STATEMENT

OF

TIMOTHY W. WESTLAKE, M.D., FFSMB, FACEP

FORMER WISCONSIN MEDICAL EXAMINING BOARD CHAIRMAN

FORMER WISCONSIN CONTROLLED SUBSTANCES BOARD MEMBER

BEFORE THE

COMMITTEE ON ENERGY AND COMMERCE

SUBCOMMITTEE ON HEALTH

U.S. HOUSE OF REPRESENTATIVES

LIVES WORTH LIVING: ADDRESSING THE FENTANYL CRISIS, PROTECTING CRITICAL LIFELINES, AND COMBATTING DISCRIMINATION AGAINST THOSE WITH DISABILITIES

FEBRUARY 1, 2023

RELEASE UPON DELIVERY

Dear Members,

Thank you for the opportunity to testify at this hearing and contribute to the discussion on this topic.

THE ISSUE

What Congress Can Do

As Congress grapples with how best to address opioid overdose deaths, it should start by making permanent a proven strategy to eliminate the creation and supply of all new deadly fentanyl related substances (FRSs), by passing the HALT Fentanyl Act. After FRS Class Scheduling was enacted in Wisconsin in 2017, the U.S. Drug Enforcement Administration enacted temporary FRS class scheduling federally in 2018, authorization of which has been extended multiple times since (including 6 times by the current administration, the most recent being a 2-year extension passed in the omnibus). In short, these efforts have resulted in shutting down the creation and flow and very existence of new fentanyl related substances into the U.S. It's why Congress must act to finally make permanent this temporary policy. **The fact is, no one can die from ingesting something never created or be incarcerated for trafficking something that does not exist.**

Background on Fentanyl Class Scheduling Legislation

By design, FRS class scheduling is preventative, not punitive. As the primary architect of current FRS class scheduling policy, my goal was to stop the creation and spread of deadly new fentanyl related substances from transnational drug trafficking organizations. It was not to incarcerate people with substance use disorder.

I am a full-time emergency physician and recent part-time medical regulator in Wisconsin. I provide medical direction for a statewide peer-to-peer recovery program that provides naloxone training and I prescribe medication-assisted treatment when needed. I'm the immediate past Chairman of the Wisconsin Medical Examining Board and a former member of the Wisconsin Controlled Substances Board (responsible for controlled substance scheduling at the state level) and was architect of the Badger State's prescription opioid reform strategy. I have testified three times before Congress in hearings focused on opioid reforms.

As well, I have been on the front lines in the opioid battle for more than 30 years. One of the most devastating aspects of my job is to inform parents and other family members their loved one is never coming home due to an opioid overdose. Inspiration for the fentanyl class scheduling reform arose out of the tragedy of my friend Lauri Badura, whose son Archie died of an overdose. Archie was an altar server with my daughters. He got hooked on prescription medicine and then snorting what he thought was heroin. I was able to resuscitate Archie on his second to last overdose. On that occasion, I showed him a body bag and warned he would end up in it if he didn't accept help. He attended rehab and stayed clean for six months. Sadly, fentanyl caught up with him once more. The last memory my friend Lauri has of her son Archie is his lifeless body being zipped up into a body bag.

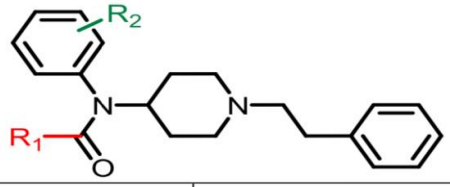
At the time I originated FRS class scheduling legislation over six years ago, doctors and other health care professionals -- in Wisconsin alone -- were battling more than nine nearly identical fentanyl variants.

While each was responsible for dozens or more overdose deaths in our state and across the U.S., they were still considered "legal" substances, having not yet been scheduled federally by the DEA or at the state level by the Controlled Substance Board (CSB). In Wisconsin, when deaths result from new novel substances, the CSB can use its emergency scheduling authority. It was like a lethal game of "Whack a Mole". We literally had to wait for the body count to pile up before we could find and schedule new fentanyl variants individually.

I knew something had to change, thus my idea to selectively schedule likely bioactive fentanyls as a class and remove the incentive foreign transnational drug trafficking organizations and chemical/ drug manufacturers had in modifying the fentanyl molecule. Knowing these entities could simply add or delete one minor chemical group and stay ahead of U.S. scheduling, my calculus was simple: stop the drugs at their source. If we could get it done in Wisconsin, we could then scale it nationally and impact global production, especially in China and elsewhere where these lethal fentanyl variants have largely been manufactured.

Working with the DEA, FRS class scheduling language was created. In part, the Stopping Overdoses of Fentanyl Analogues (SOFA) Act, or Wisconsin Act 60, which passed unanimously in the state legislature, memorialized Archie Badura. Then State Senate Leader, now Wisconsin Congressman Scott Fitzgerald (R-WI), shepherded the bill through the process. It was signed into law on November 9, 2017. Within its first week on the books, the DEA published its intent to use emergency scheduling powers to temporarily schedule FRSs as a class federally. This took effect February 2018. The results have been incontrovertible: the creation of new fentanyl related substances has ground to a halt internationally.

Table 1. Examples of recent structural modifications to fentanyl observed on the illicit market.



Substance	R_1	R_2
fentanyl[14]	$-CH_2CH_3$	H
acetyl fentanyl	$-CH_3$	H
butyryl fentanyl	$-CH_2CH_2CH_3$	H
furanyl fentanyl	-furan-2-yl	H
4-fluoroisobutyryl fentanyl	$-CH(CH_3)_2$	*para*-F
acryl fentanyl	$-CH=CH_2$	H
ortho-fluorofentanyl	$-CH_2CH_3$	*ortho*-F
tetrahydrofuranyl fentanyl	-tetrahydrofuran-2-yl	H
methoxyacetyl fentanyl	$-CH_2OCH_3$	H
cyclopropyl fentanyl	-cyclopropyl	H
valeryl fentanyl	$-CH_2CH_2CH_2CH_3$	H
isobutyryl fentanyl	$-CH(CH_3)_2$	H
para-chloroisobutyryl fentanyl	$-CH(CH_3)_2$	*para*-Cl
para-methoxybutyryl fentanyl	$-CH_2CH_2CH_3$	*para*-OCH_3
cyclopentyl fentanyl	-cyclopentyl	H
ocfentanil	$-CH_2OCH_3$	*ortho*-F
para-fluorobutyryl fentanyl	$-CH_2CH_2CH_3$	*para*-F

To date, DEA has found 36 new FRSs found to have caused thousands of overdose deaths in multiple states across the country. Since 2018, 12 new fentanyl related substances were found and with significantly fewer deaths attributed; it is suspected that many of these new FRSs may have already been in development prior to the temporary scheduling. The NFLIS (National Forensic Lab Information System) data show 7,058 encounters for FRSs in 2016-2017, and a decrease in 2018-19 to 758 encounters [a 90% decrease], and of these, the vast majority were for previously scheduled FRSs. Most importantly, the fentanyl/FRS flow from China has ground to a halt, and reports to NFLIS of overdose deaths related to new fentanyl-related substances have essentially ceased.

CONCERNS RAISED AND CONSIDERED

Increased Incarceration?

The goal of fentanyl class scheduling is singularly focused: to remove the incentive for and therefore halt development of deadly fentanyl poisons at their origin, namely, in drug labs overseas. Those opposed to fentanyl class scheduling initially suggested there would be a large increase in societal costs due to increased incarceration of people suffering from substance use disorder, but that has not proven to be the case. According to a 2021 GAO report, in the three years since FRS class scheduling was placed into regulation, there have been exactly eight prosecutions in the U.S. using the temporary scheduling language and half of these defendants had known ties to transnational criminal organizations/ drug cartels.

Opposition also mischaracterizes FRS scheduling as a partisan matter at the federal level given the years in which the policy has taken hold. I beg to differ. I have talked with federal and state policymakers across the political spectrum who care deeply about this issue and are determined to do what they can to help fix it. Plain and simple, by halting the creation and existence of new fentanyl variants, there has been significantly less availability and supply, causing a reduction in harm, overdose deaths and incarceration.

This underscores the primary strategy of overdose prevention and harm reduction. When considering societal effects, we must also consider the impact on mortality rates. In Florida alone, in 2016 and 2017, there were over 2500 deaths from FRSs. Since 2018, FRS related deaths in the US have been almost nonexistent. As such, those who have opposed this policy because of concerns related to incarceration, now suggest it is unnecessary because of the low number of prosecutions. Their pivot proves the policy is working. We have already witnessed the positive societal impacts of the fentanyl class scheduling including that thousands more Americans are alive today who would otherwise not be had new fentanyl related substances been created and trafficked in the U.S. Not only are people with opioid use disorder not being incarcerated as a result of FRS scheduling, they are alive today, in part, because of this policy.

Other false claims used by opponents of FRS class scheduling include that deaths and incarcerations due to fentanyl and FRSs have sharply increased in recent years. As mentioned previously, deaths and incarcerations from new FRSs have ground to a halt. Increases are due to illicit fentanyl which FRS scheduling is not designed to stop. Rather, it is to prevent overdoses at the hands of new FRSs by removing the incentive for their creation and distribution at foreign points of origin. **FRS class scheduling is the ultimate form of harm reduction and overdose prevention: you can't die from ingesting something never created, nor can you be incarcerated for selling something that doesn't exist**.

Effect on General Research

Concern about not wanting to impede general research was thoughtfully considered, and great care was given to ensure the language would be specific and narrowly crafted. We looked at more than structural similarity when arriving at the definition of fentanyl related substances. Structure-Activity Relationship (SAR) considers the relationship between changes in chemical structure relative to changes in pharmacological activity; it was the basis of the definition to make sure substances meeting this definition have a high probability of retaining opioid-like pharmacological and psychoactive activity. The detailed scheduling language includes specific modifications to only those portions of the fentanyl molecule with documented high likelihood of bioactivity. The language is the equivalent of a surgical scalpel, not a hand grenade.

Concerns raised about the potential negative impact of FRS scheduling on research are **purely theoretical** and have already been addressed by discussions with stakeholders. These proposed research accommodations have been signed off on and are supported by the agencies and organizations representing academic scientific research in the US - including the National Institute of Drug Abuse, the National Institutes of Health, HHS and the FDA. Why would they all support FRS class scheduling if it would harm research? The agreed upon accommodations would significantly loosen research restrictions into studying all schedule 1 substances (not just FRSs) and open up wide areas of substance abuse research.

- Those who oppose FRS scheduling point to increased numbers of illicit fentanyl deaths as reason for why FRS scheduling is not working. Some have said that "Temporary scheduling is a failed experiment that hasn't curbed the devastation of the opioid crisis." At best, this is disingenuous and a misunderstanding of the issue. In fact, the opposite is true. FRS scheduling has accomplished the one and only thing it is designed to do: stop the creation and very existence of new FRSs and therefore shut down all new FRS related deaths.

- Tragically, overdose deaths from illicit fentanyl have skyrocketed, but deaths from illicit fentanyl are a separate issue from FRSs and FRS scheduling, and one that could never be impacted by FRS class scheduling. Arguing that FRS class scheduling has not worked because illicit fentanyl deaths have risen is a complete confabulation and misrepresentation of the facts on the effects of FRS scheduling. The correct question should be whether deaths and trafficking arrests from new FRSs have slowed down or stopped as a result of FRS scheduling - which they incontrovertibly have.

- Opponents of permanent FRS scheduling have said that "Temporary scheduling has preemptively criminalized potentially life-saving antidotes to fentanyl overdoses and impeded the medical, research and scientific community's ability to develop solutions we need to effectively tackle this crisis", and that "One FRS has been shown to have similar properties to naloxone." But this is a misrepresentation and is based on one FRS (Mirfentanil) that was studied in the early 1990s that had antagonistic properties at low levels, but agonist effects at high levels and has never passed beyond phase 2 studies. Again, a purely theoretical argument about a theoretically negative effect on research when weighed against the actual death of thousands of Americans from FRSs when they were left to be reactively scheduled individually. The fact is, academic scientific research would actually be significantly advanced if research

accommodations similar to the ONDCP proposal in the HALT Fentanyl Act were to be enacted allowing easier access to research on all controlled substances.

Others have argued that FRS scheduling would impede research into new opioid versions of fentanyl. Obviously, the last thing we need is a better or more powerful opioid.

Similarly, some suggest research into new lifesaving treatments such as a FRS reversal agent or medication assisted treatment would be impeded.

- The scientific basis for this argument seems to be based on one line in testimony by Dr. Throckmorton, Deputy Director of the Center for Drug Evaluation and Research at the FDA, at a December 2021 Energy and Commerce Committee hearing, "The Overdose Crisis: Interagency Proposal to Combat Illicit Fentanyl-Related Substances": "Among the individual FRS for which pharmacological activity has been studied, FDA has identified examples of substances lacking in mu-opioid agonist activity, the presumed pharmacology that would lead to opioid-related harms."

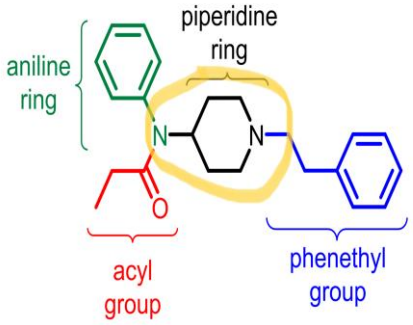
- While it is true there is a single FRS that is a predominant kappa receptor stimulator at low levels (which are thought to have lower abuse potential and theoretically beneficial antagonistic properties) as cited by Dr. Throckmorton, however at high levels it does stimulate mu receptors.

- However, when reviewing research into FRSs, every substance studied and classifiable under the FRS class scheduling language has been found to have opioid receptor bioactivity. Almost all are dozens to hundreds and even thousands of times more potent than heroin and morphine. More complete information is forthcoming from federal chemists at DEA conducting FRS research. It is my understanding this research will show that as of August, 2022 the DEA has encountered 36 FRSs and completed preliminary pharmacological investigations on 27 of them, with additional testing ongoing. It was found that all FRSs studied to date bind and activate at least one opioid receptor with varying affinities and efficacies. In short all FRSs are bioactive.

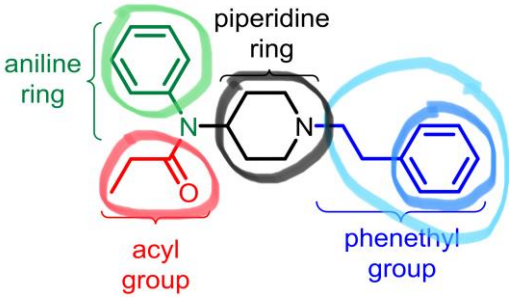
- To date, and over the past 60 years of exhaustive structure-activity relationship studies on fentanyls, research has failed to highlight any activity leading to the development of a fentanyl based antagonist/ reversal agent or medication assisted treatment.

- In contrast, prior to FRS class scheduling, legal FRSs pouring across our borders took the lives of countless Americans.

Fentanyls fall into the 4-anilinopiperidine class (defined by the aniline ring in the 4-position of the piperidine ring). By definition, in order to structurally classify as a fentanyl related substance under the FRS language, the base chemical structure must be that with Nitrogen at the 4-position of the piperidine ring (highlighted in yellow below).



Any chemical without that exact base structure and without any of the specified modifications would not be included in the scheduling. All elements of the basic fentanyl molecular chemical scaffolding must be present. If there are any deletions from the scaffold, the chemical wouldn't be included, and if there are any substitutions not specifically included in the specific language, those chemicals would also not be included in scheduling. FRS Class Scheduling Language: must include one or more of the following-



(A) By replacement of the phenyl portion of the phenethyl group by any monocycle, whether or not further substituted in or on the monocycle;
(B) By substitution in or on the phenethyl group with alkyl, alkenyl, alkoxy, hydroxy, halo haloalkyl, amino or nitro groups;
(C) By substitution in or on the piperidine ring with alkyl, alkenyl, alkoxy, ester, ether, hydroxy, halo, haloalkyl, amino or nitro groups;
(D) By replacement of the aniline ring with any aromatic monocycle whether or not further substituted in or on the aromatic monocycle and/or

(E) By replacement of the N-propionyl group by another acyl group.

The targeted language was intentionally designed to capture only the modifications [already well described in the scientific and medical literature] being used by transnational criminal organizations to exploit the legitimate research information on structure activity relationships. By staying one step ahead of the CSA and Analogues Act, they continued the spread of these deadly poisons in the U.S. and internationally. There is an excellent detailed discussion on the chemistry and history of fentanyl and fentanyl related substances in a statement from Michael Van Linn, PhD taken from testimony before the United States Sentencing Commission in December, 2017: https://www.ussc.gov/sites/default/files/pdf/amendment-process/public-hearings-and-meetings/20171205/Van-Linn.pdf

Fentanyl was first created in 1960 and has been studied extensively since then. As noted in the Van Linn testimony, many of the new FRSs responsible for recent overdose deaths in the U.S. are well described in the patent and scientific literature, often accompanied by pharmacological data and detailed instructions on synthesis. Essentially, these are precise maps that guide legal -- as well as illicit – drug labs and chemical manufacturers in creating new FRSs that are almost certain to be bioactive.

The pathway to synthesize fentanyl and FRSs is relatively straight forward and well-defined, and creation of a new FRS is as simple as plugging in or removing a different chemical precursors at one step or another in the process of synthesis. The ease of creating new FRSs is attractive to medicinal chemists and, unfortunately, also illicit chemists.

Reversing Overdoses and Medication Assisted Treatment

Some opposition in the research community suggest FRS class controls would hamper research into possible chemicals that could be used to reverse overdoses or treat opioid use disorder. To date, in over 60 years of extensive research done on fentanyls during which exhaustive structure activity relationship studies have been conducted, registered researchers and published research have failed to highlight any activity in developing a fentanyl based antagonist/ reversal agent or medication assisted treatment.

It should also be noted that the pharmacological and overdose effects including lethal respiratory depressant effects of fentanyl/FRSs are similar to those of other opioid agonist drugs such as morphine, heroin and oxycodone etc. Naloxone (Narcan) has been shown to be effective in reversing the respiratory depression that leads to death caused by opioids like heroin, as well as semisynthetic and synthetic opioids including fentanyl. In other words, Naloxone is a very effective reversal agent/ antagonist. Deaths do not occur because naloxone doesn't work or isn't strong enough. Rarely it can wear off and if it does, the solution is to give more. Overdose deaths occur because of the ingestion of lethal doses of highly potent and toxic opioids, and are not due to a lack of potency or effectiveness of naloxone in reversing opioid toxicity when given in time.

With regard to medicinal treatment of opioid use disorder (medication assisted treatment/ MAT), relapse rates have no correlation with current MAT options. Relapse or drop-out rate of patients is attributed to many factors such as cost, access to doctors/ treaters and/ or lack of behavioral treatments among other factors, and are not related to the specific opioid being abused. Nor have there been discovered or created any fentanyl/FRS based medication assisted treatments. **To recap, not one reversal agent/antagonist or MAT has been found or investigated in the six decades of research done into fentanyls.** All current research is focused on detection, analysis and understanding the harm of

these substances. The fentanyl class is not being researched as a possible therapeutic prior or since the DEA emergency control in 2018.

Sufficient Oversight & Collaboration Across Agencies

In the normal sequence of scheduling, DEA reviews and investigates chemical compounds individually, then collaborates with HHS and the FDA in making a final decision in the scheduling process. Concerns about bypassing consultation with HHS and the FDA in this circumstance by which the DEA can schedule certain fentanyl-related substances based on the specific, limited, targeted criteria were thoughtfully considered. As a result, the language was narrowly crafted to only include likely bioactive modifications based on the already known structure activity relationships.

Proactively, and also in response to research concerns raised by the Department of Health and Human Services (HHS) and other stakeholders, DEA has already addressed and significantly simplified the research requirements for FRSs including, for example, requiring a single registration for all chemicals in the fentanyl class instead of separate registrations for each individual substance like it does for all other substances. It is significant to note that more than half of the 11 new research registrants for the new fentanyl class since 2018 were for DEA subcontractor chemical analysis or submitted through the Department of Defense. Ultimately, research is driven by funding and there does not appear to be a current investment in FRS research after 6 decades of studying the class. A final point on this: nearly all development of new fentanyl-related substances has been done oversees [in China mostly] and not by American scientists and researchers.

Theoretical Research Concerns

It is interesting to note that the main groups opposing FRS scheduling for reason of theoretical negative effects on research are in fact mainly criminal justice reform based activist organizations. These same organizations initially opposed FRS scheduling due to concerns of theoretical effects of mass incarceration preferentially affecting of people of color. This did not happen. A report by the GAO in 2021 said there were eight prosecutions for drug trafficking in the U.S. in the 3 years FRS scheduling had been temporarily enacted, four of which were known cartel traffickers. As designed, "**No one can die from ingesting something never created or be incarcerated for trafficking something that does not exist."**

Lethality and Potency, as Deadly as Chemical Weapons

The most accurate way to view fentanyl-related substances is as weapons of mass destruction, not as recreational drugs or intoxicants like marijuana, cocaine, and even heroin. In a 2019 paper by John P. Caves, Jr., a Distinguished Research Fellow in the Center for the Study of Weapons of Mass Destruction (CSWMD) at the Institute for National Strategic Studies at the National Defense University, called "Fentanyl as a Chemical Weapon" covers the topic well. https://www.hsdl.org/?view&did=832803. Opposition to fentanyl class scheduling has likened it to cocaine legislation in the 1980s and as an extension of the war on drugs, but this perspective fails to account for the chemical weapon-like level of lethality that exists with fentanyl and FRSs.

The following table is a representation of the precise level of lethality [how much is required to kill an average human] of common narcotics and chemical weapons agents. It is almost incomprehensible how small a dose of fentanyl will kill someone: **2mg or approximately the equivalent of 4 grains of sand**.

Lethal Doses of Chemical Warfare Agents and Narcotics

Chemical Agent/Drug	Lethal Dose	Route
Botulinum Toxin	.00007mg	Inhaled/Ingested/Injected
Tetanus Toxin	.0001mg	Inhaled/Ingested/Injected
CARFENTANIL	**.02mg**	**Inhaled/Injected**
Tabun Nerve Agent	1-1.5mg	Inhaled/Ingested/Percutaneous
Ricin	1.78mg; 10mg	Inhaled/Injected;Percutaneous
FENTANYL	**2mg (approx. equal to 4 grains of sand)**	**Inhaled/Injected**
VX Nerve Agent	2.1mg; 10mg	Inhaled/Injected; Percutaneous
Strychnine	70-140mg	Ingested
HEROIN	**70mg**	**Inhaled/Injected**
Cyanide	100-200mg	Ingested
MORPHINE	**200mg**	**Inhaled/Injected**
Methamphetamine	200mg	Inhaled/Injected
Cocaine	200mg	Inhaled/Injected
MDMA (Ecstasy)	1000mg	Ingested
THC/Marijuana	4000mg (pure THC)	***Not realistically achievable in humans by all methods of marijuana consumption per the WHO

Lethal Doses of Chemical Warfare Agents and Narcotics

Chemical Agent/Drug	Lethal Dose	Route
	One teaspoon of Fentanyl is enough to kill 2,000 people	

In September 2018, 52 members of the National Association of Attorneys General (NAAG) sent a letter urging Congress to adopt the Wisconsin law on scheduling FRSs . When Congress failed to act, in December 2019 a second unanimous letter from NAAG was sent urging Congress to adopt FRS class scheduling showcasing the strong bipartisan support for this policy. https://1li23g1as25g1r8so11ozniw-wpengine.netdna-ssl.com/wp-content/uploads/2020/10/Letter-to-Congress-SOFA-Act-8.23-1.pdf , https://1li23g1as25g1r8so11ozniw-wpengine.netdna-ssl.com/wp-content/uploads/2020/10/NAAG-Support-for-FIGHT-Act-Letter.pdf.

Signors of both letters included HHS Secretary Xavier Becerra in his capacity as California Attorney General. It speaks to the importance of this matter as a critical national public safety measure and which has no political affiliation.

Targeted control of specific fentanyl-related substances as a class and not as discrete chemicals is not a minor change to the U.S. Controlled Substance Act (CSA). It has been carefully and thoughtfully crafted and wouldn't even be considered, but for its significant impact already seen in the worst drug epidemic in the modern era. Annualized deaths caused by illicit fentanyl and known analogues now surpass heroin and are responsible for the overdose death spike and lowering of the average life expectancy for Americans for the first time since development of immunizations and antibiotics.

Analogues Act of the CSA is Not Sufficient

Some suggest the Analogues Act of the CSA is sufficient to give DEA and DOJ the power needed to act against fentanyl-related substances. That is not accurate. In order to use the Analogues Act, a substance must be proven *substantially similar* to a listed schedule I or II, and also must be proven to be *intended for human consumption*. This is highly problematic because those findings must be adjudicated in court in each and every case, even when the substance has been proven to be an analogue in a previous case. In addition, the usual threshold to trigger looking at a substance as an analogue is purely reactive and not proactive or preventative when it is found to be killing people, usually many people across multiple states.

According to the 2019 Florida Medical Examiners Commission Report, deaths in the Sunshine State directly attributable to FRS overdose rose 65 percent in just one year: 965 in 2016 to 1,588 in 2017. Between 2017 and 2018 in New York City alone there were over 900 deaths from FRSs. Thousands have already died due to the existence and availability of fentanyl related substances. It's why the former

Governor of New York called for fentanyl class scheduling language in NY and why other states and nations including Canada are following Wisconsin's lead. We cannot go back to the way it was before fentanyl class scheduling was put in place.

Concerns over Prosecutions for Non-Bioactive FRSs

Concerns raised about increased prosecution of people distributing non-psychoactive FRSs that would be inappropriately classified as schedule I is an extremely unlikely scenario for the following reasons:

1) First and foremost - **every substance classifiable under the FRS class scheduling language (all 27) has been found to have potent opioid bioactivity - dozens or more times more potent than morphine.**

2) Simple charges of possession and lowest level dealing of FRSs are simply not aggressively prosecuted by federal prosecutors.

3) FRSs do not exist naturally. They are synthesized in illicit clandestine overseas labs by chemist suppliers to transnational criminal organizations. The process of FRS synthesis is intentional and based on researched and readily available information of the roadmaps of the Structure-Activity Relationships: it isn't grown in a backyard; there is no bathtub lab manufacturing occurring; and, there is never going to be accidental synthesis, manufacturing and distribution of a new FRS.

4) The low likelihood of transnational criminal organizations/ drug cartels synthesizing, manufacturing, and distributing new FRSs that aren't bioactive/ psychoactive. It's simply not plausible they would decide not to test their product lest they put new FRSs in their distribution networks that were duds [non-psychoactive]. How long would they be able to sell them if they didn't have potent opioid bioactivity?

Due to the specific and targeted nature of the SOFA language based on stopping the exploitation of known fentanyl/FRS structure activity relationships, it is almost certain that a newly developed FRS covered under this fentanyl related substance class scheduling language that is then manufactured and internationally trafficked would be bioactive. If the bioactivity were similar to fentanyl, it would be at the level of chemical weapons lethality: one teaspoon deadly enough to kill 2,000 people.

Those opposed to enacting permanent fentanyl class scheduling suggest a drug trafficker could be incarcerated for distributing a FRS that was actually beneficial or an antagonist like naloxone. This is simply not the case. As previously mentioned, in the over 60 years of research done on fentanyls, not one substance with antagonistic properties has ever been researched. Of importance to note, if Congress were to enact the rapid de-scheduling pathway proposed by President Biden in his ONDCP FRS scheduling recommendations (also in the HALT Fentanyl Act), rescheduling could be done rapidly in the highly unlikely circumstance of a substance being trafficked turns out to be non-psychoactive.

Sentencing Guidelines

Under current federal guidelines, the sentence is 5 years for 10 grams of fentanyl/ FRS, and 10 years for more than 100 grams. On first glance, that may seem harsh, but it is important to remember the lethality and consider that 10 grams of a FRS is enough to kill 5,000 people, and 100 grams of a FRS could kill 50,000. I would venture to guess that most, if not all, physicians [and Americans too for that matter] would agree: if you could have only one class of drug with associated mandatory minimums, it would be fentanyl and FRSs.

There is information being disseminated that there have been prosecutions for FRSs that are not bioactive. This is not correct. As mentioned previously, every FRS researched to date under the FRS language has been found to have opioid effect bioactivity far more potent than heroin and morphine. The most recent new FRS studied was found to be four to eight times more potent than fentanyl.

Benzyl fentanyl has often been pointed to as an example of a fentanyl analogue that was scheduled under emergency order and then unscheduled [in 1985 and 1986 respectively]. In fact, it would not have qualified under the fentanyl class scheduling language as a FRS. The benzyl fentanyl modification and similar modifications were specifically excluded from the scheduling language because of their known non-bioactivity. It is also misstated by opposition that since 2018, prosecutions of the List 1 precursor benzyl fentanyl have occurred under FRS scheduling. In fact, they have occurred under precursor controls. [This is because benzyl fentanyl can be easily modified to create fentanyl, therefore it was controlled as a List 1 precursor]. **There have been Zero prosecutions for FRSs that are not bioactive.**

In addition, n several occasions, substances that do not fall under the FRS class scheduling language have been misclassified as such by those arguing against FRS Class Scheduling: benzyl fentanyl, remifentanil, Imodium and AT202 adding to the confusion on the issue of impact on research. In fact, all are not classifiable as schedule 1 under the FRS scheduling language.

International Coordination (with China Especially)

In trade negotiations with the Chinese government, the U.S. included targeted FRS class scheduling among its priorities. As a result, China permanently enacted similar scheduling language in May 2019. The United Nations includes it in its toolkit of model opioid legislation for member nations. Several other countries [including Canada] and many American states have adopted similar scheduling language. In this case of harm reduction to benefit American citizens, even China sees the value in permanent FRS class scheduling. It is not inconceivable -- and many would say likely -- that if the U.S. doesn't permanently enact FRS class scheduling, China may not continue its prohibitions on fentanyls, and the incentives for the creation and distribution of new FRSs would re-open, or that some of the thousands of chemical companies in India would start on the FRS creation pathway that would re-open if FRS scheduling were to sunset.

CONCLUSION

It is incontrovertible that temporary targeted fentanyl class control has already been an extremely effective harm reduction tool and has eliminated the incentive for traffickers to create new FRSs, closing the FRS loophole at home and overseas and saving countless lives in the process. If Congress allows the FRS-class scheduling to expire, it's only a matter of time before other countries like China and India could restart fentanyl-related substance creation and unleash the devastating consequences.

My roles as an emergency physician, parent of young adult daughters and a medical regulator, drove me to design a legislative solution to prevent the development of new FRSs by illicit overseas chemists, but at the same time not incarcerate people with substance use disorder or impede critical research. The FRS class scheduling language that has been embraced by the Biden Administration/ONDCP and HALT Fentanyl Act threads that needle.

Congress has in its power to permanently enact this important FRS class scheduling legislation and continue to save countless lives. There is no question, if we turn our collective backs on the progress that's been made to stem the tide of the creation of new FRSs in America, thousands more deaths will occur annually from the reemergence, existence and widespread availability of these deadly chemical agents. **Now is the time to make this crucial reform permanent and pass the HALT Fentanyl Act.**

Thank you for the opportunity to contribute to the discussion and thank you for your leadership on this critical public health issue.

Timothy W Westlake, MD, FFSMB, FACEP
Wisconsin Medical Examining Board, Immediate-Past Chairman
Wisconsin Controlled Substance Board, Former Member