

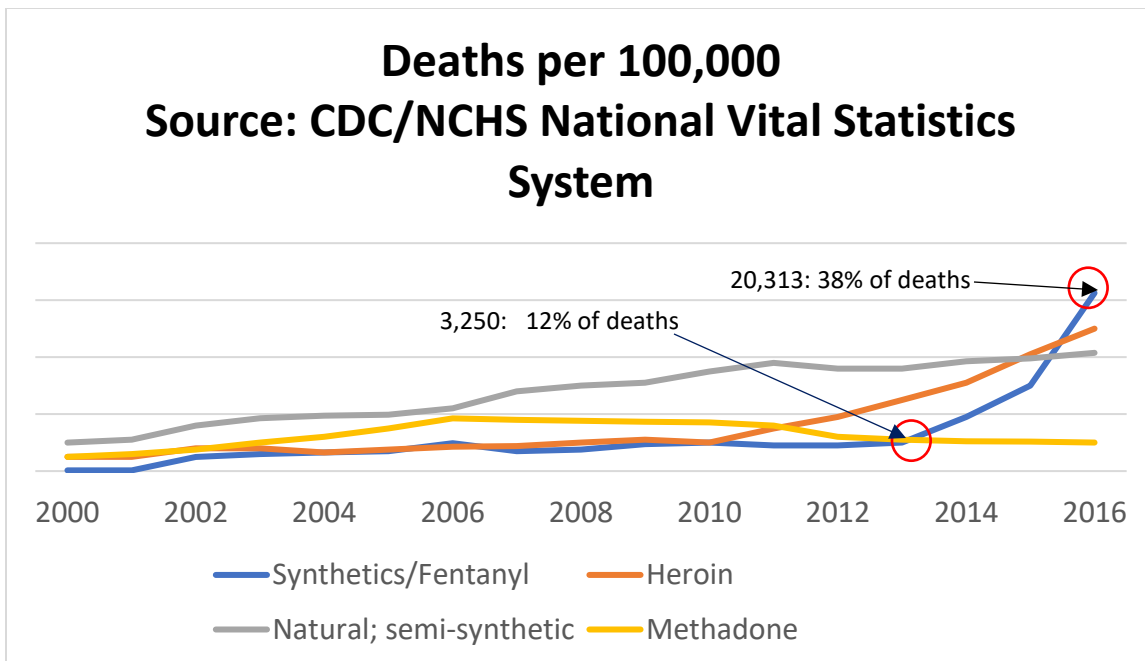
To the Editor:

Today, The Washington Post published an article titled *“The Health 202: Obscure provision in House opioids' bill could restart war on drugs”*. The very title of this article indicates the only problem of the SITSA (Stop the Importation and Trafficking of Synthetic Analogues) bill; a bill which should be a “no-brainer” piece of legislation in the fight against opioid death. What is described as “strange bedfellows” and a “bromance” is nothing strange at all. Unless, that is, if we find it strange that one party or the other sees no reason to interrupt the devastating Opioid Crisis by saving 10 or 20-thousand lives per year.

The Opioid Crisis has been made totally nuclear by the sudden growth of synthetic heroin, known to most under the too-simplistic moniker “fentanyl”. The sudden, dramatic spread of this incredible medical miracle to the illegal street market is causing 10’s of thousands of deaths per year in populations which were never at risk before. My daughter Amanda was a member of one of those populations – the mentally-ill, non-addict, who self-medicates – and she died in a manner almost unheard of 6 years ago. By the time Amanda hits the statistics (she died in 2018, so she is not in the data yet), she will be one of 10’s of thousands who didn’t need to die.

This “obscure provision” is the first step toward getting that genie back in the bottle, or at least back near the bottle. SITSA is obscure because there are three areas within which one needs to develop a more-than-casual understanding before one can credibly assess the value of SITSA: 1. The science of Synthetic Opioids; 2. The business model of the drug dealer; 3. The fact that we have always had opioid users who were not addicts and, until the rise of synthetics at the street-level in 2013, had minuscule risk of death by opioids. Ironically, they are now the most likely to die. The good news is that their deaths are very preventable. SITSA is an indispensable step in doing so.

There is no picture as compelling as the simple data from the CDC. When synthetic opioids made a surge in 2013, they changed all the paradigms



Please look carefully at the comparative curves above. The takeover of natural drugs by synthetics means that the natural and semi-synthetic numbers (the most linear, predictable and open to intervention) will move toward the slope of fentanyl. A complete takeover today calculates to a death toll in 2025 of 315,000.

1. Science of Synthetic Opioid

First a bit of education in science: “Heroin” is a meaningless word which is the brand name of Bayer’s Diacetylmorphine (extracted from poppy plants in 1874 and patented in 1897 under the brand-name “heroin”). “Fentanyl” is a meaningless word which is the name of a synthetic version of heroin; “synthetic” is a fancy word for man-made, i.e. not from a natural plant. Let’s stay on that point for a moment.

When a chemical is synthesized, i.e. man-made, a smart synthetic chemist can figure out how to tweak that molecule to be technically different than the base molecule, or backbone, but largely have the same function. We call this a “synthetic analogue”. Picture it like a living shelter being carved out of a rock vs. building a house with wood beams and bricks. You can custom design the latter example in far more detailed ways, while both provide similar shelter. In our present consideration of Fentanyl, we have carfentanil, alfentanil, sufentanil, remifentanil, acrylfentanyl, etc. In fact, scientists have computed somewhere in excess of 1400 analogues of fentanyl, approximately 400 with similar analgesic properties. Regulations and laws being what they are, the government cannot say “fentanyl and all its analogues are illegal”. It has to specify a certain chemical, which has a specific CAS number, chemical formula and molecular structure. It then spends approximately six months getting it listed on as schedule I/II. That is what they have done with “fentanyl” ($C_{22}H_{28}N_2O$, CAS ID: 437-38-7, etc.). What about the other 1400? At six months per chemical, dealers can continue to sell legal (or, better yet, non-illegal) versions of this poison for 700 years with impunity. SITSA and its Schedule A is the only way to corral this massive problem.

Here is the basic problem: Synthesized basic fentanyl is 100X the potency of “heroin”. This is a great benefit to pain patients and their prescribing doctors, but this strength becomes a scourge when the compound hits the streets. Why? The mixing of drugs (what Pharma calls “Active Pharmaceutical ingredient” or “API”) into cutting agent (what Pharma calls “excipient”) is challenging science, and even big pharma struggles to get things right with all their PhD scientists and scientific instrumentation. Drug dealers are not Pharma Blending Engineers, and they cannot manage this extra potency. This is why it kills.

Remember “analogues”, same basic idea but slightly different? Carfentanil is an analogue which has more-or-less the same effect as fentanyl or heroin but is 10,000X stronger. A dealer is never going to be able to mix this safely. *Most* of his/her customers will either get nothing, or die, and a few in the middle will actually get the expected effect. Many people have seen this famous picture by now; the relative amounts necessary to cause death of these three chemicals:



Why do I say the terms above are meaningless? Because both heroin and fentanyl, and all other “opioids”, are in a pharmacological category called “ μ -opioid receptor agonists”, which is a fancy way of saying that these chemicals cause certain receptors in the brain to flood with dopamine, which feels very good. This good-feeling is what addicts are addicted to, and spend their lives chasing.

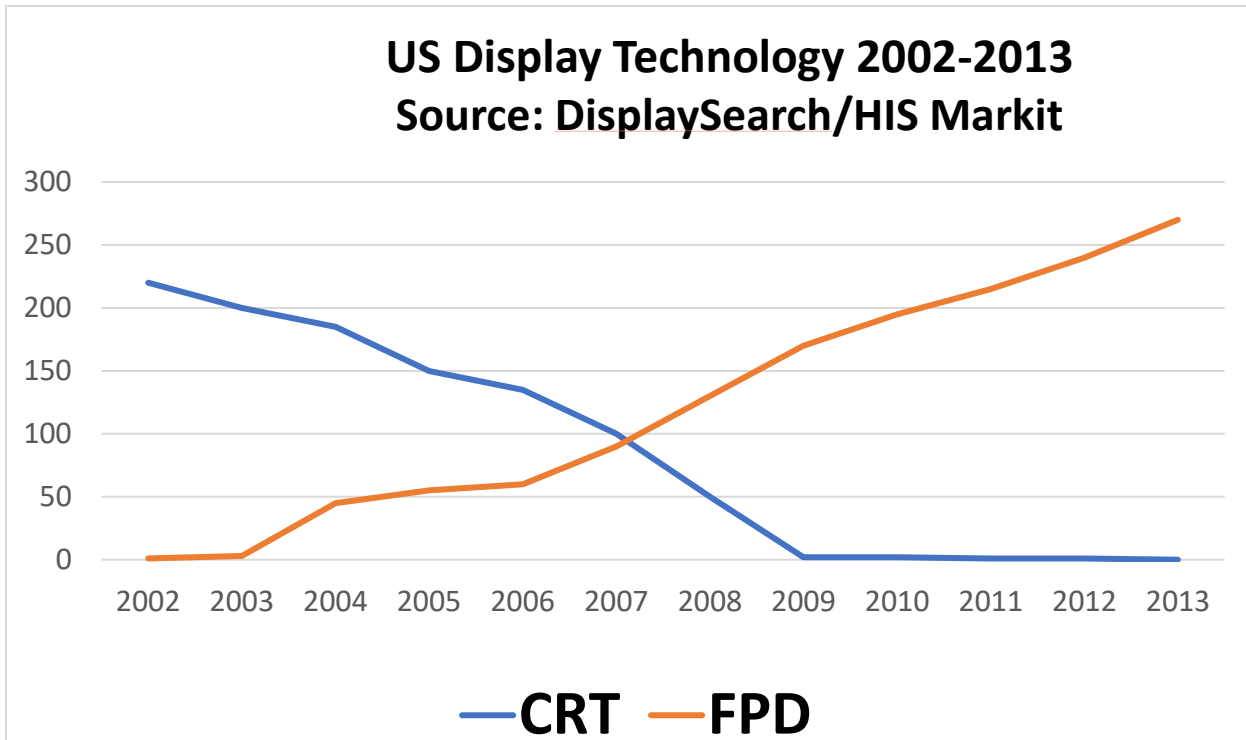
Terms like “heroin”, “fentanyl” and “Oxy” are meaningless because once a person is addicted to a μ -opioid receptor agonist, they will take whatever μ -opioid receptor agonist they find, irrespective of the name. This is the basis of our addiction problem in the US. Pill-poppers can say “I’m no junkie, I don’t use heroin”. This is a meaningless statement. If one is taking a μ -opioid receptor agonist for no other reason than to get the flood of dopamine (**which is NOT why chronic pain patients take it**), they are an addict, same as a “junkie”; in fact, they are a “junkie”. As a contrast, not all of these medications will have the same effect upon a specific pain. Therefore, people taking these drugs properly (i.e. for pain) cannot simply substitute one for the other; this makes them less apt to hit the street for their drugs since not all μ -opioid receptor agonists will work for their specific case.

The next step in an understating of the science beyond the casual, is recognition that certain people are more apt to become addicted than others. These poor folks are the ones who create the market for opioid dealers. Some portion of these afflicted souls will follow a predictable path where they will use more and more as their resistance to the euphoric effect grows, and one day give into the temptation to take enough to actually get high. Alas, that amount gets them high, and then kills them in the process. This is the classical pattern of drug overdose death. This, for the most part, is what we faced in 2012 and before.

In this pre-2012 scenario, as long as a person avoided addiction, whether through a fortuitous biology or better self-discipline when taking meds or partying, they would have a relatively low exposure to death. In the brave new world of illicit synthetic drugs, one need not be an addict or even a regular user: Run into fentanyl once and you’re dead. Factor into this concept that in my traveling around the country speaking to schools, churches and law enforcement, the law enforcement officers tell me that straight heroin, without any synthetic, is a rare find. The takeover is well on its way, and the takeover is deadly in its implications. Why is the takeover happening? Let’s turn to the “business” of drug dealing.

2. The “Business” of dealing

In my lectures around the country, I use the business case study of CRT televisions and their yielding of the market to Flat Panel Displays (FPD) in 2007, as an extraordinarily accurate analogue of what synthetic opioid (e.g. Fentanyl) will do to its natural counterpart (e.g. Heroin) in the market due to its superiority as a product; superior both in what it does for the user (more potent), and what it does for the dealer (easier to make, easier to smuggle and 100-10,000X more profitable). There are two compelling (and terrifying) factors which we can learn from the CRT/FPD saga. First is that once the two products hit a parity in the market (2007) the CRT went into total extinction within two years:



Secondly, and more importantly, once the CRT disappeared, the full economies of scale of the FPD manufacturing process were realized and we saw an explosion of manufacturing, which led to a massive expansion of the base market of displays; the FPD went places the CRT never did, like the wrist (Apple/Samsung watch).

Similarly, once we get rid of heroin (and we will), there will be an explosion in the manufacturing of fentanyl, and this synthetic will find its way into all μ -opioid receptor agonist needs. At that point, the death toll will make us long, nostalgically, for the days of **only** 72,000 Drug OD deaths.

3. Non-Addict Death Rates

Non-addicts are the leading group in the recent explosion in death rates. In our zeal to help addicts, we are forgetting many other opioid users. These non-addicted users are far more vulnerable to the potency of synthetics, since they have limited resistance, and limited experience to know that what they are ingesting is a powerful synthetic which has been mixed crudely. This group includes,

- The mentally-ill, self-medicating
- Thrill seekers/experimenters
- Those with high-risk attraction
- Those with poor impulse control/excessive partiers
- Chronic pain sufferers cut off from scripts
 - this group will grow as legal opioids become harder to acquire

There is a silver-lining here. If the increase in death is in a population which is not hard-addicted, and would not die were it not for synthetics, then anything we do to inhibit the incursion of fentanyl into the street-drug supply stream will directly translate into a reduction in death rates. SITSA is a great start to making that happen.

SITSA is not Nancy Reagan's "war on drugs". We are not talking about revisiting the Rockefeller Laws or anything of the kind, and saying we are is disingenuous politics at the very least. The paradigms of the past are gone; we must seek solutions in the new paradigm and leave the old terms – and the old prejudices – behind us.

Synthetic drugs are a terrible scourge upon our culture which even have the potential to be the worst chemical warfare agent man has ever developed. Within 2018, four men representing two arrests (NJ and NE) had enough fentanyl to kill 45,000,000 people. None of them will spend more than 10 years in jail. One of the NJ pair is 26 and he was sentenced 6 years. There was a recent arrest in Toronto where the criminal had a similar volume of carfentanil. That one man had enough poison to reach the **Billion – with a "B" – level of death**. In this case, he ingested some of the carfentanil and is now in a vegetative state; further proof of just how out-of-control this situation is.

Had any of these people been carrying a newly spun analogue, they wouldn't even be prosecuted! Can any rational person oppose a law which attempts to prevent these dealers from being beyond prosecution?

I implore all Senators to read this carefully, call me personally and get informed. This is a nuanced discussion and does not lend itself to the politics of the simplistic soundbite. Today's article does a disservice in that it was shallow and lacking in any reasonable information. That may be OK for the politics of arcane subjects such as banking regulations or international treaties; but where are the disingenuous folks going to be when we are losing 300,000/year of our young people with no way out. Without SITSA, that is our future. The President recently said that the synthetic attack on America is "almost a form of warfare...it's a disgrace and we can stop it", but not without SITSA. In addition to SITSA, it would be ideal if the President would indeed view it as a strategic issue between the US and China, the chief producer of the drug.

My daughter died a death that was totally preventable; SITSA is the prevention.

Michael J. Gray

Bereaved father of Amanda Beatrice Rose Gray (+2018)

Please feel free to visit my web site at www.actus.org for more information about what we can do to slow this assault. I can be reached at mgray@actus.org