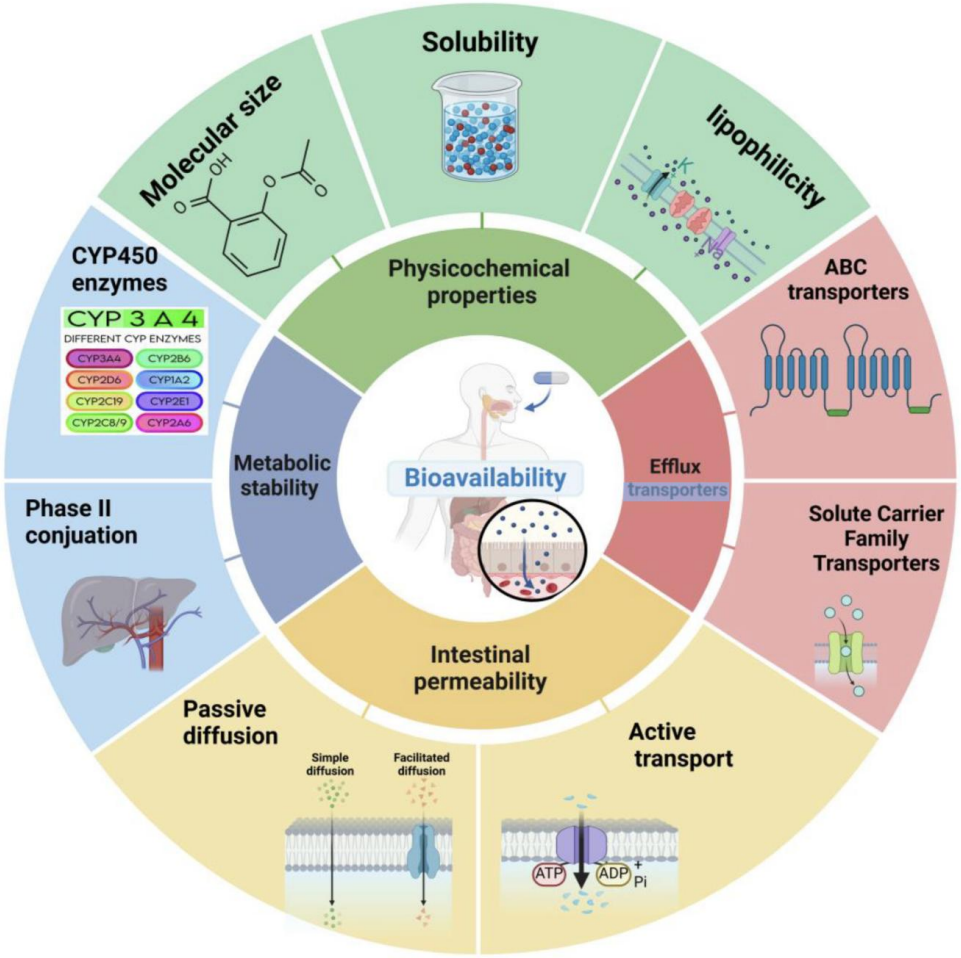
TOLERANCE

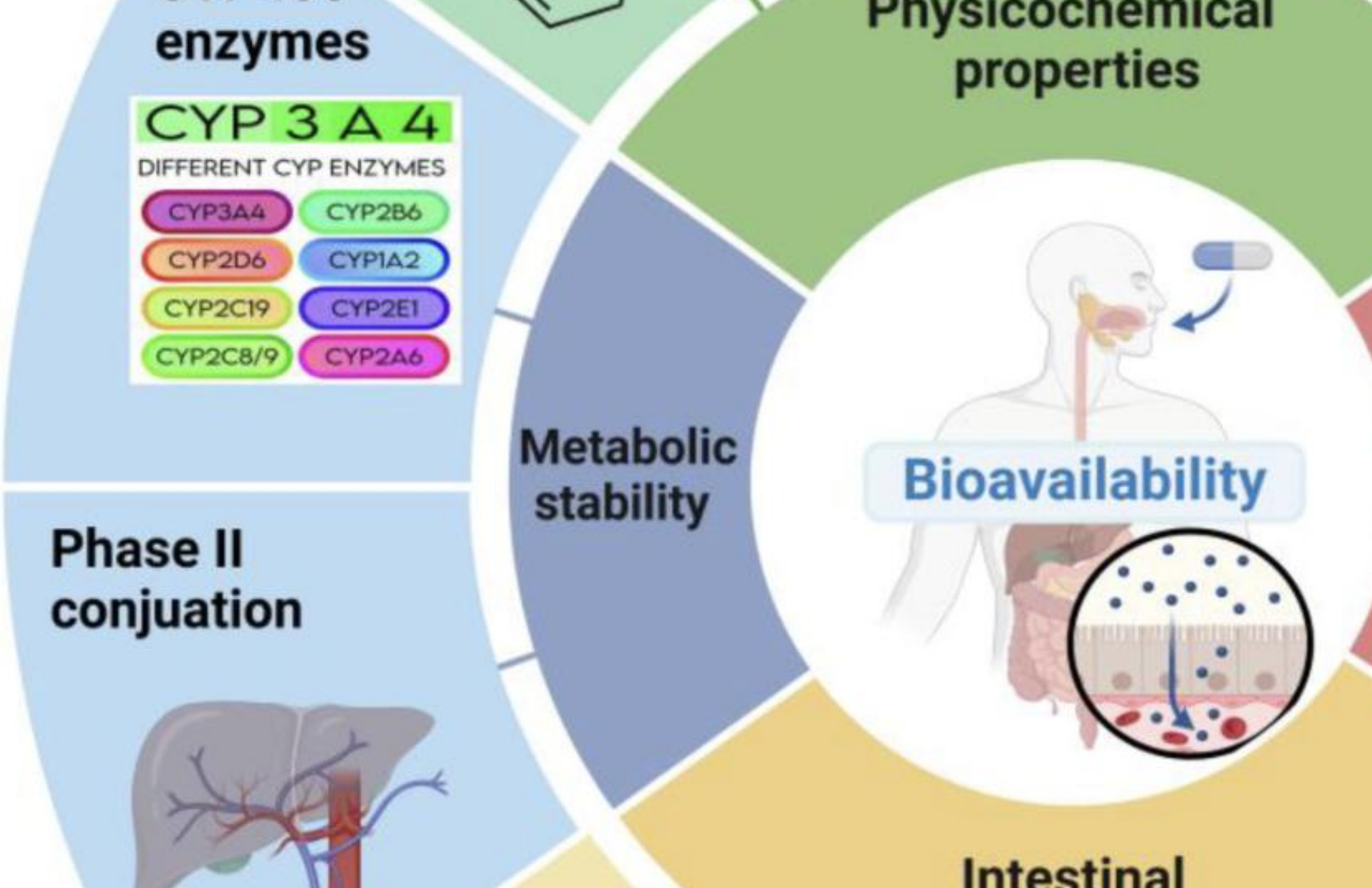
- Is not permanent
  - Will lose tolerance with cessation of use
  - This may be quick in some cases


Comorbid Diseases
Liver and kidney function
Disease States
Disease advancement
Compliance by patients
Pharmacogenomics
Key factors affecting blood drug concentration
Combination Drug
Medication literacy by patients
Compliance
Diets
Skipped or missed a dose


Key factors affecting blood drug concentration
Combination Drug
Medication literacy by pati
Diets
Skipped o
a d


Diseases
Liver and kidney function
cement
Compliance by patients
Pharmacogenomics


Solubility
Molecular size
lipophilicity
CYP450 enzymes
CYP 3 A 4
DIFFERENT CYP ENZYMES
CYP3A4
CYP2B6
CYP2D6
CYP1A2
CYP2C19
CYP2E1
CYP2C8/9
CYP2A6
Physicochemical properties
ABC transporters
Metabolic stability
Bioavailability
Efflux transporters
Phase II conjuation
Solute Carrier Family Transporters
Intestinal permeability
Passive diffusion
Simple diffusion
Facilitated diffusion
Active transport
ATP
ADP
Pi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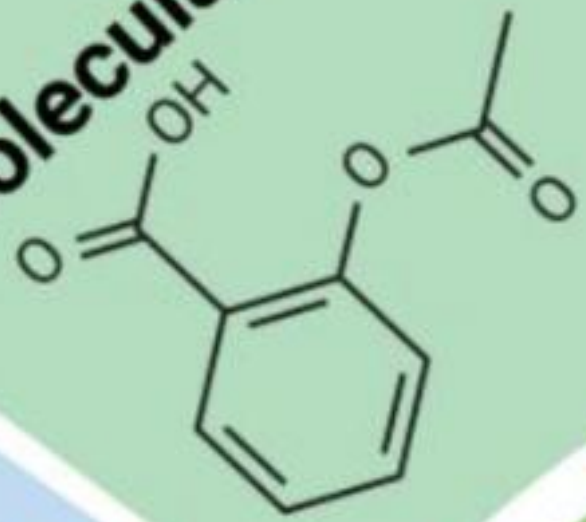
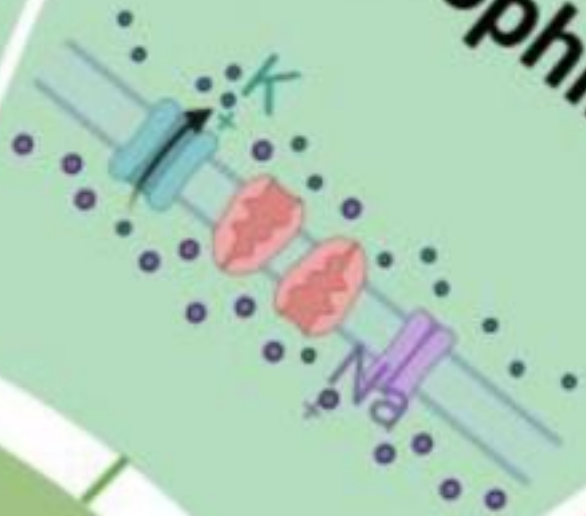


Solubility

lipophilicity



50
nes

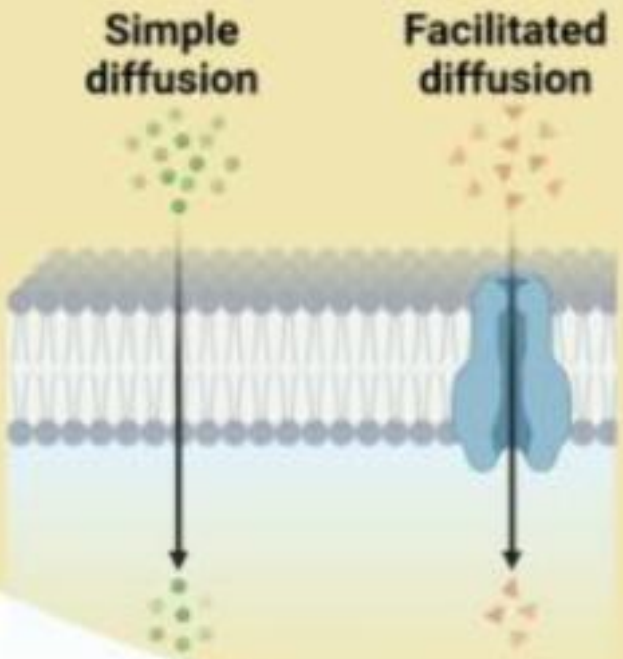
3 A 4
CYP ENZYMES
CYP2B6
CYP1A2
CYP2E1

Physicochemical properties

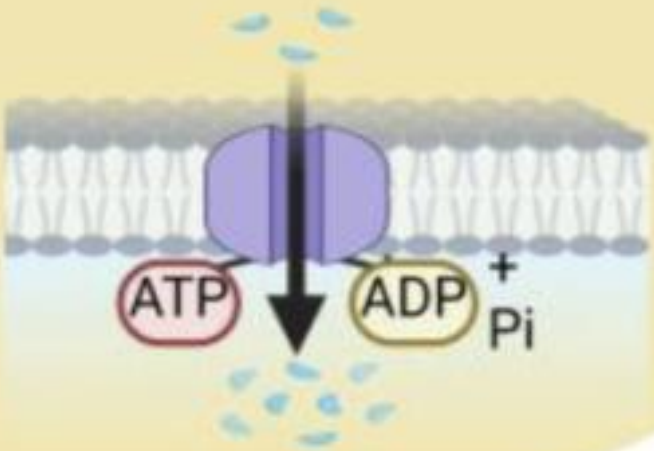
A
trans

Intestinal permeability

Passive diffusion



Active transport



INTERPRETATION OF DRUG RESULTS

- So….. how do we interpret drug results?

- Carefullly

INTERPRETATION OF DRUG RESULTS

- Need information related to the case:
  - Are other drugs present
  - What is the history of use
  - How long between the event and blood draw
  - Personal (age, sex, etc)
  - Observations (officer, witnesses, video)

INTERPRETATION OF DRUG RESULTS

- Must correlate the drugs identified as well as the concentration with the observations and context of the case

EtOH +
0.043 g%

- Amphetamine 17 ng/mL
- Methamphetamine 240 ng/mL
- Fentanyl 6.3 ng/mL
- NorFentanyl 7.1 ng/mL
- Clonazolam 13 ng/mL
- Gabapentin 17,360 ng/mL
- Buprenorphine 1.2 ng/mL
- Norbuprenorphine 2.6 ng/mL
- Tramadol 66 ng/mL
- Acetone + 0.022 g%

EtOH + 0.043 g%

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ASB 037 GUIDELINES FOR OPINIONS AND TESTIMONY

5.2 Appropriate Opinions and Testimony by a Toxicologist

Through testimony and offering an expert toxicological opinion, it is generally appropriate for a toxicologist to:

a) discuss a laboratory report and any analytical work that supports that report. Applicable limitations should also be addressed.

b) qualify a reported concentration in the context of a given case as subtherapeutic, therapeutic, toxic or lethal when that statement can be backed by appropriate references, databases and/or other relevant information.

c) address the pharmacokinetics/toxicokinetics, as well as the pharmacodynamics/ toxicodynamics of drugs or other chemicals.

d) discuss the toxicological impact of the presence, absence and/or stability of drugs or other chemicals.

e) address impairment for the average individual to the extent that effects are consistent with documented pharmacodynamic and toxicodynamic properties of the substance and within the context of a given case.

f) perform or discuss toxicological calculations that are generally accepted in the field and can be supported by research and references, provided appropriate limitations are cited. For example, ethanol back extrapolation calculations may be performed.

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5.3 Inappropriate Opinions and Testimony by a Toxicologist

d) A toxicologist should not imply impairment of an individual based on analytical findings from urine, hair or other matrices unless supported by the literature.

e) A toxicologist should not opine as to the absolute cause of an accident.

f) A toxicologist should not perform extrapolation calculations for drugs other than ethanol.

i) A toxicologist should not opine as to the effects of a drug or combination of drugs on a specific individual without context of a given case. This does not preclude a toxicologist from addressing general effects of drugs at varying concentrations (Section 5.2.).

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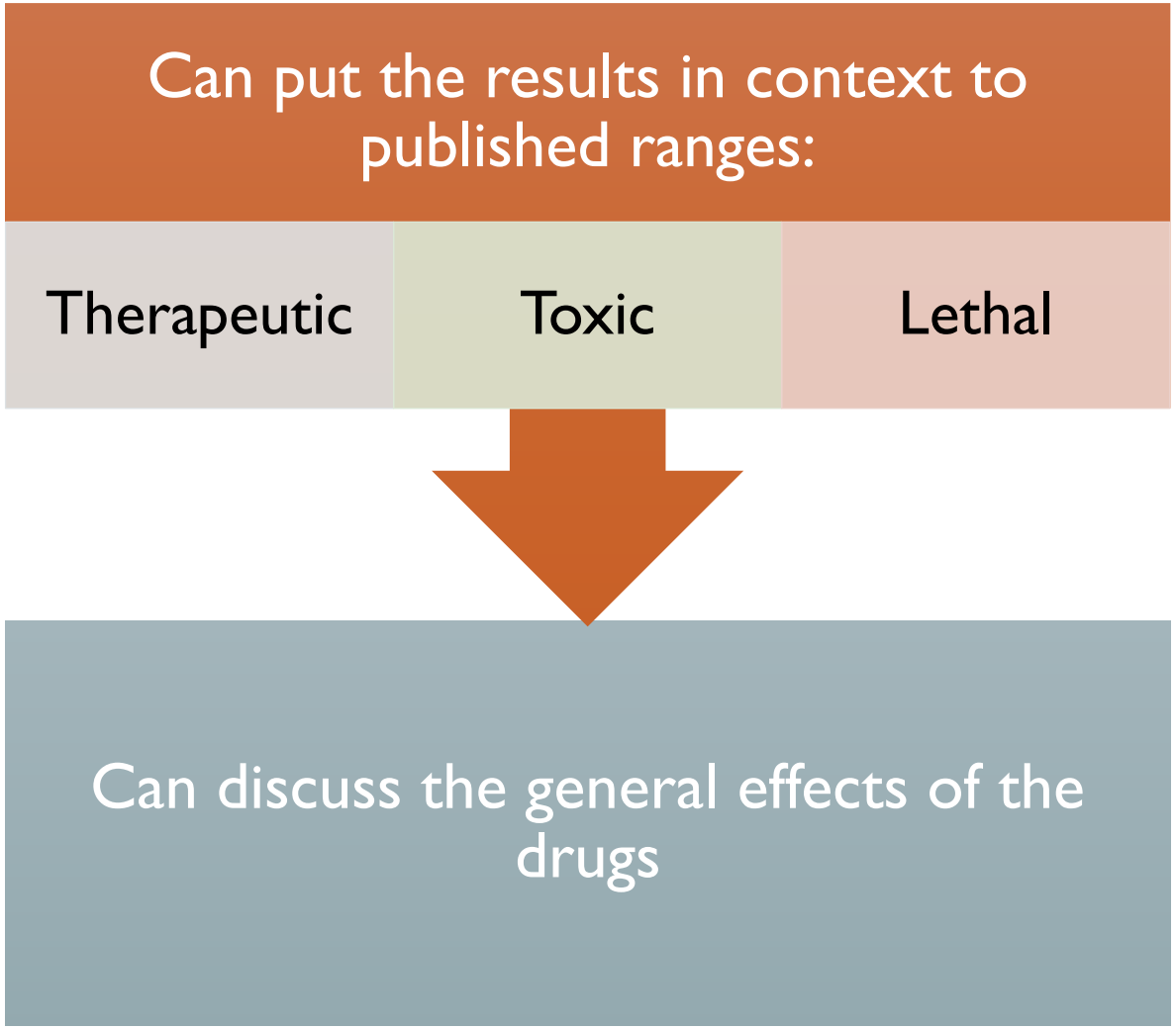
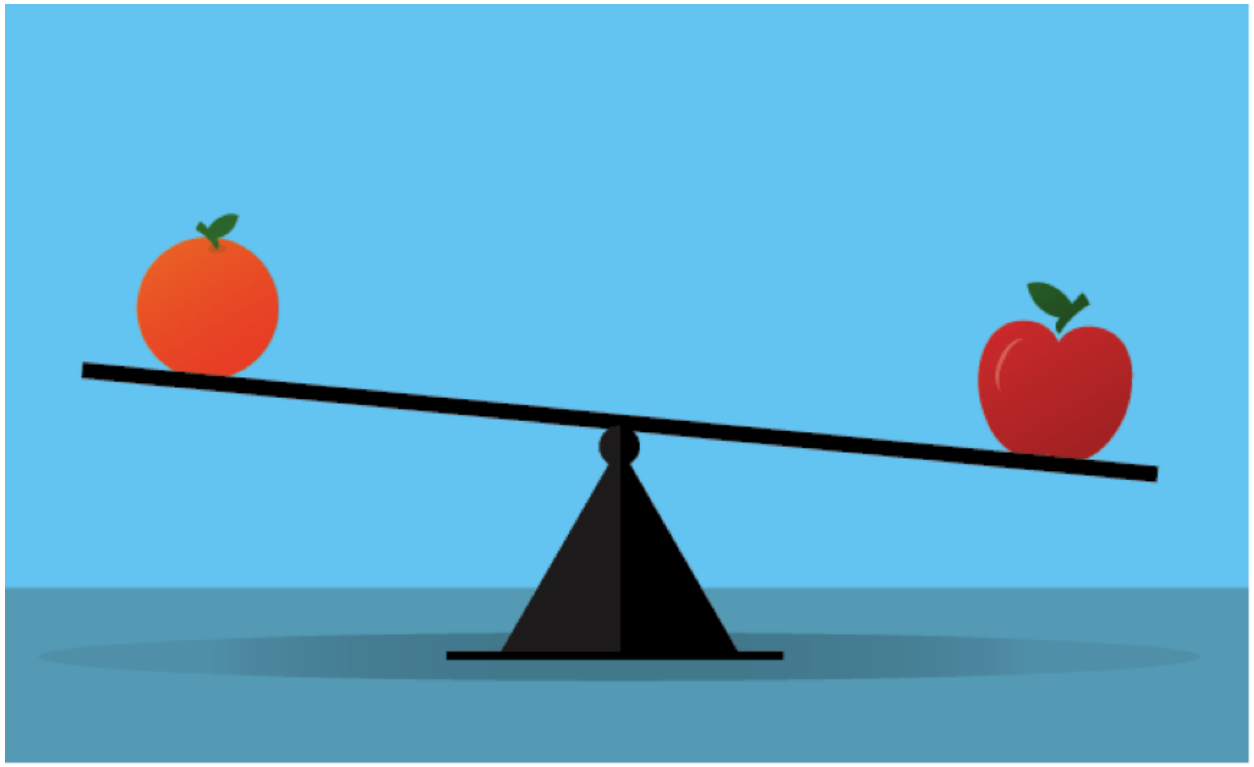
CONTEXT AND GENERAL EFFECTS



BLOOD VERSUS URINE VERSUS ORAL FLUID



URINE

Less invasive sample collection

Some on-site testing capability

Broad detection time window

Targeting metabolites for detection

No relationship to brain concentrations

No relationship between urine concentration and effect

Time delay for collection

BLOOD

Closest relationship to brain concentrations

Targeting parent drug for detection

Large literature for comparative interpretation

Somewhat invasive collection

Limited detection window

Time delay for collection

Lack of quantitative effect relationship

No on-site testing capability

ORAL FLUID

Least invasive collection

No time delay for collection

Targeting parent drug for detection

On-site testing capabilities

Limited relationship to blood concentrations

No relationship between concentrations and effect

Limited detection window

Limited specimen volume

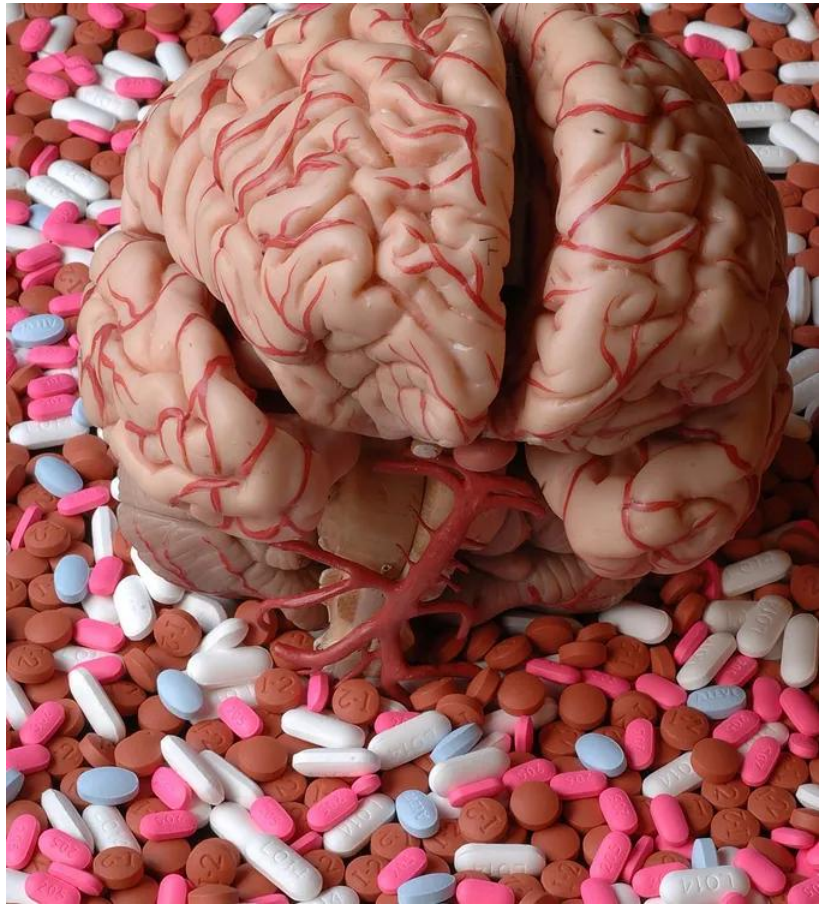
BRAIN TISSUE

Most invasive collection

Difficult to collect

Direct correlation to impairment

Significantly reduce recidivism



CLINICAL NUMBERS

Drugs are likely in urine and not confirmed

- There may be a number or may not be one

Alcohol results are typically enzymatic and in serum

Even if clinical results are confirmed or run on GC (alcohol) they are not forensic in nature.

SUMMARY

- The current research and science does not support the use of per se for drugs
  - Blood drug concentrations are poorly correlated with driving impairment
  - Blood and OF per se limits often fail to discriminate between impaired and unimpaired drivers
- The use of per se levels in urine are inappropriate to determine impairment

SUMMARY

- The use of per se may provide the public with a perception of safety below the per se value
- Drug levels below per se with signs of impairment should be evaluated as an impaired driver
- Tolerant individuals over the per se may not be impaired to the point where they cannot operate a motor vehicle

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REGIONAL
TOXICOLOGY LIAISON

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