Richard De La Garza, II, Ph.D. Written Statement for the United States Sentencing Commission July 28, 2025

This hearing is designed to help the Commission gather factual information about methamphetamine to help inform a later policy determination about whether the Commission should equalize penalties for the differing forms of methamphetamine. This report will provide answers to several questions, including: (1) What are the differences, if any, between methamphetamine of varying purity levels? (2) Are there any differences in chemical structure or pharmacological effects? (3) Does higher purity equate to stronger potency, such that higher purity methamphetamine achieves its desired effect for a longer period of time? Do individuals using higher purity methamphetamine tend to use a smaller dosage of the drug? (4) Does higher purity methamphetamine have greater adverse effects?

My expertise stems from my training as a neuroscientist with expertise in clinical pharmacology. Research from my lab has included evaluation of several candidate medications for methamphetamine use disorder, both in Phase I and Phase II clinical trials. To date, there are zero FDA-approved medications for methamphetamine use disorder highlighting the continued need for this critical research. A key part of this work involves recruiting and interviewing individuals from the community (both in California and Texas) who admit to current use of methamphetamine and a subsequent diagnostic interview assures that they meet DSM criteria for methamphetamine use disorder. Our evaluations include assessments of mood (anxiety and depression symptoms), extensive evaluations of the types of drugs used by the individual, route and frequency of usage, years of use, criminal history, and attempts to find treatment.

Methamphetamine is a potent central nervous system stimulant that promotes release and blocks reuptake of the monoamines dopamine, norepinephrine, and serotonin in presynaptic terminals, leading to euphoria, increased energy, alertness, appetite suppression, and sympathetic activity (increased heart rate and blood pressure). It also inhibits vesicular storage of monoamines and increases cytosolic neurotransmitter levels with potential downstream neurotoxicity. The toxic effects of methamphetamine include hypertension and heart disease, cognitive impairments, and increased incidences of depression and psychosis. Methamphetamine's effects are characterized by rapid absorption, prolonged elimination, and significant individual variance

According to the June 2024 report, titled Methamphetamine Trafficking Offenses in the Federal Criminal Justice System, methamphetamine is the most prevalent drug in federal drug trafficking cases. That report questions whether the current statutory and guideline structure, based on purity, meaningfully reflects offender culpability. The report revealed that seized and tested methamphetamine is extremely pure (98% median purity). On this basis, the authors recommended that the 10:1 sentencing ratio for pure methamphetamine vs. mixture is outdated and should be revised. Further, purity was consistently high regardless of region or proximity to the border, undermining assumptions that higher purity equals higher culpability.

From a pharmacological perspective, higher chemical purity (i.e., higher percentage of d-methamphetamine) increases active dose delivered per weight and amplifies central stimulant and cardiotoxic effects. Alternatively, lower purity (due to adulterants or presence of l-isomer or inert cutters) reduces potency, shortens duration, and may introduce unpleasant or non-stimulant effects. Thus, isomeric/purity composition (not just total amount) critically shapes pharmacodynamic profile: high-purity d-meth results in stronger, longer, and more addictive effects; impure or racemic formulations blunt efficacy and user reinforcement. While the assumption is that high-purity meth (often >95%) indicates production by major traffickers or labs, this is no longer reliable. The DEA's 2022 Profiling Program reported that 88% of analyzed domestic samples were over 95% pure, regardless of seizure size-even some small seizures contained ultra-pure meth. At U.S.-Mexico border entry points, samples averaged ~98% purity, even in small packages—showing that users on the street regularly obtain high-purity methamphetamine. Since the 2006 Combat Methamphetamine Epidemic Act limited access to ephedrine, cartels shifted to P2P precursor methods, leading to consistently high purity "super meth". By 2012, 96% of DEA meth samples were P2P-based—with purity levels up to ~97%, making high purity more common and less indicative of large-scale trafficking.

Trafficking-level seizures typically reflect ultra-high purity, while user-level products range widely, with average purity around 58%. Cutting methamphetamine with cheaper substances stretches the product and increases profits. Adulterants can be active drugs (e.g., opioids) or inactive fillers (e.g., caffeine). Some cuts are added to intensify the high, reduce comedown, or mask impurities. A mix of stimulants (e.g., caffeine, ephedrine) can prolong the effects produced by methamphetamine, while depressants (e.g., benzodiazepines) smooth the crash. **These adulterants significantly increase the risk of cardiotoxicity, neurotoxicity, dependence, and overdose** (especially pertinent to opioids). The unpredictable nature of

street methamphetamine supports arguments against sentencing enhancements based solely on purity, since adulterated methamphetamine can be more, not less, dangerous. Increasingly, though, street-level users can access high-purity methamphetamine (especially with the rise of Mexican "superlabs" described above), complicating assumptions that high purity equates to a high-level trafficker.

Some research suggests crystal methamphetamine is correlated with higher rates of dependence, but that reflects route of administration (smoking/injection) and concentration in use contexts, not an inherent pharmacological difference per milligram. Importantly, the pharmacodynamics of methamphetamine are largely unaffected by the purity level in street doses — a user simply consumes more or less of the drug. Methamphetamine HCl is a salt, and whether in crystalline or powder form, the biological effect per milligram of actual methamphetamine is the same. Research from my laboratory and others have shown that users will self-administer just enough methamphetamine to produce pleasurable effects, but not necessarily all doses of methamphetamine that are available. Further, our lab has shown that a history of unrestricted access to methamphetamine is associated with long-lasting increases in methamphetamine use in the future.

The discussion on methamphetamine purity may be informed by considering the evolution of THC (commonly referred to as marijuana) over time. Like, methamphetamine, marijuana purity and composition have changed significantly over the last 60 years primarily due to shifts in cultivation, processing, market demands, and regulatory oversight. In the 1960s, THC potency was typically 0.5%–1.5%, with a balanced profile of THC, CBD and minor cannabinoids (which may have moderated psychoactive effects). Most marijuana was imported, often brick weed from Mexico or Colombia, and seeds, stems, and leaves were common in retail products, reducing cannabinoid concentration. Adulterants were rare, but some low-quality street cannabis may have been sprayed with substances to increase weight or appearance (e.g., sugar water, paraffin wax). Lastly, mold and pesticide contamination were uncontrolled and untested.

In contrast, THC potency of modern marijuana (2020s) ranges from 15-95% (flower: 15–30%+ versus concentrates: 60–95%). Concentrates today contain THC levels never seen before 2010. In fact, regulatory concerns have emerged around potency caps in some states due to mental health and addiction risk. Current products are often bred to have extremely high THC and minimal CBD (inverse of older strains). In regulated markets, cannabis is tested for

pesticides, heavy metals, residual solvents (in concentrates), and microbials (e.g., mold, mildew, salmonella). Illicit market products, especially vapes and edibles, can contain Vitamin E acetate (linked to lung illness), synthetic cannabinoids (e.g., Spice, K2) misrepresented as natural THC, and mycotoxins, residual butane, or unapproved flavoring agents.

Tables 1 and 2 (below) show how marijuana and methamphetamine have changed over time regarding purity, types of adulterants, and several other factors.

Table 1: Marijuana Then versus Now

Category	1960s Marijuana	2020s Marijuana
THC Potency	0.5%-1.5%	15%–30%+ (flower) 60%–95% (concentrates)
CBD Content	Moderate	Very low
Adulterants	Rare (sugar, wax)	Rare in legal, common in illicit (Vitamin E acetate, synthetics)
Contaminants	No testing, mold/seeds	Strictly tested (legal) Risky in illicit
Cultivation Method	Outdoor, landrace	Indoor, hydroponic, genetic optimization
Common Form	Brick weed (flower)	Flower, vapes, dabs, edibles
Concentrates	Nonexistent	Widespread: wax, shatter, rosin, distillates
Vape Products	Nonexistent	Very common; regulated (legal) Risk of adulterants (illicit)
Legal vs Illicit Market	Mostly illegal; smuggled imports	Legal in many states with testing Illicit still prevalent and risky

Table 2: Methamphetamine Then versus Now

Category	Past Methamphetamine (Pre-1990s)	Current Methamphetamine (2020s–2025)
Purity	10%-30%	90%+ (street level)
Common Form	Powder or pills	Crystalline ('ice')
Primary Source	Domestic (small labs)	Mexico (superlabs, industrial scale)
Production Method	Ephedrine/pseudoephedrine-based (Nazi method)	P2P (phenyl-2-propanone method), no cold meds required
Contaminants/Adulterants	Household chemicals, toxic byproducts	Very high purity; occasional fentanyl or cutting agents
Legal Status	Some pharmaceutical use (e.g., Desoxyn)	Desoxyn still legal in rare prescriptions; most use is illicit
Route of Administration	Oral, snorting, occasional injection	Smoking, injection, occasional vaping
Health Impact Trends	Addiction and cognitive impairment over time	More severe psychosis, overdoses, and rapid deterioration

Acknowledging how these and other drugs change over time is critical for ultimately understanding why individuals use their drug of choice. Generally, it is not a matter of seeking out more or less pure forms of methamphetamine, it is mostly about purchasing and using what is readily available at that given time. For THC, sentencing is usually based on the total weight of the product, regardless of purity. Specifically, there is no federal sentencing distinction based on the percentage of THC in a mixture (e.g., comparing 20% THC flower vs. 90% THC extract). This is in stark contrast to the current approach for methamphetamine, in which federal law explicitly distinguishes between pure methamphetamine versus mixture with a 10:1 sentencing disparity.

Overall, the pharmacological effects of methamphetamine do not vary meaningfully based on purity. Whether methamphetamine is adulterated or nearly pure, the impact on the user's brain, health, and behavior is the same for the same dose of active methamphetamine. As such, I agree with the primary recommendation of the June 2024 report Methamphetamine Trafficking Offenses in the Federal Criminal Justice System – that the 10:1 sentencing ratio for pure methamphetamine vs. mixture should be revised.

Relevant Literature

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<u>Abbreviations</u>: CBD - Cannabidiol; DSM – Diagnostic and Statistical Manual for Psychiatric Disorders; HCl – hydrocholoride; P2P – methamphetamine produced using phenyl-2-propanone as a precursor; THC – Tetrahydrocannabinol.