Welcome

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NIDA's Role in the Scheduling Process

Should we (HHS and the Pharmaceutical Industry) Follow the DEA's Example Related to Product Scheduling?

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Abuse Liability Testing Under NIDA Contracts

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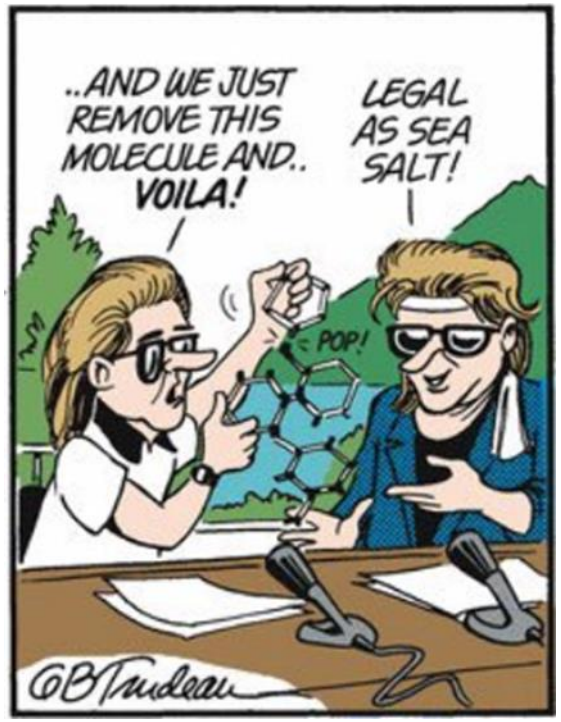

NIDA's Role in the Scheduling Process

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HHS Scheduling Recommendations

Jane Acri
Nathan Appel
David McCann

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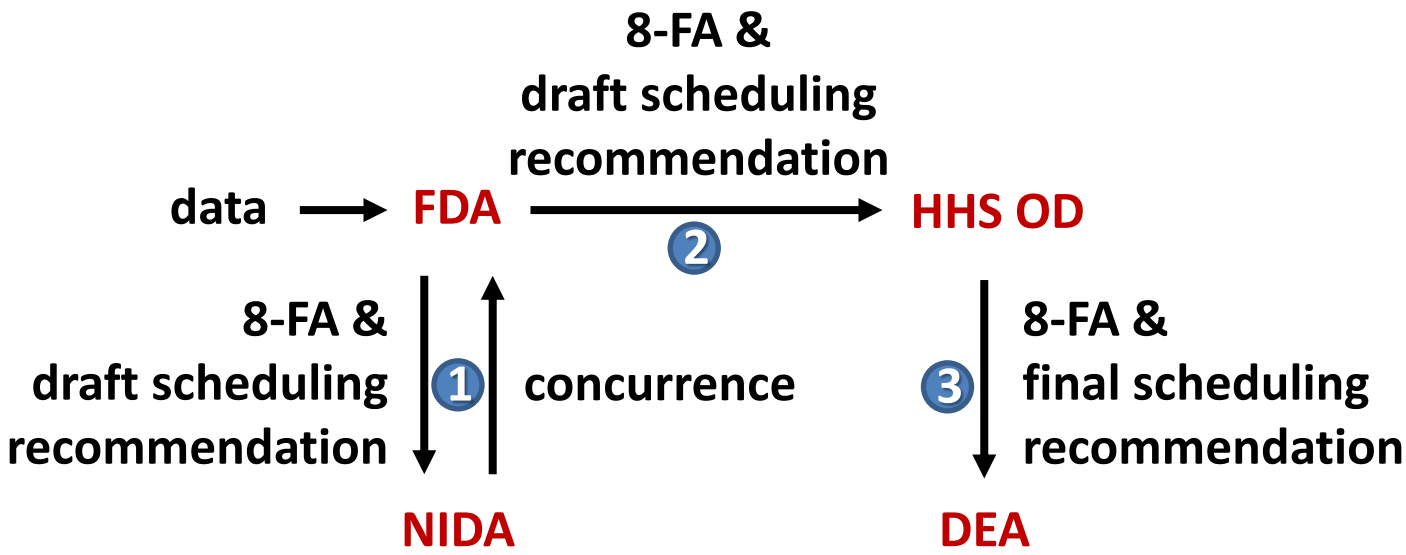

If control is required by US obligations under international treaties, the DEA can order control of a drug under the schedule it deems most appropriate without regard to HHS recommendations.

(paraphrased from the CSA)

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Differential Scheduling of Products and Drug Substance

1985: Marinol® (THC in sesame oil) placed in Schedule II
THC Schedule I

1999: Marinol® changed to Schedule III
THC Schedule I

2017: Syndros® (THC oral solution) placed in Schedule II
Marinol® Schedule III
THC Schedule I

2018: Epidiolex® (CBD product) placed in Schedule V;
CBD Schedule I

What about abuse-deterrent formulations?

When taken by the intended (oral) route, current abuse-deterrent formulations of oxycodone and other Schedule II opioids appear to carry the same risk of overdose death as non-abuse-deterrent formulations.

Buprenorphine (Schedule III) appears to carry a lower risk of overdose death due to partial agonist activity at *mu*-opioid and NOP receptors.

What if the risk of overdose death can be decreased through formulation?

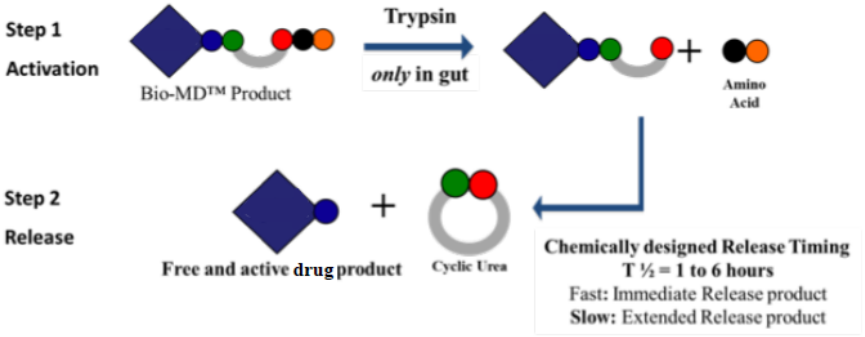
Both Ensysce Biosciences and Elysium Therapeutics received NIDA grants in 2018 for the development of "overdose-deterrent" opioid formulations.

Ensysce™ biosciences

Abuse Deterrent Prodrug: ADP

BIO-MD™ prodrugs:

Two Step 'Oral Activation' Technology



Overdose Protection

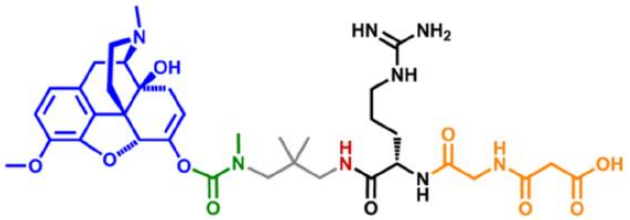
MPAR™ platform:

Combination product: BIO-MD™ and Trypsin Inhibitor

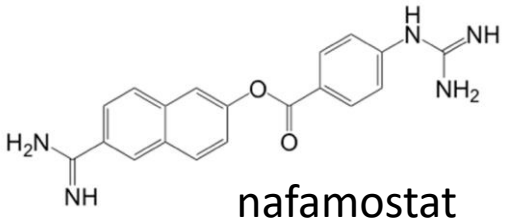
Small amount of trypsin inhibitor does not affect release if taken as per prescription.

An overdose provides enough trypsin inhibitor to prevent full activation and release of opioid.

Ensysce™ biosciences



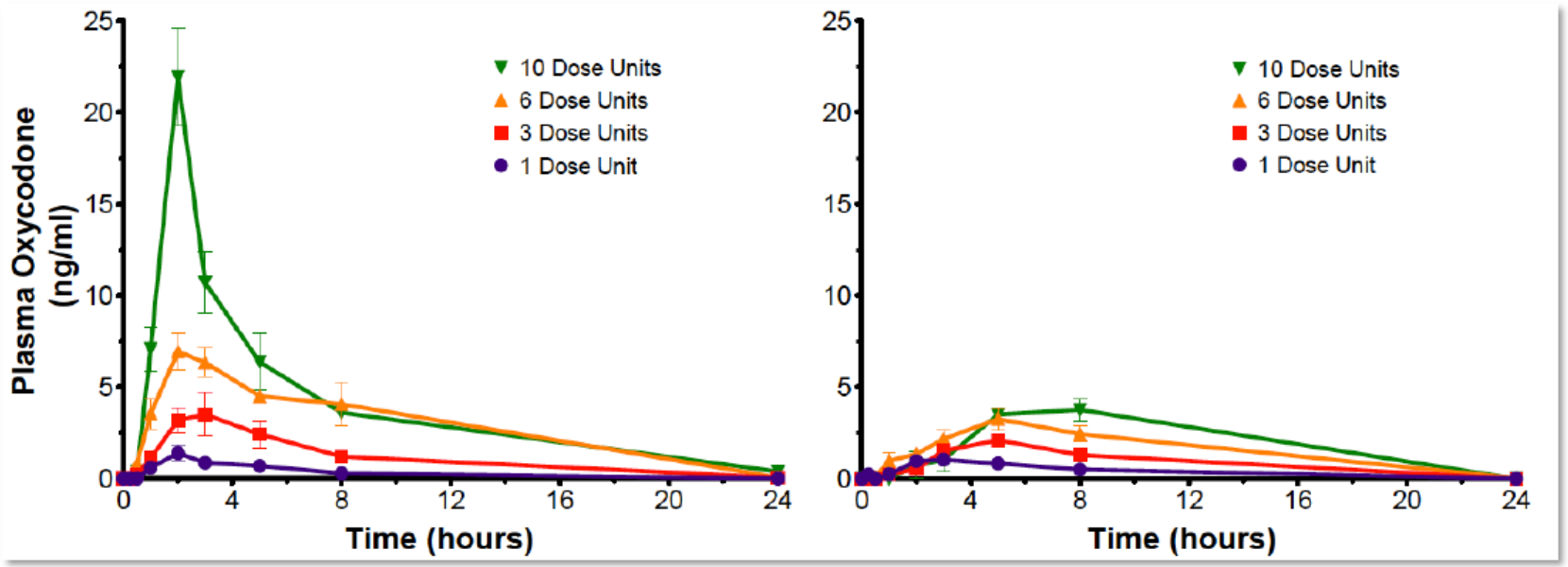
PF614 (OC prodrug)



nafamostat

Without nafamostat (trypsin inhibitor)

With nafamostat



In rats n=4/dose
OC = oxycodone
MPAR™ = PF614 with nafamostat

The combination of PF614 with trypsin inhibitor, nafamostat shows attenuation of activation of prodrug with muti-pill administration.

If we embrace the concept of product-specific scheduling, it may stimulate further innovation in the development of overdose-deterrent products.