2017 SENATE JUDICIARY

SB 2096

2017 SENATE STANDING COMMITTEE MINUTES

Judiciary Committee
Fort Lincoln Room, State Capitol

SB 2096
1/4/2017
26567

☐ Subcommittee
☐ Conference Committee

Committee Clerk Signature	

Explanation or reason for introduction of bill/resolution:

To amend a bill relating to the scheduling of controlled substances; and to declare an emergency.

Minutes: **Testimony attached #** 1, 2, 3

Chairman Armstrong called the committee to order. All committee members were present.

Attorney General Wayne Stenehjem – Introduced the bill (No written testimony.) He stated he supports the proposed bill and amendments. Attorney General Stenehjem laid the groundwork for the bill, he gave statistics of prescription drug overdoses and he proclaimed the seriousness of the bill. He described how the Attorney General's office works with the crime lab and other law enforcement agencies to limit the amount of illegal prescription drugs being sold illegally on the streets.

Mark Hardy, Executive Director of the State Board of Pharmacy – Testified in support of the bill (see attachment 1.) He also proposed recommended amendments (see attachment 3)

Senator Nelson: "Can you go through what the different drug schedules are?"

Mark Hardy – Elaborated the different types of drug schedules and what they mean.

Chairman Armstrong: "What mechanisms do we have in place that happened over the interim when we discussed this? A lot of things happen over two years which is when we meet for this bill."

Mark Hardy: "Legislature granted the Board of Pharmacy the ability to create emergency rules to add drug compounds to drug schedules."

Senator Luick: "Are your amendments basically typographical?"

Mark Hardy: "Yes, some are. First subset is, second subset we request to be added to the bill, and last subset is language modification on some specific drugs."

Charlene Rittenbach, ND Forensic Crime Specialist – Testified in support of the bill (see attachment 2)

Senator Larson: "Fentanyl has medicinal value?"

Charlene Rittenbach: "Yes. It's Schedule II."

Chairman Armstrong" "Most of the Fentanyl you see in overdoses is black market Fentanyl, I presume?"

Charlene Rittenbach: "Correct."
Charlene completed her testimony by discussing how the Fentanyl organic compound can be chemically manipulated to produce related Fentanyl compounds.

Chairman Armstrong closed the hearing on SB 2096.

Senator Nelson motioned to Adopt the Amendment with a Do Pass.
Senator Myrdal seconded.

A Roll Call Vote was taken to Adopt the Amendment. Yea: 6 Nay: 0 Absent: 0
The motion carried.

Senator Nelson motioned for a Do Pass as Amended. Senator Myrdal seconded.

A Roll Call Vote was taken for a Do Pass as Amended. Yea: 6 Nay: 0 Absent: 0
The motion carried.

Bill carried by Senator Nelson.

17.8013.01001
Title.02000

Adopted by the Judiciary Committee

January 5, 2017

CR 1/6/17

PROPOSED AMENDMENTS TO SENATE BILL NO. 2096

Page 4, line 2, replace the underscored period with an underscored comma

Page 4, line 4, replace the underscored period with an underscored comma

Page 4, line 29, after the first underscored closing parenthesis insert an underscored hyphen

Page 4, line 29, replace "Butyrvl" with "Butyryl"

Page 5, line 7, replace "Acrvlfentanyl" with "Acrylfentanyl"

Page 5, line 9, replace "Valervl" with "Valeryl"

Page 11, line 6, replace "Hindazole" with "H-indazole"

Page 11, line 7, replace "ADBCHMINACA" with "ADB-CHMINACA"

Page 11, after line 7, insert:

[17] Methyl 2-(1-(5-fluoropentyl)-1H-indazole-3-carboxamido)-3,3-dimethylbutanoate - Other names: 5F-ADB and 5F-MDMB-PINACA.

[18] N-(adamantan-1-yl)-1-(5-fluoropentyl)-1H-indazole-3-carboxamide - Other names: 5F-APINACA and 5F-AKB48.

[19] Methyl 2-(1-(cyclohexylmethyl)-1H-indole-3-carboxamido)-3,3-dimethylbutanoate - Other names: MDMB-CHMICA and MMB-CHMINACA.

[20] Methyl 2-(1-(4-fluorobenzyl)-1H-indazole-3-carboxamido)-3,3-dimethylbutanoate - Other names: MDMB-FUBINACA.

Page 20, line 1, replace "a" with "alpha"

Page 27, line 16, after "Epidiolex" insert "or its successor name as determined by the United States food and drug administration"

Renumber accordingly

Date: 1/4/17
Roll Call Vote #: 1

2017 SENATE STANDING COMMITTEE
ROLL CALL VOTES
BILL/RESOLUTION NO. SB 2096

Senate Judiciary Committee

☐ Subcommittee

Amendment LC# or Description: 17.8013.01001

Recommendation: ☒ Adopt Amendment
☐ Do Pass ☐ Do Not Pass ☐ Without Committee Recommendation
☐ As Amended ☐ Rerefer to Appropriations
☐ Place on Consent Calendar

Other Actions: ☐ Reconsider ☐ _____

Motion Made By Sen. Nelson Seconded By Sen. Myrdal

Senators	Yes	No	Senators	Yes	No
Chairman Armstrong	X		Senator Osland	X	
Vice-Chair Larson					
Senator Luick					
Senator Myrdal					
Senator Nelson					

Total (Yes) 6 No 0

Absent 0

Floor Assignment _____

If the vote is on an amendment, briefly indicate intent:

Date: 1/4/17
Roll Call Vote #: 2

2017 SENATE STANDING COMMITTEE
ROLL CALL VOTES
BILL/RESOLUTION NO. SB 2096

Senate Judiciary Committee

☐ Subcommittee

Amendment LC# or Description: 17.8013.01001

Recommendation: ☐ Adopt Amendment
☒ Do Pass ☐ Do Not Pass ☐ Without Committee Recommendation
☒ As Amended ☐ Rerefer to Appropriations
☐ Place on Consent Calendar

Other Actions: ☐ Reconsider ☐ _____

Motion Made By Sen. Nelson Seconded By Sen. Myrdal

Senators	Yes	No	Senators	Yes	No
Chairman Armstrong	X		Senator Osland	X	
Vice-Chair Larson					
Senator Luick					
Senator Myrdal					
Senator Nelson					

Total (Yes) 6 No 0

Absent 0

Floor Assignment Sen. Nelson

If the vote is on an amendment, briefly indicate intent:

REPORT OF STANDING COMMITTEE

SB 2096: Judiciary Committee (Sen. Armstrong, Chairman) recommends **AMENDMENTS AS FOLLOWS** and when so amended, recommends **DO PASS** (6 YEAS, 0 NAYS, 0 ABSENT AND NOT VOTING). SB 2096 was placed on the Sixth order on the calendar.

Page 4, line 2, replace the underscored period with an underscored comma

Page 4, line 4, replace the underscored period with an underscored comma

Page 4, line 29, after the first underscored closing parenthesis insert an underscored hyphen

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Renumber accordingly

2017 HOUSE JUDICIARY

SB 2096

2017 HOUSE STANDING COMMITTEE MINUTES

Judiciary Committee
Prairie Room, State Capitol

SB 2096
3/1/2017
28575

☐ Subcommittee
☐ Conference Committee

Committee Clerk Signature

Explanation or reason for introduction of bill/resolution:

Relating to the scheduling of controlled substances; and to declare an emergency.

Minutes: 1,2

Chairman K. Koppelman: Opened the hearing on SB 2096.

Mark Hardy, Executive Director, ND Board of Pharmacy: (#1) Went through the bill. (1:00-9:30)

Representative Jones: On page 27 when you were talking about the epidiolex; you said it is a divertive of a marijuana plant. What is it? Is it an oil or a pill form?
What is it?

Mark Hardy: it is going to be an oil and be capsulized. It will be a standardized doze which an epileptic patient would take to have the seizures subside.

Representative Jones: This is in a schedule 4 or schedule 5 classification and you said if it was left up to the federal government that would be considered a class 1?

Mark Hardy; Now with the state control substance; the federal government would change that upon the approval of the drug coming to market. With our state legislation this is a unique drug that is coming to the market and it would look at our state control substance act and where would it fit in it. Now we have marijuana in a schedule 1 substance in the state of ND; it could be conceived that Dravidics of marijuana as a dial as a schedule 1 substance. When it comes to the market it will be a schedule 4 or schedule 5 federally and for us in the state as far as dispensing and subscribing it makes no difference if it is in schedule 4 or 5.

Representative Jones: Page 23 you were talking about a medicine that immobilizes animals; is that veterinary use or are we talking about putting them down?

Mark Hardy: If a human came into contact it would lead to immediate death of a patient.

Chairman K. Koppelman: Over the years when we have had to classify various substances that it was always to stay ahead of the game when designer drugs were formulated and we would classify something by a specific definition and they would change the formula a little bit and then it didn't fit that definition anymore, but it was just as problematic. Is that what we are we capturing some of that creativity?

Mark Hardy: Yes that is what we are doing here. We have had to do emergency rules as far as to protection of the public in some of these synthetic products in the past.

Chairman K. Koppelman: Epidiolex was discussed. If they make ten changes three years ago that is not part of that statute? Did you discuss that at all? Adopting future actions through reference?

Mark Hardy; That is something the Senate judiciary did not discuss when we brought the amendments to them. We did have extensive conversation with the pharmacy that is bringing it to market; GW Pharmaceutical about the appropriate language that they felt comfortable with. We need to do investigation to be sure it complies with this. What happens when the FDA looks at the naming of the drug; they look at the name at the dialects and are there any drugs going to be confused with that in the market that may lead to potential drug errors.

Chairman K. Koppelman: We already have medication that contains the essence of the marijuana plant. How do we deal with this with respect to scheduling because one of the issues we have dealt with in ND years ago we passed a law allowing the growing of industrial hemp for our farmers? It looks a lot like marijuana and it is not smoke able; but the federal government at the time said we are not going to let you grow this because we think you might be able to grow a marijuana plant somewhere in the middle of this hemp field and it would be undetectable and that concerns us because marijuana is illegal under federal law. Now it is still illegal under the federal law how do you see all of this shaking out and how is it reflected in this?

Mark Hardy: There is complexities to marijuana and how it is scheduled and how each state deals with it on the individual level.

Representative Klemin: With this medical marijuana measure that passed you still have to get a prescription to get it.

Mark Hardy: You do not need a prescription for it. A doctor has to certify that you have a debilitating disease.

Representative Klemin: Where is it in the bill?

Mark Hardy; Page 6, line 23.

Chairman K. Koppelman: It sounds like one of the problems when states legalize marijuana use whether it is medicinal or recreation they have a financial problem. The banks say this is illegal under federal law so we won't touch the money. So it is a cash business. Is that the same thing that occurs in the pharmacy world so if the state does legalize this and a doctor

could write a prescription for some kind of derivative that might be municipal are pharmacy's afraid to deal with that for the same reason?

Mark Hardy: Yes.

Representative Klemin: You said Schedule 1 was substances with no medical use yet we have medical marijuana listed under schedule 1?

Mark Hardy: The drug has to be approved by the FDA in order to come to market and have specific doze ranges and safety profiles and those kind of things. Marijuana and medicinal would be outside that context on how medicines are brought to the market. DEA and FDA looked at marijuana in 2015 as far as changing the scheduling and they decided to leave it in schedule I.

Representative Vetter: Who has access to that card list? Is there any other drug out there that is going to have a special card?

Mark Hardy: Dept. of Health tracks that information. The patient would get a card and they would take it and they have to renew it etc.

Representative Vetter: So the Department of Health has this list. So does law enforcement have this list too?

Mark Hardy: I don't know if I can answer that question.

Charlene Rittenbach, Forensic Scientist, ND Crime Lab Division, Office of Attorney General: (#2) (27:20-34:00)

Representative Satrom: Who makes this stuff?

Charlene Rittenbach: A lot of these chemicals that are legal highs are being made in China. There is a lot of money in this. They are number 1 and it is sold through the internet.

Representative Klemin: Once we add this in here do we anticipate we will have less of this type of illegal substance being sold in ND?

Charlene Rittenbach: It will be harder to obtain. A lot of these compounds are already added to heroin now and it is already a schedule substance. It is a tool to help the seller so someone couldn't order from the internet. They have some control so they can't just order in ND.

Representative Klemin: You say in your testimony that you are going to make these analog drugs harder to obtain. Is there any way we can predict where the next substance is going to be?

Charlene Rittenbach: That is what we are trying to do with this type of legislation with the group molecule with any substitutions. This is a proactive approach where if they tweet the fentanyl molecules a little bit it would be covered in our law.

Chairman K. Koppelman: Is there a way to have some overarching language in some of these statutes that captures slight difference; can we somehow find a way to adopt language that will capture whatever class because they are just messing with the words.

Charlene Rittenbach: That is a good point. We already do have a controlled substance analog definition in our state code, but it only covers a schedule 1 or 2. We have to meet some criteria so a lot of these newer compounds because there is no research or literature on some of these. The seller is representing it as a drug.

Chairman K. Koppelman: Wouldn't it be a loophole represented to be a drug. In the past they have been sold like bath salts and other things in various shops as something else?

Charlene Rittenbach: The wording in our state law is that it must be chemically similar; and either or has to be met.

Chairman K. Koppelman: In looking at the schedule I and 2 substances there seems to be morphine derivatives; are there similar substances to morphine for example that are schedule 1 and if so why and why is it not schedule 2? How is it that they are under both schedule 1 and 2?

Charlene Rittenbach: Morphine or opioid divertive are gotten from the plant opium so there are five naturally occurring optimize in the opium plant. You also have opioids why are synthetic produced. They produce the same effects in the body and the receptors in the brain, but it is how you start with it.

Chairman K. Koppelman: So those specific ones may not have a municipal purpose where morphine may or does?

Opposition: None

Neutral: None

Hearing closed.

Do Pass Motion Made by Rep. Karls; Seconded by Rep. Satrom

Discussion:

Representative Klemin: I am concerned about the schedule 1 marijuana and relationship to legality of marijuana under the initiated measure and for medical uses when it is a schedule 1 substance that has no medical use according to the definition but yet it confusing and inconsistent.

Representative Simons: What you said is only in commerce. If the state kept it in the state, then the federal government couldn't do anything. Is that correct?

Chairman K. Koppelman: They would camp on the supremacy clause with respect to federal law superseding state law with respect to scheduled drugs and the FDA's authority.

Representative Jones: We have 29 states have medical marijuana legalized and we are fighting the federal government about the fact they won't take it off the schedule 1 classification. I thought it was going to be taken off 3-4 months ago.

Representative Nelson: The federal government made all marijuana extracts schedule 1 and epidiolex so it is a schedule 1 drug under FDA rules right now. Here we are putting it in schedule 4 or 5? It does look like we have some leeway doing state schedule different from federal schedule.

Chairman K. Koppelman: Marijuana in many forms the way it is sold illegally will remain in crime in ND.

Representative Nelson: Industrial hemp is marijuana so maybe that specific law supersedes this schedule?

Chairman K. Koppelman: Marijuana listed under schedule 1 is the street drug and the exceptions are what they are for the moment.

Representative Jones: I asked my sheriff what the biggest problem we have and it is drugs. They are trying lead the curve and have tools so they can try to stop this.

Chairman K. Koppelman: It is hard to stay ahead of that curve. I think ND has done better than most states have.

Representative Klemin: We can't say it is a schedule 1 substance that has no medical use and one the one hand and then have this inconsistent state law that we are having this big Senate bill on through the initiated measure saying that some medical marijuana doesn't require a prescription.

Chairman K. Koppelman: We could solve that is this bill passes with the emergency clause first is dealt with so that would be an exception with the schedule without muddying the term logy with something that might turn out to be not explicit with what we end up with/.

Roll Call Vote: 11 Yes 2 No 2 Absent Carrier: Rep. Satrom

Closed.

Date: 3/1/2017
Roll Call Vote 1

2017 HOUSE STANDING COMMITTEE
ROLL CALL VOTES
BILL/RESOLUTION NO. SB 2096

House **Judiciary** Committee

☐ Subcommittee

Amendment LC# or Description: _____

Recommendation: ☐ Adopt Amendment
☒ Do Pass ☐ Do Not Pass ☐ Without Committee Recommendation
☐ As Amended ☐ Rerefer to Appropriations
☐ Place on Consent Calendar

Other Actions: ☐ Reconsider ☐ _____

Motion Made By Rep. Karls Seconded By Rep Satrom

Representatives	Yes	No	Representatives	Yes	No
Chairman K. Koppelman	X			X	
Vice Chairman Karls	X			X	
Rep. Blum	X				
Rep. Johnston		X			
Rep. Jones	X				
Rep. Klemin	X				
Rep. Magrum	--				
Rep. Maragos	X				
Rep. Paur	---				
Rep. Roers-Jones	X				
Rep. Satrom	X				
Rep. Simons		X			
Rep. Vetter	X				

Total (Yes) 11 No 2

Absent 2

Floor Assignment Rep. Satrom

If the vote is on an amendment, briefly indicate intent:

REPORT OF STANDING COMMITTEE

SB 2096, as engrossed: Judiciary Committee (Rep. K. Koppelman, Chairman) recommends **DO PASS** (11 YEAS, 2 NAYS, 2 ABSENT AND NOT VOTING). Engrossed SB 2096 was placed on the Fourteenth order on the calendar.

2017 TESTIMONY

SB 2096

OFFICE OF THE EXECUTIVE DIRECTOR
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STATE BOARD OF PHARMACY

State of North Dakota
Doug Burgum, Governor

E-mail= Mhardy@btinet.net www.nodakpharmacy.com

Mark J. Hardy, PharmD, R.Ph.
Executive Director

Senate Bill No 2096 – Controlled Substances Rescheduling
Senate Judiciary Committee – Fort Lincoln Room
1:00 PM - Wednesday – January 4, 2017

Chairman Armstrong, members of the Senate Judiciary Committee, for the record I am Mark J. Hardy, PharmD, Executive Director of the North Dakota State Board of Pharmacy. I appreciate the opportunity to be here to speak to you today.

Senate Bill 2096 is the biennial bill introduced by State Board of Pharmacy to bring the Controlled Substances scheduling up-to-date with what the Food and Drug Administration [FDA] and Drug Enforcement Administration [DEA] have done over the past two years. This bill also adds a new category for derivatives of Fentanyl within the Schedule I controlled substances. The drafting of this bill, specifically the Schedule I substances was done in conjunction with the ND Crime Lab. A representative with the ND Crime Lab is here and will present testimony to explain much of the chemistry and reasons for the new category listed in this proposed legislation. The intention for these changes is to try to be proactive and ensure that we have future chemical modifications that can be made to these substances, identified as controlled substances. This bill is very lengthy and, we feel, as comprehensive as possible with the information that we have at this time.

I would like to highlight each provision of the bill to ensure you have an understanding of the changes we have in the drafting of this bill.

On page 4, line 1 – we have added the previously mentioned new category for derivatives of Fentanyl compounds, as schedule I opioids.

In the previous pages 1-3 you will notice multiply compounds that were struck from schedule I and were specifically added under the Fentanyl derivatives section as compounds which would chemically fall under that new section. Of course, these compounds have recently garnished a great deal of attention, specifically, furanyl fentanyl which is specifically listed on page 4 line 26 of this bill. The intention is to have the core structure listed with future illicit modifications considered a schedule I substance while still having the statement that Fentanyl derivatives which are FDA approved and listed in another schedule would be exempted.

On page 3, starting on line 27-31 are three opioid compounds separate from Fentanyl derivatives, which the DEA has scheduled since our last legislative session and we are adding as well.

On page 11, line 5 is the addition of a new Indole Carboxamide compound which was also scheduled by DEA. Other similar compounds were also made Schedule I compounds by DEA at the same time but, have already been specifically identified in past legislative sessions.

On page 18, beginning on line 17 through page 20 line 2 we made some modifications to the other known names of substituted cathinones and made the addition of Pentylone and 4-MePPP consistent with the DEA's scheduling.

Again, these changes in the Schedule I Controlled Substances lists the core chemical compounds as well as the individual compound in attempt to be proactive in the complex nature of modifying these dangers drugs by chemists in foreign countries to circumvent laws. This is our best approach for protecting our citizens and of being proactive in assisting the legal system, by specifically listing the known chemicals for their legal cases.

On page 22, line 30 the addition of Thiafentanil which is a new controlled substance which has been scheduled by DEA since our last legislative session, into Schedule II.

On page 24, lines 16-17 are the addition of the chemical name for Tramadol as a Schedule IV substance to mirror that of DEA. The 2013 Legislative Session was proactive in scheduling Tramadol in North Dakota prior to the DEA scheduling it as we had such large abuse reports.

On Page 25, line 14 the addition of Flunitrazepam as a Schedule IV controlled substance to be consistent with DEA scheduling.

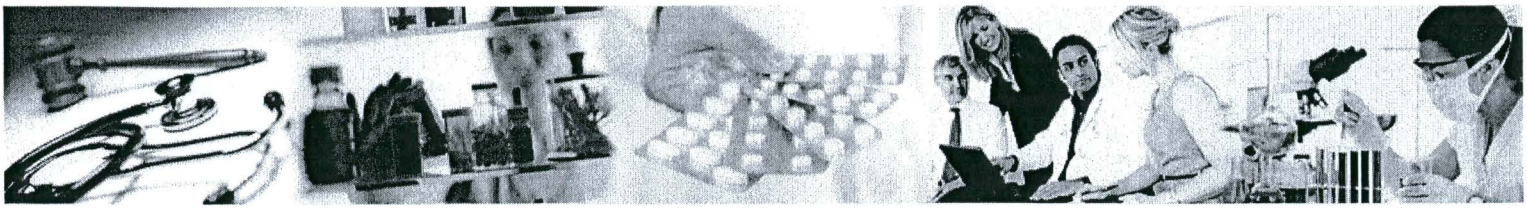
On page 27, starting with line 12 the addition of Eluxadone as a Schedule IV controlled substance to be consistent with DEA scheduling.

Also on page 27, line 16 we are proposing the addition of Epidiolex as a Schedule IV controlled substance to be consistent with DEA scheduling and respectfully request the amendment to add the terminology " or it's successor name as determined by the Food and Drug Administration". This medication is a drug currently in phase 3 trials and is a cannabidiol derived medication. Cannabidiol is one of the compounds in the marijuana plant. This product will specifically be utilized to treat epilepsy conditions in children. The reason for the language offered in the amendments is due to Epidiolex as it currently stands would now fall as a Schedule I compound without this specific addition. The request for the amendment is to address the circumstances that the FDA would change the brand name of the drug in it's approval process. It is likely to be brought to market in late 2017

Page 28, line 25 Brivaracetam is added as a Schedule IV controlled substance to be consistent with DEA scheduling.

Lastly, I am handing out proposed amendments to address typographical errors in the legislative council's draft, along with three additional Indole Carboxamide compounds, which were recently scheduled by DEA.

We respectfully request that this legislation be considered an emergency measure to put these changes into effect as soon as possible. I do appreciate your time and consideration on this legislation and am available for any questions you may have.



Rules - 2015

Drug Scheduling Actions

Final Rule: Placement of Eluxadoline Into Schedule IV; Correction (December 17, 2015)

Final Rule: Placement of Eluxadoline Into Schedule IV; Correction (November 16, 2015)

Proposed Rule: Placement of Three Synthetic Phenethylamines Into Schedule I (November 13, 2015)

Final Order: Extension of Temporary Placement of Three Synthetic Phenethylamines in Schedule I (November 13, 2015)

Final Rule: Placement of Eluxadoline Into Schedule IV (November 12, 2015)

Notice of Intent: Temporary Placement of the Synthetic Cannabinoid MAB-CHMINACA Into Schedule I (September 16, 2015)

Final Rule: Removal of [^{123}I]Ioflupane From Schedule II of the Controlled Substances Act (September 11, 2015)

Proposed Rule: Placement of Eluxadoline Into Schedule IV (August 11, 2015)

Final Order: Temporary Placement of Acetyl Fentanyl Into Schedule I (July 17, 2015)

Proposed Rule: Removal of [^{123}I]Ioflupane From Schedule II of the Controlled Substances Act (June 3, 2015)

Notice of Intent: Temporary Placement of Acetyl Fentanyl into Schedule I (May 21, 2015)

Final Order: Extension of Temporary Placement of UR-144, XLR11, and AKB48 in Schedule I of the Controlled Substances Act (May 15, 2015)

Proposed Rule: Placement of UR-144, XLR11, and AKB48 Into Schedule I (May 14, 2015)

Final Rule: Substances Temporarily Controlled Under Schedule I of the Controlled Substances Act (March 20, 2015)

Final Order: Temporary Placement of Three Synthetic Cannabinoids Into Schedule I (January 30, 2015)

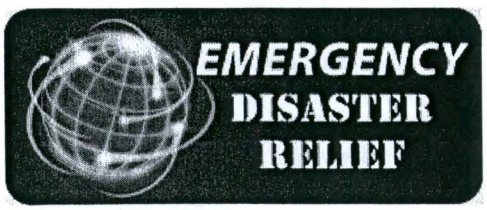
Final Rule: Removal of Naloxegol From Control (January 23, 2015)

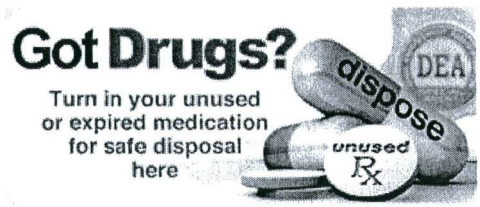
Excluded Nonnarcotic Products

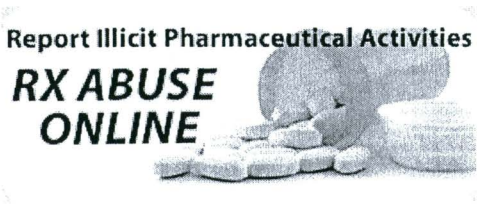
Interim Final Rule: Table of Excluded Nonnarcotic Products: Nasal Decongestant Inhaler/Vapor Inhaler (October 27, 2015)

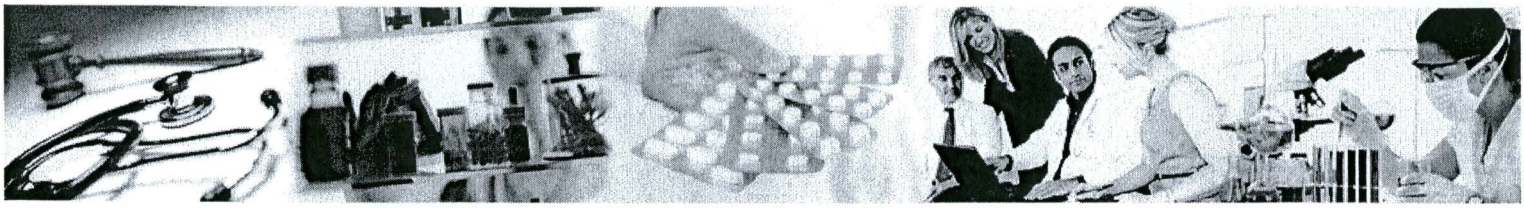
Interim Final Rule: Table of Excluded Nonnarcotic Products: Vicks® VapoInhaler® (October 27, 2015)

Cases Against Doctors
Chemical Control Program
CMEA (Combat Meth Epidemic Act)
Controlled Substance Schedules
DATA Waived Physicians
Drug Disposal Information
Drug and Chemical Information
E-commerce Initiatives
Federal Agencies & Related Links
Federal Register Notices
National Take-Back Initiative
NFLIS
Publications & Manuals
Questions & Answers
Significant Guidance Documents
Synthetic Drugs
Title 21 Code of Federal Regulations
Title 21 USC Codified CSA









Rules - 2016

Cases Against Doctors
Chemical Control Program
CMEA (Combat Meth Epidemic Act)
Controlled Substance Schedules
DATA Waived Physicians
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NFLIS
Publications & Manuals
Questions & Answers
Significant Guidance Documents
Synthetic Drugs
Title 21 Code of Federal Regulations
Title 21 USC Codified CSA

Combat Methamphetamine Enhancement Act of 2010 (MEA)

Final Rule: Self-Certification and Employee Training of Mail-Order Distributors of Scheduled Listed Chemical Products (January 25, 2016)

Drug Scheduling Actions

Notice of Intent: Temporary Placement of Six Synthetic Cannabinoids (5F-ADB, 5F-AMB, 5F-APINACA, ADB-FUBINACA, MDMB-CHMICA and MDMB-FUBINACA) Into Schedule I (December 21, 2016)

Final Rule : Establishment of a New Drug Code for Marihuana Extract (December 14, 2016)

Proposed Rule : Designation of Alpha-Phenylacetoacetonitrile (APAAN), a Precursor Chemical Used in the Illicit Manufacture of Phenylacetone, Methamphetamine, and Amphetamine, as a List I Chemical (December 12, 2016)

Final Order: Temporary Placement of Furanyl Fentanyl Into Schedule I (November 29, 2016)

Final Order: Temporary Placement of U-47700 Into Schedule I (November 14, 2016)

Withdrawal of Notice of Intent to Temporarily Place Mitragynine and 7-Hydroxymitragynine Into Schedule I (October 13, 2016)

Notice of Intent: Temporary Placement of Furanyl Fentanyl Into Schedule I (September 27, 2016)

Final Rule: Placement of Three Synthetic Phenethylamines Into Schedule I (September 27, 2016)

Notice of Intent: Temporary Placement of U-47700 Into Schedule I (September 7, 2016)

Final Rule: Placement of PB-22, 5F-PB-22, AB-FUBINACA and ADB-PINACA into Schedule I (September 6, 2016)

Notice of Intent: Temporary Placement of Mitragynine and 7-Hydroxymitragynine Into Schedule I (August 31, 2016)

Interim Final Rule: Placement of Thiafentanil Into Schedule II (August 26, 2016)

Interim Final Rule: Placement of Brivaracetam Into Schedule V (May 12, 2016)

Final Order: Temporary Placement of Butyryl Fentanyl and Beta-Hydroxythiofentanyl Into Schedule I (May 12, 2016)

Final Rule: Placement of UR-144, XLR11, and AKB48 into Schedule I (May 11, 2016)

Final Order: Placement of AH-7921 Into Schedule I (April 14, 2016)

Notice of Intent: Temporary Placement of Butyryl Fentanyl and Beta-Hydroxythiofentanyl Into Schedule I (March 23, 2016)

Proposed Rule: Placement of UR-144, XLR11, and AKB48 Into Schedule I; Correction (March 22, 2016)

Proposed Rule: Placement of 10 Synthetic Cathinones Into Schedule I (March 4, 2016)

Final Order: Extension of Temporary Placement of 10 Synthetic Cathinones in Schedule I of the Controlled Substances Act (March 4, 2016)

Proposed Rule: Placement of PB-22, 5F-PB-22, AB-FUBINACA and ADB-PINACA into Schedule I (February 5, 2016)

Final Order: Temporary Placement of the Synthetic Cannabinoid MAB-CHMINACA Into Schedule I (February 5, 2016)

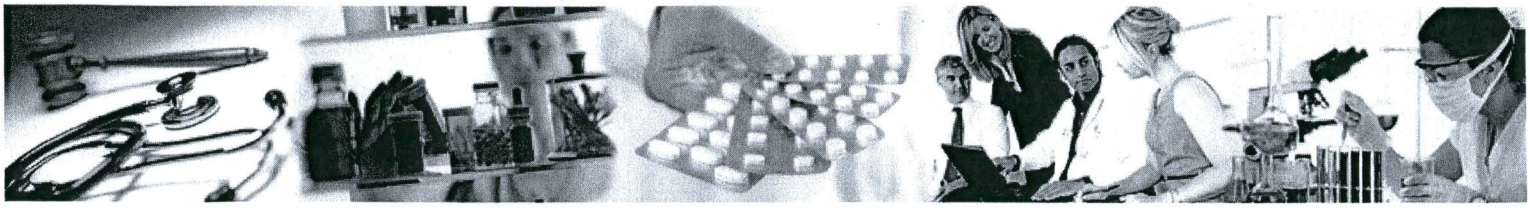
Final Order: Extension of Temporary Placement of PB-22, 5F-PB-22, AB-FUBINACA and ADB-PINACA in Schedule I of the Controlled Substances Act (February 5, 2016)

Excluded Nonnarcotic Products

Final Rule: Table of Excluded Nonnarcotic Products: Vicks® VapoInhaler® (February 8, 2016)

Final Rule: Table of Excluded Nonnarcotic Products: Nasal Decongestant Inhaler/Vapor Inhaler (February 8, 2016)

Exempt Chemical Preparations Under the Controlled Substances Act



Rules - 2015

[Federal Register Volume 80, Number 242 (Thursday, December 17, 2015)]
[Rules and Regulations]
[Page 78657]
From the Federal Register Online via the Government Publishing Office [www.gpo.gov]
[FR Doc No: 2015-31843]

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA-419F]

Schedules of Controlled Substances: Placement of Eluxadoline Into Schedule IV; Correction

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Final rule; correction.

SUMMARY: The Drug Enforcement Administration (DEA) is correcting a final rule that appeared in the Federal Register of November 12, 2015 (80 FR 69861). The document issued an action placing the substance 5-[[[(2S)-2-amino-3-[4-aminocarbonyl)-2,6-dimethylphenyl]-1-oxopropyl][(1S)-1-(4-phenyl-1H-imidazol-2-yl)ethyl] amino]methyl]-2-methoxybenzoic acid (eluxadoline), including its salts, isomers, and salts of isomers, into schedule IV of the Controlled Substances Act. This document inadvertently included a paragraph in the regulatory text that was not intended for publication, and was unable to be removed before being placed on public inspection. This document corrects the final rule by removing this paragraph.

DATES: Effective December 17, 2015.

FOR FURTHER INFORMATION CONTACT: John R. Scherbenske, Office of Diversion Control, Drug Enforcement Administration; Mailing Address: 8701 Morrissette Drive, Springfield, Virginia 22152, Telephone: (202) 598-6812.

SUPPLEMENTARY INFORMATION: In **FR Doc. 2015-28718** appearing on page 69864 in the Federal Register of Thursday, November 12, 2015, the following correction is made:

Administrative Procedure Act [Corrected]

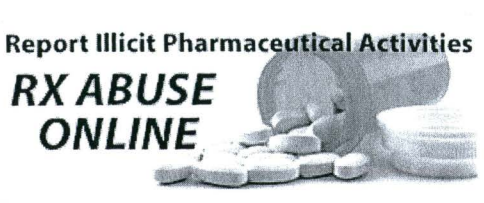
1. On page 69864, in the preamble, at the bottom of the first and top of the second columns, the section titled *Administrative Procedure Act* is removed entirely.

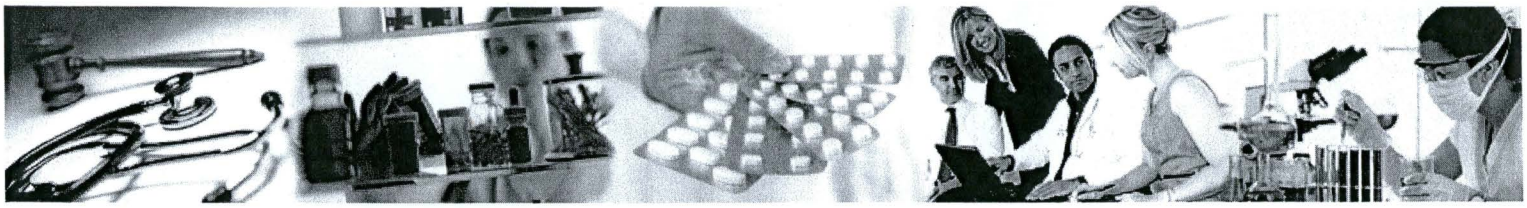
Dated: December 11, 2015.

Chuck Rosenberg,
Acting Administrator.

[FR Doc. 2015-31843 Filed 12-16-15; 8:45 am]

BILLING CODE 4410-09-P





Rules - 2016

[Federal Register Volume 81, Number 166 (Friday, August 26, 2016)]
[Rules and Regulations]
[Pages 58834-58840]
From the Federal Register Online via the Government Publishing Office [www.gpo.gov]
[FR Doc No: 2016-20463]

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Parts 1301, 1305, and 1308

[Docket No. DEA-375]

Schedules of Controlled Substances: Placement of Thiafentanil Into Schedule II

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Interim final rule with request for comments.

SUMMARY: The Drug Enforcement Administration is placing the substance thiafentanil (4-(methoxycarbonyl)-4-(N-phenmethoxyacetamido)-1-[2-(thienyl)ethyl] piperidine), including its isomers, esters, ethers, salts and salts of isomers, esters and ethers as possible, into schedule II of the Controlled Substances Act. This scheduling action is pursuant to the Controlled Substances Act, as revised by the Improving Regulatory Transparency for New Medical Therapies Act which was signed into law on November 25, 2015.

DATES: The effective date of this rule is August 26, 2016. Interested persons may file written comments on this rule in accordance with **21 U.S.C. 811**(j)(3) and **21 CFR 1308.43**(g). Electronic comments must be submitted, and written comments must be postmarked, on or before September 26, 2016. Commenters should be aware that the electronic Federal Docket Management System will not accept comments after 11:59 p.m. Eastern Time on the last day of the comment period.

Interested persons, defined at **21 CFR 1300.01** as those "adversely affected or aggrieved by any rule or proposed rule issuable pursuant to section 201 of the Act (**21 U.S.C. 811**)," may file a request for hearing or waiver of hearing pursuant to **21 CFR 1308.44** and in accordance with **21 CFR 1316.45** and/or **1316.47**, as applicable. Requests for hearing and waivers of an opportunity for a hearing or to participate in a hearing must be received on or before September 26, 2016.

ADDRESSES: To ensure proper handling of comments, please reference "Docket No. DEA-375" on all correspondence, including any attachments.

- *Electronic comments:* The Drug Enforcement Administration encourages that all comments be submitted electronically through the Federal eRulemaking Portal, which provides the ability to type short comments directly into the comment field on the Web page or attach a file for lengthier comments. Please go to http://www.regulations.gov and follow the online instructions at that site for submitting comments. Upon completion of your submission, you will receive a Comment Tracking Number for your comment. Please be aware that submitted comments are not instantaneously available for public view on Regulations.gov. If you have received a Comment Tracking Number, your comment has been successfully submitted and there is no need to resubmit the same comment.
- *Paper comments:* Paper comments that duplicate the electronic submission are not necessary and are discouraged. Should you wish to mail a paper comment in lieu of an electronic comment, it should be sent via regular or express mail to: Drug Enforcement Administration, Attn: DEA Federal Register Representative/ODW, 8701 Morrissette Drive, Springfield, Virginia 22152.
- *Hearing requests:* All requests for hearing and waivers of participation must be sent to: Drug Enforcement Administration, Attn: Administrator, 8701 Morrissette Drive, Springfield, Virginia 22152. All requests for hearing and waivers of participation should also be sent to: (1) Drug Enforcement Administration, Attn: Hearing Clerk/LJ, 8701 Morrissette Drive, Springfield, Virginia 22152; and (2) Drug Enforcement Administration, Attn: DEA Federal Register Representative/ ODW, 8701 Morrissette Drive, Springfield, Virginia 22152.

FOR FURTHER INFORMATION CONTACT: Michael J. Lewis, Office of Diversion Control, Drug Enforcement Administration; Mailing Address: 8701 Morrissette Drive, Springfield, Virginia 22152; Telephone: (202) 598-6812.

SUPPLEMENTARY INFORMATION:

Posting of Public Comments

Please note that all comments received are considered part of the public record. They will, unless reasonable cause is given, be made available by the Drug Enforcement

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Administration (DEA) for public inspection online at http://www.regulations.gov. Such information includes personal identifying information (such as your name, address, etc.) voluntarily submitted by the commenter. The Freedom of Information Act (FOIA) applies to all comments received. If you want to submit personal identifying information (such as your name, address, etc.) as part of your comment, but do not want it to be made publicly available, you must include the phrase

"PERSONAL IDENTIFYING INFORMATION" in the first paragraph of your comment. You must also place all of the personal identifying information you do not want made publicly available in the first paragraph of your comment and identify what information you want redacted.

If you want to submit confidential business information as part of your comment, but do not want it to be made publicly available, you must include the phrase "CONFIDENTIAL BUSINESS INFORMATION" in the first paragraph of your comment. You must also prominently identify the confidential business information to be redacted within the comment.

Comments containing personal identifying information and confidential business information identified as directed above will generally be made publicly available in redacted form. If a comment has so much confidential business information or personal identifying information that it cannot be effectively redacted, all or part of that comment may not be made publicly available. Comments posted to http://www.regulations.gov may include any personal identifying information (such as name, address, and phone number) included in the text of your electronic submission that is not identified as directed above as confidential.

An electronic copy of this document and supplemental information, including the complete Department of Health and Human Services and Drug Enforcement Administration eight-factor analyses, to this interim final rule are available at http://www.regulations.gov for easy reference.

Request for Hearing, Notice of Appearance at Hearing, or Waiver of Participation in Hearing

Pursuant to **21 U.S.C. 811**(a), this action is a formal rulemaking "on the record after opportunity for a hearing." Such proceedings are conducted pursuant to the provisions of the Administrative Procedure Act (APA), 5 U.S.C. 551-559. **21 CFR 1308.41-1308.45**; **21 CFR part 1316**, subpart D. In accordance with **21 CFR 1308.44**(a)-(c), requests for a hearing, notices of appearance, and waivers of an opportunity for a hearing or to participate in a hearing may be submitted only by interested persons, defined as those "adversely affected or aggrieved by any rule or proposed rule issuable pursuant to section 201 of the Act (21 U.S.C. 811)." **21 CFR 1300.01**. Requests for a hearing and notices of participation must conform to the requirements of **21 CFR 1308.44**(a) or (b), as applicable, and include a statement of the interest of the person in the proceeding and the objections or issues, if any, concerning which the person desires to be heard. Any waiver of an opportunity for a hearing must conform to the requirements of 21 CFR 1308.44(c), including a written statement regarding the interested person's position on the matters of fact and law involved in any hearing.

Please note that pursuant to **21 U.S.C. 811**(a), the purpose and subject matter of the hearing are restricted to "(A) find[ing] that such drug or other substance has a potential for abuse, and (B) mak[ing] with respect to such drug or other substance the findings prescribed by subsection (b) of **section 812** of this title for the schedule in which such drug is to be placed . . . ." Requests for a hearing and waivers of participation in the hearing should be submitted to the DEA on or before the deadline specified above, using the address information provided therein.

Background, Legal Authority, and Basis for This Scheduling Action

Thiafentanil, known chemically as 4-(methoxycarbonyl)-4-(N-phenylmethoxyacetamido)-1-[2-(2-thienyl)ethyl]piperidine, a potent opioid, is an analogue of fentanyl. The product Thianil (thiafentanil oxalate, a salt form of thiafentanil) was reviewed by the Food and Drug Administration (FDA) to determine whether it meets the requirements for addition to the Index of Legally Marketed Unapproved New Animal Drugs for Minor Species (the Index) (21 U.S.C. 360ccc-1) as set forth by the Minor Use and Minor Species Animal Health Act of 2004 (MUMS Act, 2004). The MUMS Act amended the Federal Food, Drug, and Cosmetic Act (FDCA) to allow for the legal marketing of unapproved new animal drugs intended for use in minor species. In a letter from the Department of Health and Human Services (HHS) dated June 20, 2016, the DEA received notification that HHS/FDA added Thianil (thiafentanil oxalate) to the Index under section 572 of the FDCA. In this same notification, HHS/FDA stated that on June 16, 2016, HHS/FDA granted the request for the addition of Thianil to the Index under Minor Species Index File (MIF) 900000. Thianil is indicated for use in the immobilization of non-domestic, non-food-producing minor species hoofstock.

Thiafentanil will be marketed as thiafentanil oxalate, 4-(methoxycarbonyl)-4-(N-phenylmethoxyacetamido)-1-[2-(2-thienyl)ethyl]piperidinium oxalate. Thiafentanil should not be confused with thiofentanyl (N-phenyl-N-(1-(2-(thiophen-2-yl)ethyl)piperidin-4-yl)propionamide), which is currently listed as a controlled schedule I substance.

Under the Controlled Substances Act (CSA), as amended in 2015 by the Improving Regulatory Transparency for New Medical Therapies Act (Pub. L. 114-89), where the DEA receives notification from HHS that the Secretary has indexed a drug under section 572 of the FDCA, the DEA is required to issue an interim final rule controlling the drug not later than 90 days after receiving such notification from HHS. **21 U.S.C. 811**(j). Accordingly, the DEA is issuing this interim final rule controlling thiafentanil.

When controlling a drug pursuant to **section 811**(j), the DEA must apply the scheduling criteria of subsections 811(b), (c), and (d) and **section 812**(b). 21 U.S.C. 811(j)(3). In accordance with these criteria, the DEA has reviewed the scientific and medical evaluation and scheduling recommendation provided by the HHS, along with all other relevant data, and completed its own eight-factor review document on thiafentanil pursuant to 21 U.S.C. 811(c). As explained below, based on these considerations, the DEA concludes that thiafentanil meets the criteria for placement in schedule II of the CSA.

On November 28, 2011, the HHS provided the DEA with its initial scientific and medical evaluation and scheduling recommendation regarding thiafentanil. Pursuant to **21 U.S.C. 811**(b), this document contained an eight-factor analysis of the abuse potential of thiafentanil as a new drug, along with the HHS' recommendation to control thiafentanil and its salts under schedule II of the CSA. Subsequently, on March 23, 2016, the HHS provided the DEA with a supplement to its 2011 analysis, which indicated that the HHS/FDA planned to add Thianil (thiafentanil oxalate) to the Index for use in the immobilization of non-domestic, non-food-producing minor species hoofstock and reiterated their recommendation that thiafentanil be placed in schedule II of the CSA. By

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letter dated June 20, 2016, the DEA received notification from the HHS that the FDA had granted the request on June 16, 2016, for Thianil (thiafentanil oxalate) to be added to the Index.

Pursuant to **21 U.S.C. 811**(j), and based on the HHS recommendation, MUMS Act indication by the HHS/FDA, and the DEA's determination, the DEA finds that thiafentanil has a high potential for abuse, a currently accepted medical use with severe restrictions, and that abuse of thiafentanil may lead to severe psychological or physical dependence. Accordingly, the DEA is issuing this interim final rule to add thiafentanil (4-(methoxycarbonyl)-4-(N-phenylmethoxyacetamido)-1-[2-(2-thienyl) ethyl]piperidine) and its isomers, esters, ethers, salts and salts of isomers, esters and ethers, whenever the existence of such, to schedule II of the CSA.

Included below is a brief summary of each factor as analyzed by the HHS and the DEA, and as considered by the DEA in its scheduling action. Please note that the DEA and HHS analyses, along with the HHS supplement, are available in their entirety under "Supporting Documents" in the public docket for this interim final rule at http://www.regulations.gov, under Docket Number "DEA-375." Full analysis of, and citations to, the information referenced in the summary may also be found in the supporting and related material.

1. *The Drug's Actual or Relative Potential for Abuse:* Thiafentanil is a chemical substance that has not been marketed in the United States, however, it is approved and marketed in the Republic of South Africa as a salt form under the brand name Thianil (thiafentanil oxalate). There is no information available which details actual abuse of thiafentanil.

According to the HHS, thiafentanil is a synthetic analogue of fentanyl and is structurally related to other fentanyl-like opioids such as sufentanil (schedule II) and carfentanil (schedule II). It acts as a potent [micro]-opioid receptor agonist and produces strong morphine-like effects in animals. It is only intended for the immobilization of non-domestic, non-food-producing minor species hoofstock. Thiafentanil has been used in a manner similar to other opioid immobilizing agents such as etorphine hydrochloride (schedule II) and carfentanil (schedule II), which are approved only for veterinary use as animal immobilization agents. The abuse potential of thiafentanil has not been evaluated in humans or in animal behavioral models that are predictors of abuse by humans. Because thiafentanil shares chemical and pharmacological similarities with schedule II fentanyl and its analogues, the abuse potential of thiafentanil is considered similar to that of schedule II opioid substances such as sufentanil and carfentanil.

Pharmacologically, as a potent [micro] opioid receptor agonist, thiafentanil is slightly less potent than carfentanil, which is 100 times more potent than fentanyl and 10,000 times more potent than morphine. Thiafentanil is a potent fentanyl analogue. Thus, it is reasonable to assume that there will be potentially significant diversion of thiafentanil from legitimate channels by people who have access to it, and that thiafentanil would be used without medical advice, therefore causing substantial hazards to the users or to the safety of the community if not controlled. The chemical and potent opioid-like pharmacological properties of thiafentanil predict that its risk to the public health is likely to be similar to fentanyl (schedule II) and its analogues such as carfentanil (schedule II), sufentanil (schedule II) and alpha-methylfentanyl (schedule I).

2. *Scientific Evidence of the Drug's Pharmacological Effects, if Known:* According to HHS' scientific and medical review, there are no data on the effects of thiafentanil in humans. Thiafentanil's effects in humans are predicted from its effects in animals and its chemical and pharmacological similarity to other schedule II potent opioids such as fentanyl and carfentanil.

The HHS eight-factor review document described a study directly comparing the immobilizing effects of thiafentanil (15 mg) and carfentanil (2 or 4 mg) in elk in which thiafentanil produced a faster immobilization effect (0.7 to 2.2 minutes) than carfentanil. In addition, the elk returned to standing 0.9 to 1.4 minutes faster under the thiafentanil condition. This study appears to support a faster immobilization and recovery time with thiafentanil relative to carfentanil. However, the authors stated that the role of the increased dose of thiafentanil is unknown.

Animal studies described by the HHS demonstrated that the effects of thiafentanil and carfentanil are completely reversed by naltrexone. As a [micro]-opioid recep antagonist, naltrexone can reverse the effects of a variety of opioid drugs including thiafentanil and carfentanil. Those studies suggest that thiafentanil possesses a neuro-pharmacological mechanism of action similar to other schedule II opioid drugs with a high abuse potential.

According to HHS' review, Thianil (thiafentanil) is currently approved and registered for use in the Republic of South Africa. Thiafentanil oxalate is suggested as a drug of choice in the capture of exotic and ungulate wildlife species.

3. *The State of Current Scientific Knowledge Regarding Thiafentanil:* The chemical name of free base thiafentanil is 4-(methoxycarbonyl) -4-(N-phenylmethoxyacetamido)-1-[2-(2-thienyl)ethyl]piperidine. It has a molecular formula of C22H28N2O4S and a molecular weight of 416.52 g/mol with a Chemical Abstract Registry Number (CAS) of 101345-60-2. Thiafentanil oxalate is also known as A3080 with a CAS number of 101365-73-5 and has a molecular formula of C24H30N2O8S with a molecular weight of 506.57 g/mol. Thiafentanil oxalate is a white crystalline powder with a melting point of 190-192 [deg]C and its salt crystalizes from absolute alcohol. Thiafentanil should not be confused with thiofentanyl (N-phenyl-N-(1-(2-(thiophen-2-yl)ethyl)piperidin-4-yl)propionamide), which is currently listed as a schedule I substance.

4. *Its History and Current Pattern of Abuse:* According to the HHS' review, there are no reports of actual abuse and misuse of thiafentanil. This may be due to the limited use of thiafentanil as an immobilizing agent by trained veterinarians.

Current data from the National Forensic Laboratory System (NFLIS),\1\ the System to Retrieve Information from Drug Evidence (STRIDE),\2\ and the STARLiMS databases show that there is no evidence of law enforcement encounters of thiafentanil in the United States. However, thiafentanil's pharmacological and structural properties suggest that its pattern of abuse would be similar to other potent

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schedule II [micro]-opioid receptor agonists such as fentanyl and carfentanil.

\1\ The National Forensic Laboratory System (NFLIS) is a program of the DEA, Office of Diversion Control. NFLIS systematically collects drug identification results and associated information from drug cases submitted to and analyzed by State and local forensic laboratories. NFLIS represents an important resource in monitoring illicit drug abuse and trafficking, including the diversion of legally manufactured pharmaceuticals into illegal markets. NFLIS is a comprehensive information system that includes data from forensic laboratories that handle approximately 90% of an estimated 1.0 million distinct annual State and local drug analysis cases. NFLIS includes drug chemistry results from completed analyses only. While NFLIS data is not direct evidence of abuse, it can lead to an inference that a drug has been diverted and abused. See 76 FR 77330, 77332, Dec. 12, 2011.

\2\ The System to Retrieve Information from Drug Evidence (STRIDE) is a database of drug exhibits sent to DEA laboratories for analysis. Exhibits from the database are from the DEA, other federal agencies, and local law enforcement agencies. Reporting via STRIDE ceased on September 30, 2014. STRIDE was succeeded by STARLiMS.

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5. *The Scope, Duration, and Significance of Abuse:* An assessment of the scope, duration, and significance of thiafentanil abuse is not available since it has only been used in a limited market. However, as stated in the HHS review, the structural and pharmacological properties of thiafentanil suggest that it could lead to an abuse pattern with a scope, duration, and significance of abuse similar to that observed with other opioid drugs and opioid analogues if it were marketed in a non-controll status or were the subject of clandestine synthesis. The HHS and DEA note that thiafentanil is not known to be or to have been the subject of abuse in the United States.

6. *What, if any, Risk There is to the Public Health:* The HHS review indicates that thiafentanil presents a significant risk to the public health and, in this vein, that thiafentanil should only be used in certain animals for very limited purposes and with extreme caution. Based on the review of the structural and pharmacological properties of thiafentanil, the HHS concluded that the abuse of thiafentanil is likely to pose a similar risk to public health as that of other potent opioid drugs such as sufentanil (schedule II), fentanyl (schedule II), carfentanil (schedule II) and clandestinely synthesized alpha-methylfentanyl (schedule I). Thus, inappropriate use of thiafentanil poses a high risk to the public health. Among other things, HHS noted that as a fentanyl derivative, and assuming that thiafentanil can be aerosolized, the use of thiafentanil presents a significant risk to the public health.

HHS described that thiafentanil's labeling indicates that it is solely intended for use by zoologic, wildlife, or exotic animal veterinarians or field biologists who have received training and are supervised by veterinarians. The sponsor recommends the use of handling protocols similar to those in place for other scheduled potent opioids such as carfentanil. HHS further indicated that thiafentanil should be handled in teams consisting of at least two individuals knowledgeable about the hazards of working with potent [mu]-opioid agonist substances. Personal protective equipment such as latex gloves and protective eyewear should be used and syringes must be disposed of properly. If exposure to thiafentanil occurs in a remote or distant environment, veterinary naltrexone is recommended for use as a reversal agent. The label information will further state that thiafentanil must never be used unless an adequate amount of reversal agent (naltrexone hydrochloride) is immediately available.

HHS also describes the risk of thiafentanil intoxication upon ingestion of animals immobilized with thiafentanil. The label information states that thiafentanil is not intended for human or animal consumption or in non-food producing minor species that become eligible for consumption by humans or food-producing animals. Because thiafentanil, similar to carfentanil, etorphine hydrochloride and diprenorphine, is a potent [mu]-opioid receptor agonist, it will be subject to specialized handling, distribution and storage procedures similar to those applicable for carfentanil, etorphine hydrochloride and diprenorphine as set forth in **21 CFR parts 1301** and **1305**. As a result, this interim final rule revises **21 CFR 1301.74**(g), **1301.75**(e), **1305.07** introductory text and paragraph (a), and **1305.17**(d) to include "thiafentanil."

7. *Its Psychic or Physiological Dependence Liability:* HHS' review states that the structural and pharmacological properties of thiafentanil suggest that it possesses a psychic and physiological dependence liability that is similar to other schedule II related [micro]-opioid receptor agonist drugs such as sufentanil, fentanyl and carfentanil.

As cited by the HHS review, a double-blind abuse liability study examining intravenous fentanyl, buprenorphine, heroin, morphine, and oxycodone in methadone-maintained patients reported that fentanyl produced subjective effects similar to heroin (schedule I) on several outcome measures indicating that the two drugs produce similar subjective effects. It also demonstrates the psychic dependence liability of fentanyl, and thiafentanil is expected to produce effects similar to fentanyl and to present a similar risk of psychic and physiological dependence. There has been a major increase in abuse of opioids analgesics in the United States (HHS review document, 2011; Compton and Volkow, 2006). Thiafentanil, similar to these opioid analgesics, presents a risk of severe psychic and physiological dependence.

8. *Whether the Substance is an Immediate Precursor of a Substance Already Controlled under the CSA:* Thiafentanil is not considered an immediate precursor of any controlled substance.

Determination of Appropriate Schedule

The CSA lists the findings required to place a drug or other substance in any particular schedule (I, II, III, IV, or V). **21 U.S.C. 812**(b). After consideration of the analysis and recommendation of the Assistant Secretary for Health of the HHS and review of all available data, the Acting Administrator of the DEA, pursuant to 21 U.S.C. 812(b)(2), finds that:

1. Thiafentanil has a high potential for abuse. Based on its structural and pharmacological properties, thiafentanil has an abuse potential that is comparable to other schedule II opioid drugs such as fentanyl, carfentanil, and sufentanil;

2. FDA determined that Thianil (thiafentanil oxalate) meets the requirements for addition to the Index as set forth by the MUMS Act, 2004 and accordingly added Thianil (thiafentanil oxalate) to the Index of Legally Marketed Unapproved New Animal Drugs for Minor Species (the Index) under section 572 of the Federal Food, Drug, and Cosmetic Act. Thianil (thiafentanil oxalate) will be legally marketed in the United States and will have an accepted medical use with severe restrictions; \3\ and

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\3\ According to the HHS analysis, "[u]se of a new animal indexed drug is subject to significant restrictions. For example, use of an indexed new animal drug for minor species is limited to a minor species for which there is a reasonable certainty that the animal or edible products from the animal will not be consumed by humans or food producing animals. 21 U.S.C. Sec. 360ccc-l(a)(1). The requester must label, distribute, and promote the new animal drug in accordance with the Index entry, and the FDA may remove a new animal drug from the Index if the conditions and limitations of use have not been followed. 21 U.S.C. 360ccc-l(d)(l)(G); (f)(l)(F). The labeling of an indexed new animal drug must prominently state that the extra-label use of the product is prohibited. 21 U.S.C. 360ccc-l(h). Such restrictions are not imposed upon approved human or animal drugs."

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3. Due to the chemical and pharmacological similarities of thiafentanil to other schedule II fentanyl derivatives, abuse of thiafentanil may lead to severe psychological or physical dependence.

Based on these findings, the Acting Administrator of the DEA concludes that thiafentanil, including its isomers, esters, ethers, salts and salts of isomers, esters and ethers whenever the existences of such isomers, esters, ethers, and salts is possible warrants control in schedule II of the CSA. **21 U.S.C. 812**(b)(2).

Requirements for Handling Thiafentanil

Thiafentanil is subject to the CSA's schedule II regulatory controls and administrative, civil, and criminal sanctions applicable to the manufacture, distribution, reverse distribution, dispensing, importing, exporting, research, and conduct of instructional

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activities and chemical analysis with, and possession involving schedule II substances, including the following:

1. *Registration.* Any person who desires to handle thiafentanil (manufacture, distribute, reverse distribute, dispense, import, export, engage in research, or conduct instructional activities or chemical analysis with, or possess), must be registered with the DEA to conduct such activities pursuant to **21 U.S.C. 822**, **823**, **957**, and **958** and in accordance with **21 CFR parts 1301** and **1312**.

2. *Quota.* Only registered manufacturers are permitted to manufacture thiafentanil in accordance with a quota assigned pursuant to **21 U.S.C. 826** and in accordance with **21 CFR part 1303**.

3. *Disposal of stocks.* Upon obtaining a schedule II registration to handle thiafentanil, and if subsequently, any person who does not desire or is not able to maintain a schedule II registration must surrender all quantities of currently held thiafentanil, or may transfer all quantities of currently held thiafentanil to a person registered with the DEA in accordance with **21 CFR part 1317**, in addition to all other applicable federal, state, local, and tribal laws.

4. *Security.* Thiafentanil is subject to schedule II security requirements and must be handled and stored pursuant to **21 U.S.C. 821** and **823**, and in accordance with **21 CFR 1301.71-1301.93**.

5. *Labeling and Packaging.* All labels, labeling, and packaging for commercial containers of thiafentanil must comply with **21 U.S.C. 825** and **958**(e), and be in accordance with **21 CFR part 1302**. In addition, thiafentanil is subject to additional labeling requirements provided by FDA. Thiafentanil must be labeled, distributed, and promoted in accordance with the Index entry of the new animal drug and the FDA may remove a new animal drug from the Index if the conditions and limitations of use have not been followed. 21 U.S.C. 360ccc-l(d)(l)(G); (f)(l)(F). The labeling of an indexed new animal drug must prominently state that the extra-label use of the product is prohibited. 21 U.S.C. 360ccc-l(h).

6. *Inventory.* Every DEA registrant who desires to possess any quantity of thiafentanil must take an inventory of thiafentanil on hand, pursuant to **21 U.S.C. 827** and **958**, and in accordance with **21 CFR 1304.03**, **1304.04**, and **1304.11**.

Any person who becomes registered with the DEA to handle thiafentanil must take an initial inventory of all stocks of controlled substances (including thiafentanil) on hand on the date the registrant first engages in the handling of controlled substances, pursuant to **21 U.S.C. 827** and **958**, and in accordance with **21 CFR 1304.03**, **1304.04**, and **1304.11**.

After the initial inventory, every DEA registrant must take a new inventory of all stocks of controlled substances (including thiafentanil) on hand every two years, pursuant to **21 U.S.C. 827** and **958**, and in accordance with **21 CFR 1304.03**, **1304.04**, and **1304.11**.

7. *Records and Reports.* Every DEA registrant must maintain records and submit reports for thiafentanil, or products containing thiafentanil, pursuant to **21 U.S.C. 827** and **958**(e), and in accordance with **21 CFR parts 1304**, **1312**, and **1317**.

8. *Orders for thiafentanil.* Every DEA registrant who distributes thiafentanil is required to comply with order form requirements, pursuant to **21 U.S.C. 828**, and in accordance with **21 CFR part 1305**.

9. *Prescriptions and other dispensing.* All prescriptions for thiafentanil or products containing thiafentanil must comply with **21 U.S.C. 829**, and be issued in accordance with **21 CFR parts 1306** and **1311**, subpart C. Moreover, given that thiafentanil is not the subject of an approved new drug application under the FDCA, and that it is only allowed under the MUMS Act amendments to the FDCA to be marketed for extremely limited use in minor species, DEA would not consider any dispensing of thiafentanil for human use to be for a legitimate medical purpose within the meaning of the CSA. Likewise, DEA would not consider any dispensing of thiafentanil for animal use beyond the scope of the drug's labeling authorized under the MUMS Act amendments to the FDCA to be for a legitimate medical purpose within the meaning of the CSA.

10. *Manufacturing and Distributing.* In addition to the general requirements of the CSA and DEA regulations that are applicable to manufacturers and distributors of schedule II controlled substances, such registrants should be advised that (consistent with the foregoing considerations) any manufacturing or distribution of thiafentanil may only be for the legitimate purposes consistent with the drug's labeling authorized under the MUMS Act, or for research activities authorized by the FDCA and CSA.

11. *Importation and Exportation.* All importation and exportation of thiafentanil must be in compliance with **21 U.S.C. 952**, **953**, **957**, and **958**, and in accordance with **21 CFR part 1312**.

12. *Liability.* Any activity involving thiafentanil not authorized by, or in violation of, the CSA or its implementing regulations, is unlawful, and may subject the person to administrative, civil, and/or criminal sanctions.

Regulatory Analyses

Administrative Procedure Act

Public Law 114-89 was signed into law, amending **21 U.S.C. 811**. This amendment provides that in cases where a new drug is (1) approved or indexed by the Department of Health and Human Services (HHS) and (2) HHS recommends control in CSA schedule II-V, the DEA shall issue an interim final rule scheduling the drug within 90 days. Additionally, the law specifies that the rulemaking shall become immediately effective as an interim final rule without requiring the DEA to demonstrate good cause. Therefore, the DEA has determined that the notice and comment requirements of section 553 of the APA, 5 U.S.C. 553, do not apply to this scheduling action.

Executive Orders 12866, Regulatory Planning and Review, and 13563, Improving Regulation and Regulatory Review

In accordance with Public Law 114-89, this scheduling action is subject to formal rulemaking procedures performed "on the record after opportunity for a hearing," which are conducted pursuant to the provisions of 5 U.S.C. 556 and 557. The CSA sets forth the procedures and criteria for scheduling a drug or other substance. Such actions are exempt from review by the Office of Management and Budget (OMB) pursuant to section 3(d)(1) of Executive Order 12866 and the principles reaffirmed in Executive Order 13563.

Executive Order 12988, Civil Justice Reform

This regulation meets the applicable standards set forth in sections 3(a) and 3(b)(2) of Executive Order 12988 to eliminate drafting errors and ambiguity, minimize litigation, provide a clear legal standard for affected conduct, and promote simplification and burden reduction.

Executive Order 13132, Federalism

This rulemaking does not have federalism implications warranting the application of Executive Order 13132. The rule does not have substantial direct effects on the States, on the relationship between the national government and the States, or on the distribution of power and

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responsibilities among the various levels of government.

Executive Order 13175, Consultation and Coordination With Indian Tribal Governments

This rule does not have tribal implications warranting the application of Executive Order 13175. It does not have substantial direct effects on one or more Indian tribes, on the relationship between the Federal government and Indian tribes, or on the distribution of power and responsibilities between the Federal government and Indian tribes.

Regulatory Flexibility Act

In accordance with 5 U.S.C. 603(a), "[w]henever an agency is required by [5 U.S.C. 553], or any other law, to publish general notice of proposed rulemaking for any proposed rule, or publishes a notice of proposed rulemaking for an interpretive rule involving the internal revenue laws of the United States, the agency shall prepare and make available for public comment an initial regulatory flexibility analysis." As noted in the above discussion regarding applicability of the Administrative Procedure Act, the DEA has determined that the notice and comment requirements of section 553 of the APA, 5 U.S.C. 553, do not apply to this scheduling action. Consequently, the RFA does not apply to this interim final rule.

Unfunded Mandates Reform Act of 1995

In accordance with the Unfunded Mandates Reform Act (UMRA) of 1995, 2 U.S.C. 1501 et seq., the DEA has determined and certifies that this action would not result in any Federal mandate that may result "in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted for inflation) in any one year." Therefore, neither a Small Government Agency Plan nor any other action is required under UMRA of 1995.

Paperwork Reduction Act of 1995

This action does not impose a new collection of information requirement under the Paperwork Reduction Act of 1995. 44 U.S.C. 3501-3521. This action would not impose recordkeeping or reporting requirements on State or local governments, individuals, businesses, or organizations. An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Congressional Review Act

This rule is not a major rule as defined by section 804 of the Small Business Regulatory Enforcement Fairness Act of 1996 (Congressional Review Act (CRA)). This rule will not result in: An annual effect on the economy of $100,000,000 or more; a major increase in costs or prices for consumers, individual industries, Federal, State, or local government agencies, or geographic regions; or significant adverse effects on competition, employment, investment, productivity, innovation, or on the ability of U.S.-based companies to compete with foreign based companies in domestic and export markets. However, pursuant to the CRA, the DEA has submitted a copy of this interim final rule to both Houses of Congress and to the Comptroller General.

List of Subjects

21 CFR Part 1301

Administrative practice and procedure, Drug traffic control, Security measures.

21 CFR Part 1305

Drug traffic control, Reporting and recordkeeping requirements.

21 CFR Part 1308

Administrative practice and procedure, Drug traffic control, Reporting and recordkeeping requirements.

For the reasons set out above, the DEA amends **21 CFR parts 1301, 1305** and **1308** as follows:

PART 1301--REGISTRATION OF MANUFACTURERS, DISTRIBUTORS, AND DISPENSERS OF CONTROLLED SUBSTANCES

- 1. The authority citation for 21 CFR part 1301 continues to read as follows:

  Authority: 21 U.S.C. 821, 822, 823, 824, 831, 871(b), **875, 877, 886a, 951, 952, 953, 956, 957, 958, 965.**

- 2. In **Sec. 1301.74,** revise paragraph (g) to read as follows:

Sec. 1301.74 Other security controls for non-practitioners; narcotic treatment programs and compounders for narcotic treatment programs.

* * * * *

(g) Before the initial distribution of thiafentanil, carfentanil, etorphine hydrochloride and/or diprenorphine to any person, the registrant must verify that the person is authorized to handle the substance(s) by contacting the Drug Enforcement Administration.

* * * * *

- 3. In **Sec. 1301.75,** revise paragraph (e) to read as follows:

Sec. 1301.75 Physical security controls for practitioners.

* * * * *

(e) Thiafentanil, carfentanil, etorphine hydrochloride and diprenorphine shall be stored in a safe or steel cabinet equivalent to a U.S. Government Class V security container.

PART 1305--ORDERS FOR SCHEDULE I AND II CONTROLLED SUBSTANCES

- 4. The authority citation for 21 CFR part 1305 continues to read as follows:

  Authority: **21 U.S.C. 821, 828, 871**(b), unless otherwise noted.

- 5. In **Sec. 1305.07,** revise the introductory text and paragraph (a) to read as follows:

Sec. 1305.07 Special procedure for filling certain orders.

A supplier of thiafentanil, carfentanil, etorphine hydrochloride, or diprenorphine, if he or she determines that the purchaser is a veterinarian engaged in zoo and exotic animal practice, wildlife management programs, or research, and is authorized by the Administrator to handle these substances, may fill the order in accordance with the procedures set forth in **Sec. 1305.17** except that:

(a) A DEA Form 222 or an electronic order for thiafentanil, carfentanil, etorphine hydrochloride, and diprenorphine must contain only these substances in reasonable quantities.

* * * * *

- 6. In **Sec. 1305.17**, revise paragraph (d) to read as follows:

Sec. 1305.17 Preservation of DEA Forms 222.

* * * * *

(d) The supplier of thiafentanil, carfentanil, etorphine hydrochloride, and diprenorphine must maintain DEA Forms 222 for these substances separately from all other DEA Forms 222 and records required to be maintained by the registrant.

PART 1308--SCHEDULES OF CONTROLLED SUBSTANCES

- 7. The authority citation for 21 CFR part 1308 continues to read as follows:

  Authority: **21 U.S.C. 811, 812, 871**(b), unless otherwise noted.

- 8. In **Sec. 1308.12**, add paragraph (c)(29) to read as follows:

Sec. 1308.12 Schedule II.

* * * * *

(c) * * *

(29) Thiafentanil 9729

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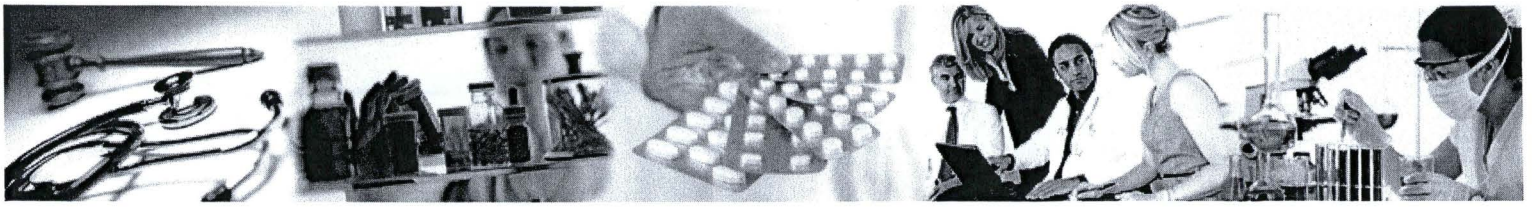
Dated: August 18, 2016.

Chuck Rosenberg,
Acting Administrator.

[FR Doc. 2016-20463 Filed 8-25-16; 8:45 am]

BILLING CODE 4410-09-P



Rules - 2016

[Federal Register Volume 81, Number 43 (Friday, March 4, 2016)]
[Proposed Rules]
[Pages 11479-11486]
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[FR Doc No: 2016-05002]

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA-436]

Schedules of Controlled Substances: Placement of 10 Synthetic Cathinones Into Schedule I

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Notice of proposed rulemaking.

SUMMARY: The Drug Enforcement Administration proposes placing 10 synthetic cathinones: 4-methyl-N-ethylcathinone (4-MEC); 4-methyl-alpha-pyrrolidinopropiophenone (4-MePPP); alpha-pyrrolidinopentiophenone (α-PVP); 1-(1,3-benzodioxol-5-yl)-2-(methylamino)butan-1-one (butylone); 2-(methylamino)-1-phenylpentan-1-one (pentedrone); 1-(1,3-benzodioxol-5-yl)-2-(methylamino)pentan-1-one (pentylone); 4-fluoro-N-methylcathinone (4-FMC); 3-fluoro-N-methylcathinone (3-FMC); 1-(naphthalen-2-yl)-2-(pyrrolidin-1-yl)pentan-1-one (naphyrone); alpha-pyrrolidinobutiophenone (α-PBP) and their optical, positional, and geometric isomers, salts and salts of isomers into schedule I of the Controlled Substances Act. This proposed scheduling action is pursuant to the Controlled Substances Act which requires that such actions be made on the record after opportunity for a hearing through formal rulemaking. If finalized, this action would impose the regulatory controls and administrative, civil, and criminal sanctions applicable to schedule I controlled substances on persons who handle (manufacture, distribute, import, export, engage in research, conduct instructional activities or chemical analysis, or possess), or propose to handle 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, or α-PBP.

DATES: Interested persons may file written comments on this proposal in accordance with **21 CFR 1308.43**(g). Comments must be submitted electronically or postmarked on or before April 4, 2016. Commenters should be aware that the electronic Federal Docket Management System will not accept comments after 11:59 p.m. Eastern Time on the last day of the comment period.

Interested persons, defined at **21 CFR 1300.01** as those "adversely affected or aggrieved by any rule or proposed rule issuable pursuant to section 201 of the Act (**21 U.S.C. 811**)," may file a request

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for hearing or waiver of hearing pursuant to **21 CFR 1308.44** and in accordance with **21 CFR 1316.45** and/or **1316.47**, as applicable. Requests for hearing and waivers of an opportunity for a hearing or to participate in a hearing must be received on or before April 4, 2016.

ADDRESSES: To ensure proper handling of comments, please reference "Docket No. DEA-436" on all correspondence, including any attachments.

- *Electronic comments:* The Drug Enforcement Administration encourages that all comments be submitted electronically through the Federal eRulemaking Portal which provides the ability to type short comments directly into the comment field on the Web page or to attach a file for lengthier comments. Please go to http://www.regulations.gov and follow the online instructions at that site for submitting comments. Upon completion of your submission you will receive a Comment Tracking Number for your comment. Please be aware that submitted comments are not instantaneously available for public view on Regulations.gov. If you have received a Comment Tracking Number, your comment has been successfully submitted and there is no need to resubmit the same comment.
- *Paper comments:* Paper comments that duplicate the electronic submission are not necessary. Should you wish to mail a paper comment in lieu of an electronic comment, it should be sent via regular or express mail to: Drug Enforcement Administration, Attn: DEA Federal Register Representative/ODW, 8701 Morrissette Drive, Springfield, Virginia 22152.
- *Hearing requests:* All requests for hearing and waivers of participation must be sent to: Drug Enforcement Administration, Attn: Administrator, 8701 Morrissette Drive, Springfield, Virginia 22152. All requests for hearing and waivers of participation should also be sent to: Drug Enforcement Administration, Attn: Hearing Clerk/LJ, 8701 Morrissette Drive, Springfield, Virginia 22152; and (2) Drug Enforcement Administration, Attn: DEA Federal Register Representative/ ODW, 8701 Morrissette Drive, Springfield, Virginia 22152.

FOR FURTHER INFORMATION CONTACT: Barbara J. Boockholdt, Office of Diversion Control, Drug Enforcement Administration; Mailing Address: 8701 Morrissette Drive, Springfield, Virginia 22152; Telephone: (202) 598-6812.

SUPPLEMENTARY INFORMATION:

Posting of Public Comments

Please note that all comments received in response to this docket are considered part of the public record. They will, unless reasonable cause is given, be made available by the Drug Enforcement Administration (DEA) for public inspection online at http://www.regulations.gov. Such information includes personal identifying information (such as your name, address, etc.) voluntarily submitted by the commenter. The Freedom of Information Act (FOIA) applies to all comments received. If you want to submit personal identifying information (such as your name, address, etc.) as part of your comment, but do not want it to be made publicly available, you must include the phrase "PERSONAL IDENTIFYING INFORMATION" in the first paragraph of your comment. You must also place all of the personal identifying information you do not want made publicly available in the first paragraph of your comment and identify what information you want redacted.

If you want to submit confidential business information as part of your comment, but do not want it to be made publicly available, you must include the phrase "CONFIDENTIAL BUSINESS INFORMATION" in the first paragraph of your comment. You must also prominently identify confidential business information to be redacted within the comment.

Comments containing personal identifying information and confidential business information identified as directed above will generally be made publicly available in redacted form. If a comment has so much confidential business information or personal identifying information that it cannot be effectively redacted, all or part of that comment may not be made publicly available. Comments posted to http://www.regulations.gov may include any personal identifying information (such as name, address, and phone number) included in the text of your electronic submission that is not identified as directed above as confidential.

An electronic copy of this document and supplemental information to this proposed rule are available at http://www.regulations.gov for easy reference.

Request for Hearing or Waiver of Participation in a Hearing

Pursuant to **21 U.S.C. 811**(a), this action is a formal rulemaking "on the record after opportunity for a hearing." Such proceedings are conducted pursuant to the provisions of the Administrative Procedure Act (APA), 5 U.S.C. 551-559. **21 CFR 1308.41-1308.45**; **21 CFR part 1316**, subpart D. In accordance with **21 CFR 1308.44** (a)-(c), requests for hearing, notices of appearance, and waivers of an opportunity for a hearing or to participate in a hearing may be submitted only by interested persons, defined as those "adversely affected or aggrieved by any rule or proposed rule issuable pursuant to section 201 of the Act (21 U.S.C. 811)." **21 CFR 1300.01**. Such requests or notices must conform to the requirements of 21 CFR 1308.44 (a) or (b), and **1316.47** or **1316.48**, as applicable, and include a statement of interest of the person in the proceeding and the objections or issues, if any, concerning which the person desires to be heard. Any waiver must conform to the requirements of 21 CFR 1308.44(c) and may include a written statement regarding the interested person's position on the matters of fact and law involved in any hearing.

Please note that pursuant to **21 U.S.C. 811**(a), the purpose and subject matter of a hearing held in relation to this rulemaking are restricted to: "(A) find[ing] that such drug or other substance has a potential for abuse, and (B) mak[ing] with respect to such drug or other substance the findings prescribed by subsection (b) of **section 812** of this title for the schedule in which such drug is to be placed . . ." All requests for hearing and waivers of participation must be sent to the DEA using the address information provided above.

Legal Authority

The DEA implements and enforces Titles II and III of the Comprehensive Drug Abuse Prevention and Control Act of 1970, as amended. Titles II and III are referred to as the "Controlled Substances Act" and the "Controlled Substances Import and Export Act," respectively, and are collectively referred to as the "Controlled Substances Act" or the "CSA" for the purposes of this action. **21 U.S.C. 801-971**. The DEA publishes the implementing regulations for these statutes in title 21 of the Code of Federal Regulations (CFR), chapter II. The CSA and its implementing regulations are designed to prevent, detect, and eliminate the diversion of controlled substances and listed chemicals into the illicit market while providing for the legitimate medical, scientific, research, and industrial needs of the United States. Controlled substances have the potential for abuse and dependence and are controlled to protect the public health and safety.

Under the CSA, controlled substances are classified into one of five schedules

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based upon their potential for abuse, their currently accepted medical use in treatment in the United States, and the degree of dependence the substance may cause. **21 U.S.C. 812**. The initial schedules of controlled substances established by Congress are found at 21 U.S.C. 812(c), and the current list of scheduled substances is published at **21 CFR part 1308**.

Pursuant to **21 U.S.C. 811**(a)(1), the Attorney General may, by rule, "add to such a schedule or transfer between such schedules any drug or other substance if he (A) finds that such drug or other substance has a potential for abuse, and (B) makes with respect to such drug or other substance the findings prescribed by subsection (b) of **section 812** of this title for the schedule in which such drug is to be placed . . ." The Attorney General has delegated scheduling authority under 21 U.S.C. 811 to the Administrator of the DEA. 28 CFR 0.100.

The CSA provides that proceedings for the issuance, amendment, or repeal of the scheduling of any drug or other substance may be initiated by the Attorney General (1) on her own motion; (2) at the request of the Secretary of the Department of Health and Human Services (HHS); \1\ or (3) on the petition of any interested party. **21 U.S.C. 811**(a). This proposed action is supported by a recommendation from the Assistant Secretary of the HHS and an evaluation of all other relevant data by the DEA. If finalized, this action would impose the regulatory controls and administrative, civil, and criminal sanctions of schedule I controlled substances on any person who handles or proposes to handle 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-;FMC, 3-FMC, naphyrone, or α-PBP.

\1\ As discussed in a memorandum of understanding entered into by the Food and Drug Administration (FDA) and the National Institute on Drug Abuse (NIDA), the FDA acts as the lead agency within the HHS in carrying out the Secretary's scheduling responsibilities under the CSA, with the concurrence of NIDA. 50 FR 9518, Mar. 8, 1985. The Secretary of the HHS has delegated to the Assistant Secretary for Health of the HHS the authority to make domestic drug scheduling recommendations. 58 FR 35460, July 1, 1993.

Background

On March 7, 2014, the DEA published a final order in the Federal Register amending **21 CFR 1308.11**(h) to temporarily place 4-methyl-N-ethylcathinone (4-MEC); 4-methyl-alpha-pyrrolidinopropiophenone (4-MePPP); alpha-pyrrolidinopentiophenone (α-PVP); 1-(1,3-benzodioxol-5-yl)-2-(methylamino)butan-1-one (butylone); 2-(methylamino)-1-phenylpentan-1-one (pentedrone); 1-(1,3-benzodioxol-5-yl)-2-(methylamino)pentan-1-one (pentylone); 4-fluoro-N-methylcathinone (4-FMC); 3-fluoro-N-methylcathinone (3-FMC); 1-(naphthalen-2-yl)-2-(pyrrolidin-1-yl)pentan-1-one (naphyrone); and alpha-pyrrolidinobutiophenone (α-PBP) into schedule I of the CSA pursuant to the temporary scheduling provisions of **21 U.S.C. 811**(h). 79 FR 12938. That final order, which became effective on the date of publication, was based on findings by the Deputy Administrator of the DEA that the temporary scheduling of these 10 synthetic cathinones was necessary to avoid an imminent hazard to public safety pursuant to 21 U.S.C. 811(h)(1). At the time the final order took effect, section 201(h)(2) of the CSA (21 U.S.C. 811(h)(2)), required that the temporary scheduling of a substance expire at the end of two years from the date of issuance of the scheduling order, and it provided that, during the pendency of proceedings under 21 U.S.C. 811(a)(1) with respect to the substance, temporary scheduling of that substance could be extended for up to 1 year. Pursuant to 21 U.S.C. 811(h)(2), the temporary scheduling of 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP expires on March 6, 2016, unless extended. An extension of the temporary order is being ordered by the DEA Administrator in a separate action.

As described in the final order published on March 7, 2014, 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP are structurally and pharmacologically similar to amphetamine, 3,4-methylenedioxymethamphetamine (MDMA), cathinone, and other related substances. While 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP have been used as research chemicals and/or studied due to their misuse and abuse, based on the review of the scientific literature, there are no known currently accepted medical uses for these substances. The Assistant Secretary of Health for the U.S. Department of Health and Human Services (HHS) has advised that there are no exemptions or approvals in effect for 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, or α-PBP under section 505 (21 U.S.C. 355) of the Federal Food, Drug and Cosmetic Act. As stated by the HHS, 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP have no known accepted medical use. They are not the subject of any approved new drug applications (NDAs) or investigational new drug applications (INDs), and are not currently marketed as approved drug products. The HHS recommends that 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP and their salts be placed into schedule I of the Controlled Substances Act (CSA).

Proposed Determination To Schedule 4-MEC, 4-MePPP, α-PVP, Butylone, Pentedrone, Pentylone, 4-FMC, 3-FMC, Naphyrone, and α-PBP

Pursuant to **21 U.S.C. 811**(a)(1), proceedings to add a drug or substance to those controlled under the CSA may be initiated by the Attorney General, or her delegate, the DEA Administrator. On December 30, 2014, the DEA requested scientific and medical evaluations and scheduling recommendations from the Assistant Secretary of Health for the HHS for 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP pursuant to 21 U.S.C. 811(b). Upon receipt of the scientific and medical evaluation and scheduling recommendations from the HHS on March 2, 2016, the DEA reviewed the documents and all other relevant data, and conducted its own eight-factor analysis of the abuse potential of 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP pursuant to 21 U.S.C. 811(c). Included below is a brief summary of each of the eight factors as analyzed by the HHS and the DEA, and as considered by the DEA in its proposed scheduling action. Please note that both the DEA 8-Factor and the HHS 8-Factor analyses are available in their entirety under the tab "Supporting Documents" of the public docket for this action at http://www.regulations.gov under Docket Number "DEA-436."

1. *The Drug's Actual or Relative Potential for Abuse:* The term "abuse" is not defined in the CSA. However, the legislative history of the CSA suggests that the [redacted] consider the following criteria when determining whether a particular drug or substance has a potential for abuse: \2\

\2\ Comprehensive Drug Abuse Prevention and Control Act of 1970, H.R. Rep. No. 91-1444, 91st Cong., Sess. 1 (1970); reprinted in 1970 U.S.C.C.A.N. 4566, 4603.

(a) There is evidence that individuals are taking the drug or drugs containing such a substance in amounts sufficient to create a hazard to their health or to the safety of other individuals or of the community; or

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(b) There is significant diversion of the drug or drugs containing such a substance from legitimate drug channels; or

(c) Individuals are taking the drug or drugs containing such a substance on their own initiative rather than on the basis of medical advice from a practitioner licensed by law to administer such drugs in the course of his professional practice; or

(d) The drug or drugs containing such a substance are new drugs so related in their action to a drug or drugs already listed as having a potential for abuse to make it likely that the drug will have the same potentiality for abuse as such drugs, thus making it reasonable to assume that there may be significant diversions from legitimate channels, significant use contrary to or without medical advice, or that it has a substantial capability of creating hazards to the health of the user or to the safety of the community.

As described by the HHS, the abuse potentials of 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP are associated with their abilities to produce psychoactive effects that are similar to those produced by mephedrone, methylone, MDPV, and other schedule I and II substances such as amphetamine, methamphetamine, cocaine, methcathinone, and MDMA that have a high potential for abuse.

The substances 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP have no approved medical uses in the United States and they have been encountered on the illicit market with adverse outcomes on the public health and safety. Because these substances are not approved drug products, a practitioner may not legally prescribe them, and they cannot be dispensed to an individual. Therefore, the use of these substances is without medical advice, leading to the conclusion that the 10 synthetic cathinones are being abused for their psychoactive properties. There are no legitimate drug channels for these synthetic cathinones as marketed drugs but the DEA notes that the 10 synthetic cathinones have use in scientific research. However, despite the limited legitimate use of these substances, reports from public health and law enforcement communicate that these substances are being abused and taken in amounts sufficient to create a hazard to an individual's health. This misuse is evidenced by emergency department admissions and deaths, representing a significant safety issue for those in the community. Papers published in the medical literature (e.g., case reports) related to 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, or α-PBP describe the effects of these substances to be similar to those of the schedule I cathinone substances MDPV, mephedrone, and methylone and other stimulant and hallucinogenic substances to include methamphetamine, cocaine and MDMA. In particular, the responses in humans to the 10 synthetic cathinones are stimulant-like and include paranoia, agitation, palpitations, tachycardia, hypertension, hyperthermia, and seizures. Data from forensic databases are used as indicators of illicit activity with drugs and abuse \3\ within the United States and include data from the System to Retrieve Information from Drug Evidence (STRIDE),\4\ STARLiMS, and the National Forensic Laboratory Information System (NFLIS).\5\ From January 2010 through December 2015 (query dates: Februa[redacted] & 11, 2016), STRIDE, STARLiMS and NFLIS databases registered a total of 20,090 reports pertaining to the 10 synthetic cathinones (4-MEC--2,820 reports; 4-M[redacted] 438 reports; α-PVP--13,295 reports; butylone--789 reports; pentedrone--1,645 reports; pentylone--411 reports; FMC--375 reports; naphyrone--84 reports; α-P[redacted] 233 reports). These drug reports represent all of the 10 synthetic cathinones reported to these databases by participating DEA, State, local, and other forensic laboratories. Consequently, the data indicate that these substances are being abused, and they present safety hazards to the health of individuals who consume them due to their stimulant properties, making them a hazard to the safety of the community.

\3\ While law enforcement data is not direct evidence of abuse, it can lead to an inference that a drug has been diverted and abused. See 76 FR 77330, 77332, Dec. 12, 2011.

\4\ STRIDE was a database that collected analyses of results from drug evidence sent to DEA laboratories. Evidence was submitted by the DEA, other Federal agencies, and select local law enforcement agencies. On October 1, 2014, STARLiMS replaced STRIDE as the DEA system of record for forensic laboratory drug evidence data.

\5\ NFLIS is a DEA program and a national forensic laboratory reporting system that systematically collects results from drug chemistry analyses conducted by state and local forensic laboratories in the United States. The NFLIS database also contains Federal data from U.S. Customs and Border Protection (CBP). NFLIS only includes drug chemistry results from completed analyses.

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2. *Scientific Evidence of the Drug's Pharmacological Effects, if Known:* Studies show that 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP produce pharmacological effects that are similar to those produced by schedule I and II substances such as methamphetamine, cocaine, MDMA, mephedrone, MDPV, and methylone. Similar to schedule I and II stimulants, the 10 synthetic cathinone substances affect monoamine transmission. The 10 synthetic cathinones, similar to methamphetamine, cocaine, MDMA, mephedrone, MDPV, methylone, and other related schedule I and II substances, bind to transporters for the dopamine, serotonin, and/or norephinephrine neurotransmitters and are uptake inhibitors of these neurotransmitters. Additionally, behavioral studies in animals demonstrate that the 10 synthetic cathinones produce locomotor behavior and discriminative stimulus effects that are similar to those of the schedule I and II substances methamphetamine and cocaine. Furthermore, the 10 synthetic cathinone produce rewarding properties as demonstrated in self-administration and conditioned place preference (CPP) studies. Drugs that have rewarding effects in animals are likely to produce rewarding effects in humans, which is indicative of abuse potential. Overall, these data indicate that the 10 synthetic cathinones produce pharmacological effects and stimulant-like behaviors that are similar to those of the schedule I substances (MDMA, mephedrone, MDPV, methylone), as well as the schedule II stimulants (methamphetamine and cocaine).

3. *The State of Current Scientific Knowledge Regarding the Drug or Other Substance:* 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP are synthetic cathinones (β-keto-phenethylamines) of the larger phenethylamine structural class (amphetamines, cathinones, 2C compounds, aminoindanes, etc.). These substances share the core phenethylamine structure with a keto functional group [carbonyl (C=O)] at the β-position and substitutions at the α-position and on the phenyl ring and nitrogen atom. Available data demonstrate that 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP are β-ketophenethylamines (i.e., synthetic cathinones) and are structurally and pharmacologically similar to amphetamine, MDMA, cathinone, mephedrone, methylone, MDPV, and other related substances. Metabolism studies demonstrate that humans metabolize synthetic cathinones to their corresponding amphetamines followed by reduction of the beta-keto group to the corresponding alcohol. According to the HHS, 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone,

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and α-PBP have no known accepted medical use. They are not the subject of any approved new drug applications (NDAs) or investigational new drug applications (INDs), and are not currently marketed as approved drug products in the U.S or in any other country. The HHS also states that there are no reported clinical trials with the 10 synthetic cathinones. Accordingly, the DEA is not aware of any accepted medical use for 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP in the United States. In addition, although the chemistry of 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP is known and has been reproduced, no studies have been undertaken to evaluate the efficacy, toxicology, and safety of these substances in humans.

4. *Its History and Current Pattern of Abuse:* 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP are synthetic cathinones that emerged on the U.S. illicit drug market around the time of the scheduling of mephedrone, methylone, and MDPV on October 21, 2011. These synthetic cathinone substances, like the schedule I synthetic cathinones (mephedrone, methylone, and MDPV), are promoted as being 'legal' alternatives to cocaine, methamphetamine, and MDMA. As reported in the medical literature, synthetic cathinones can induce stimulant effects, especially under high dose conditions, including tachycardia, palpitations, hypertension, tremor, seizures, hallucinations, paranoia, delusions, hyperthermia, sweating, headache, hyponatremia, and rhabdomyolysis. Products that contain 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP are falsely marketed as "research chemicals," "jewelry cleaner," "stain remover," "plant food or fertilizer," "insect repellants," or "bath salts" and are sold at smoke shops, head shops, convenience stores, adult book stores, and gas stations. They can also be purchased on the Internet under a variety of product names (e.g., "White Dove," "Explosion," "Tranquility"). They are commonly encountered in the form of powders, crystals, resins, tablets, and capsules. The packages of these commercial products usually contain the warning "not for human consumption." Information from published scientific studies indicate that the most common routes of administration for synthetic cathinone substances is ingestion by swallowing capsules or tablets, or nasal insufflation by snorting the powder tablets. Evidence from poison centers and published reports suggest that the main users of methylone are young adults. There is evidence that these synthetic cathinone substances are ingested with other substances including other synthetic cathinones, common cutting agents, or other recreational substances.

5. *The Scope, Duration, and Significance of Abuse:* 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP, like mephedrone, methylone, and MDPV, are popular recreational drugs. Evidence that these synthetic cathinone substances are being abused and trafficked is confirmed by law enforcement encounters of these substances and reports from national databases. Forensic laboratories have analyzed drug exhibits received from state, local, or Federal law enforcement agencies that were found to contain 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, or α-PBP. NFLIS registered over 17,000 reports from State, local, and other forensic laboratories identifying these substances in drug-related reports for the period from January 2010 to December 2015 from 47 states. STRIDE & STARLiMS registered over 2,000 reports from DEA forensic laboratories from January 2010 to December 2015. Encounters of 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP by law enforcement have occurred in several states. Additionally, large seizures of these substances have occurred by the U.S. Customs and Border Protection (CBP). Concerns over the abuse of these synthetic cathinone substances have prompted many States to regulate them. These data demonstrate that 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP have a scope, duration, and significance of abuse that supports scheduling under the CSA.

6. *What, if Any, Risk There is to the Public Health:* Available evidence on the overall public health risks associated with the use of synthetic cathinones indicates that 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP can cause acute health problems leading to emergency department (ED) admissions, violent behaviors causing harm to self or others, or death. Law enforcement, forensic laboratories, case reports, and public health officials have reported toxic exposure to some of the 10 synthetic cathinones that demonstrate the public health risks associated with these substances. Serious adverse effects have resulted in documented hospital ED admissions from the ingestion of butylone, 4-FMC, or naphyrone. Individuals under the influence of 4-MEC or α-PVP have acted violently and unpredictably causing harm, or even death, to themselves or others. Butylone has been directly implicated in two fatalities reported in the medical literature. Other synthetic cathinones, such as α-PVP, pentedrone, and pentylone, have also been implicated in the deaths of individuals. Acute effects of these substances are those typical of a sympathomimeticagent (e.g., cocaine, methamphetamine, amphetamine) and include among other effects tachycardia, headache, palpitations, agitation, anxiety, mydriasis, tremor, fever or sweating, and hypertension. Other effects, with possible public health risk implications, that have been reported from the use of synthetic cathinone substances include psychological effects such as psychosis, paranoia, hallucinations, and agitation. Finally, the possibility of death for individuals abusing 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP also indicates that these substances pose a serious public health threat. In addition to the recognized harm from ingesting and abusing synthetic cathinones, abusers risk harm when they obtain these drugs through unknown sources. Products containing these synthetic cathinone substances often do not bear labeling information regarding their ingredients and if they do, they may not contain the expected active ingredients or identify the health risks and potential hazards associated with these products. Thus, the limited knowledge about product contents, its purity and lack of information about its effects may pose another level of risk to users.

7. *Its Psychic or Physiological Dependence Liability:* The DEA is unaware of any clinical studies that have evaluated the dependence potential of 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, or α-PBP; however, according to the HHS, synthetic cathinones have rewarding properties in rodents similar to those of schedule II stimulants. Generally, there is a strong correlation between drugs that serve as reinforcers in animals, and drugs associated with problems of addiction, dependence, or abuse by humans. In a self-administration study,

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α-PVP and pentedrone were self-administered by rodents. In the intracranial self-stimulation (ICSS) assay, α-PVP and 4-MEC significantly reduced the ICSS threshold compared to vehicle control. In drug discrimination studies, all 10 synthetic cathinone substances fully generalize to the discriminative stimulus effects produced by the schedule II stimulants--cocaine and methamphetamine. In conditioned place preference (CPP) studies, α-PBP, α-PVP, and pentedrone produce CPP in rodents. Thus, these data indicate that 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP have behavioral and rewarding properties in rodents similar to those of schedule II stimulants and, consequently, psychic dependence on these substances can develop and may contribute to the continued use among individuals who abuse them despite their adverse consequences.

8. *Whether the Substance is an Immediate Precursor of a Substance Already Controlled Under the CSA:* 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP are not considered immediate precursors of any controlled substance of the CSA.

Conclusion: After considering the scientific and medical evaluation conducted by the HHS, the HHS's recommendation, and the DEA's own eight-factor analysis, the DEA finds that the facts and all relevant data constitute substantial evidence of the potential for abuse of 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP. As such, the DEA hereby proposes to schedule 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP as controlled substances under the CSA.

Proposed Determination of Appropriate Schedule

The CSA establishes five schedules of controlled substances known as schedules I, II, III, IV, and V. The CSA also outlines the findings required to place a drug or other substance in any particular schedule. **21 U.S.C. 812**(b). After consideration of the analysis and recommendation of the Assistant Secretary for the HHS and review of all other available data, the Administrator of the DEA, pursuant to **21 U.S.C. 811**(a) and 21 U.S.C. 812(b)(1), finds that:

1. 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP have a high potential for abuse that is comparable to other schedule I and schedule II substances such as mephedrone, methylone, MDPV, methcathinone, MDMA, amphetamine, methamphetamine, and cocaine;

2. 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP have no currently accepted medical use in treatment in the United States; and

3. There is a lack of accepted safety for use of 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP under medical supervision.

Based on these findings, the Administrator of the DEA concludes that 4-methyl-N-ethylcathinone (4-MEC); 4-methyl-alpha-pyrrolidinopropiophenone (4-MePPP); alpha-pyrrolidinopentiophenone (α-PVP); 1-(1,3-benzodioxol-5-yl)-2-(methylamino)butan-1-one (butylone); 2-(methylamino)-1-phenylpentan-1-one (pentedrone); 1-(1,3-benzodioxol-5-yl)-2-(methylamino)pentan-1-one (pentylone); 4-fluoro-N-methylcathinone (4-FMC); 3-fluoro-N-methylcathinone (3-FMC); 1-(naphthalen-2-yl) -2-(pyrrolidin-1-yl)pentan-1-one (naphyrone); alpha-pyrrolidinobutiophenone (α-PBP) and their optical, positional, and geometric isomers, salts and salts of isomers, warrant control in schedule I of the CSA. **21 U.S.C. 812**(b)(1).

Requirements for Handling 4-MEC, 4-MePPP, α-PVP, Butylone, Pentedrone, Pentylone, 4-FMC, 3-FMC, Naphyrone, and α-PBP

If this rule is finalized as proposed, 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP would continue \6\ to be subject to the regulatory controls and administrative, civil, and criminal sanctions applicable to the manufacture, distribution, possession, importing, research, conduct of instructional activities, and exporting of schedule I controlled substances, including the following:

\6\ 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, or α-PBP are currently subject to schedule I controls on a temporary basis, pursuant to **21 U.S.C. 811**(h). 79 FR 12938, Mar. 7, 2014.

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1. *Registration.* Any person who handles (manufactures, distributes, dispenses, imports, exports, engages in research, conducts instructional activities or chemical analysis with, or possesses) 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, or α-PBP, or who desires to handle 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, or α-PBP would be required to be registered with the DEA to conduct such activities pursuant to **21 U.S.C. 822**, **823**, **957**, and **958**, and in accordance with **21 CFR parts 1301** and **1312**.

2. *Security.* 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, or α-PBP would be subject to schedule I security requirements and would need to be handled and stored pursuant to **21 U.S.C. 821** and **823**, and in accordance with **21 CFR 1301.71-1301.93**.

3. *Labeling and Packaging.* All labels, labeling, and packaging for commercial containers of 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, naphyrone, or α-PBP would need to be in compliance with **21 U.S.C. 825** and **958**(e), and be in accordance with **21 CFR part 1302**.

4. *Quota.* Only registered manufacturers would be permitted to manufacture 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, or α-PBP in accordance with a quota assigned pursuant to **21 U.S.C. 826**, and in accordance with **21 CFR part 1303**.

5. *Inventory.* Any person who becomes registered with the DEA on or after the effective date of the final rule must take an initial inventory of all stocks of controlled substances (including 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP) on hand on the date the registrant first engages in the handling of controlled substances pursuant to **21 U.S.C. 827** and **958**, and in accordance with **21 CFR 1304.03**, **1304.04**, and **1304.11**.

After the initial inventory, every DEA registrant must take a new inventory of all stocks of controlled substances (including 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP) on hand every two years pursuant to **21 U.S.C. 827** and **958**, and in accordance with **21 CFR 1304.03**, **1304.04**, and **1304.11**.

6. *Records and Reports.* Every DEA registrant would be required to maintain records and submit reports with respect to 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and/ or α-PBP pursuant to **21 U.S.C. 827** and **958**(e), and in accordance with **21 CFR parts 1304** and **1312**.

7. *Order Forms.* Every DEA registrant who distributes 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, or α-PBP would be required to comply with the order form requirements, pursuant to **21 U.S.C. 828**, and **21 CFR part 1305**.

8. *Importation and Exportation.* All importation and exportation of 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC,

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naphyrone, or α-PBP would need to be in compliance with **21 U.S.C. 952**, **953**, **957**, and **958**, and in accordance with **21 CFR part 1312**.

9. *Liability.* Any activity involving 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, or α-PBP not authorized by, or in violation of, the CSA or its implementing regulations would be unlawful, and could subject the person to administrative, civil, and/ or criminal sanctions.

Regulatory Analyses

Executive Orders 12866 and 13563

In accordance with **21 U.S.C. 811**(a), this proposed scheduling action is subject to formal rulemaking procedures done "on the record after opportunity for a hearing," which are conducted pursuant to the provisions of 5 U.S.C. 556 and 557. The CSA sets forth the criteria for scheduling a drug or other substance. Such actions are exempt from review by the Office of Management and Budget (OMB) pursuant to section 3(d)(1) of Executive Order 12866 and the principles reaffirmed in Executive Order 13563.

Executive Order 12988

This proposed regulation meets the applicable standards set forth in sections 3(a) and 3(b)(2) of Executive Order 12988 to eliminate drafting errors and ambiguity, minimize litigation, provide a clear legal standard for affected conduct, and promote simplification and burden reduction.

Executive Order 13132

This proposed rulemaking does not have federalism implications warranting the application of Executive Order 13132. The proposed rule does not have substantial direct effects on the States, on the relationship between the national government and the States, or the distribution of power and responsibilities among the various levels of government.

Executive Order 13175

This proposed rule does not have tribal implications warranting the application of Executive Order 13175. It does not have substantial direct effects on one or more Indian tribes, on the relationship between the Federal Government and Indian tribes, or on the distribution of power and responsibilities between the Federal Government and Indian tribes.

Regulatory Flexibility Act

The Administrator, in accordance with the Regulatory Flexibility Act (RFA), 5 U.S.C. 601-602, has reviewed this proposed rule and by approving it, certifies that it will not have a significant economic impact on a substantial number of small entities. On March 7, 2014, the DEA published a final order to temporarily place 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP into schedule I of the CSA pursuant to the temporary scheduling provisions of **21 U.S.C. 811**(h). The DEA estimates that all entities handling or planning to handle 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, or α-PBP are currently registered to handle these substances. There are currently 43 registrations authorized to handle 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, or α-PBP, as well as a number of registered analytical labs that are authorized to handle schedule I controlled substances generally. These 43 registrations represent 31 entities, of which 11 are small entities. Therefore, the DEA estimates that 11 small entities are affected by this proposed rule.

A review of the 43 registrations indicates that all entities that currently handle 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, or α-PBP also handle other schedule I controlled substances, and have established and implemented (or currently maintain) the systems and processes required to handle 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, or α-PBP. Therefore, the DEA anticipates that this proposed rule will impose minimal or no economic impact on any affected entities; and thus, will not have a significant economic impact on any of the 11 affected small entities. Therefore, the DEA has concluded that this proposed rule will not have a significant effect on the small entities.

Unfunded Mandates Reform Act of 1995

In accordance with the Unfunded Mandates Reform Act (UMRA) of 1995, 2 U.S.C. 1501 et seq., the DEA has determined and certifies that this action would not result in any Federal mandate that may result "in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted for inflation) in any one year . . ." Therefore, neither a Small Government Agency Plan nor any other action is required under UMRA of 1995.

Paperwork Reduction Act of 1995

This action does not impose a new collection of information under the Paperwork Reduction Act of 1995. 44 U.S.C. 3501-3521. This action would not impose recordkeeping or reporting requirements on State or local governments, individuals, businesses, or organizations. An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

List of Subjects in 21 CFR Part 1308

Administrative practice and procedure, Drug traffic control, Reporting and recordkeeping requirements.

For the reasons set out above, 21 CFR part 1308 is proposed to be amended to read as follows:

PART 1308--SCHEDULES OF CONTROLLED SUBSTANCES

- 1. The authority citation for 21 CFR part 1308 continues to read as follows:

Authority: 21 U.S.C. 811, 812, 871(b), unless otherwise noted. 2. In Sec. 1308.11:

- a. Add paragraphs (d)(58) through (d)(67);
- b. Remove paragraphs (h)(11) through (h)(20),
- c. Redesignate paragraphs (h)(21) through (h)(25) as (h)(11) through (h)(15);

The additions to read as follows:

Sec. 1308.11 Schedule I.

* * * * *

(d) * * *

(58) 4-methyl-*N*-ethylcathinone (4MEC)	(1249)
(59) 4-methyl-*alpha*-pyrrolidinopropiophenone (4-MePPP)	(7498)
(60) *alpha*-pyrrolidinopentiophenone (α-PVP)	(7545)
(61) 1-(1,3-benzodioxol-5-yl)-2-(methylamino)butan-1-one (butylone, bk-MB	(7541)
(62) 2-(methylamino)-1-phenylpentan-1-one (pentedrone)	(1246)
(63) 1-(1,3-benzodioxol-5-yl)-2-(methylamino)pentan-1-one (pentylone, bk-MBDP)	(7542)
(64) 4-fluoro-*N*-methylcathinone (4-FMC; flephedrone)	(1238)
(65) 3-fluoro-*N*-methylcathinone (3-FMC)	(1233)
(66) 1-(naphthalen-2-yl)-2-(pyrrolidin-1-yl)pentan-1-one (naphyrone)	(1258)
(67) *alpha*-pyrrolidinobutiophenone	(7546)

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Dated: March 2, 2016.

Chuck Rosenberg,
Acting Administrator.

[FR Doc. 2016-05002 Filed 3-3-16; 8:45 am]

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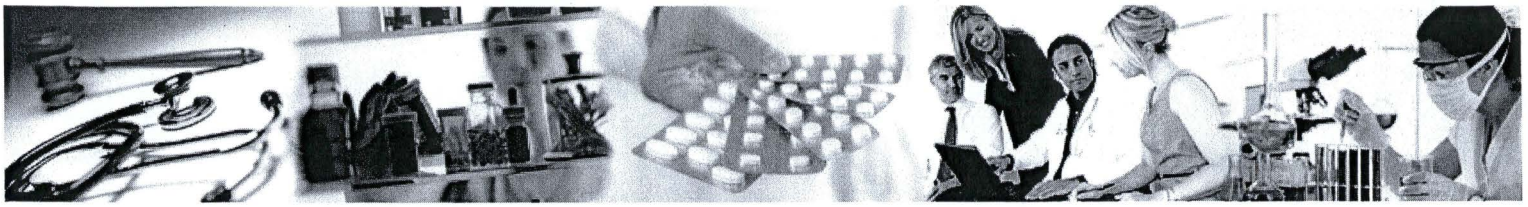

Rules - 2015

[Federal Register Volume 80, Number 179 (Wednesday, September 16, 2015)]
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[Pages 55565-55568]
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DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA-421N]

Schedules of Controlled Substances: Temporary Placement of the Synthetic Cannabinoid MAB-CHMINACA Into Schedule I

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Notice of intent.

SUMMARY: The Administrator of the Drug Enforcement Administration is issuing this notice of intent to temporarily schedule the synthetic cannabinoid N-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-(cyclohexylmethyl)-1H-indazole-3-carboxamide (common names, MAB-CHMINACA and ADB-CHMINACA) into schedule I pursuant to the temporary scheduling provisions of the Controlled Substances Act. This action is based on a finding by the Administrator that the placement of this synthetic cannabinoid into schedule I of the Controlled Substances Act is necessary to avoid an imminent hazard to the public safety. Any final order will impose the administrative, civil, and criminal sanctions and regulatory controls applicable to schedule I controlled substances under the Controlled Substances Act on the manufacture, distribution, possession, importation, exportation, research, and conduct of instructional activities of this synthetic cannabinoid.

DATES: September 16, 2015.

FOR FURTHER INFORMATION CONTACT: John R. Scherbenske, Office of Diversion Control, Drug Enforcement Administration; Mailing Address: 8701 Morrissette Drive, Springfield, Virginia 22152; Telephone: (202) 598-6812.

SUPPLEMENTARY INFORMATION: Any final order will be published in the Federal Register and may not be effective prior to October 16, 2015.

Legal Authority

The Drug Enforcement Administration (DEA) implements and enforces titles II and III of the Comprehensive Drug Abuse Prevention and Control Act of 1970, as amended. Titles II and III are referred to as the "Controlled Substances Act" and the "Controlled Substances Import and Export Act," respectively, and are collectively referred to as the "Controlled Substances Act" or the "CSA" for the purpose of this action. The DEA publishes the implementing regulations for these statutes in title 21 of the Code of Federal Regulations (CFR), chapter II. The CSA and its implementing regulations are designed to prevent, detect, and eliminate the diversion of controlled substances and listed chemicals into the illicit market while ensuring an adequate supply is available for the legitimate medical, scientific, research, and industrial needs of the United States. Controlled substances have the potential for abuse and dependence and are controlled to protect the public health and safety.

Under the CSA, every controlled substance is classified into one of five schedules based upon its potential for abuse, its currently accepted medical use in treatment in the United States, and the degree of dependence the drug or other substance may cause. **21 U.S.C. 812**. The initial schedules of controlled substances established by Congress are found at 21 U.S.C. 812(c), and the current list of all scheduled substances is published at **21 CFR part 1308**.

Section 201 of the CSA, **21 U.S.C. 811**, provides the Attorney General with the authority to temporarily place a substance into schedule I of the CSA for two years without regard to the requirements of 21 U.S.C. 811(b) if she finds that such action is necessary to avoid imminent hazard to the public safety. 21 U.S.C. 811(h)(1). In addition, if proceedings to control a substance are initiated under 21 U.S.C. 811(a)(1), the Attorney General may extend the temporary scheduling for up to one year. 21 U.S.C. 811(h)(2).

Where the necessary findings are made, a substance may be temporarily scheduled if it is not listed in any other schedule under section 202 of the CSA, **21 U.S.C. 812**, or if there is no exemption or approval in effect for the substance under section 505 of the Federal Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. 355. **21 U.S.C. 811**(h)(1). The Attorney General has delegated her scheduling authority under 21 U.S.C. 811 to the Administrator of the DEA. 28 CFR 0.100.

Background

Section 201(h)(4) of the CSA, **21 U.S.C. 811**(h)(4), requires the Administrator to notify the Secretary of the Department of Health and Human Services (HHS) of t Administrator's intention to temporarily place a substance into schedule I of the CSA.\1\ The Administrator transmitted notice of intent to place N-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-(cyclohexylmethyl)-1H-indazole-3-carboxamide (hereinafter referred to as MAB-CHMINACA) into schedule I on a temporary basis to the Assistant Secretary by letter dated May 14, 2015. The Assistant Secretary responded to this notice by letter dated June 3, 2015, and advised that based on review by the Food and Drug Administration (FDA), there are currently no investigational new drug applications or approved new drug applications for MAB-CHMINACA. The Assistant Secretary also stated that HHS has no objection to the temporary placement of MAB-CHMINACA into schedule I of the CSA. The DEA has taken into consideration the Assistant Secretary's comments. MAB-CHMINACA is not currently listed in any schedule under the CSA, and no exemptions or

approvals are in effect for MAB-CHMINACA under section 505 of the FDCA, 21 U.S.C. 355. The DEA has found that the control of MAB-CHMINACA in schedule I on a temporary basis is necessary to avoid an imminent hazard to public safety.

\1\ Because the Secretary of the HHS has delegated to the Assistant Secretary for Health of the HHS the authority to make domestic drug scheduling recommendations, for purposes of this notice of intent, all subsequent references to "Secretary" have been replaced with "Assistant Secretary." As set forth in a memorandum of understanding entered into by the HHS, the Food and Drug Administration (FDA), and the National Institute on Drug Abuse (NIDA), the FDA acts as the lead agency within the HHS in carrying out the Assistant Secretary's scheduling responsibilities under the CSA, with the concurrence of NIDA. 50 FR 9518, Mar. 8, 1985.

To find that placing a substance temporarily into schedule I of the CSA is necessary to avoid an imminent hazard to the public safety, the Administrator is required to consider three of the eight factors set forth in section 201(c) of the CSA, **21 U.S.C. 811**(c): the substance's history and current pattern of abuse; the scope, duration and significance of abuse; and what, if any, risk there is to the public health. 21 U.S.C. 811(h)(3). Consideration of these factors includes actual abuse, diversion from legitimate channels, and clandestine importation, manufacture, or distribution. 21 U.S.C. 811(h)(3).

A substance meeting the statutory requirements for temporary scheduling may only be placed in schedule I. **21 U.S.C. 811**(h)(1). Substances in schedule I are those that have a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. **21 U.S.C. 812**(b)(1).

MAB-CHMINACA

Available data and information for MAB-CHMINACA, summarized below,

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indicate that this synthetic cannabinoid (SC) has a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. The DEA analysis is available in its entirety under the tab "Supporting and Related Material" of the public docket of this action at www.regulations.gov under Docket Number DEA-421N.

Synthetic Cannabinoids

Synthetic cannabinoids are substances synthesized in laboratories that mimic the biological effects of delta-9-tetrahydrocannabinol (THC), the main psychoactive ingredient in marijuana. It is believed SCs were first introduced on the designer drug market in several European countries as "herbal incense" before the initial encounter in the United States by U.S. Customs and Border Protection (CBP) in November 2008. From 2009 to present, misuse of SCs has increased in the United States with law enforcement encounters describing plant material laced with SCs intended for human consumption. It has been demonstrated that the substances and the associated designer products are abused for their psychoactive properties. With many generations of SCs being encountered since 2009, MAB-CHMINACA is one of the latest, and based upon reports from public health and law enforcement, the misuse and abuse of this substance is negatively impacting the public health and communities.

The designer drug products laced with SCs, including MAB-CHMINACA, are often sold under the guise of "herbal incense" or "potpourri," use various product names, and are routinely labeled "not for human consumption." Additionally, these products are marketed as a "legal high" or "legal alternative to marijuana" and are readily available over the Internet, in head shops, or sold in convenience stores. There is an incorrect assumption that these products are safe, and that labeling these products as "not for human consumption" is a legal defense to criminal prosecution.

MAB-CHMINACA is a SC that has pharmacological effects similar to the schedule I hallucinogen THC and other temporarily and permanently controlled schedule I substances. MAB-CHMINACA has been shown to cause severe toxicity and adverse health effects following ingestion, including seizures, excited delirium, cardiotoxicity and death. With no approved medical use and limited safety or toxicological information, MAB-CHMINACA has emerged on the illicit drug market and is being abused for its psychoactive properties.

[redacted]ctor 4. History and Current Pattern of Abuse

SCs have been developed over the last 30 years as tools for investigating the cannabinoid system. SCs were first encountered by CBP within the United States in November 2008. Since then, the popularity of SCs and their associated products has increased steadily as evidenced by law enforcement seizures, public health information, and media reports. Amidst multiple administrative and legislative actions to place SCs found on the illicit market into schedule I of the CSA, new versions of SCs intended to circumvent current law continue to be encountered. MAB-CHMINACA is a SC that was encountered following the hospitalization of 125 individuals around the Baton Rouge, Louisiana area in October 2014 (see factor 6 of supporting materials). Since that time, multiple overdoses and deaths involving MAB-CHMINACA have been reported. For example, overdose clusters attributed to MAB-CHMINACA have been reported in Shreveport, Louisiana; Bryan, Texas; Beaumont, Texas; multiple cities in the State of Mississippi; Hampton, Virginia; and Hagerstown, Maryland (see factor 6 of supporting materials). Specifically, in April 2015, the largest nationwide outbreak involving SCs was reported by multiple news outlets. In addition, State public health entities have collectively reported over 2,000 overdoses and at least 33 deaths across at least 11 States attributed to the misuse of SCs. Of these overdoses and deaths, currently available toxicology results have determined that a number of overdoses from this most recent cluster were connected to ingestion of MAB-CHMINACA (see factor 6 of supporting materials).

On April 29, 2015, the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) reported multiple outbreaks of intoxications within the United States resulting from the ingestion of products believed to contain SCs. EMCDDA further reported that MAB-CHMINACA had been implicated in at least some of those cases. EMCDDA also reported on two deaths involving MAB-CHMINACA, one in Hungary and the other in Japan.

A major concern, as reiterated by public health officials and medical professionals, remains the targeting and direct marketing of SCs and SC-containing products to adolescents and youth. This is supported by law enforcement encounters and reports from emergency departments: however, all age groups have been reported by the media as abusing these substances and related products. Individuals, including minors, are purchasing SCs from the Internet, gas stations, convenience stores, and head shops.

Smoking mixtures of these substances for the purpose of achieving intoxication have resulted in numerous emergency department visits and calls to poison control centers. As reported by the American Association of Poison Control Centers (AAPCC), adverse effects including severe agitation, anxiety, racing heartbeat, high blood pressure, nausea, vomiting, seizures, tremors, intense hallucinations, psychotic episodes, suicide, and other harmful thoughts and/or actions can occur following ingestion of SCs. Presentations at emergency departments directly linked to the abuse of MAB-CHMINACA have resulted in similar symptoms, including severe agitation, seizures and/or death (see factor 6).

As discussed previously, it is believed most abusers of SCs or SC-related products smoke the product following application to plant material. Until recently, this was the preferred route of administration. Law enforcement has also begun to encounter new variations of SCs in liquid form. It is believed abusers have been applying the liquid to hookahs or "e-cigarettes," which allows the user to administer a vaporized liquid that can be inhaled.

Factor 5. Scope, Duration and Significance of Abuse

Following multiple scheduling actions designed to safeguard the public from the adverse effects and safety issues associated with SCs, encounters by law enforcement and health care professionals indicate the continued abuse of these substances and their associated products. With each action to control SCs, drug manufacturers and suppliers are adapting at an alarmingly quick pace to design new SCs that circumvent regulatory controls. Even before DEA temporarily controlled the latest group of SCs, AB-CHMINACA, AB-PINACA, and THJ-2201, on January 30, 2015, MAB-CHMINACA was already available on the illicit market and responsible for overdoses and deaths (see factor 6 of supporting materials). From October 2014 to the present, multiple overdoses and deaths have been attributed to the abuse of MAB-CHMINACA.

[redacted]n October 29, 2014, the State of Louisiana issued an emergency rule adding N-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-(cyclohexylmethyl)-1H-indazole-3-carboxamide (MAB-

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CHMINACA) to the list of schedule I Controlled Dangerous Substances section of the Louisiana Administrative Code (La. Admin. Code tit. 46, section 2704 (2014)), upon the determination that it had a high potential for abuse and should be scheduled as a controlled substance to avoid an imminent peril to the public health, safety, and welfare.

Poison control centers continue to report the abuse of SCs and their associated products. These substances remain a threat to both the short- and long-term public health and safety. Exposures to SCs were first reported to the AAPCC in 2011. The most alarming report via the AAPCC was published on April 23, 2015. The AAPCC reported a dramatic spike in poison center exposure calls throughout the United States in 2015. The AAPCC reported 1,512 exposure calls in April 2015, representing an almost three-fold increase in exposures to SCs as compared to the previous largest monthly tally (657 exposures in January 2012) since reporting began in 2011. It is likely that many of the calls are directly attributable to the abuse of MAB-CHMINACA based on its high prevalence in drug seizure reports and specimen test reports (see factor 6 and table 3 of supporting materials). Further, exposure calls to the AAPCC from within the first five months of 2015 (January 1 to June 1) are greater than the total exposure calls involving SCs from all of 2014. In addition, a majority of exposure incidents from 2011 to the present resulted in individuals seeking medical attention at health care facilities.

The following information regarding MAB-CHMINACA was obtained through NFLIS \2\ (queried on May 27, 2015):

\2\ National Forensic Laboratory Information System (NFLIS) is a national drug forensic laboratory reporting system that systematically collects results from drug chemistry analyses conducted by state and local forensic laboratories in the United States.

MAB-CHMINACA: NFLIS-451 reports; first encountered in September 2014; locations include Arkansas, Indiana, Kansas, Louisiana, Missouri, Oklahoma, Texas, Virginia, and Wisconsin.

Factor 6. What, if Any, Risk There Is to the Public Health

MAB-CHMINACA was identified in a cluster of 125 subjects that presented to emergency facilities within the Baton Rouge and Shreveport, Louisiana areas in October 2014. On October 29, 2014, the Louisiana Secretary of the Department of Health and Hospitals announced the addition of MAB-CHMINACA into schedule I of the Controlled Dangerous Substances section of the Louisiana Administrative Code (La. Admin. Code tit. 46, section 2704 (2014)). From October 2014 to the present, multiple clusters of overdoses involving MAB-CHMINACA and at least four deaths attributed to the misuse and abuse of MAB-CHMINACA have been reported. (see factor 6 and table 3 of supporting materials). Adverse health effects reported from use of MAB-CHMINACA have included: seizures, coma, severe agitation, loss of motor control, loss of consciousness, difficulty breathing, altered mental status, and convulsions that in some cases resulted in death.

Since abusers obtain these drugs through unknown sources, the identity, purity, and quantity of these substances is uncertain and inconsistent, thus posing significant adverse health risks to users. The SCs encountered on the illicit drug market have no accepted medical use within the United States. Regardless, SC products continue to be easily available and abused by diverse populations. Unknown factors including detailed product analysis and dosage variations between various packages and batches present a significant danger to an abusing individual. Designer drug products have been found to vary in the amount and type of SC that plant material is laced with, which could be one explanation for the numerous emergency department admissions that have been connected to these substances. Similar to previous SCs, MAB-CHMINACA has been found on plant material.

Finding of Necessity of Schedule I Placement To Avoid Imminent Hazard to Public Safety

Based on the data and information summarized above, the continued uncontrolled manufacture, distribution, importation, exportation, and abuse of MAB-CHMINACA poses an imminent hazard to the public safety. The DEA is not aware of any currently accepted medical uses for MAB-CHMINACA in the United States. A substance meeting the statutory requirements for temporary scheduling, **21 U.S.C. 811**(h)(1), may only be placed in schedule I. Substances in schedule I are those that have a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. Available data and information for MAB-CHMINACA indicate that this substance has a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. As required by section 201(h)(4) of the CSA, 21 U.S.C. 811(h)(4), the DEA, through a letter dated May 14, 2015, notified the Assistant Secretary of the DEA's intention to temporarily this substance in schedule I.

Conclusion

This notice of intent initiates an expedited temporary scheduling action and provides the 30-day notice pursuant to section 201(h) of the CSA, **21 U.S.C. 811**(h). In accordance with the provisions of section 201(h) of the CSA, 21 U.S.C. 811(h), the Administrator considered available data and information, herein set forth the grounds for his determination that it is necessary to temporarily schedule MAB-CHMINACA in schedule I of the CSA, and finds that placement of this SC into sch of the CSA is necessary to avoid an imminent hazard to the public safety.

Because the Administrator hereby finds that it is necessary to temporarily place this SC into schedule I to avoid an imminent hazard to the public safety, any subsequent final order temporarily scheduling these substances will be effective on the date of publication in the Federal Register, and will be in effect for a period of two years, with a possible extension of one additional year, pending completion of the regular (permanent) scheduling process. **21 U.S.C. 811**(h) (1) and (2). It is the intention of the Administrator to issue such a final order as soon as possible after the expiration of 30 days from the date of publication of this document. MAB-CHMINACA will then be subject to the regulatory controls and administrative, civil, and criminal sanctions applicable to the manufacture, distribution, possession, importation, exportation, research, and conduct of instructional activities of a schedule I controlled substance.

The CSA sets forth specific criteria for scheduling a drug or other substance. Regular scheduling actions in accordance with **21 U.S.C. 811**(a) are subject to formal rulemaking procedures done "on the record after opportunity for a hearing" conducted pursuant to the provisions of 5 U.S.C. 556 and 557. 21 U.S.C. 811. The regular scheduling process of formal rulemaking affords interested parties with appropriate process and the government with any additional relevant information needed to make a determination. Final decisions that conclude the regular scheduling process of formal rulemaking are subject to judicial review. **21 U.S.C. 877**. Temporary

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scheduling orders are not subject to judicial review. **21 U.S.C. 811**(h)(6).

Regulatory Matters

Section 201(h) of the CSA, **21 U.S.C. 811**(h), provides for an expedited temporary scheduling action where such action is necessary to avoid an imminent hazard to the public safety. As provided in this subsection, the Attorney General may, by order, schedule a substance in schedule I on a temporary basis. Such an order may not be issued before the expiration of 30 days from (1) the publication of a notice in the Federal Register of the intention to issue such order and the grounds upon which such order is to be issued, and (2) the date that notice of the proposed temporary scheduling order is transmitted to the Assistant Secretary. 21 U.S.C. 811(h)(1).

Inasmuch as section 201(h) of the CSA directs that temporary scheduling actions be issued by order and sets forth the procedures by which such orders are to be issued, the DEA believes that the notice and comment requirements of the Administrative Procedure Act (APA) at 5 U.S.C. 553, do not apply to this notice of intent. In the alternative, even assuming that this notice of intent might be subject to section 5 U.S.C. 553, the Administrator finds that there is good cause to forgo the notice and comment requirements of section 553, as any further delays in the process for issuance of temporary scheduling orders would be impracticable and contrary to the public interest in view of the manifest urgency to avoid an imminent hazard to the public safety.

Although the DEA believes this notice of intent to issue a temporary scheduling order is not subject to the notice and comment requirements of the APA, the DEA notes that in accordance with **21 U.S.C. 811**(h)(4), the Administrator will take into consideration any comments submitted by the Assistant Secretary with regard to the proposed temporary scheduling order.

Further, the DEA believes that this temporary scheduling action is not a "rule" as defined by 5 U.S.C. 601(2), and, accordingly, is not subject to the requirements of the Regulatory Flexibility Act. The requirements for the preparation of an initial regulatory flexibility analysis in 5 U.S.C. 603(a) are not applicable where, as here, the DEA is not required by the APA or any other law to publish a general notice of proposed rulemaking.

Additionally, this action is not a significant regulatory action as defined by Executive Order 12866 (Regulatory Planning and Review), section 3(f), and, according this action has not been reviewed by the Office of Management and Budget.

This action will not have substantial direct effects on the States, on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government. Therefore, in accordance with Executive Order 13132 (Federalism), it is determined that this action does not have sufficient federalism implications to warrant the preparation of a Federalism Assessment.

List of Subjects in 21 CFR Part 1308

Administrative practice and procedure, Drug traffic control, Reporting and recordkeeping requirements.

For the reasons set out above, the DEA proposes to amend 21 CFR part 1308 as follows:

PART 1308--SCHEDULES OF CONTROLLED SUBSTANCES

- 1. The authority citation for part 1308 continues to read as follows:

Authority: 21 U.S.C. 811, 812, 871(b), unless otherwise noted.

- 2. In **Sec. 1308.11**, add paragraph (h)(25) to read as follows:

Sec. 1308.11 Schedule I.

* * * * *

(h) * * *

(25) N-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-(cyclohexylmethyl)-1H-indazole-3-carboxamide, its optical, positional, and geometric isomers, salts and salts of isomers—7032 (Other names: MAB-CHMINACA; ADB-CHMINACA)

Dated: September 10, 2015.

Chuck Rosenberg,
Acting Administrator.

[FR Doc. 2015-23198 Filed 9-15-15; 8:45 am]

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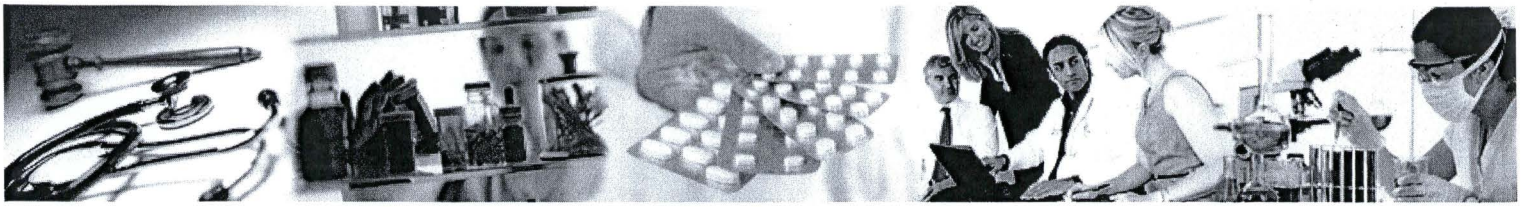

Rules - 2016

[Federal Register Volume 81, Number 92 (Thursday, May 12, 2016)]
[Rules and Regulations]
[Pages 29492-29496]
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[FR Doc No: 2016-11219]

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA-434F]

Schedules of Controlled Substances: Temporary Placement of Butyryl Fentanyl and Beta-Hydroxythiofentanyl Into Schedule I

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Final order.

SUMMARY: The Administrator of the Drug Enforcement Administration is issuing this final order to temporarily schedule the synthetic opioids, N-(1-phenethylpiperidin-4-yl)-N-phenylbutyramide, also known as N-(1-phenethylpiperidin-4-yl)-N-phenylbutanamide, (butyryl fentanyl) and N-[1-[2-hydroxy-2-(thiophen-2-yl)ethyl]piperidin-4-yl]-N-phenylpropionamide, also known as N-[1-[2-hydroxy-2-(2-thienyl)ethyl]-4-piperidinyl]-N-phenylpropanamide, (beta-hydroxythiofentanyl), and their isomers, esters, ethers, salts and salts of isomers, esters and ethers, into schedule I pursuant to the temporary scheduling provisions of the Controlled Substances Act. This action is based on a finding by the Administrator that the placement of butyryl fentanyl and beta-hydroxythiofentanyl into schedule I of the Controlled Substances Act is necessary to avoid an imminent hazard to the public safety. As a result of this order, the regulatory controls and administrative, civil, and criminal sanctions applicable to schedule I controlled substances will be imposed on persons who handle (manufacture, distribute, reverse distribute, import, export, engage in research, conduct instructional activities or chemical analysis, or possess), or propose to handle, butyryl fentanyl and beta-hydroxythiofentanyl.

DATES: This final order is effective on May 12, 2016.

FOR FURTHER INFORMATION CONTACT: Barbara J. Boockholdt, Office of Diversion Control, Drug Enforcement Administration; Mailing Address: 8701 Morrissette Drive, Springfield, Virginia 22152; Telephone: (202) 598-6812.

SUPPLEMENTARY INFORMATION:

Legal Authority

The Drug Enforcement Administration (DEA) implements and enforces titles II and III of the Comprehensive Drug Abuse Prevention and Control Act of 1970, as amended. **21 U.S.C. 801-971**. Titles II and III are referred to as the "Controlled Substances Act" and the "Controlled Substances Import and Export Act," respectively, and are collectively referred to as the "Controlled Substances Act" or the "CSA" for the purpose of this action. The DEA publishes the implementing regulations for these statutes in title 21 of the Code of Federal Regulations (CFR), chapter II. The CSA and its implementing regulations are designed to prevent, detect, and eliminate the diversion of controlled substances and listed chemicals into the illicit market while ensuring an adequate supply is available for the legitimate medical, scientific, research, and industrial needs of the United States. Controlled substances have the potential for abuse and dependence and are controlled to protect the public health and safety.

Under the CSA, every controlled substance is classified into one of five schedules based upon its potential for abuse, its currently accepted medical use in treatment in the United States, and the degree of dependence the drug or other substance may cause. **21 U.S.C. 812**. The initial schedules of controlled substances established by Congress are found at 21 U.S.C. 812(c), and the current list of all scheduled substances is published at **21 CFR part 1308**.

Section 201 of the CSA, **21 U.S.C. 811**, provides the Attorney General with the authority to temporarily place a substance into schedule I of the CSA for two years without regard to the requirements of 21 U.S.C. 811(b) if she finds that such action is necessary to avoid an imminent hazard to the public safety. 21 U.S.C. 811(h)(1). In addition, if proceedings to control a substance are initiated under 21 U.S.C. 811(a)(1), the Attorney General may extend the temporary scheduling for up to one year. 21 U.S.C. 811(h)(2).

Where the necessary findings are made, a substance may be temporarily scheduled if it is not listed in any other schedule under section 202 of the CSA, **21 U.S.C. 812**, or if there is no exemption or approval in effect for the substance under section 505 of the Federal Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. 355. **21 U.S.C. 811**(h)(1). The Attorney General has delegated her scheduling authority under 21 U.S.C. 811 to the Administrator of the DEA. 28 CFR 0.100.

Background

Section 201(h)(4) of the CSA, **21 U.S.C. 811**(h)(4), requires the Administrator to notify the Secretary of the Department of Health and Human Services (HHS) of his intention to temporarily place a substance into schedule I of the CSA.\1\ The Administrator transmitted the notice of intent to place butyryl fentanyl and beta-hydroxythiofentanyl into schedule I on a temporary basis to the Assistant Secretary by letter dated December 21, 2015. The Assistant Secretary responded to this notice by letter dated January 13, 2016, and advised that based on review by the Food and Drug Administration (FDA), there are currently no investigational new drug

applications or approved new drug applications for butryl fentanyl or beta-hydroxythiofentanyl. The Assistant Secretary also stated that the HHS has no objection to the temporary placement of butryl fentanyl or beta-hydroxythiofentanyl into schedule I of the CSA. The DEA has taken into consideration the Assistant Secretary's comments as required by **21 U.S.C. 811**(h)(4). Neither butryl fentanyl nor beta-hydroxythiofentanyl is currently listed in any schedule under the CSA, and no exemptions or approvals are in effect for butryl fentanyl or beta-hydroxythiofentanyl under section 505 of the FDCA, 21 U.S.C. 355. The DEA has found that the control of butryl fentanyl and beta-hydroxythiofentanyl in schedule I on a temporary basis is necessary to avoid an imminent hazard to public safety, and as required by 21 U.S.C. 811(h)(1)(A), a notice of intent to temporarily schedule butryl fentanyl and beta-hydroxythiofentanyl was published in the Federal Register on March 23, 2016. 81 FR 15485.

\1\ As discussed in a memorandum of understanding entered into by the Food and Drug Administration (FDA) and the National Institute on Drug Abuse (NIDA), the FDA acts as the lead agency within the HHS in carrying out the Secretary's scheduling responsibilities under the CSA, with the concurrence of NIDA. 50 FR 9518, Mar. 8, 1985. The Secretary of the HHS has delegated to the Assistant Secretary for Health of the HHS the authority to make domestic drug scheduling recommendations. 58 FR 35460, July 1, 1993.

To find that placing a substance temporarily into schedule I of the CSA is necessary to avoid an imminent hazard to the public safety, the

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Administrator is required to consider three of the eight factors set forth in section 201(c) of the CSA, **21 U.S.C. 811**(c): The substance's history and current pattern of abuse; the scope, duration and significance of abuse; and what, if any, risk there is to the public health. 21 U.S.C. 811(h)(3). Consideration of these factors includes actual abuse, diversion from legitimate channels, and clandestine importation, manufacture, or distribution. 21 U.S.C. 811(h)(3).

A substance meeting the statutory requirements for temporary scheduling may only be placed into schedule I. **21 U.S.C. 811**(h)(1). Substances in schedule I are those that have a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. **21 U.S.C. 812**(b)(1). Available data and information for butryl fentanyl and beta-hydroxythiofentanyl, summarized below, indicate that these synthetic opioids have a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. The DEA's three-factor analysis, and the Assistant Secretary's January 13, 2016, letter, are available in their entirety under the tab "Supporting Documents" of the public docket of this action at www.regulations.gov under FDMS Docket ID: DEA-2016-0005 (Docket Number DEA-434).

Factor 4. History and Current Pattern of Abuse

Clandestinely produced substances structurally related to the schedule II opioid analgesic fentanyl were trafficked and abused on the West Coast in the late 1970s and 1980s. These clandestinely produced fentanyl-like substances were commonly known as designer drugs, and recently there has been a reemergence in the trafficking and abuse of designer drug substances, including fentanyl-like substances. Alpha-methylfentanyl, the first fentanyl analogue identified in California, was placed into schedule I of the CSA in September 1981. 46 FR 46799. Following the control of alpha-methylfentanyl, the DEA identified several other fentanyl analogues (3-methylthiofentanyl, acetyl-alpha-methylfentanyl, beta-hydroxy-3-methylfentanyl, alpha-methylthiofentanyl, thiofentanyl, beta-hydroxyfentanyl, para-fluorofentanyl, and 3-methylfentanyl) in submissions to forensic laboratories. These substances were temporarily controlled \2\ in 1985-1987 under schedule I of the CSA after finding that they posed an imminent hazard to public safety and were subsequently permanently placed in schedule I of the CSA. On July 17, 2015, acetyl fentanyl was temporarily controlled under schedule I of the CSA after a finding by the Administrator that it posed an imminent hazard to public safety. 80 FR 42381.

\2\ 50 FR 43698, 51 FR 42834, 50 FR 11690, 51 FR 15474, and 51 FR 4722. [The temporary scheduling of para-fluorofentanyl was extended in 1987, at 52 FR 7270.

Prior to October 1, 2014, the System to Retrieve Information from Drug Evidence (STRIDE) collected the results of drug evidence analyzed at DEA laboratories and reflected evidence submitted by the DEA, other federal law enforcement agencies, and some local law enforcement agencies. STRIDE data were queried through September 30, 2014, by date submitted to federal forensic laboratories. Since October 1, 2014, STARLiMS (a web-based, commercial laboratory information management system) has replaced STRIDE as the DEA laboratory drug evidence data system of record. DEA laboratory data submitted after September 30, 2014, are reposited in STARLiMS. Data from STRIDE and STARLiMS were queried on December 21, 2015. The National Forensic Laboratory Information System (NFLIS) is a program of the DEA that collects drug identification results from drug cases analyzed by other federal, state, and local forensic laboratories. NFLIS reports from other federal, state, and local forensic laboratories were queried on December 22, 2015.\3\

\3\ Data are still being reported for September-November 2015 due to normal lag time for laboratories to report to NFLIS.

The first laboratory submission of butyryl fentanyl was recorded in Kansas in March 2014 according to NFLIS. STRIDE, STARLiMS, and NFLIS registered seven reports containing butyryl fentanyl in 2014 in Illinois, Kansas, Minnesota, and Pennsylvania; 81 reports of butyryl fentanyl were recorded in 2015 in California, Connecticut, Florida, Indiana, North Dakota, New York, Ohio, Oregon, Tennessee, Virginia, and Wisconsin. A total of three reports of beta-hydroxythiofentanyl were recorded by STARLiMS, all of which were reported in 2015 from Florida. As of December 22, 2015, beta-hydroxythiofentanyl had not been reported in NFLIS; however, this substance was identified in June 2015 by a forensic laboratory in Oregon.

Evidence also suggests that the pattern of abuse of fentanyl analogues, including butyryl fentanyl and beta-hydroxythiofentanyl, parallels that of heroin and prescription opioid analgesics. Seizures of butyryl fentanyl have been encountered in tablet and powder form. Butyryl fentanyl was identified on bottle caps and spoons and residue was detected within glassine bags, on digital scales, and on sifters which demonstrates the abuse of this substance as a replacement for heroin or other opioids, either knowingly or unknowingly. Butyryl fentanyl has been encountered as a single substance as well as in combination with other illicit substances, such as acetyl fentanyl, heroin, cocaine, or methamphetamine. Like butyryl fentanyl, beta-hydroxythiofentanyl has been encountered in both tablet and powder form. Both butyryl fentanyl and beta-hydroxythiofentanyl have caused fatal overdoses, in which intravenous routes of administration are documented.

Factor 5. Scope, Duration and Significance of Abuse

The DEA is currently aware of at least 40 confirmed fatalities associated with butyryl fentanyl and 7 confirmed fatalities associated with beta-hydroxythiofentanyl. The information on these deaths occurring in 2015 was collected from toxicology and medical examiner reports and was reported from four states--Florida (7, beta-hydroxythiofentanyl), Maryland (1, butyryl fentanyl), New York (38, butyryl fentanyl), and Oregon (1, butyryl fentanyl). STRIDE, STARLiMS, and NFLIS have a total of 88 drug reports in which butyryl fentanyl was identified in drug exhibits submitted in 2014 and 2015 from California, Connecticut, Florida, Illinois, Indiana, Kansas, Minnesota, North Dakota, New York, Ohio, Oregon, Pennsylvania, Tennessee, Virginia, and Wisconsin. STARLiMS has a total of three drug reports in which beta-hydroxythiofentanyl was identified in drug exhibits submitted in 2015 from Florida. It is likely that the prevalence of butyryl fentanyl and beta-hydroxythiofentanyl in opioid analgesic-related emergency room admissions and deaths is underreported as standard immunoassays cannot differentiate these substances from fentanyl.

The population likely to abuse butyryl fentanyl and beta-hydroxythiofentanyl overlaps with the populations abusing prescription opioid analgesics and heroin. This is evidenced by the routes of administration and drug use history documented in butyryl fentanyl and beta-hydroxythiofentanyl fatal overdose cases. Because abusers of these fentanyl analogues are likely to obtain these

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substances through illicit sources, the identity, purity, and quantity is uncertain and inconsistent, thus posing significant adverse health risks to abusers of butyryl fentanyl and beta-hydroxythiofentanyl. Individuals who initiate (i.e., use an illicit drug for the first time) butyryl fentanyl or beta-hydroxythiofentanyl abuse are likely to be at risk of developing substance use disorder, overdose, and death similar to that of other opioid analgesics (e.g., fentanyl, morphine, etc.).

Factor 6. What, if Any, Risk There Is to the Public Health

Butyryl fentanyl and beta-hydroxythiofentanyl exhibit pharmacological profiles similar to that of fentanyl and other mu-opioid receptor agonists. Due to limited scientific data, their potency and toxicity are not known; however, the toxic effects of both butyryl fentanyl and beta-hydroxythiofentanyl in humans are demonstrated

by overdose fatalities involving these substances. Abusers of these fentanyl analogues may not know the origin, identity, or purity of these substances, thus posing significant adverse health risks when compared to abuse of pharmaceutical preparations of opioid analgesics, such as morphine and oxycodone.

Based on the documented case reports of overdose fatalities, the abuse of butyryl fentanyl and beta-hydroxythiofentanyl leads to the same qualitative public health risks as heroin, fentanyl and other opioid analgesic substances. The public health risks attendant to the abuse of heroin and opioid analgesics are well established and have resulted in large numbers of drug treatment admissions, emergency department visits, and fatal overdoses.

Butyryl fentanyl and beta-hydroxythiofentanyl have been associated with numerous fatalities. At least 40 confirmed overdose deaths involving butyryl fentanyl ab have been reported in Maryland (1), New York (38), and Oregon (1) in 2015. At least seven confirmed overdose fatalities involving beta-hydroxythiofentanyl hav been reported in Florida in 2015. This indicates that both butyryl fentanyl and beta-hydroxythiofentanyl pose an imminent hazard to the public safety.

Finding of Necessity of Schedule I Placement To Avoid Imminent Hazard to Public Safety

In accordance with **21 U.S.C. 811**(h)(3), based on the data and information summarized above, the continued uncontrolled manufacture, distribution, importation, exportation, and abuse of butyryl fentanyl and beta-hydroxythiofentanyl pose an imminent hazard to the public safety. The DEA is not aware of any currently accepted medical uses for these substances in the United States. A substance meeting the statutory requirements for temporary scheduling, 21 U.S.C. 811(h)(1), may only be placed into schedule I. Substances in schedule I are those that have a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. Available data and information for butyryl fentanyl and beta-hydroxythiofentanyl indicate that these substances have a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. As required by section 201(h)(4) of the CSA, 21 U.S.C. 811(h)(4), the Administrator, through a letter dated December 21, 2015, notified the Assistant Secretary of the DEA's intention to temporarily place these substances into schedule I.

Conclusion

In accordance with the provisions of section 201(h) of the CSA, **21 U.S.C. 811**(h), the Administrator considered available data and information, herein sets forth the grounds for his determination that it is necessary to temporarily schedule butyryl fentanyl and beta-hydroxythiofentanyl into schedule I of the CSA, and finds that placement of these synthetic opioids into schedule I of the CSA is necessary to avoid an imminent hazard to the public safety. Because the Administrator hereby finds it necessary to temporarily place these synthetic opioids into schedule I to avoid an imminent hazard to the public safety, this final order temporarily scheduling butyryl fentanyl and beta-hydroxythiofentanyl will be effective on the date of publication in the Federal Register, and will be in effect for a period of two years, with a possible extension of one additional year, pending completion of the regular (permanent) scheduling process. 21 U.S.C. 811(h)(1) and (2).

The CSA sets forth specific criteria for scheduling a drug or other substance. Permanent scheduling actions in accordance with **21 U.S.C. 811**(a) are subject to formal rulemaking procedures done "on the record after opportunity for a hearing" conducted pursuant to the provisions of 5 U.S.C. 556 and 557. 21 U.S.C. 811. The permanent scheduling process of formal rulemaking affords interested parties with appropriate process and the government with any additional relevant information needed to make a determination. Final decisions that conclude the permanent scheduling process of formal rulemaking are subject to judicial review. **21 U.S.C. 877**. Temporary scheduling orders are not subject to judicial review. 21 U.S.C. 811(h)(6).

Requirements for Handling

Upon the effective date of this final order, butyryl fentanyl and beta-hydroxythiofentanyl will become subject to the regulatory controls and administrative, civil, and criminal sanctions applicable to the manufacture, distribution, reverse distribution, importation, exportation, engagement in research, and conduct of instructional activities or chemical analysis with, and possession of schedule I controlled substances including the following:

1. *Registration.* Any person who handles (manufactures, distributes, reverse distributes, imports, exports, engages in research, or conducts instructional activities or chemical analysis with, or possesses), or who desires to handle, butyryl fentanyl and beta-hydroxythiofentanyl must be registered with the DEA to conduct such activities pursuant to **21 U.S.C. 822**, **823**, **957**, and **958** and in accordance with **21 CFR parts 1301** and **1312**, as of May 12, 2016. Any person who currently handles butyryl fentanyl and beta-hydroxythiofentanyl, and is not registered with the DEA, must submit an application for registration and may not continue to handle butyryl fentanyl or beta-hydroxythiofentanyl as of May 12, 2016, unless the DEA has approved that application for registration pursuant to 21 U.S.C. 822, 823, 957, 958, and in accordance with 21 CFR parts 1301 and 1312. Retail sales of schedule I controlled substances to the general public are not allowed under the CSA. Possession of any quantity of this substance in a manner not authorized by the CSA on or after May 12, 2016 is unlawful and those in possession of any quantity o this substance may be subject to prosecution pursuant to the CSA.

2. *Disposal of stocks.* Any person who does not desire or is not able to obtain a schedule I registration to handle butyryl fentanyl and beta-hydroxythiofentanyl, must surrender all quantities of currently held butyryl fentanyl and beta-hydroxythiofentanyl.

3. *Security.* Butyryl fentanyl and beta-hydroxythiofentanyl are subject to schedule I security requirements and must be handled and stored pursuant to **21 U.S.C. 821**, **823**, **871**(b), and in accordance with **21 CFR 1301.71-1301.93**, as of May 12, 2016.

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4. *Labeling and packaging.* All labels, labeling, and packaging for commercial containers of butyryl fentanyl and beta-hydroxythiofentanyl must be in compliance with **21 U.S.C. 825**, **958**(e), and be in accordance with **21 CFR part 1302**. Current DEA registrants shall have 30 calendar days from May 12, 2016, to comply with all labeling and packaging requirements.

5. *Inventory.* Every DEA registrant who possesses any quantity of butyryl fentanyl and beta-hydroxythiofentanyl on the effective date of this order must take an inventory of all stocks of this substance on hand, pursuant to **21 U.S.C. 827** and **958**, and in accordance with **21 CFR 1304.03**, **1304.04**, and **1304.11**. Current DEA registrants shall have 30 calendar days from the effective date of this order to be in compliance with all inventory requirements. After the initial inventory, every DEA registrant must take an inventory of all controlled substances (including butyryl fentanyl and beta-hydroxythiofentanyl) on hand on a biennial basis, pursuant to 21 U.S.C. 827 and **958**, and in accordance with **21 CFR 1304.03**, **1304.04**, and **1304.11**.

6. *Records.* All DEA registrants must maintain records with respect to butyryl fentanyl and beta-hydroxythiofentanyl pursuant to **21 U.S.C. 827** and **958**, and in accordance with **21 CFR parts 1304**, and **1312**, **1317** and **Sec. 1307.11**. Current DEA registrants authorized to handle butyryl fentanyl and beta-hydroxythiofentanyl shall have 30 calendar days from the effective date of this order to be in compliance with all recordkeeping requirements.

7. *Reports.* All DEA registrants who manufacture or distribute butyryl fentanyl and beta-hydroxythiofentanyl must submit reports pursuant to **21 U.S.C. 827** and in accordance with **21 CFR parts 1304**, and **1312** as of May 12, 2016.

8. *Order Forms.* All DEA registrants who distribute butyryl fentanyl and beta-hydroxythiofentanyl must comply with order form requirements pursuant to **21 U.S.C. 828** and in accordance with **21 CFR part 1305** as of May 12, 2016.

9. *Importation and Exportation.* All importation and exportation of butyryl fentanyl and beta-hydroxythiofentanyl must be in compliance with **21 U.S.C. 952**, **953**, **957**, **958**, and in accordance with **21 CFR part 1312** as of May 12, 2016.

10. *Quota.* Only DEA registered manufacturers may manufacture butyryl fentanyl and beta-hydroxythiofentanyl in accordance with a quota assigned pursuant to **21 U.S.C. 826** and in accordance with **21 CFR part 1303** as of May 12, 2016.

11. *Liability.* Any activity involving butyryl fentanyl and beta-hydroxythiofentanyl not authorized by, or in violation of the CSA, occurring as of May 12, 2016, is unlawful, and may subject the person to administrative, civil, and/or criminal sanctions.

Regulatory Matters

Section 201(h) of the CSA, **21 U.S.C. 811**(h), provides for an expedited temporary scheduling action where such action is necessary to avoid an imminent hazard t the public safety. As provided in this subsection, the Attorney General may, by order, schedule a substance in schedule I on a temporary basis. Such an order may be issued before the expiration of 30 days from (1) the publication of a notice in the Federal Register of the intention to issue such order and the grounds upon which such order is to be issued, and (2) the date that notice of the proposed temporary scheduling order is transmitted to the Assistant Secretary. 21 U.S.C. 811(h)(1).

Inasmuch as section 201(h) of the CSA directs that temporary scheduling actions be issued by order and sets forth the procedures by which such orders are to be issued, the DEA believes that the notice and comment requirements of the Administrative Procedure Act (APA) at 5 U.S.C. 553, do not apply to this temporary scheduling action. In the alternative, even assuming that this action might be subject to 5 U.S.C. 553, the Administrator finds that there is good cause to forgo the

notice and comment requirements of 5 U.S.C. 553, as any further delays in the process for issuance of temporary scheduling orders would be impracticable and contrary to the public interest in view of the manifest urgency to avoid an imminent hazard to the public safety.

Further, the DEA believes that this temporary scheduling action is not a "rule" as defined by 5 U.S.C. 601(2), and, accordingly, is not subject to the requirements of the Regulatory Flexibility Act. The requirements for the preparation of an initial regulatory flexibility analysis in 5 U.S.C. 603(a) are not applicable where, as here, the DEA is not required by the APA or any other law to publish a general notice of proposed rulemaking.

Additionally, this action is not a significant regulatory action as defined by Executive Order 12866 (Regulatory Planning and Review), section 3(f), and, accordingly, this action has not been reviewed by the Office of Management and Budget (OMB).

This action will not have substantial direct effects on the States, on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government. Therefore, in accordance with Executive Order 13132 (Federalism) it is determined that this action does not have sufficient federalism implications to warrant the preparation of a Federalism Assessment.

As noted above, this action is an order, not a rule. Accordingly, the Congressional Review Act (CRA) is inapplicable, as it applies only to rules. However, if this were a rule, pursuant to the Congressional Review Act, "any rule for which an agency for good cause finds that notice and public procedure thereon are impracticable, unnecessary, or contrary to the public interest, shall take effect at such time as the federal agency promulgating the rule determines." 5 U.S.C. 808(2). It is in the public interest to schedule these substances immediately because they pose a public health risk. This temporary scheduling action is taken pursuant to **21 U.S.C. 811** (h), which is specifically designed to enable the DEA to act in an expeditious manner to avoid an imminent hazard to the public safety. 21 U.S.C. 811(h) exempts the temporary scheduling order from standard notice and comment rulemaking procedures to ensure that the process moves swiftly. For the same reasons that underlie 21 U.S.C. 811(h), that is, the DEA's need to move quickly to place these substances into schedule I because they pose an imminent hazard to public safety, it would be contrary to the public interest to delay implementation of the temporary scheduling order. Therefore, this order shall take effect immediately upon its publication. The DEA has submitted a copy of this final order to both Houses of Congress and to the Comptroller General, although such filing is not required under the Small Business Regulatory Enforcement Fairness Act of 1996 (Congressional Review Act), 5 U.S.C. 801-808 because, as noted above, this action is an order, not a rule.

List of Subjects in 21 CFR Part 1308

Administrative practice and procedure, Drug traffic control, Reporting and recordkeeping requirements.

For the reasons set out above, the DEA amends 21 CFR part 1308 as follows:

PART 1308--SCHEDULES OF CONTROLLED SUBSTANCES

- 1. The authority citation for part 1308 continues to read as follows:

  Authority: 21 U.S.C. 811, 812, 871(b), unless otherwise noted.

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- 2. Amend **Sec. 1308.11** by adding paragraphs (h)(26) and (27) to read as follows:

Sec. 1308.11 Schedule I.

* * * * *

(h) * * *

(26) *N*-(1-phenethylpiperidin-4-yl)-*N*-phenylbutyramide, its isomers, esters, ethers, salts and salts of isomers, esters and ethers (Other names: Butyryl fentanyl) ..... (9822)

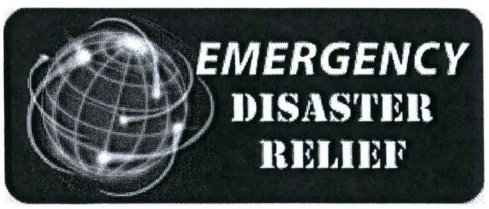
(27) *N*-[1-[2-hydroxy-2-(thiophen-2-yl)ethyl]piperidin-4-yl]-*N*-phenylpropionamide, its isomers, esters, ethers, salts and salts of isomers, esters and ethers (Other names: beta-hydroxythiofentanyl) ..... (9836)

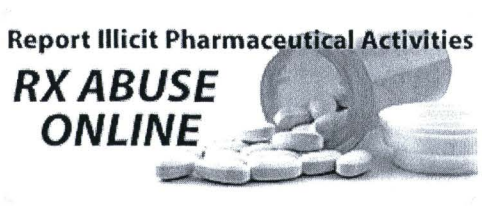
Dated: May 6, 2016.

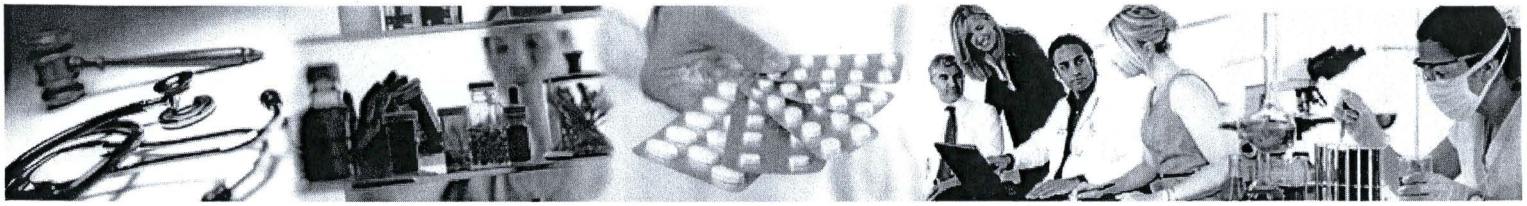
Chuck Rosenberg,
Acting Administrator.

[FR Doc. 2016-11219 Filed 5-11-16; 8:45 am]

BILLING CODE 4410-09-P







Rules - 2016

[Federal Register Volume 81, Number 72 (Thursday, April 14, 2016)]
[Rules and Regulations]
[Pages 22023-22025]
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[FR Doc No: 2016-08566]

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA-432]

Schedules of Controlled Substances: Placement of AH-7921 Into Schedule I

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Final order.

SUMMARY: With the issuance of this final order, the Administrator of the Drug Enforcement Administration places the substance AH-7921 (Systematic IUPAC Name: 3,4-dichloro-N-[(1dimethylamino)cyclohexylmethyl]benzamide), including its isomers, esters, ethers, salts, and salts of isomers, esters and ethers, into schedule I of the Controlled Substances Act. This scheduling action is pursuant to the Controlled Substances Act and is required in order for the United States to discharge its obligations under the Single Convention on Narcotic Drugs, 1961. This action imposes the regulatory controls and administrative, civil, and criminal sanctions applicable to schedule I controlled substances on persons who handle (manufacture, distribute, import, export, engage in research or conduct instructional activities with, or possess), or propose to handle, AH-7921.

DATES: Effective May 16, 2016.

FOR FURTHER INFORMATION CONTACT: Barbara J. Boockholdt, Office of Diversion Control, Drug Enforcement Administration; Mailing Address: 8701 Morrissette Drive, Springfield, Virginia 22152; Telephone: (202) 598-6812.

SUPPLEMENTARY INFORMATION:

Legal Authority

The Drug Enforcement Administration (DEA) implements and enforces titles II and III of the Comprehensive Drug Abuse Prevention and Control Act of 1970, as amended. Titles II and III are referred to as the "Controlled Substances Act" and the "Controlled Substances Import and Export Act," respectively, and are collectively referred to as the "Controlled Substances Act" or the "CSA" for the purpose of this action. **21 U.S.C. 801-971**. The DEA publishes the implementing regulations for these statutes in title 21 of the Code of Federal Regulations (CFR), chapter II. The CSA and its implementing regulations are designed to prevent, detect, and eliminate the diversion of controlled substances and listed chemicals into the illicit market while providing for the legitimate medical, scientific, research, and industrial needs of the United States. Controlled substances have the potential for abuse and dependence and are controlled to protect the public health and safety.

Under the CSA, controlled substances are classified into one of five schedules based upon their potential for abuse, their currently accepted medical use in treatment in the United States, and the degree of dependence the substance may cause. **21 U.S.C. 812**. The initial schedules of controlled substances established by Congress are found at 21 U.S.C. 812(c), and the current list of scheduled substances is published at **21 CFR part 1308**.

Section 201(d)(1) of the CSA (**21 U.S.C. 811**(d)(1)) states that, if control of a substance is required "by United States obligations under international treaties, conventions, or protocols in effect on October 27, 1970, the Attorney General shall issue an order controlling such drug under the schedule he deems most appropriate to carry out such obligations, without regard to the findings and procedures required by section 201(a) and (b) (21 U.S.C. 811(a) and (b)) and section 202(b) (**21 U.S.C. 812**(b)) of the Act." 21 U.S.C. 811(d)(1), **21 CFR 1308.46**. If a substance is added to one of the schedules of the Single Convention on Narcotic Drugs, 1961, then, in accordance with article 3, paragraph 7 of the Convention, as a signatory Member State, the United States is obligated to control that substance under its national drug control legislation, the CSA. The Attorney General has delegated scheduling authority under 21 U.S.C. 811 to the Administrator of the DEA. 28 CFR 0.100.

Background

On May 8, 2015, the Secretary-General of the United Nations advised the Secretary of State of the United States, that during the 58th session of the Commission on Narcotic Drugs, AH-7921 was added to schedule I of the Single Convention on Narcotic Drugs, 1961. This letter was prompted by a decision at the 58th session of the Commission on Narcotic Drugs in March 2015 to schedule AH-7921 under schedule I of the Single Convention on Narcotic Drugs. As a signatory Member State to the Single Convention on Narcotic Drugs, the United States is obligated to control AH-7921 under its national drug control legislation, the CSA, in the schedule deemed most appropriate to carry out its international obligations. **21 U.S.C. 811**(d)(1).

AH-7921

AH-7921 is an N-substituted cyclohexylmethyl benzamide developed in 1962 by Allen and Hanbury's, Ltd., a pharmaceutical company in the United Kingdom. AH-7921 is a [micro]-opioid receptor agonist with analgesic activity similar to that of morphine. The DEA is not aware of any commercial or medical uses for this substance. In animals, withdrawal symptoms are observed following repeated administration of AH-7921. Currently, clinical studies evaluating the safety and pharmacological effects of AH-7921 in humans have not been reported in the scientific literature. Usage of AH-7921 for eliciting euphoria and relaxation has been documented. There have been several reports of overdoses and deaths from AH-7921 reported worldwide including at least one published case report of a death resulting from AH-7921 in the United States. Given the increasing abuse of opioid prescription drugs (e.g., oxycodone, hydrocodone and fentanyl) and increased use of heroin in the United States, there are legitimate concerns about an increased potential of abuse of AH-7921.

[redacted] is not aware of any claims or any medical or scientific literature suggesting that AH-7921 has a currently accepted medical use in treatment in the United States. Accordingly, DEA has not requested that HHS conduct a scientific and medical evaluation of the substance's medical utility.

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Furthermore, DEA is not required under **21 U.S.C. 811**(d)(1) to make any findings required by 21 U.S.C. 811(a) or **812**(b), and is not required to follow the procedures prescribed by 21 U.S.C. 811(a) and (b). Therefore, consistent with the framework of 21 U.S.C. 811(d), DEA concludes that AH-7921 has no currently accepted medical use in treatment in the United States and is most appropriately placed in schedule I of the CSA.

Conclusion

In order to meet the obligations of the Single Convention on Narcotic Drugs, 1961 and because AH-7921 has no currently accepted medical use in treatment in the United States, the Administrator of the Drug Enforcement Administration has determined that this substance should be placed in schedule I of the Controlled Substances Act.

Requirements for Handling

Upon the effective date of this final order, AH-7921 is subject to the CSA's schedule I regulatory controls and administrative, civil, and criminal sanctions applicable to the manufacture, distribution, importation, exportation, engagement in research, and conduct of instructional activities with, and possession of schedule I controlled substances including the following:

1. *Registration.* Any person who handles (manufactures, distributes, imports, exports, engages in research or conducts instructional activities with, or possesses), or who desires to handle, AH-7921 must be registered with the DEA to conduct such activities pursuant to **21 U.S.C. 822**, **823**, **957**, and **958** and in accordance with **21 CFR parts 1301** and **1312**, as of May 16, 2016. Any person who currently handles AH-7921, and is not registered with the DEA, must submit an application for registration and may not continue to handle AH-7921 as of May 16, 2016, unless the DEA has approved that application for registration pursuant to 21 U.S.C. 822, 823, 957, 958, and in accordance with 21 CFR parts 1301 and 1312.

2. *Disposal of stocks.* Any person who does not desire or is not able to obtain a schedule I registration must surrender all quantities of currently held AH-7921, or may transfer all quantities of currently held AH-7921 to a person registered with the DEA on or before May 16, 2016 in accordance with all applicable federal, state, local, and tribal laws. As of May 16, 2016, controlled substances must be disposed of in accordance with **21 CFR part 1317**, in additional to all other applicable federal, state, local, and tribal laws.

3. *Security.* AH-7921 is subject to schedule I security requirements and must be handled and stored pursuant to **21 U.S.C. 821**, **823**, **871**(b), and in accordance with **21 CFR 1301.71-1301.93**, as of May 16, 2016.

4. *Labeling and packaging.* All labels, labeling, and packaging for commercial containers of AH-7921 must be in compliance with **21 U.S.C. 825**, **958**(e), and be in accordance with **21 CFR part 1302** as of May 16, 2016.

5. *Quota.* A quota assigned pursuant to **21 U.S.C. 826** and in accordance with **21 CFR part 1303** is required in order to manufacture AH-7921 as of May 16, 2016.

6. *Inventory.* Every DEA registrant who possesses any quantity of AH-7921 on the effective date of this order must take an inventory of all stocks of this substance on hand as of May 16, 2016, pursuant to **21 U.S.C. 827** and **958**, and in accordance with **Sec. Sec. 1304.03**, **1304.04**, and **1304.11**.

[redacted] person who becomes registered with the DEA after May 16, 2016 must take an initial inventory of all stocks of controlled substances (including AH-7921) on hand [redacted]he date the registrant first engages in the handling of controlled substances, pursuant to **21 U.S.C. 827** and **958** and in accordance with **21 CFR 1304.03**, [redacted]**304.04**, and **1304.11**.

After the initial inventory, every DEA registrant must take an inventory of all controlled substances (including AH-7921) on hand on a biennial basis, pursuant to **21 U.S.C. 827** and **958**, and in accordance with **Sec. Sec. 1304.03**, **1304.04**, and **1304.11**.

7. *Records and Reports.* Every DEA registrant would be required to maintain records and submit reports with respect to AH-7921 pursuant to **21 U.S.C. 827** and **958**, and in accordance with **21 CFR parts 1304** and **1312**.

8. *Order Forms.* All DEA registrants who distribute AH-7921 must comply with order form requirements pursuant to **21 U.S.C. 828** and in accordance with **21 CFR part 1305** as of May 16, 2016.

9. *Importation and Exportation.* All importation and exportation of AH-7921 must be in compliance with **21 U.S.C. 952**, **953**, **957**, **958**, and in accordance with **21 CFR part 1312** as of May 16, 2016.

10. *Liability.* Any activity involving AH-7921 not authorized by, or in violation of the CSA, occurring as of May 16, 2016, is unlawful, and may subject the person to administrative, civil, and/or criminal sanctions.

Regulatory Analyses

Administrative Procedure Act

The CSA provides for an expedited scheduling action where control is required by the United States obligations under international treaties, conventions, or protocols. **21 U.S.C. 811**(d)(1). If control is required pursuant to such international treaty, convention, or protocol, the Attorney General must issue an order controlling such drug under the schedule he deems most appropriate to carry out such obligations, without regard to the findings or procedures otherwise required for scheduling actions. Id.

To the extent that **21 U.S.C. 811**(d)(1) directs that if control is required by the United States obligations under international treaties, conventions, or protocols in effect on October 27, 1970, scheduling actions shall be issued by order (as compared to scheduling pursuant to 21 U.S.C. 811(a) by rule), the DEA believes that the notice and comment requirements of section 553 of the Administrative Procedure Act (APA), 5 U.S.C. 553, do not apply to this scheduling action. In the alternative, even if this action does constitute "rule making" under 5 U.S.C. 551(5), this action is exempt from the notice and comment requirements of 5 U.S.C. 553 pursuant to 21 U.S.C. 553(a)(1) as an action involving a foreign affairs function of the United States given that this action is being done in accordance with 21 U.S.C. 811(d)(1)'s requirement that such action be taken to comply with the United States obligations under the specified international agreements.

Executive Order 12866

This action is not a significant regulatory action as defined by Executive Order 12866 (Regulatory Planning and Review), section 3(f), and, accordingly, this action has not been reviewed by the Office of Management and Budget (OMB).

[redacted]*ecutive Order 13132*

[redacted]s action does not have federalism implications warranting the application of Executive Order 13132. This action will not have substantial direct effects on the [redacted]States, on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government. Therefore, in accordance with Executive Order 13132 (Federalism) it is determined that this action does not have sufficient federalism implications to warrant the preparation of a Federalism Assessment.

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Executive Order 13175

This action does not have tribal implications warranting the application of Executive Order 13175. The action does not have substantial direct effects on one or more Indian tribes, on the relationship between the Federal government and Indian tribes, or on the distribution of power and responsibilities between the Federal government and Indian tribes.

Regulatory Flexibility Act

The Regulatory Flexibility Act (RFA) (5 U.S.C. 601-612) applies to rules that are subject to notice and comment under section 553(b) of the APA or any other la[redacted] explained above, the CSA exempts this final order from notice and comment. Consequently, the RFA does not apply to this action.

Paperwork Reduction Act of 1995

This action does not impose a new collection of information requirement under the Paperwork Reduction Act of 1995. 44 U.S.C. 3501-3521. An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Congressional Review Act

This action is not a major rule as defined by section 804 of the Small Business Regulatory Enforcement Fairness Act of 1996 (Congressional Review Act). However, the DEA has submitted a copy of this final order to both Houses of Congress and to the Comptroller General.

List of Subjects in 21 CFR Part 1308

Administrative practice and procedure, Drug traffic control, Narcotics, Prescription drugs.

For the reasons set out above, the DEA amends 21 CFR part 1308 as follows:

PART 1308--SCHEDULES OF CONTROLLED SUBSTANCES

- 1. The authority citation for part 1308 continues to read as follows:

  Authority: 21 U.S.C. 811, 812, 871(b), unless otherwise noted.

- 2. Amend **Sec. 1308.11** by redesignating paragraphs (b)(3) through (55) as (b)(4) through (56) and adding a new (b)(3)to read as follows:

Sec. 1308.11 Schedule I.

* * * * *

(b) * * *

(3) AH-7921 (3,4-dichloro-*N*-[(1-dimethylamino) cyclohexylmethyl]benzamide 9551

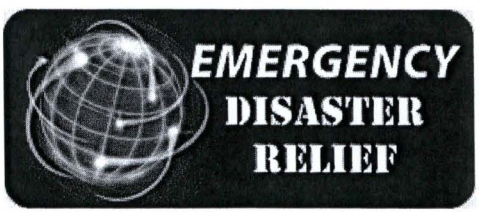
* * * * *

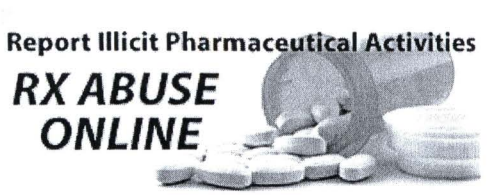
Dated: April 8, 2016

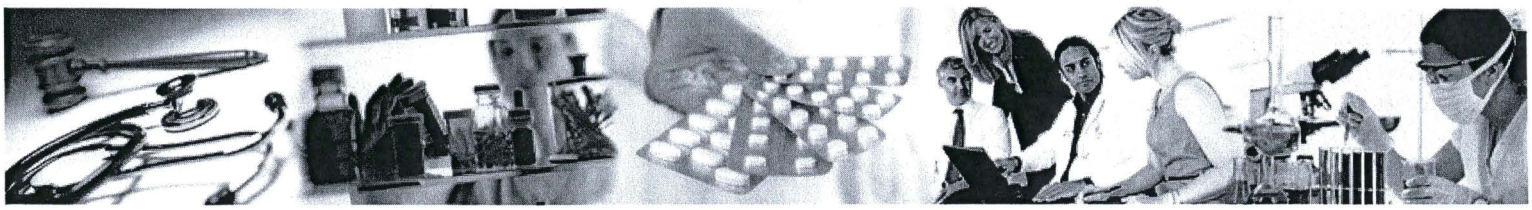
Chuck Rosenberg,
Acting Administrator.

[FR Doc. 2016-08566 Filed 4-13-16; 8:45 am]

BILLING CODE 4410-09-P







Rules - 2016

[Federal Register Volume 81, Number 219 (Monday, November 14, 2016)]
[Rules and Regulations]
[Pages 79389-79393]
From the Federal Register Online via the Government Publishing Office [www.gpo.gov]
[FR Doc No: 2016-27357]

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA-440]

Schedules of Controlled Substances: Temporary Placement of U-47700 Into Schedule I

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Final Order

SUMMARY: The Administrator of the Drug Enforcement Administration is issuing this final order to temporarily schedule the synthetic opioid, 3,4-dichloro-N-[2-(dimethylamino)cyclohexyl]-N-methylbenzamide (also known as U-47700), and its isomers, esters, ethers, salts and salts of isomers, esters and ethers, into schedule I pursuant to the temporary scheduling provisions of the Controlled Substances Act. This action is based on a finding by the Administrator that the placement of U-47700 into schedule I of the Controlled Substances Act is necessary to avoid an imminent hazard to the public safety. As a result of this order, the regulatory controls and administrative, civil, and criminal sanctions applicable to schedule I controlled substances will be imposed on persons who handle (manufacture, distribute, reverse distribute, import, export, engage in research, conduct instructional activities or chemical analysis, or possess), or propose to handle, U-47700.

DATES: This final order is effective on November 14, 2016.

FOR FURTHER INFORMATION CONTACT: Michael J. Lewis, Diversion Control Division, Drug Enforcement Administration; Mailing Address: 8701 Morrissette Drive, Springfield, Virginia 22152; Telephone: (202) 598- 6812.

SUPPLEMENTARY INFORMATION:

Legal Authority

The Drug Enforcement Administration (DEA) implements and enforces titles II and III of the Comprehensive Drug Abuse Prevention and Control Act of 1970, as amended. **21 U.S.C. 801-971**. Titles II and III are referred to as the "Controlled Substances Act" and the "Controlled Substances Import and Export Act," respectively, and are collectively referred to as the "Controlled Substances Act" or the "CSA" for the purpose of this action. The DEA publishes the implementing regulations

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for these statutes in title 21 of the Code of Federal Regulations (CFR), chapter II. The CSA and its implementing regulations are designed to prevent, detect, and eliminate the diversion of controlled substances and listed chemicals into the illicit market while ensuring an adequate supply is available for the legitimate medical, scientific, research, and industrial needs of the United States. Controlled substances have the potential for abuse and dependence and are controlled to protect the public health and safety.

Under the CSA, every controlled substance is classified into one of five schedules based upon its potential for abuse, its currently accepted medical use in treatment in the United States, and the degree of dependence the drug or other substance may cause. 21 U.S.C. 812. The initial schedules of controlled substances established by Congress are found at **21 U.S.C. 812**(c), and the current list of all scheduled substances is published at **21 CFR part 1308.**

Section 201 of the CSA, **21 U.S.C. 811**, provides the Attorney General with the authority to temporarily place a substance into schedule I of the CSA for two years without regard to the requirements of 21 U.S.C. 811(b) if she finds that such action is necessary to avoid an imminent hazard to the public safety. 21 U.S.C. 811(h)(1). In addition, if proceedings to control a substance are initiated under 21 U.S.C. 811(a)(1), the Attorney General may extend the temporary scheduling for up to one year. 21 U.S.C. 811(h)(2).

Where the necessary findings are made, a substance may be temporarily scheduled if it is not listed in any other schedule under section 202 of the CSA, 21 U.S.C. 812, or if there is no exemption or approval in effect for the substance under section 505 of the Federal Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. 355. 21 U.S.C. 811(h)(1). The Attorney General has delegated her scheduling authority under 21 U.S.C. 811 to the Administrator of the DEA. 28 CFR 0.100.

Background

Section 201(h)(4) of the CSA, 21 U.S.C. 811(h)(4), requires the Administrator to notify the Secretary of the Department of Health and Human Services (HHS) of his intention to temporarily place a substance into schedule I of the CSA.\1\ The Administrator transmitted the notice of intent to place U-47700 into schedule I on a temporary basis to the Assistant Secretary by letter dated April 18, 2016. The Assistant Secretary responded to this notice by letter dated April 28, 2016, and advised

that based on review by the Food and Drug Administration (FDA), there are currently no investigational new drug applications or approved new drug applications for U-47700. The Assistant Secretary also stated that the HHS has no objection to the temporary placement of U-47700 into schedule I of the CSA. The DEA has taken into consideration the Assistant Secretary's comments as required by 21 U.S.C. 811(h)(4). U-47700 is not currently listed in any schedule under the CSA, and no exemptions or approvals are in effect for U-47700 under section 505 of the FDCA, 21 U.S.C. 355. The DEA has found that the control of U-47700 in schedule I on a temporary basis is necessary to avoid an imminent hazard to the public safety, and as required by 21 U.S.C. 811(h)(1)(A), a notice of intent to temporarily schedule U-47700 was published in the Federal Register on September 7, 2016. 81 FR 61636.

\1\ As discussed in a memorandum of understanding entered into by the Food and Drug Administration (FDA) and the National Institute on Drug Abuse (NIDA), the FDA acts as the lead agency within the HHS in carrying out the Secretary's scheduling responsibilities under the CSA, with the concurrence of NIDA. 50 FR 9518, Mar. 8, 1985. The Secretary of the HHS has delegated to the Assistant Secretary for Health of the HHS the authority to make domestic drug scheduling recommendations. 58 FR 35460, July 1, 1993.

To find that placing a substance temporarily into schedule I of the CSA is necessary to avoid an imminent hazard to the public safety, the Administrator is required to consider three of the eight factors set forth in section 201(c) of the CSA, 21 U.S.C. 811(c): The substance's history and current pattern of abuse; the scope, duration and significance of abuse; and what, if any, risk there is to the public health. 21 U.S.C. 811(h)(3). Consideration of these factors includes actual abuse, diversion from legitimate channels, and clandestine importation, manufacture, or distribution. 21 U.S.C. 811(h)(3).

A substance meeting the statutory requirements for temporary scheduling may only be placed into schedule I. 21 U.S.C. 811(h)(1). Substances in schedule I are those that have a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. 21 U.S.C. 812(b)(1). Available data and information for U- 47700, summarized below, indicate that this synthetic opioid has a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. The DEA's updated three-factor analysis, and the Assistant Secretary's April 28, 2016, letter, are available in their entirety under the tab "Supporting Documents" of the public docket of this action at www.regulations.gov under FDMS Docket ID: DEA-2016-0016 (Docket Number DEA-440).

Factor 4. History and Current Pattern of Abuse

The recreational abuse of novel opioids continues to be a significant concern. These substances are distributed to users with often unpredictable outcomes. The novel synthetic opioid U-47700 has recently been encountered by law enforcement and public health officials and the adverse health effects and outcomes are documented in the scientific literature. Self-reporting by users describes the effects of U-47700 to be similar to other opioids. The negative effects documented in the scientific literature are also consistent with other opioids. The National Forensic Laboratory Information System (NFLIS) is a national drug forensic laboratory reporting system that systematically collects results from drug chemistry analyses conducted by participating Federal, State, and local forensic laboratories across the country. The DEA utilizes NFLIS to monitor for drug trends. The first laboratory submission of U-47700 was recorded in October 2015; a total of 88 records were reported from State and local forensic laboratories between October 2015--September 2016 according to NFLIS (query date: October 24, 2016).

On October 1, 2014, the DEA implemented STARLiMS (a web-based, commercial laboratory information management system) as its laboratory drug evidence data system of record. DEA laboratory data submitted after September 30, 2014, are reposited in STARLiMS; data from STARLiMS were queried on November 1, 2016. STARLiMS registered 45 reports containing U-47700 in 2016 from California, Connecticut, Florida, Maryland, Montana, North Dakota, New Jersey, New York, Tennessee, Texas, Virginia, West Virginia, and the District of Columbia. Through information collected from NFLIS, law enforcement reports, and email communications, the DEA is aware of the identification of U-47700 from toxicology reports and submitted evidence to forensic laboratories in several states, including Arkansas, California, Colorado, Connecticut, Florida, Georgia, Iowa, Kentucky, Missouri, Montana, New

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Hampshire, New Jersey, New York, North Carolina, North Dakota, Ohio, Oklahoma, Oregon, Pennsylvania, Texas, and Wisconsin. These identifications occurred in 2015 and 2016.

Evidence suggests that the pattern of abuse of U-47700 parallels that of heroin, prescription opioid analgesics, and other novel opioids. Seizures of U-47700 have been encountered in powder form and in counterfeit tablets that mimic pharmaceutical opioids. U-47700 has also been encountered in glassine bags and envelopes and knotted corners of plastic bags. These clandestine forms of distribution demonstrate the abuse of this substance as a replacement for heroin or other opioids, either knowingly or unknowingly. Further, U-47700 has been encountered as a single substance as well as in combination with other substances, including heroin, fentanyl, and furanyl fentanyl in drug exhibits.

The scientific literature and information collected by DEA demonstrate U-47700 is being abused for its opioid properties. The distribution of U-47700 and the increased prevalence of abuse remain deeply concerning to the DEA.

Factor 5. Scope, Duration and Significance of Abuse

The scientific literature and reports collected by the DEA demonstrate U-47700 is being abused for its opioid properties. This abuse of U-47700 has resulted in morbidity and mortality (see updated DEA 3-Factor Analysis for full discussion). The DEA has received reports for at least 46 confirmed fatalities \2\ associated with U-47700. The information on these deaths occurring in 2015 and 2016 was collected from email communications and toxicology and medical examiner reports and was reported from New Hampshire (1), New York (31), North Carolina (10), Ohio (1), Texas (2), and Wisconsin (1). The scientific literature notes additional fatal overdoses connected to U-47700. The population likely to abuse U-47700 appears to overlap with the populations abusing prescription opioid analgesics, other "designer opioids," and heroin, as evidenced by drug use history documented in U-47700 fatal overdose cases. This observation is further supported by U-47700 being sold on the illicit market in glassine bags, some of which are marked with stamped logos, imitating the sale of heroin. Additionally, U-47700 has been found in counterfeit pills. Because abusers of U-47700 are likely to obtain this substance through non- regulated sources (i.e., on-line purchases or drug dealers), the identity, purity, and quantity are uncertain and inconsistent, thus posing significant adverse health risks to the end user. Individuals who initiate (i.e., use a drug for the first time) U-47700 abuse are likely to be at risk of developing substance use disorder, overdose, and death similar to that of other opioid analgesics (e.g., fentanyl, morphine, etc.).

\2\ Due to a proofreading error, the number of fatalities listed in the U-47700 NOI, which was 15, is incorrect. The correct number, 46, has been added to this Final Order.

STARLiMS contains 45 reports in which U-47700 was identified in drug exhibits submitted in 2016. A query of NFLIS returned 88 records of U-47700 being identified in exhibits submitted to State and local forensic laboratories between October 2015--September 2016. The DEA is not aware of any laboratory analyses of drug evidence identifying U- 47700 prior to 2015, indicating that this synthetic opioid only recently became available as a replacement for other opioids that are commonly abused (i.e. oxycodone, heroin, fentanyl). U-47700 is available over the Internet and is marketed as a "research chemical." The on-line sale and marketing of U-47700 are similar to other new psychoactive substances that have rapidly appeared on the recreational drug market and also resulted in negative consequences for the user.

Factor 6. What, if Any, Risk There Is to the Public Health

U-47700 exhibits pharmacological profiles similar to that of morphine and other mu-opioid receptor agonists. Cases of intoxication are reported in the literature with morbidity and mortality associated with U-47700 use. The toxic effects of U-47700 in humans are demonstrated by overdoses and overdose fatalities associated with this substance, as reported in the scientific literature. Abusers of U-47700 may not know the origin, identity, or purity of this substance, thus posing significant adverse health risks when compared to abuse of pharmaceutical preparations of opioid analgesics, such as morphine and oxycodone. Additionally, the potent opioid U-47700 may serve as a precursor to problematic opioid use and dependence.

Based on reports in the scientific literature and information received by the DEA, the abuse of U-47700 leads to the same qualitative public health risks as heroin, fentanyl and other opioid analgesic substances. As with any non-medically approved opioid, the health and safety risks for users are great. The public health risks

attendant to the abuse of heroin and opioid analgesics are well established and have resulted in large numbers of drug treatment admissions, emergency department visits, and fatal overdoses.

U-47700 has been associated with a number of fatalities and non- fatal overdoses as detailed in the scientific literature. The DEA has received information connecting U-47700 to at least 46 confirmed overdose deaths, occurring in 2015 and 2016 in New Hampshire (1), New York (31), North Carolina (10), Ohio (1), Texas (2), and Wisconsin (1).

Finding of Necessity of Schedule I Placement To Avoid Imminent Hazard to Public Safety

[redacted]ccordance with **21 U.S.C. 811**(h)(3), based on the data and information summarized above, the continued uncontrolled manufacture, distribution, importation, [redacted]portation, and abuse of U-47700 pose an imminent hazard to the public safety. The DEA is not aware of any currently accepted medical uses for this substance in [redacted]he United States. A substance meeting the statutory requirements for temporary scheduling, 21 U.S.C. 811(h)(1), may only be placed into schedule I. Substances in schedule I are those that have a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. Available data and information for U-47700 indicate that this substance has a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. As required by section 201(h)(4) of the CSA, 21 U.S.C. 811(h)(4), the Administrator, through a letter dated April 18, 2016, notified the Assistant Secretary of the DEA's intention to temporarily place this substance into schedule I.

Conclusion

In accordance with the provisions of section 201(h) of the CSA, 21 U.S.C. 811(h), the Administrator considered available data and information, herein sets forth the grounds for his determination that it is necessary to temporarily schedule U-47700 into schedule I of the CSA, and finds that placement of this synthetic opioid into schedule I of the CSA is necessary to avoid an imminent hazard to the public safety. Because the Administrator hereby finds it necessary to temporarily place this synthetic opioid into schedule I to avoid an imminent hazard

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to the public safety, this final order temporarily scheduling U-47700 will be effective on the date of publication in the Federal Register, and will be in effect for a period of two years, with a possible extension of one additional year, pending completion of the regular (permanent) scheduling process. 21 U.S.C. 811(h) (1) and (2).

The CSA sets forth specific criteria for scheduling a drug or other substance. Permanent scheduling actions in accordance with 21 U.S.C. 811(a) are subject to formal rulemaking procedures done "on the record after opportunity for a hearing" conducted pursuant to the provisions of 5 U.S.C. 556 and 557. 21 U.S.C. 811. The permanent scheduling process of formal rulemaking affords interested parties with appropriate process and the government with any additional relevant information needed to make a determination. Final decisions that conclude the permanent scheduling process of formal rulemaking are subject to judicial review. 21 U.S.C. 877. Temporary scheduling orders are not subject to judicial review. 21 U.S.C. 811(h)(6).

Requirements for Handling

Upon the effective date of this final order, U-47700 will become subject to the regulatory controls and administrative, civil, and criminal sanctions applicable to the manufacture, distribution, reverse distribution, importation, exportation, engagement in research, and conduct of instructional activities or chemical analysis with, and possession of schedule I controlled substances including the following:

1. Registration. Any person who handles (manufactures, distributes, reverse distributes, imports, exports, engages in research, or conducts instructional activities or chemical analysis with, or possesses), or who desires to handle, U-47700 must be registered with the DEA to conduct such activities pursuant to 21 U.S.C. 822, 823, 957, and 958 and in accordance with 21 CFR parts 1301 and 1312, as of November 14, 2016. Any person who currently handles U-47700, and is not registered with the DEA, must submit an application for registration and may not continue to handle U-47700 as of November 14, 2016, unless the DEA has approved that application for registration pursuant to 21 U.S.C. 822, 823, 957, 958, and in accordance with 21 CFR parts 1301 and 1312. Retail sales of schedule I controlled substances to the general public are not allowed under the CSA. Possession of any quantity of this substance in a manner not authorized by the CSA on or after November 14, 2016 is unlawful and those in possession of any quantity of this substance may be subject to prosecution pursuant to the CSA.

[redacted]2. Disposal of stocks. Any person who does not desire or is not able to obtain a schedule I registration to handle U-47700, must surrender all quantities of currently [redacted]d U-47700.

[redacted]Security. U-47700 is subject to schedule I security requirements and must be handled and stored pursuant to **21 U.S.C. 821**, **823**, **871**(b), and in accordance with **21 CFR 1301.71-1301.93**, as of November 14, 2016.

4. Labeling and packaging. All labels, labeling, and packaging for commercial containers of U-47700 must be in compliance with **21 U.S.C. 825**, **958**(e), and be in accordance with **21 CFR part 1302**. Current DEA registrants shall have 30 calendar days from November 14, 2016, to comply with all labeling and packaging requirements.

5. Inventory. Every DEA registrant who possesses any quantity of U- 47700 on the effective date of this order must take an inventory of all stocks of this substance on hand, pursuant to **21 U.S.C. 827** and **958**, and in accordance with **21 CFR 1304.03, 1304.04, and 1304.11**. Current DEA registrants shall have 30 calendar days from the effective date of this order to be in compliance with all inventory requirements. After the initial inventory, every DEA registrant must take an inventory of all controlled substances (including U-47700) on hand on a biennial basis, pursuant to 21 U.S.C. 827 and 958, and in accordance with **21 CFR 1304.03, 1304.04, and 1304.11.**

6. Records. All DEA registrants must maintain records with respect to U-47700 pursuant to 21 U.S.C. 827 and 958, and in accordance with **21 CFR parts 1304**, and **1312**, **1317** and **Sec. 1307.11**. Current DEA registrants shall have 30 calendar days from the effective date of this order to be in compliance with all recordkeeping requirements.

7. Reports. All DEA registrants who manufacture or distribute U- 47700 must submit reports pursuant to 21 U.S.C. 827 and in accordance with 21 CFR parts 1304, and 1312 as of November 14, 2016.

8. Order Forms. All DEA registrants who distribute U-47700 must comply with order form requirements pursuant to 21 U.S.C. 828 and in accordance with **21 CFR part 1305** as of November 14, 2016.

9. Importation and Exportation. All importation and exportation of U-47700 must be in compliance with 21 U.S.C. 952, 953, 957, 958, and in accordance with **21 CFR part 1312** as of November 14, 2016.

10. Quota. Only DEA registered manufacturers may manufacture U- 47700 in accordance with a quota assigned pursuant to 21 U.S.C. 826 and in accordance with **21 CFR part 1303** as of November 14, 2016.

11. Liability. Any activity involving U-47700 not authorized by, or in violation of the CSA, occurring as of November 14, 2016, is unlawful, and may subject the person to administrative, civil, and/or criminal sanctions.

Regulatory Matters

Section 201(h) of the CSA, 21 U.S.C. 811(h), provides for a temporary scheduling action where such action is necessary to avoid an imminent hazard to the public safety. As provided in this subsection, the Attorney General may, by order, schedule a substance in schedule I on a temporary basis. Such an order may not be issued before the expiration of 30 days from (1) the publication of a notice in the Federal Register of the intention to issue such order and the grounds upon which such order is to be issued, and (2) the date that notice of the proposed temporary scheduling order is transmitted to the Assistant Secretary. 21 U.S.C. 811(h)(1).

[redacted]asmuch as section 201(h) of the CSA directs that temporary scheduling actions be issued by order and sets forth the procedures by which such orders are to be [redacted]ued, the DEA believes that the notice and comment requirements of the Administrative Procedure Act (APA) at 5 U.S.C. 553, do not apply to this temporary [redacted]cheduling action. In the alternative, even assuming that this action might be subject to 5 U.S.C. 553, the Administrator finds that there is good cause to forgo the notice and comment requirements of 5 U.S.C. 553, as any further delays in the process for issuance of temporary scheduling orders would be impracticable and contrary to the public interest in view of the manifest urgency to avoid an imminent hazard to the public safety.

Further, the DEA believes that this temporary scheduling action is not a "rule" as defined by 5 U.S.C. 601(2), and, accordingly, is not subject to the requirements of the Regulatory Flexibility Act. The requirements for the preparation of an initial regulatory flexibility analysis in 5 U.S.C. 603(a) are not applicable where, as here, the DEA is not required by the APA or any other law to publish a general notice of proposed rulemaking.

Additionally, this action is not a significant regulatory action as defined by Executive Order 12866 (Regulatory Planning and Review), section 3(f), and, accordingly, this action has not been

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reviewed by the Office of Management and Budget (OMB). This action will not have substantial direct effects on the States, on the relationship between the na government and the States, or on the distribution of power and responsibilities among the various levels of government. Therefore, in accordance with Executiv Order 13132 (Federalism) it is determined that this action does not have sufficient federalism implications to warrant the preparation of a Federalism Assessment.

As noted above, this action is an order, not a rule. Accordingly, the Congressional Review Act (CRA) is inapplicable, as it applies only to rules. However, if this were a rule, pursuant to the Congressional Review Act, "any rule for which an agency for good cause finds that notice and public procedure thereon are impracticable, unnecessary, or contrary to the public interest, shall take effect at such time as the federal agency promulgating the rule determines." 5 U.S.C. 808(2). It is in the public interest to schedule this substance immediately because it poses a public health risk. This temporary scheduling action is taken pursuant to 21 U.S.C. 811(h), which is specifically designed to enable the DEA to act in an expeditious manner to avoid an imminent hazard to the public safety. 21 U.S.C. 811(h) exempts the temporary scheduling order from standard notice and comment rulemaking procedures to ensure that the process moves swiftly. For the same reasons that underlie 21 U.S.C. 811(h), that is, the DEA's need to move quickly to place this substance into schedule I because it poses an imminent hazard to the public safety and it would be contrary to the public interest to delay implementation of the temporary scheduling order. Therefore, this order shall take effect immediately upon its publication. The DEA has submitted a copy of this final order to both Houses of Congress and to the Comptroller General, although such filing is not required under the Small Business Regulatory Enforcement Fairness Act of 1996 (Congressional Review Act), 5 U.S.C. 801-808, because, as noted above, this action is an order, not a rule.

List of Subjects in 21 CFR Part 1308

Administrative practice and procedure, Drug traffic control, Reporting and recordkeeping requirements.

For the reasons set out above, the DEA amends 21 CFR part 1308 as follows:

PART 1308--SCHEDULES OF CONTROLLED SUBSTANCES

1. The authority citation for part 1308 continues to read as follows:

Authority: 21 U.S.C. 811, 812, 871(b), unless otherwise noted.

2. Amend Sec. 1308.11 by adding paragraph (h)(18) to read as follows:

Sec. 1308.11 Schedule I.

* * * * *

(h) * * *

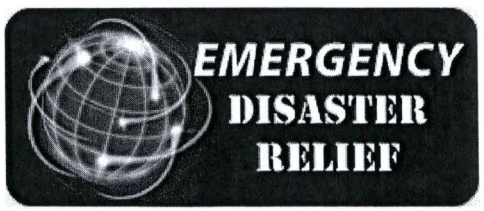
(18) 3,4-Dichloro-N-[2-(dimethylamino)cyclohexyl]-N-methylbenzamide, its isomers, esters, ethers, salts and salts of isomers, esters and ethers (Other name: U-47700).....(9547)

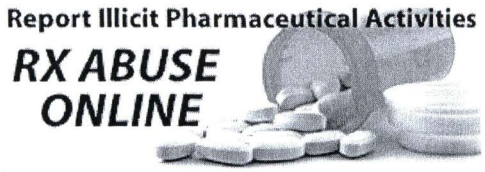
* * * * *

Dated: November 7, 2016.

Chuck Rosenberg,
Acting Administrator.

[FR Doc. 2016-27357 Filed 11-10-16; 8:45 am]
BILLING CODE 4410-09-P





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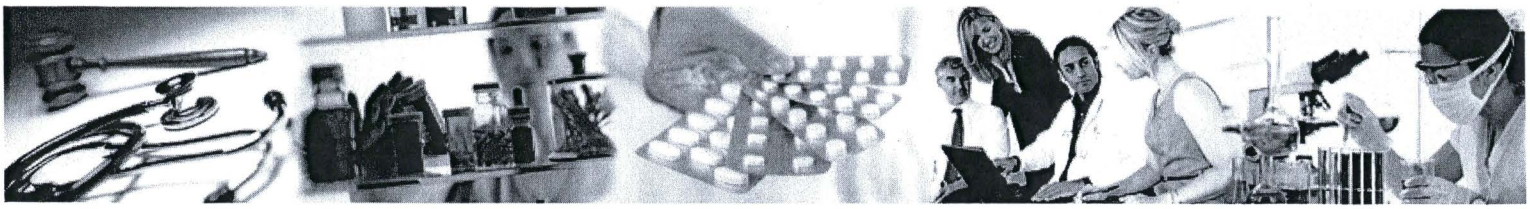

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[Federal Register Volume 81, Number 229 (Tuesday, November 29, 2016)]
[Rules and Regulations]
[Pages 85873-85877]
From the Federal Register Online via the Government Publishing Office [www.gpo.gov]
[FR Doc No: 2016-28693]

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA-448]

Schedules of Controlled Substances: Temporary Placement of Furanyl Fentanyl Into Schedule I

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Final Order

SUMMARY: The Administrator of the Drug Enforcement Administration is issuing this final order to temporarily schedule the synthetic opioid, N-(1-phenethylpiperidin-4-yl)-N-phenylfuran-2-carboxamide (furanyl fentanyl), and its isomers, esters, ethers, salts and salts of isomers, esters and ethers, into schedule I pursuant to the temporary scheduling provisions of the Controlled Substances Act. This action is based on a finding by the Administrator that the placement of furanyl fentanyl into schedule I of the Controlled Substances Act is necessary to avoid an imminent hazard to the public safety. As a result of this order, the regulatory controls and administrative, civil, and criminal sanctions applicable to schedule I controlled substances will be imposed

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on persons who handle (manufacture, distribute, reverse distribute, import, export, engage in research, conduct instructional activities or chemical analysis, or possess), or propose to handle, furanyl fentanyl.

DATES: This final order is effective on November 29, 2016.

FOR FURTHER INFORMATION CONTACT: Michael J. Lewis, Diversion Control Division, Drug Enforcement Administration; Mailing Address: 8701 Morrissette Drive, Springfield, Virginia 22152; Telephone: (202) 598-6812.

SUPPLEMENTARY INFORMATION:

Legal Authority

The Drug Enforcement Administration (DEA) implements and enforces titles II and III of the Comprehensive Drug Abuse Prevention and Control Act of 1970, as amended. 21 U.S.C. 801-971. Titles II and III are referred to as the "Controlled Substances Act" and the "Controlled Substances Import and Export Act," respectively, and are collectively referred to as the "Controlled Substances Act" or the "CSA" for the purpose of this action. The DEA publishes the implementing regulations for these statutes in title 21 of the Code of Federal Regulations (CFR), chapter II. The CSA and its implementing regulations are designed to prevent, detect, and eliminate the diversion of controlled substances and listed chemicals into the illicit market while ensuring an adequate supply is available for the legitimate medical, scientific, research, and industrial needs of the United States. Controlled substances have the potential for abuse and dependence and are controlled to protect the public health and safety. Under the CSA, every controlled substance is classified into one of five schedules based upon its potential for abuse, its currently accepted medical use in treatment in the United States, and the degree of dependence the drug or other substance may cause. 21 U.S.C. 812. The initial schedules of controlled substances established by Congress are found at 21 U.S.C. 812(c), and the current list of all scheduled substances is published at 21 CFR part 1308.

Section 201 of the CSA, **21 U.S.C. 811**, provides the Attorney General with the authority to temporarily place a substance into schedule I of the CSA for two years without regard to the requirements of 21 U.S.C. 811(b) if she finds that such action is necessary to avoid an imminent hazard to the public safety. 21 U.S.C. 811(h)(1). In addition, if proceedings to control a substance are initiated under 21 U.S.C. 811(a)(1), the Attorney General may extend the temporary scheduling for up to one year. 21 U.S.C. 811(h)(2).

Where the necessary findings are made, a substance may be temporarily scheduled if it is not listed in any other schedule under section 202 of the CSA, 21 U.S.C. 812, or if there is no exemption or approval in effect for the substance under section 505 of the Federal Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. 355. 21 U.S.C. 811(h)(1). The Attorney General has delegated her scheduling authority under 21 U.S.C. 811 to the Administrator of the DEA. 28 CFR 0.100.

Background

Section 201(h)(4) of the CSA, 21 U.S.C. 811(h)(4), requires the Administrator to notify the Secretary of the Department of Health and Human Services (HHS) of his intention to temporarily place a substance into schedule I of the CSA.\1\ The Administrator transmitted the notice of intent to place furanyl fentanyl into schedule I on a temporary basis to the Assistant Secretary by letter dated June 22, 2016. The Assistant Secretary responded to this notice by letter dated July 8, 2016, and advised that based on review by the Food and Drug Administration (FDA), there are currently no investigational new drug applications or approved new drug applications for furanyl fentanyl. The Assistant Secretary also stated that the HHS has no objection to the temporary placement of furanyl fentanyl into schedule I of the CSA. The DEA

has taken into consideration the Assistant Secretary's comments as required by 21 U.S.C. 811(h)(4). Furanyl fentanyl is not currently listed in any schedule under the CSA, and no exemptions or approvals are in effect for furanyl fentanyl under section 505 of the FDCA, 21 U.S.C. 355. The DEA has found that the control of furanyl fentanyl in schedule I on a temporary basis is necessary to avoid an imminent hazard to the public safety, and as required by 21 U.S.C. 811(h)(1)(A), a notice of intent to temporarily schedule furanyl fentanyl was published in the Federal Register on September 27, 2016. 81 FR 66224.

\1\ As discussed in a memorandum of understanding entered into by the Food and Drug Administration (FDA) and the National Institute on Drug Abuse (NIDA), the FDA acts as the lead agency within the HHS in carrying out the Secretary's scheduling responsibilities under the CSA, with the concurrence of NIDA. 50 FR 9518, Mar. 8, 1985. The Secretary of the HHS has delegated to the Assistant Secretary for Health of the HHS the authority to make domestic drug scheduling recommendations. 58 FR 35460, July 1, 1993.

To find that placing a substance temporarily into schedule I of the CSA is necessary to avoid an imminent hazard to the public safety, the Administrator is required to consider three of the eight factors set forth in section 201(c) of the CSA, 21 U.S.C. 811(c): The substance's history and current pattern of abuse; the scope, duration and significance of abuse; and what, if any, risk there is to the public health. 21 U.S.C. 811(h)(3). Consideration of these factors includes actual abuse, diversion from legitimate channels, and clandestine importation, manufacture, or distribution. 21 U.S.C. 811(h)(3).

A substance meeting the statutory requirements for temporary scheduling may only be placed into schedule I. 21 U.S.C. 811(h)(1). Substances in schedule I are those that have a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. **21 U.S.C. 812**(b)(1). Available data and information for furanyl fentanyl, summarized below, indicate that this synthetic opioid has a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. The DEA's updated three-factor analysis, and the Assistant Secretary's July 8, 2016, letter, are available in their entirety under the tab "Supporting Documents" of the public docket of this action at www.regulations.gov under FDMS Docket ID: DEA-2016-0018 (Docket Number DEA-448).

Factor 4. History and Current Pattern of Abuse

The recreational abuse of fentanyl-like substances continues to be a significant concern. These substances are distributed to users with often unpredictable outcomes. Furanyl fentanyl has recently been encountered by law enforcement and public health officials and the adverse health effects and outcomes are documented in the scientific literature. The documented negative effects of furanyl fentanyl are consistent with those of other opioids. On October 1, 2014, the DEA implemented STARLiMS (a Web-based, commercial laboratory information management system) to replace the System to Retrieve Information from Drug Evidence (STRIDE) as its laboratory drug evidence data system of record. DEA laboratory data submitted after September 30, 2014, are reposited in STARLiMS; data from STRIDE and STARLiMS were queried on November 2, 2016. STARLiMS registered 113

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reports containing furanyl fentanyl, all reported in 2016, from Alabama, California, Connecticut, Delaware, Florida, Georgia, Illinois, Maryland, Mississippi, Missouri, Montana, New Jersey, New York, North Carolina, North Dakota, Rhode Island, Tennessee, Texas, Utah, Virginia, Wisconsin, West Virginia, and the District of Columbia.

The National Forensic Laboratory Information System (NFLIS) is a national drug forensic laboratory reporting system that systematically collects results from drug chemistry analyses conducted by participating Federal, State and local forensic laboratories across the country. According to NFLIS, the first report of furanyl fentanyl was recorded in December 2015 in Oregon. From December 2015 through September 2016, a total of 494 submissions to state and local forensic laboratories identifying furanyl fentanyl were reported in NFLIS as a result of law enforcement encounters in California, Connecticut, Florida, Iowa, Kentucky, Massachusetts, Minnesota, Missouri, New Jersey, North Dakota, Ohio, Oklahoma, Oregon, Pennsylvania, Virginia, and Wisconsin (query date: November 2, 2016). The DEA is not aware of any laboratory identifications of furanyl fentanyl prior to 2015.

Evidence suggests that the pattern of abuse of fentanyl analogues, including furanyl fentanyl, parallels that of heroin and prescription opioid analgesics. Seizures of furanyl fentanyl have been encountered in powder form. Furanyl fentanyl has also been encountered in drug paraphernalia commonly associated with heroin or oth opioid abuse including glassine bags, and as a residue on spoons and bottle caps. Furanyl fentanyl has been encountered as a single substance as well as in combination with other substances of abuse, including heroin, fentanyl, butyryl fentanyl, and U-47700. Furanyl fentanyl has been connected to fatal overdoses, in which intravenous routes of administration are documented.

Factor 5. Scope, Duration and Significance of Abuse

The scientific literature and reports collected by the DEA demonstrate furanyl fentanyl is being abused for its opioid properties. This abuse of furanyl fentanyl has resulted in morbidity and mortality (see updated DEA 3-Factor Analysis for full discussion). The DEA has received reports for at least 128 confirmed fatalities associated with furanyl fentanyl. The information on these deaths occurring in 2015 and 2016 was collected from email communications or toxicology and medical examiner reports received by the DEA. These deaths were reported from five states--Illinois (36), Maryland (41), New Jersey (1), North Carolina (49), and Ohio (1). The scientific literature notes additional fatal overdoses connected to furanyl fentanyl. STARLiMS and NFLIS have a total of 607 drug reports in which furanyl fentanyl was identified in drug exhibits submitted to forensic laboratories from December 2015 through September 2016 from law enforcement encounters. It is likely that the prevalence of furanyl fentanyl in opioid analgesic-related emergency room admissions and deaths is underreported as standard immunoassays may not differentiate this substance from fentanyl.

The population likely to abuse furanyl fentanyl overlaps with the population abusing prescription opioid analgesics and heroin. This is evidenced by the routes of drug administration and drug use history documented in furanyl fentanyl fatal overdose cases. Because abusers of furanyl fentanyl are likely to obtain this substance through unregulated sources (i.e. on-line purchases or drug dealers), the identity, purity, and quantity are uncertain and inconsistent, thus posing significant adverse health risks to the end user. Individuals who initiate (i.e. use a drug for the first time) furanyl fentanyl abuse are likely to be at risk of developing substance use disorder, overdose, and death similar to that of other opioid analgesics (e.g., fentanyl, morphine, etc.).

Factor 6. What, if Any, Risk There Is to the Public Health

Furanyl fentanyl exhibits pharmacological profiles similar to that of fentanyl and other [micro]-opioid receptor agonists. The toxic effects of furanyl fentanyl in humans are demonstrated by overdose fatalities involving this substance. Abusers of furanyl fentanyl may not know the origin, identity, or purity of this substance, thus posing significant adverse health risks when compared to abuse of pharmaceutical preparations of opioid analgesics, such as morphine and oxycodone.

Based on reports in the scientific literature and information received by the DEA, the abuse of furanyl fentanyl leads to the same qualitative public health risks as heroin, fentanyl and other opioid analgesic substances. As with any non-medically approved opioid, the health and safety risks for users are great. The public health risks attendant to the abuse of heroin and opioid analgesics are well established and have resulted in large numbers of drug treatment admissions, emergency department visits, and fatal overdoses. Furanyl fentanyl has been associated with a number of fatalities and non-fatal overdoses as detailed in the scientific literature. The DEA has received information connecting furanyl fentanyl to at least 128 confirmed overdose deaths occurring in 2015 and 2016 in Illinois (36), Maryland (41), New Jersey (1), North Carolina (49), and Ohio (1).

Finding of Necessity of Schedule I Placement To Avoid Imminent Hazard to Public Safety

In accordance with **21 U.S.C. 811**(h)(3), based on the data and information summarized above, the continued uncontrolled manufacture, distribution, importation, exportation, and abuse of furanyl fentanyl pose an imminent hazard to the public safety. The DEA is not aware of any currently accepted medical uses for this substance in treatment in the United States. A substance meeting the statutory requirements for temporary scheduling, 21 U.S.C. 811(h)(1), may only be placed into schedule I. Substances in schedule I are those that have a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. Available data and information for furanyl fentanyl indicate that this substance has a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. As required by section 201(h)(4) the CSA, 21 U.S.C. 811(h)(4), the Administrator, through a letter dated June 22, 2016, notified the Assistant Secretary of the DEA's intention to temporarily place th substance into schedule I.

Conclusion

In accordance with the provisions of section 201(h) of the CSA, 21 U.S.C. 811(h), the Administrator considered available data and information, herein sets forth the grounds for his determination that it is necessary to temporarily schedule furanyl fentanyl into schedule I of the CSA, and finds that placement of this synthetic opioid into schedule I of the CSA is necessary to avoid an imminent hazard to the public safety. Because the Administrator hereby finds it necessary to temporarily place this synthetic opioid into schedule I to avoid an imminent hazard to the public safety, this final order temporarily scheduling furanyl fentanyl will be effective on the date of publication in the Federal Register, and will be in effect for a period of two

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[redacted]rs, with a possible extension of one additional year, pending completion of the regular (permanent) scheduling process. 21 U.S.C. 811(h) (1) and (2).

[redacted] CSA sets forth specific criteria for scheduling a drug or other substance. Permanent scheduling actions in accordance with **21 U.S.C. 811**(a) are subject to formal [redacted]lemaking procedures done "on the record after opportunity for a hearing" conducted pursuant to the provisions of 5 U.S.C. 556 and 557. 21 U.S.C. 811. The permanent scheduling process of formal rulemaking affords interested parties with appropriate process and the government with any additional relevant information needed to make a determination. Final decisions that conclude the permanent scheduling process of formal rulemaking are subject to judicial review. 21 U.S.C. 877. Temporary scheduling orders are not subject to judicial review. 21 U.S.C. 811(h)(6).

Requirements for Handling

Upon the effective date of this final order, furanyl fentanyl will become subject to the regulatory controls and administrative, civil, and criminal sanctions applicable to the manufacture, distribution, reverse distribution, importation, exportation, engagement in research, and conduct of instructional activities or chemical analysis with, and possession of schedule I controlled substances including the following:

1. *Registration*. Any person who handles (manufactures, distributes, reverse distributes, imports, exports, engages in research, or conducts instructional activities or chemical analysis with, or possesses), or who desires to handle, furanyl fentanyl must be registered with the DEA to conduct such activities pursuant to 21 U.S.C. 822, 823, 957, and 958 and in accordance with 21 CFR parts 1301 and 1312, as of November 29, 2016. Any person who currently handles furanyl fentanyl, and is not registered with the DEA, must submit an application for registration and may not continue to handle furanyl fentanyl as of November 29, 2016, unless the DEA has approved that application for registration pursuant to 21 U.S.C. 822, 823, 957, 958, and in accordance with 21 CFR parts 1301 and 1312. Retail sales of schedule I controlled substances to the general public are not allowed under the CSA. Possession of any quantity of this substance in a manner not authorized by the CSA on or after November 29, 2016 is unlawful and those in possession of any quantity of this substance may be subject to prosecution pursuant to the CSA.

2. *Disposal of stocks*. Any person who does not desire or is not able to obtain a schedule I registration to handle furanyl fentanyl, must surrender all quantities of currently held furanyl fentanyl.

3. *Security*. Furanyl fentanyl is subject to schedule I security requirements and must be handled and stored pursuant to **21 U.S.C. 821**, **823**, **871**(b), and in accordance with **21 CFR 1301.71-1301.93**, as of November 29, 2016.

4. *Labeling and packaging*. All labels, labeling, and packaging for commercial containers of furanyl fentanyl must be in compliance with 21 U.S.C. 825, 958(e), and be in accordance with **21 CFR part 1302**. Current DEA registrants shall have 30 calendar days from November 29, 2016, to comply with all labeling and packaging requirements.

5. *Inventory*. Every DEA registrant who possesses any quantity of furanyl fentanyl on the effective date of this order must take an inventory of all stocks of this substance on hand, pursuant to 21 U.S.C. 827 and 958, and in accordance with 21 CFR 1304.03, 1304.04, and 1304.11. Current DEA registrants shall have 30 calendar days from the effective date of this order to be in compliance with all inventory requirements. After the initial inventory, every DEA registrant must take an inventory of all controlled substances (including furanyl fentanyl) on hand on a biennial basis, pursuant to **21 U.S.C. 827** and **958**, and in accordance with **21 CFR 1304.03, 1304.04, and 1304.11.**

6. *Records*. All DEA registrants must maintain records with respect to furanyl fentanyl pursuant to 21 U.S.C. 827 and 958, and in accordance with **21 CFR parts 1304**, and **1312**, **1317** and Sec. **1307.11**. Current DEA registrants shall have 30 calendar days from the effective date of this order to be in compliance with all recordkeeping requirements.

[redacted] *Reports*. All DEA registrants who manufacture or distribute furanyl fentanyl must submit reports pursuant to 21 U.S.C. 827 and in accordance with 21 CFR parts [redacted]4, and 1312 as of November 29, 2016.

[redacted]. *Order Forms*. All DEA registrants who distribute furanyl fentanyl must comply with order form requirements pursuant to **21 U.S.C. 828** and in accordance with 21 CFR part 1305 as of November 29, 2016.

9. *Importation and Exportation*. All importation and exportation of furanyl fentanyl must be in compliance with **21 U.S.C. 952**, **953**, **957**, **958**, and in accordance with **21 CFR part 1312** as of November 29, 2016.

10. *Quota*. Only DEA registered manufacturers may manufacture furanyl fentanyl in accordance with a quota assigned pursuant to **21 U.S.C. 826** and in accordance with **21 CFR part 1303** as of November 29, 2016.

11. *Liability*. Any activity involving furanyl fentanyl not authorized by, or in violation of the CSA, occurring as of November 29, 2016, is unlawful, and may subject the person to administrative, civil, and/or criminal sanctions.

Regulatory Matters

Section 201(h) of the CSA, 2**1 U.S.C. 811**(h), provides for a temporary scheduling action where such action is necessary to avoid an imminent hazard to the public safety. As provided in this subsection, the Attorney General may, by order, schedule a substance in schedule I on a temporary basis. Such an order may not be issued before the expiration of 30 days from (1) the publication of a notice in the Federal Register of the intention to issue such order and the grounds upon which such order is to be issued, and (2) the date that notice of the proposed temporary scheduling order is transmitted to the Assistant Secretary. 21 U.S.C. 811(h)(1).

Inasmuch as section 201(h) of the CSA directs that temporary scheduling actions be issued by order and sets forth the procedures by which such orders are to be issued, the DEA believes that the notice and comment requirements of the Administrative Procedure Act (APA) at 5 U.S.C. 553, do not apply to this temporary scheduling action. In the alternative, even assuming that this action might be subject to 5 U.S.C. 553, the Administrator finds that there is good cause to forgo the notice and comment requirements of 5 U.S.C. 553, as any further delays in the process for issuance of temporary scheduling orders would be impracticable and contrary to the public interest in view of the manifest urgency to avoid an imminent hazard to the public safety.

Further, the DEA believes that this temporary scheduling action is not a "rule" as defined by 5 U.S.C. 601(2), and, accordingly, is not subject to the requirements of the Regulatory Flexibility Act. The requirements for the preparation of an initial regulatory flexibility analysis in 5 U.S.C. 603(a) are not applicable where, as here, the DEA is not required by the APA or any other law to publish a general notice of proposed rulemaking.

Additionally, this action is not a significant regulatory action as defined by Executive Order 12866 (Regulatory Planning and Review), section 3(f), and, accordingly, this action has not been reviewed by the Office of Management and Budget (OMB).

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This action will not have substantial direct effects on the States, on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government. Therefore, in accordance with Executive Order 13132 (Federalism) it is determined that this action does not have sufficient federalism implications to warrant the preparation of a Federalism Assessment.

[redacted] noted above, this action is an order, not a rule. Accordingly, the Congressional Review Act (CRA) is inapplicable, as it applies only to rules. However, if this were a [redacted]e, pursuant to the Congressional Review Act, "any rule for which an agency for good cause finds that notice and public procedure thereon are impracticable, [redacted]nnecessary, or contrary to the public interest, shall take effect at such time as the federal agency promulgating the rule determines." 5 U.S.C. 808(2). It is in the public interest to schedule this substance immediately to avoid an imminent hazard to the public safety. This temporary scheduling action is taken pursuant to 21 U.S.C. 811(h), which is specifically designed to enable the DEA to act in an expeditious manner to avoid an imminent hazard to the public safety. 21 U.S.C. 811(h) exempts the temporary scheduling order from standard notice and comment rulemaking procedures to ensure that the process moves swiftly. For the same reasons that underlie 21 U.S.C. 811(h), that is, the DEA's need to move quickly to place this substance into schedule I because it poses an imminent hazard to the public safety, it would be contrary to the public interest to delay implementation of the temporary scheduling order. Therefore, this order shall take effect immediately upon

its publication. The DEA has submitted a copy of this final order to both Houses of Congress and to the Comptroller General, although such filing is not required under the Small Business Regulatory Enforcement Fairness Act of 1996 (Congressional Review Act), 5 U.S.C. 801-808 because, as noted above, this action is an order, not a rule.

List of Subjects in 21 CFR Part 1308

Administrative practice and procedure, Drug traffic control, Reporting and recordkeeping requirements.

- For the reasons set out above, the DEA amends 21 CFR Part 1308 as follows:

PART 1308--SCHEDULES OF CONTROLLED SUBSTANCES

- 1. The authority citation for part 1308 continues to read as follows:

Authority: 21 U.S.C. 811, 812, 871(b), unless otherwise noted.

- 2. Amend Sec. 1308.11 by adding paragraph (h)(19) to read as follows:

Sec. 1308.11 Schedule I.

* * * * *

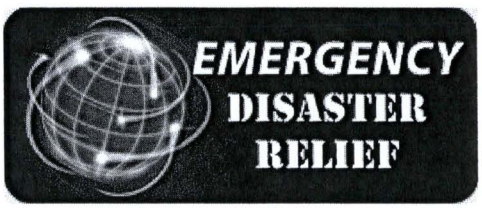
(h) * * *

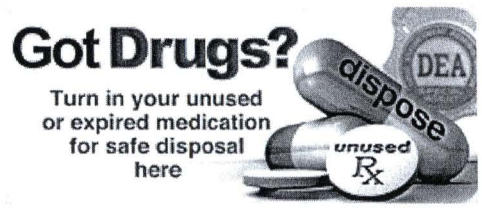
(19) N-(1-phenethylpiperidin-4-yl)-N-phenylfuran-2-carboxamide, its isomers, esters, ethers, salts and salts of isomers, esters and ethers (Other name: Furanyl fentanyl) (9834).

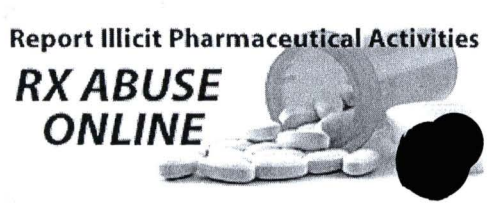
Dated: November 22, 2016

Chuck Rosenberg,
Acting Administrator.

[FR Doc. 2016-28693 Filed 11-28-16; 8:45 am]
BILLING CODE 4410-09-P







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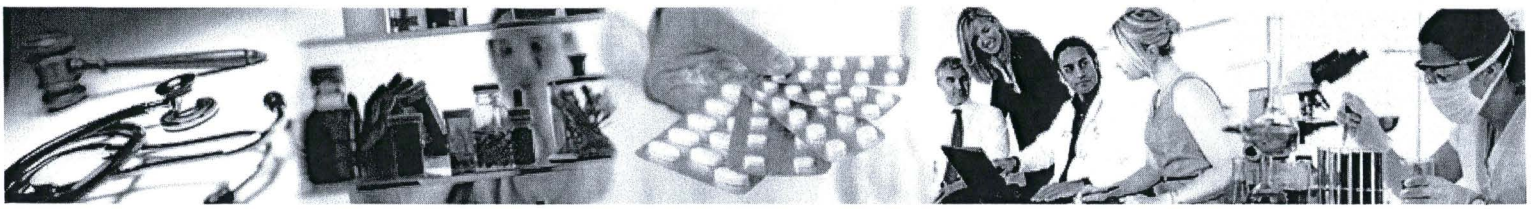

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[FR Doc No: 2016-11245]

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA-435]

Schedules of Controlled Substances: Placement of Brivaracetam Into Schedule V

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Interim final rule, with request for comments.

SUMMARY: The Drug Enforcement Administration is placing the substance brivaracetam ((2S)-2-[(4R)-2-oxo-4-propylpyrrolidin-1-yl] butanamide) (also referred to as BRV; UCB-34714; Briviact) (including its salts) into schedule V of the Controlled Substances Act. This scheduling action is pursuant to the Controlled Substances Act, as revised by the Improving Regulatory Transparency for New Medical Therapies Act which was signed into law on November 25, 2015.

DATES: The effective date of this rulemaking is May 12, 2016. Interested persons may file written comments on this rulemaking in accordance with **21 CFR 1308.43** (g). Electronic comments must be submitted, and written comments must be postmarked, on or before June 13, 2016. Commenters should be aware that the electronic Federal Docket Management System will not accept comments after 11:59 p.m. Eastern Time on the last day of the comment period.

Interested persons, defined at **21 CFR 1300.01** as those "adversely affected or aggrieved by any rule or proposed rule issuable pursuant to section 201 of the Act (**21 U.S.C. 811**)," may file a request for hearing or waiver of hearing pursuant to **21 CFR 1308.44**. Requests for hearing and waivers of an opportunity for a hearing or to participate in a hearing must be received on or before June 13, 2016.

ADDRESSES: To ensure proper handling of comments, please reference "Docket No. DEA-435" on all correspondence, including any attachments.

- *Electronic comments:* The Drug Enforcement Administration encourages that all comments be submitted electronically through the Federal eRulemaking Portal, which provides the ability to type short comments directly into the comment field on the Web page or attach a file for lengthier comments. Please go to http://www.regulations.gov and follow the online instructions at that site for submitting comments. Upon completion of your submission, you will receive a Comment Tracking Number for your comment. Please be aware that submitted comments are not instantaneously available for public view on Regulations.gov. If you have received a Comment Tracking Number, your comment has been successfully submitted and there is no need to resubmit the same comment.
- *Paper comments:* Paper comments that duplicate the electronic submission are not necessary and are discouraged. Should you wish to mail a paper comment in lieu of an electronic comment, it should be sent via regular or express mail to: Drug Enforcement Administration, Attn: DEA Federal Register Representative/ODW, 8701 Morrissette Drive, Springfield, VA 22152.
- *Hearing requests:* All requests for hearing and waivers of participation must be sent to: Drug Enforcement Administration, Attn: Administrator, 8701 Morrissette Drive, Springfield, Virginia 22152. All requests for hearing and waivers of participation should also be sent to: (1) Drug Enforcement Administration, Attn: Hearing Clerk/LJ, 8701 Morrissette Drive, Springfield, Virginia 22152; and (2) Drug Enforcement Administration, Attn: DEA Federal Register Representative/ ODW, 8701 Morrissette Drive, Springfield, Virginia 22152.

FOR FURTHER INFORMATION CONTACT: Barbara J. Boockholdt, Office of Diversion Control, Drug Enforcement Administration; Mailing Address: 8701 Morrissette Drive, Springfield, Virginia 22152; Telephone: (202) 598-6812.

SUPPLEMENTARY INFORMATION:

Posting of Public Comments

Please note that all comments received are considered part of the public record. They will, unless reasonable cause is given, be made available by the Drug Enforcement Administration (DEA) for public inspection online at http://www.regulations.gov. Such information includes personal identifying information (such as your name, address, etc.) voluntarily submitted by the commenter. The Freedom of Information Act (FOIA) applies to all comments received. If you want to submit personal identifying information (such as your name, address, etc.) as part of your comment, but do not want it to be made publicly available, you must include the phrase "PERSONAL IDENTIFYING INFORMATION" in the first paragraph of your comment. You must also place all of the personal identifying information you do not want made publicly available in the first paragraph of your comment and identify what information you want redacted.

If you want to submit confidential business information as part of your comment, but do not want it to be made publicly available, you must include the phrase "CONFIDENTIAL BUSINESS INFORMATION" in the first paragraph of your comment. You must also prominently identify the confidential business information to be redacted within the comment.

Comments containing personal identifying information and confidential business information identified as directed above will generally be made publicly available in redacted form. If a comment has so much confidential business information or personal identifying information that it cannot be effectively redacted, all or part of that comment may not be made publicly available. Comments posted to http://www.regulations.gov may include any personal identifying information (such as name, address, and phone number) included in the text of your electronic submission that is not identified as directed above as confidential.

An electronic copy of this document and supplemental information, including the complete Department of Health and Human Services and Drug Enforcement Administration eight-factor analyses, to this interim final rule are available at http://www.regulations.gov for easy reference.

Request for Hearing, Notice of Appearance at Hearing, or Waiver of Participation in Hearing

Pursuant to **21 U.S.C. 811**(a), this action is a formal rulemaking "on the record after opportunity for a hearing." Such proceedings are conducted pursuant to the provisions of the Administrative Procedure Act (APA), 5 U.S.C. 551-559. **21 CFR 1308.41-1308.45**; **21 CFR part 1316**, subpart D. In accordance with **21 CFR 1308.44**(a)-

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(c), requests for a hearing, notices of appearance, and waivers of an opportunity for a hearing or to participate in a hearing may be submitted only by interested persons, defined as those "adversely affected or aggrieved by any rule or proposed rule issuable pursuant to section 201 of the Act (**21 U.S.C. 811**)." **21 CFR 1300.01**. Requests for a hearing and notices of participation must conform to the requirements of **21 CFR 1308.44**(a) or (b), as applicable, and include a statement of the interest of the person in the proceeding and the objections or issues, if any, concerning which the person desires to be heard. Any waiver of an opportunity for a hearing must conform to the requirements of **21 CFR 1308.44**(c) including a written statement regarding the interested person's position on the matters of fact and law involved in any hearing.

Please note that pursuant to **21 U.S.C. 811**(a), the purpose and subject matter of the hearing are restricted to "(A) find[ing] that such drug or other substance has a potential for abuse, and (B) mak[ing] with respect to such drug or other substance the findings prescribed by subsection (b) of **section 812** of this title for the schedule in which such drug is to be placed. * * *" Requests for a hearing and waivers of participation in the hearing should be submitted to DEA using the address information provided above.

Legal Authority

The DEA implements and enforces titles II and III of the Comprehensive Drug Abuse Prevention and Control Act of 1970, as amended. **21 U.S.C. 801-971**. Titles II and III are referred to as the "Controlled Substances Act" and the "Controlled Substances Import and Export Act," respectively, and are collectively referred to as the "Controlled Substances Act" or the "CSA" for the purpose of this action. The DEA publishes the implementing regulations for these statutes in title 21 of the Code of Federal Regulations (CFR), chapter II. The CSA and its implementing regulations are designed to prevent, detect, and eliminate the diversion of controlled substances and listed chemicals into the illicit market while providing for the legitimate medical, scientific, research, and industrial needs of the United States. Controlled substances have the potential for abuse and dependence and are controlled to protect the public health and safety.

Under the CSA, controlled substances are classified into one of five schedules based upon their potential for abuse, their currently accepted medical use in treatment in the United States, and the degree of dependence the substance may cause. **21 U.S.C. 812**. The initial schedules of controlled substances established by Congress are found at 21 U.S.C. 812(c), and the current list of all scheduled substances is published at **21 CFR part 1308**.

Pursuant to **21 U.S.C. 811**(a)(1), the Attorney General may, by rule, "add to such a schedule or transfer between such schedules any drug or other substance if he * * * finds that such drug or other substance has a potential for abuse, and * * * makes with respect to such drug or other substance the findings prescribed by subsection (b) of **section 812** of this title for the schedule in which such drug is to be placed * * *" The Attorney General has delegated this scheduling authority under 21 U.S.C. 811 to the Administrator of the DEA. 28 CFR 0.100.

The CSA provides that scheduling of any drug or other substance may be initiated by the Attorney General (1) on her own motion; (2) at the request of the Secre of Health and Human Services (HHS); or (3) on the petition of any interested party. **21 U.S.C. 811**(a). This action imposes the regulatory controls and administra civil, and criminal sanctions of schedule V controlled substances for any person who handles or proposes to handle BRV.

The Improving Regulatory Transparency for New Medical Therapies Act (Pub. L. 114-89) was signed into law on November 25, 2015. This law amended **21 U.S.C. 811** and states that in cases where a new drug is (1) approved by the Department of Health and Human Services (HHS) and (2) HHS recommends control in CSA schedule II-V, DEA shall issue an interim final rule scheduling the drug, within 90 days.

The law further states that the 90-day timeframe starts the later of (1) the date DEA receives the HHS scientific and medical evaluation/ scheduling recommendation or (2) the date DEA receives notice of drug approval by HHS. In addition, the law specifies that the rulemaking shall become immediately effective as an interim final rule without requiring the DEA to demonstrate good cause therefor.

Specifically, Public Law 114-89 revised section 201 of the CSA (**21 U.S.C. 811**) by inserting after subsection (i) a new paragraph (j), which requires that with respect to a drug referred to in subsection (f), if the Secretary recommends that the Attorney General control the drug in schedule II, III, IV, or V pursuant to subsections (a) and (b), the Attorney General is required to, within 90 days, issue an interim final rule controlling the drug in accordance with such subsections and **21 U.S.C. 812**(b) using the specified procedures. For purposes of calculating the 90 days, Public Law 114-89 states that such date shall be the later of the date on which the Attorney General receives the scientific and medical evaluation and the scheduling recommendation from the Secretary in accordance with subsection (b), or the date on which the Attorney General receives notification from the Secretary that the Secretary has approved an application under section 505(c), 512, or 571 of the Federal Food, Drug, and Cosmetic Act or section 351(a) of the Public Health Service Act, or indexed a drug under section 572 of the Federal Food, Drug, and Cosmetic Act, with respect to the drug described in paragraph (1). Public Law 114-89 further stipulates that a rule issued by the Attorney General under paragraph (1) becomes immediately effective as an interim final rule without requiring the Attorney General to demonstrate good cause and requires that the interim final rule give interested persons the opportunity to comment and to request a hearing. After the conclusion of such proceedings, the Attorney General must issue a final rule in accordance with the scheduling criteria of subsections **21 U.S.C. 811**(b), (c), and (d) of this section and 21 U.S.C. 812(b).

Background

Brivaracetam ((2S)-2-[(4R)-2-oxo-4-propylpyrrolidin-1-yl] butanamide) (also referred to as BRV; UCB-34714; Briviact) is a new molecular entity with central nervous system (CNS) depressant properties. BRV is known to be a high affinity ligand for the synaptic vesicle protein, SV2A, which is found on excitatory synapses in the brain. On November 22, 2014, UCB Inc. (Sponsor) submitted three New Drug Applications (NDAs) to the U.S. Food and Drug Administration (FDA) for the tablet, oral, and intravenous formulations of BRV. The FDA accepted the NDA filings for BRV on January 21, 2015.

On March 28, 2016 the DEA received notification that HHS/FDA approved BRV as an add-on treatment to other medications to treat partial onset seizures in patients age 16 years and older with epilepsy.

Determination to Schedule BRV

Pursuant to **21 U.S.C. 811**(a)(1), proceedings to add a drug or substance to those controlled under the CSA may be initiated by request of the Secretary

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of the HHS.\1\ On September 8, 2015, the HHS provided the DEA with a scientific and medical evaluation document prepared by the FDA entitled "Basis for the Recommendation to Place Brivaracetam in Schedule V of the Controlled Substances Act." Pursuant to **21 U.S.C. 811**(b), this document contained an eight-factor analysis of the abuse potential of BRV as a new drug, along with the HHS' recommendation to control BRV under schedule V of the CSA.

\1\ As set forth in a memorandum of understanding entered into by the HHS, the FDA, and the National Institute on Drug Abuse (NIDA), the FDA acts as the lead agency within the HHS in carrying out the Secretary's scheduling responsibilities under the CSA, with the concurrence of the NIDA. 50 FR 9518, Mar. 8, 1985. The

Secretary of the HHS has delegated to the Assistant Secretary for Health of the HHS the authority to make domestic drug scheduling recommendations. 58 FR 35460, July 1, 1993.

In response, in December 2015, the DEA reviewed the scientific and medical evaluation and scheduling recommendation provided by the HHS, along with all other relevant data, and completed its own eight-factor review document pursuant to **21 U.S.C. 811**(c). The DEA concluded that BRV met the **21 U.S.C. 812**(b)(5) criteria for placement in schedule V of the CSA. Subsequently, on March 28, 2016, the DEA received notification that HHS/FDA approved three NDAs for BRV (see Background section).

Pursuant to the provisions of the Improving Regulatory Transparency for New Medical Therapies Act (Pub. L. 114-89), and based on the HHS recommendation, NDA approvals by HHS/FDA, and DEA's determination, DEA is issuing this interim final rule to schedule brivaracetam ((2S)-2-[(4R)-2-oxo-4-propylpyrrolidin-1-yl] butanamide) (including its salts) as a controlled substance under the CSA.

Included below is a brief summary of each factor as analyzed by the HHS and the DEA, and as considered by the DEA in its scheduling action. Please note that both the DEA and HHS analyses are available in their entirety under "Supporting Documents" in the public docket for this interim final rule at http://www.regulations.gov, under Docket Number "DEA-435." Full analysis of, and citations to, the information referenced in the summary may also be found in the supporting and related material.

1. *The Drug's Actual or Relative Potential for Abuse:* BRV is a new chemical entity and has not been marketed in the United States or in any other country; information on actual abuse of BRV is not available. The HHS characterized BRV as related in its action to lacasamide and ezogabine, which are both schedule V CNS depressant anti-epileptics (AEDs). Based on data submitted by the Sponsor in their NDAs, the HHS indicated that administration of BRV in mice, rats, and dogs resulted in CNS depressant effects, including decreased locomotor activity and reactivity, motor incoordination, and ataxia.

BRV is not self-administered in animals and, unlike schedule IV benzodiazepines and the schedule III AED perampanel, lacks pentobarbital-like (schedule II) discriminative stimulus and reinforcing effects (HHS review, 2015). In humans, BRV is most similar to the schedule V AEDs lacosamide, ezogabine, and pregabalin in producing positive subjective effects without producing sedation and withdrawal following drug discontinuation that is observed with schedule IV benzodiazepines. Based on this collective evidence, the HHS concluded that BRV has an abuse potential that is most similar to AEDs in schedule V.

2. *Scientific Evidence of the Drug's Pharmacological Effects, if Known:* BRV selectively binds with high affinity to synaptic vesicle protein 2A (SV2A). It produces reverse inhibition caused by negative modulators of gamma aminobutyric acid (GABA) and glycine and inhibits sodium (Na+) channels. These sites appear to underlie pharmacological activity of BRV.

In rats, BRV at high doses partially generalizes to the schedule IV benzodiazepine chlordiazepoxide. BRV, across a wide range of doses, neither initiates nor maintains self-administration in rats trained to self-administer cocaine. Human studies have reported that healthy individuals may experience euphoria, sedation, and a drunken-like feeling following BRV administration. When treatment-emergent adverse events (TEAEs) \2\ were pooled across several clinical BRV studies, the most common TEAEs were dizziness and sedative-related events such as fatigue, extreme drowsiness, and extreme weakness. In a human abuse potential study, the oral abuse potential, safety, tolerability, and pharmacokinetics of BRV (50 mg, 200 mg, and 1000 mg) were compared to 1.5 and 3.0 mg of the schedule IV CNS depressant alprazolam (ALP) and placebo. When surveyed, for all doses of BRV, there was an increase of drug likability, feeling of a high, and taking the drug again in comparison to placebo. The HHS mentioned that individuals who took BRV had fewer sedative, euphoric, stimulant, dizziness, and overall negative subjective effects compared to ALP.

\2\ Treatment-emergent adverse event (TEAE): An event or unexpected medical occurrence (e.g. adverse event) which first appears during treatment with a drug or substance. TEAEs are typically absent prior to the onset of treatment or would have been exacerbated relative to pre-treatment conditions.

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3. *The State of Current Scientific Knowledge Regarding Brivaracetam:* The chemical name for brivaracetam is (2S)-2-[(4R)-2-oxo-4-propylpyrrolidin-1-yl] butanamide. Other names include BRV and UCB-34714. The Chemical Abstract Services number (CAS #) of BRV is: 357336-20-0. BRV is a racetam derivative.\3\ As the HHS noted, BRV does not have structural similarities to any other scheduled AED or to any major classes of abused sedative drugs with noted euphoric effects. Chemical synthesis of BRV is considered highly complex and includes several steps, reagents and specialized equipment.

\3\ Racetams are a class of drugs that have a pyrrolidoline center.

BRV is readily soluble in water at up to 700 mg/mL. In an in vitro oral tablet dissolution evaluation, BRV oral tablets were placed in a buffer (pH 6.4) for 16 hours. Approximately 86-96% of BRV was released after 16 hours in the buffer; 14-30% of BRV was released following 1 hour and 40-66% BRV was released after 4 hours.

Following oral ingestion, BRV is rapidly and completely absorbed. In healthy young males, the half-life of BRV was determined to be approximately 9 hours. According to the HHS, the half-life of BRV is decreased to 6 hours when a repeated oral dose of 800 mg/day BRV is administered. The HHS noted that BRV binds weakly to plasma proteins and is extensively metabolized through several pathways. Clearance through the kidneys represents 5-10% of the total clearance and only 3-7% of the parent compound (BRV) was detected in the urine. The three main metabolites of BRV were detected in urine and according to the HHS, these metabolites are relatively inactive. One BRV metabolite was characterized as having a potency that was 20 times less than BRV, and this metabolite was not detected in human plasma and represented less than 3% of the dose in urine.

4. *Its History and Current Pattern of Abuse:* As noted by the HHS, information on the history and current pattern of abuse of BRV is not available since this drug is currently not marketed in any country. A review of the animal and human data indicates that BRV has an abuse potential similar to other schedule V AEDs. If BRV were to be

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approved for medical use, the HHS indicated that BRV would be abused for its euphoric properties and other abuse-related TEAEs that were reported in human clinical studies. Based on the available information, the HHS concluded that the history and pattern of abuse of BRV will be similar to other schedule V CNS depressants.

5. *The Scope, Duration, and Significance of Abuse:* As noted by the HHS, information on the scope, duration, and significance of abuse of BRV is not available since this drug is currently not marketed in any country. Results from animal and human studies suggest that there is abuse potential associated with BRV and if marketed in the United States, it is likely that BRV will be abused similar to other AEDs that are CNS depressants. The HHS stated that it is unlikely that epileptic individuals (the population expected to take this drug) will abuse BRV. The HHS concluded that based on abuse potential similarities between BRV and other schedule V AEDs, it is likely that the scope, duration, and significance of abuse of BRV will be similar to these compounds.

6. *What, if any, Risk There is to the Public Health:* The HHS characterized BRV's drug abuse potential to be similar to schedule V AEDs. As such, the public health risk with BRV will also be similar to other schedule V AEDs. The HHS noted that if BRV were approved for medical use, it would be abused for its rewarding properties. In healthy volunteers administered 600 mg or higher of BRV, cognitive and motor impairment and sedation were observed. It is unknown how BRV would interact in combination with other CNS depressants and if the sedative effects would be additive or even a lethal combination. In an interaction study with BRV and intravenous ethanol in healthy individuals, it was determined that BRV enhanced the effects of ethanol.

7. *Its Psychic or Physiological Dependence Liability:* BRV has limited psychological dependence and does not appear to have physical dependence. When rats were administered BRV for 30 days, no signs of physical dependence were noted in comparison to the schedule IV comparator, chlordiazepoxide. Similarly, in human clinical studies with healthy volunteers, there were no reports or adverse events that noted physical dependence or a withdrawal syndrome associated with BRV use. The low potential for physical dependence observed with BRV is consistent with other schedule V AEDs. There is limited evidence for psychological dependence with BRV. Clinical studies have reported individuals experiencing increasing euphoria with increasing doses of BRV. Tolerance does not appear to develop with respect to BRV treatment on epileptic seizure reduction.

8. *Whether the Substance is an Immediate Precursor of a Substance Already Controlled under the CSA:* BRV is not an immediate precursor of any controlled substance.

Conclusion: After considering the scientific and medical evaluation conducted by the HHS, the HHS' recommendation, and its own eight-factor analysis, the DEA has determined that these facts and all relevant data constitute substantial evidence of a potential for abuse of BRV. As such, the DEA hereby schedules BRV as a controlled substance under the CSA.

Determination of Appropriate Schedule

The CSA outlines the findings required to place a drug or other substance in any particular schedule (I, II, III, IV, or V). **21 U.S.C. 812**(b). After consideration of the analysis and recommendation of the Assistant Secretary for Health of the HHS and review of all available data, the Acting Administrator of the DEA, pursuant to 2[redacted] U.S.C. 812(b)(5), finds that:

1. BRV has a low potential for abuse relative to the drugs or other substances in schedule IV. The overall abuse potential of BRV is comparable to schedule V controlled substances such as ezogabalin, pregabalin, and lacosamide;

2. With FDA's approval of the new drug applications, BRV has a currently accepted medical use in the United States as adjunctive treatment of partial onset seizures in epileptic individuals ages 16 and older; and

3. Human and animal studies demonstrate that BRV has limited psychological dependence and does not appear to have physical dependence. There was no evidence of physical dependence associated with BRV in human and animal studies since there have been no reports of withdrawal syndromes or other physical dependence effects. Based on these data, abuse of BRV may lead to limited psychological dependence similar to schedule V AEDs but less than that of drugs in schedule IV.

Based on these findings, the Acting Administrator of the DEA concludes that brivaracetam ((2S)-2-[(4R)-2-oxo-4-propylpyrrolidin-1-yl] butanamide) (also referred to as BRV; UCB-34714; Briviact), including its salts, warrants control in schedule V of the CSA. **21 U.S.C. 812**(b)(5).

Requirements for Handling Brivaracetam

BRV is subject to the CSA's schedule V regulatory controls and administrative, civil, and criminal sanctions applicable to the manufacture, distribution, reverse distribution, dispensing, importing, exporting, research, and conduct of instructional activities and chemical analysis with, and possession involving schedule V substances, including the following:

1. *Registration.* Any person who handles (manufactures, distributes, reverse distributes, dispenses, imports, exports, engages in research, or conducts instructional activities or chemical analysis with, or possesses) BRV, or who desires to handle BRV, must be registered with the DEA to conduct such activities pursuant to **21 U.S.C. 822**, **823**, **957**, and **958** and in accordance with **21 CFR parts 1301** and **1312**. Any person who currently handles BRV, and is not registered with the DEA, must submit an application for registration and may not continue to handle BRV, unless the DEA has approved that application for registration, pursuant to 21 U.S.C. 822, 823, 957, and 958, and in accordance with 21 CFR parts 1301 and 1312.

2. *Disposal of stocks.* Any person who does not desire or is not able to obtain a schedule V registration must surrender all quantities of currently held BRV, or may transfer all quantities of currently held BRV to a person registered with the DEA in accordance with **21 CFR part 1317**, in additional to all other applicable federal, state, local, and tribal laws.

3. *Security.* BRV is subject to schedule III-V security requirements and must be handled and stored pursuant to **21 U.S.C. 821**, **823**, and **871**(b), and in accordance with **21 CFR 1301.71-1301.93**.

4. *Labeling and Packaging.* All labels, labeling, and packaging for commercial containers of BRV must comply with **21 U.S.C. 825** and **958**(e), and be in accordance with **21 CFR part 1302**.

5. *Inventory.* Every DEA registrant who possesses any quantity of BRV must take an inventory of BRV on hand, pursuant to **21 U.S.C. 827** and **958**, and in accordance with **21 CFR 1304.03**, **1304.04**, and **1304.11**.

Any person who becomes registered with the DEA must take an initial inventory of all stocks of controlled substances (including BRV) on hand on the date the registrant first engages in the handling of controlled substances, pursuant to **21 U.S.C. 827** and **958**, and in accordance with **21 CFR 1304.03**, **1304.04**, and **1304.11**.

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After the initial inventory, every DEA registrant must take a new inventory of all stocks of controlled substances (including BRV) on hand every two years, pursuant to **21 U.S.C. 827** and **958**, and in accordance with **21 CFR 1304.03**, **1304.04**, and **1304.11**.

6. *Records and Reports.* Every DEA registrant must maintain records and submit reports for BRV, or products containing BRV, pursuant to **21 U.S.C. 827** and **958**(e), and in accordance with **21 CFR parts 1304**, **1312**, and **1317**.

7. *Prescriptions.* All prescriptions for BRV or products containing BRV must comply with **21 U.S.C. 829**, and be issued in accordance with **21 CFR parts 1306** and **1311**, subpart C.

8. *Importation and Exportation.* All importation and exportation of BRV must be in compliance with **21 U.S.C. 952**, **953**, **957**, and **958**, and in accordance with **21 CFR part 1312**.

9. *Liability.* Any activity involving BRV not authorized by, or in violation of, the CSA or its implementing regulations, is unlawful, and may subject the person to administrative, civil, and/or criminal sanctions.

Regulatory Analyses

Administrative Procedure Act

Public Law 114-89 was signed into law, amending **21 U.S.C. 811**. This amendment provides that in cases where a new drug is (1) approved by the Department of Health and Human Services (HHS) and (2) HHS recommends control in CSA schedule II-V, the DEA shall issue an interim final rule scheduling the drug within 90 days. Additionally, the law specifies that the rulemaking shall become immediately effective as an interim final rule without requiring the DEA to demonstrate good cause. Therefore, the DEA has determined that the notice and comment requirements of section 553 of the APA, 5 U.S.C. 553, do not apply to this scheduling action.

Executive Orders 12866, Regulatory Planning and Review, and 13563, Improving Regulation and Regulatory Review

In accordance with Public Law 114-89, this scheduling action is subject to formal rulemaking procedures performed "on the record after opportunity for a hearing," which are conducted pursuant to the provisions of 5 U.S.C. 556 and 557. The CSA sets forth the procedures and criteria for scheduling a drug or other substance. Such actions are exempt from review by the Office of Management and Budget (OMB) pursuant to section 3(d)(1) of Executive Order 12866 and the principles reaffirmed in Executive Order 13563.

Executive Order 12988, Civil Justice Reform

This regulation meets the applicable standards set forth in sections 3(a) and 3(b)(2) of Executive Order 12988 to eliminate drafting errors and ambiguity, minimize litigation, provide a clear legal standard for affected conduct, and promote simplification and burden reduction.

Executive Order 13132, Federalism

This rulemaking does not have federalism implications warranting the application of Executive Order 13132. The rule does not have substantial direct effects on the States, on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government.

Executive Order 13175, Consultation and Coordination With Indian Tribal Governments

This rule does not have tribal implications warranting the application of Executive Order 13175. It does not have substantial direct effects on one or more Indian tribes, on the relationship between the Federal government and Indian tribes, or on the distribution of power and responsibilities between the Federal government and Indian tribes.

Regulatory Flexibility Act

In accordance with 5 U.S.C. 603(a), "[w]henever an agency is required by [5 U.S.C. 553], or any other law, to publish general notice of proposed rulemaking for any proposed rule, or publishes a notice of proposed rulemaking for an interpretive rule involving the internal revenue laws of the United States, the agency shall prepare and make available for public comment an initial regulatory flexibility analysis." As noted in the above discussion regarding applicability of the Administrative Procedure Act, the DEA has determined that the notice and comment requirements of section 553 of the APA, 5 U.S.C. 553, do not apply to this scheduling action. Consequently, the RFA does not apply to this interim final rule.

Unfunded Mandates Reform Act of 1995

In accordance with the Unfunded Mandates Reform Act (UMRA) of 1995, 2 U.S.C. 1501 et seq., the DEA has determined and certifies that this action would not result in any Federal mandate that may result "in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted for inflation) in any one year." Therefore, neither a Small Government Agency Plan nor any other action is required under UMRA of 1995.

Paperwork Reduction Act of 1995

This action does not impose a new collection of information requirement under the Paperwork Reduction Act of 1995. 44 U.S.C. 3501-3521. This action would not impose recordkeeping or reporting requirements on State or local governments, individuals, businesses, or organizations. An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Congressional Review Act

This rule is not a major rule as defined by section 804 of the Small Business Regulatory Enforcement Fairness Act of 1996 (Congressional Review Act (CRA)). This rule will not result in: An annual effect on the economy of $100,000,000 or more; a major increase in costs or prices for consumers, individual industries, Federal, State, or local government agencies, or geographic regions; or significant adverse effects on competition, employment, investment, productivity, innovation, or on the ability of U.S.-based companies to compete with foreign based companies in domestic and export markets. However, pursuant to the CRA, the DEA has submitted a copy of this interim final rule to both Houses of Congress and to the Comptroller General.

List of Subjects in 21 CFR Part 1308

Administrative practice and procedure, Drug traffic control, Reporting and recordkeeping requirements.

For the reasons set out above, the DEA amends 21 CFR part 1308:

PART 1308--SCHEDULES OF CONTROLLED SUBSTANCES

- 1. The authority citation for 21 CFR part 1308 continues to read as follows:

  Authority: 21 U.S.C. 811, 812, 871(b), unless otherwise noted.

- 2. Amend **Sec. 1308.15** by redesignating paragraphs (e)(1) through (e)(3) as paragraphs (e)(2) through (e)(4) and adding new paragraph (e)(1) to read as follows:

Sec. 1308.15 Schedule V.

* * * * *

(e) * * *

[Page 29492]]

(1) Brivaracetam ((2S)-2-[(4R)-2-oxo-4-propylpyrrolidin-1-yl]butanamide) (also referred to as BRV; UCB–34714; Briviact) (including its salts) 2710

* * * * *

Dated: May 6, 2016.

Chuck Rosenberg,
Acting Administrator.

[FR Doc. 2016-11245 Filed 5-11-16; 8:45 am]

BILLING CODE 4410-09-P

GW pharmaceuticals

April 25, 2016

Mark Hardy
Executive Director
North Dakota State Board of Pharmacy
1906 E. Broadway Ave.
Bismarck, ND 58501-1354

Dear Mr. Hardy,

Please allow me to introduce myself. I am the Vice President of U.S. Professional Relations for GW Pharmaceuticals. GW is the developer of Epidiolex®, a pure cannabidiol (CBD) investigational product that is being studied as a potential anti-convulsive treatment for children with certain types of childhood-onset, medication-resistant epilepsies, including Dravet Syndrome and Lennox Gastaut Syndrome (LGS).

We have just announced that the results of our first study in Dravet Syndrome were highly statistically significant in favor of Epidiolex® over placebo. Epidiolex® achieved the primary endpoint of a significant reduction in convulsive seizures assessed over the entire treatment period compared with placebo (p=0.01). The results from our two trials in LGS will become available over the next few months, and the results from our second Dravet study will be available in the second half of the year. I include the press release announcing the first Dravet study results. Epidiolex® has both Orphan Drug Designation and Fast Track Designation from the U.S. Food and Drug Administration (FDA) in the treatment of Dravet syndrome and also Orphan designation for LGS.

Dravet Syndrome is a severe infantile-onset and highly treatment-resistant epileptic syndrome. Over time, people with Dravet Syndrome can develop multiple types of seizures and are prone to prolonged seizures called status epilepticus, which can be life threatening. Risk of premature death including SUDEP (sudden expected death in epilepsy) is elevated in people with Dravet Syndrome. Additionally, the majority will develop moderate to severe intellectual and development disabilities and require lifelong supervision and care. **There are currently no FDA-approved treatments**, and nearly all patients continue to have uncontrolled seizures and other medical needs throughout their lifetime.

Patients with Lennox Gastaut Syndrome commonly have frequent seizures of a wide variety, including convulsive, atonic seizures, which can cause abrupt falls and serious injury. LGS is also highly medication resistant. Most children with LGS experience some degree of impaired intellectual functioning or information processing, as well as developmental delays and behavioral disturbances.

5800 Armada Drive Suite 210 Carlsbad, CA 92008
Telephone: 760-795-2200 - Facsimile: 760-795-2219 - www.gwpharm.com

GW pharmaceuticals

As you can see, there is a pressing need for new treatment options for patients with Dravet Syndrome and LGS. These syndromes have serious consequences for both the patients and for their families.

GW intends to file a New Drug Application with the FDA as soon as possible within the next year. Since Epidiolex has Fast Track status, we hope that the FDA will afford it a Priority Review cycle, which could result in approval within eight months of submission. Because CBD is a purified derivative of the cannabis plant, it is currently classified in Schedule I of the U.S. Controlled Substances Act (CSA). If Epidiolex® were approved by FDA, it would then be rescheduled by DEA to a lower schedule so that it could be prescribed. Under recent federal legislation, that rescheduling should be accomplished within 90 days of FDA approval. Almost all states have their own state controlled drug laws, and CBD is a Schedule I substance under those laws. ***Therefore, despite being approved by FDA and rescheduled by DEA, Epidiolex® could not be made available to patients in your state until it is also rescheduled under state law.*** In summary:

- Late 2016/beginning of 2017 - GW files a New Drug Application with FDA
- Potential FDA approval within 8 months of submission - based on Fast Track status and Priority Review Cycle
- 90 days after FDA approval - DEA reschedules Epidiolex® from Schedule I to lower schedule.
- Subsequently, the state reschedules Epidiolex® under state law similarly to DEA rescheduling.

We understand that your agency is responsible for implementing the administrative process that must occur in order for such rescheduling to take place. Therefore, we are reaching out to you with this information in order to minimize any delays in patient access in your state to a much-needed treatment option.

We would very much like to speak with you in the very near future to provide you with additional information about our research and answer any questions you might have about the development path of Epidiolex®. Thank you so much for considering our request.

Best wishes,

Alice P. Mead

Alice P. Mead
Vice President, U.S. Professional Relations
GW Pharmaceuticals

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For Patients

GW's Epidiolex® Clinical Program

GW is committed to developing new medicines to treat rare, treatment-resistant epilepsy conditions where there are limited or in some cases, no approved treatment options.

Epidiolex is GW's lead cannabinoid product candidate and is a proprietary oral solution of pure plant-derived cannabidiol, or CBD. GW's Epidiolex development is initially concentrating on severe, orphan, early-onset, treatment-resistant epilepsy syndromes including Dravet syndrome, Lennox-Gastaut syndrome (LGS), Tuberous Sclerosis Complex (TSC) and Infantile Spasms (IS).

GW's Epidiolex development includes two distinct programs:

FDA-authorized clinical trials program

- We have commenced a series of clinical trials designed to obtain safety and efficacy data on Epidiolex to provide to the FDA and other regulatory authorities around the world, which is necessary to be considered for approval as a prescription medicine. Target indications currently include Dravet syndrome, Lennox-Gastaut syndrome, Tuberous Sclerosis Complex, and Infantile Spasms. In these trials, eligible patients are randomly assigned to receive Epidiolex or placebo added to their current treatment and evaluated over a specific period of time. These trials are "blinded" meaning that patients, families, and physicians do not know which treatment arm they have been assigned.
- GW's current Phase 3 pivotal trials program for Epidiolex includes two Phase 3 trials in Dravet syndrome, two in LGS, one in TSC, and one in IS. The first two of these Phase 3 trials, one in Dravet syndrome and one in LGS, have showed significantly greater reductions in specific seizure types for patients taking Epidiolex compared to those taking placebo. (see GW press releases: 14 March 2016 & 27 June 2016, 26 September 2016).
- To learn more about GW's Epidiolex clinical trials please see the ClinicalTrials.gov website here.
- Link to a form for your health care professional to fill out to reach GW's medical affairs group. Please note: You must be a health care professional (HCP) to fill out this form. By clicking submit, you are confirming you are a health care professional. Please do not include any patient-identifying information.

FDA-authorized, independent Physician-led program or Expanded Access (which are at times called Compassionate Use programs in some countries) and for which GW supplies Epidiolex*

- The FDA may authorize expanded access programs to facilitate access to investigational drugs for treatment use for patients with a serious or immediately life-threatening disease or condition who lack therapeutic alternatives. This is done through FDA granting Investigational New Drug (IND) applications.
- The FDA has granted individual patient emergency INDs to physicians as well as INDs to physicians and state programs to treat groups of patients suffering from intractable epilepsy with Epidiolex.
- The most recent physician-reported data from this Expanded Access Program was presented in December 2015 at the American Epilepsy Society's annual meeting. Results from 261 patients receiving Epidiolex under these INDs showed promising signals of clinical effect in reducing seizures (link to press release and poster).

Support and Advocacy Organizations

- There are a number of organizations which provide invaluable help, information, and support to people living with epilepsy. They are also a useful resource for caregivers, friends, and relatives. The following list includes links to some websites of patient organizations that may be useful.
  - **Epilepsy Foundation**
  - **Dravet syndrome**
  - **Lennox-Gastaut syndrome**
  - **Tuberous Sclerosis Complex**
  - **Infantile Spasms**

GW is committed to respecting the primary role of healthcare providers in the treatment of epilepsy disorders. Therefore, we cannot respond to medical questions about your personal health situation, nor can we accept private medical information. Please contact your healthcare provider with any questions pertaining to your or a family member's medical condition

If you are interested in participating in a GW-sponsored clinical trial, please have your physician contact GW at: medicalinformation@gwpharm.com

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SB 2096

Senate Judiciary Committee, January 4, 2017
Testimony of Charlene Rittenbach, Forensic Scientist
ND Crime Laboratory Division, Office of Attorney General

Mr. Chairman, members of the Judiciary Committee.

This is my fourth legislative session helping to update North Dakota's laws to extend to the new designer drug compounds being identified in forensic casework. The original concept of these designer drugs was to produce and sell drugs that are not regulated, but can give the same effects as drugs that are already controlled, thus producing legal highs. It started 8 years ago, with the surge of Synthetic Cannabinoid compounds – sold as incense or potpourri giving users a high similar to THC (Marijuana). Then six years ago, I was here explaining the Substituted Cathinones - sold as Bath Salts producing central nervous system stimulant effects and the potent synthetic hallucinogens (Substituted Phenethylamines and Substituted Tryptamines) that were groups of compounds that were being added to the law. I am happy to say that this legislation has proved to be sufficient, as new compounds emerging today are covered in this group language. Last legislative session, three additional Synthetic Cannabinoid groups were added that were more comprehensive therefore replacing four existing groups. I am pleased to say that these changes have been effective and all current synthetic cannabinoids that have been identified in casework thus far have fallen into one of these groups and been included under our law.

Today I am talking about a different class of drugs – synthetic opioids. Recently synthetic opioid analgesics have been emerging that are extremely potent and are increasing the number of overdoses. One of the most abundant drugs being produced and abused is fentanyl, which is about 100 times more potent than morphine (30-50 times more potent than heroin) as an analgesic. Fentanyl is a schedule II controlled substance and has many legitimate uses to treat pain. It is used during surgical procedures, and also administered to patents via transdermal patches and transmucosal lozenges also known as lollipops. Prescription fentanyl medications have led to overdoses and fatalities in the past, but the large increase in fatal overdoses since 2013 is primarily due to clandestine produced fentanyl that is distributed in tablet, capsule, powder and liquid form. In addition to fentanyl, various analogs of fentanyl such as furanyl fentanyl, butyryl fentanyl and others are surfacing on the street and causing problems with user overdoses.

Fentanyl and fentanyl analogs are traditionally mixed into or sold as heroin, oftentimes without the customer's knowledge. The typical dosage (by IV) for fentanyl is 125 µg, which is roughly equivalent to 2 grains of salt. The average lethal dose for fentanyl is 2 mg, which is the average weight of a mosquito. This means the user taking fentanyl for its euphoric effects has a very small window between a recreational dose and a lethal overdose. The United States is in the midst of a fentanyl crisis, with law enforcement reporting and public health data indicating higher availability of fentanyl and fentanyl analogs, increased seizures of fentanyl and fentanyl analogs and more known overdose deaths from fentanyl and fentanyl analogs than at any other time since the drugs were first created in 1959.

The DEA's data query system, NFLIS (National Forensic Laboratory Information System) collects drug chemistry analysis results from cases analyzed by state, local and federal forensic laboratories. The following national statistics from 2012 to 2016 show the dramatic rise in fentanyl and fentanyl analogue identifications from state, local and federal forensic laboratories throughout the United States:

2012 – 686
2013 – 787
2014 – 4,456
2015 – 14,953
2016 – 47,749 (Not including statistics for the month of December)

The proposed changes include adding a section called Fentanyl Derivatives. This group will account for the newer analog compounds which use a chemical class approach that defines a core molecular structure (Fentanyl) and lists possible substitutions and modifications. Some compounds that would fall into this class are already specifically listed schedule I opiates so they would be moved under this class and listed as an example. The definition does state that unless specifically excepted, listed in another schedule or are not FDA approved drugs to account for legitimate fentanyl analogs already listed in Schedule II or new compounds that may be FDA approved in the future.

In addition to the fentanyl derivative language, three other synthetic opioids are being specifically listed as they are structurally different than the fentanyls. The potent synthetic opioids AH-7921, MT-45 and U-47700 are compounds that have been identified in forensic casework and numerous deaths associated with each have been reported.

I have stated in previous years that North Dakota has some of the best all inclusive laws encompassing hundreds of compounds when you compare our law to some other states. The addition of the fentanyl derivative section and the addition of some compounds specifically, will strengthen our laws to include potent synthetic opioids being identified in forensic casework which have the potential to cause overdose deaths. The opioid epidemic cannot simply be solved by controlling all the compounds but at least it is one step that will make obtaining these currently legal analogs harder to obtain and a tool to prosecute the sellers of these harmful substances.

(3)

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Doug Burgum, Governor

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Mark J. Hardy, PharmD, R.Ph.
Executive Director

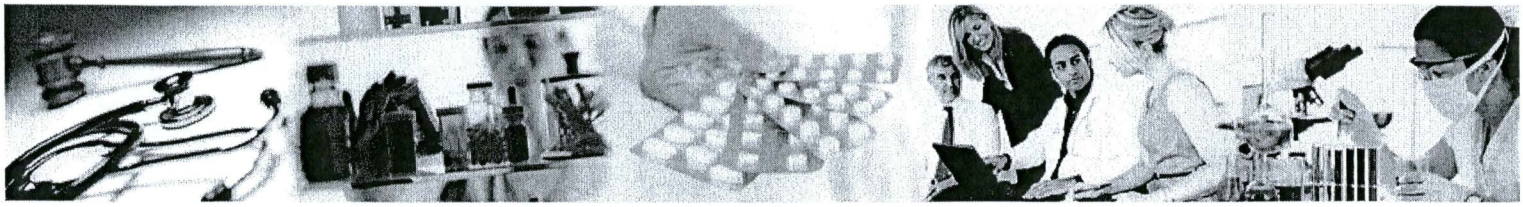
January 4, 2017

RE: Proposed Amendments to SB2096

Page 4 Line 2 – should be a comma instead of a period between "drugs, and"
Page 4 Line 4 – should be a comma instead of a period at the end of the line after "ring,"
Page 4 Line 29 – should have a dash between ")-N-phenylbutanamide"
Page 4 Line 29– should be a y instead of a v in "Butyryl"
Page 5 Line 7 – should be a y instead of a v in "Acrylfentanyl"
Page 5 Line 9 – should be a y instead of a v in "Valeryl"
Page 11 Line 6 – should have a dash between "H-indazole-3-carboxamide"
Page 11 Line 7 – should have a dash between "ADB-CHMINACA"
Page 20 Line 1 – instead of "a" should either be the alpha symbol (α) or say alpha

Page 11 after line 7 the additions of:
[17] methyl 2-(1-(5-fluoropentyl)-1H-indazole-3-carboxamido)-3,3-dimethylbutanoate – Other names: 5F-ADB and 5F-MDMB-PINACA
[18] N-(adamantan-1-yl)-1-(5-fluoropentyl)-1H-indazole-3-carboxamide –other names: 5F-APINACA and 5F-AKB48
[19] methyl 2-(1-(cyclohexylmethyl)-1H-indole-3-carboxamido)-3,3-dimethylbutanoate – Other names: MDMB-CHMICA and MMB-CHMINACA
[20] methyl 2-(1-(4-fluorobenzyl)-1H-indazole-3-carboxamido)-3,3-dimethylbutanoate – Other names: MDMB-FUBINACA

Page 27 line 16- Add language after Epidiolex "or its successor name as determined by the Food and Drug Administration"



Rules - 2016

[Federal Register Volume 81, Number 245 (Wednesday, December 21, 2016)]
[Rules and Regulations]
[Pages 93595-93599]
From the Federal Register Online via the Government Publishing Office [www.gpo.gov]
[FR Doc No: 2016-30595]

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA-446]

Schedules of Controlled Substances: Temporary Placement of Six Synthetic Cannabinoids (5F-ADB, 5F-AMB, 5F-APINACA, ADB-FUBINACA, MDMB-CHMICA and MDMB-FUBINACA) Into Schedule I

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Notice of intent.

SUMMARY: The Administrator of the Drug Enforcement Administration is issuing this notice of intent to temporarily schedule six synthetic cannabinoids: methyl 2-(1-(5-fluoropentyl)-1H-indazole-3-carboxamido)-3,3-dimethylbutanoate [5F-ADB; 5F-MDMB-PINACA]; methyl 2-(1-(5-fluoropentyl)-1H-indazole-3-carboxamido)-3-methylbutanoate [5F-AMB]; N-(adamantan-1-yl)-1-(5-fluoropentyl)-1H-indazole-3-carboxamide [5F-APINACA, 5F-AKB48]; N-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-(4-fluorobenzyl)-1H-indazole-3-carboxamide [ADB-FUBINACA]; methyl 2-(1-(cyclohexylmethyl)-1H-indole-3-carboxamido)-3,3-dimethylbutanoate [MDMB-CHMICA, MMB-CHMINACA] and methyl 2-(1-(4-fluorobenzyl)-1H-indazole-3-carboxamido)-3,3-dimethylbutanoate [MDMB-FUBINACA], into schedule I pursuant to the temporary scheduling provisions of the Controlled Substances Act (CSA). This action is based on a finding by the Administrator that the placement of these synthetic cannabinoids into schedule I of the Controlled Substances Act is necessary to avoid an imminent hazard to the public safety. Any final order will impose the administrative, civil, and criminal sanctions and regulatory controls applicable to schedule I substances under the Controlled Substances Act on the manufacture, distribution, possession, importation, exportation of, and research and conduct with, instructional activities of these synthetic cannabinoids.

DATES: December 21, 2016.

FOR FURTHER INFORMATION CONTACT: Michael J. Lewis, Office of Diversion Control, Drug Enforcement Administration; Mailing Address: 8701 Morrissette Drive, Springfield, Virginia 22152; Telephone: (202) 598-6812.

SUPPLEMENTARY INFORMATION: Any final order will be published in the Federal Register and may not be effective prior to January 20, 2017.

Legal Authority

The Drug Enforcement Administration (DEA) implements and enforces titles II and III of the Comprehensive Drug Abuse Prevention and Control Act of 1970, as amended. **21 U.S.C. 801-971**. Titles II and III are referred to as the "Controlled Substances Act" and the "Controlled Substances Import and Export Act," respectively, and are collectively referred to as the "Controlled Substances Act" or the "CSA" for the purpose of this action. The DEA publishes the implementing regulations for these statutes in title 21 of the Code of Federal Regulations (CFR), chapter II. The CSA and its implementing regulations are designed to prevent, detect, and eliminate the diversion of controlled substances and listed chemicals into the illicit market while providing for the legitimate medical, scientific, research, and industrial needs of the United States. Controlled substances have the potential for abuse and dependence and are controlled to protect the public health and safety.

Under the CSA, every controlled substance is classified into one of five schedules based upon its potential for abuse, its currently accepted medical use in treatment in the United States, and the degree of dependence the drug or other substance may cause. 21 U.S.C. 812. The initial schedules of controlled substances established by Congress are found at **21 U.S.C. 812**(c), and the current list of all scheduled substances is published at 21 CFR part 1308.

Section 201 of the CSA, **21 U.S.C. 811**, provides the Attorney General with the authority to temporarily place a substance into schedule I of the CSA for two years without regard to the requirements of 21 U.S.C. 811(b) if she

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finds that such action is necessary to avoid an imminent hazard to the public safety. 21 U.S.C. 811(h)(1). In addition, if proceedings to control a substance are initiated under 21 U.S.C. 811(a)(1), the Attorney General may extend the temporary scheduling for up to one year. 21 U.S.C. 811(h)(2).

Where the necessary findings are made, a substance may be temporarily scheduled if it is not listed in any other schedule under section 202 of the CSA, 21 U.S.C. 812, or if there is no exemption or approval in effect for the substance under section 505 of the Federal Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. 355. 21 U.S.C. 811(h)(1); **21 CFR part 1308**. The Attorney General has delegated scheduling authority under 21 U.S.C. 811 to the Administrator of the DEA. 28 CFR 0.100.

Background

Section 201(h)(4) of the CSA 21 U.S.C. 811(h)(4), requires the Administrator to notify the Secretary of the Department of Health and Human Services (HHS) of any intention to temporarily place a substance into schedule I of the CSA.\1\ The Acting Administrator transmitted notice of his intent to place 5F-ADB, 5F-AMB, 5F-APINACA, ADB-FUBINACA, MDMB-CHMICA and MDMB-FUBINACA in schedule I on a temporary basis to the Assistant Secretary by letter dated April 22, 2016. The Assistant Secretary responded to this notice by letter dated May 2, 2016, and advised that based on a review by the Food and Drug Administration (FDA), there were no investigational new drug applications or approved new drug applications for 5F-ADB, 5F-AMB, 5F-APINACA, ADB-FUBINACA, MDMB-CHMICA or MDMB-FUBINACA. The Assistant Secretary also stated that the HHS had no objection to the temporary placement of 5F-ADB, 5F-AMB, 5F-APINACA, ADB-FUBINACA, MDMB-CHMICA or MDMB-FUBINACA into schedule I of the CSA. 5F-ADB, 5F-AMB, 5F-APINACA, ADB-FUBINACA, MDMB-CHMICA or MDMB-FUBINACA are not currently listed in any schedule under the CSA.

\1\ As discussed in a memorandum of understanding entered into by the Food and Drug Administration (FDA) and the National Institute on Drug Abuse (NIDA), the FDA acts as the lead agency within the Department of Health and Human Service (HHS) in carrying out the Secretary's scheduling responsibilities under the CSA, with the concurrence of NIDA. 50 FR 9518, Mar. 8, 1985. The Secretary of the HHS has delegated to the Assistant Secretary for Health of the HHS the authority to make domestic drug scheduling recommendations. 58 FR 35460, July 1, 1993.

To find that placing a substance temporarily into schedule I of the CSA is necessary to avoid an imminent hazard to the public safety, the Administrator is required to consider three of the eight factors set forth in 21 U.S.C. 811(c): The substance's history and current pattern of abuse; the scope, duration and significance of abuse; and what, if any, risk there is to the public health. 21 U.S.C. 811(h)(3). Consideration of these factors includes actual abuse, diversion from legitimate channels, and clandestine importation, manufacture, or distribution. 21 U.S.C. 811(h)(3).

A substance meeting the statutory requirements for temporary scheduling may only be placed in schedule I. 21 U.S.C. 811(h)(1). Substances in schedule I are those that have a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. 21 U.S.C. 812(b)(1).

5F-ADB, 5F-AMB, 5F-APINACA, ADB-FUBINACA, MDMB-CHMICA and MDMB-FUBINACA

Available data and information for 5F-ADB, 5F-AMB, 5F-APINACA, ADB- FUBINACA, MDMB-CHMICA and MDMB-FUBINACA indicate that these synthetic cannabinoids (SCs) have a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision.

Synthetic Cannabinoids

SCs are substances synthesized in laboratories that mimic the biological effects of delta-9-tetrahydrocannabinol (THC), the main psychoactive ingredient in marijuana. It is believed that SCs were first introduced on the designer drug market in several European countries as "herbal incense" before the initial encounter in the United States by U.S. Customs and Border Protection (CBP) in November 2008. From 2009 to the present, misuse and abuse of SCs has increased in the United States with law enforcement encounters describing SCs applied onto plant material and in designer drug products intended for human consumption. It has been demonstrated that the substances and the associated designer drug products are abused for their psychoactive properties. With many generations of SCs having been encountered since 2009, 5F-ADB, 5F-AMB, 5F-APINACA, ADB-FUBINACA, MDMB-CHMICA and MDMB- FUBINACA are some of the latest, and the abuse of these substances is negatively impacting communities.

As observed by the DEA and CBP, SCs originate from foreign sources, such as China. Bulk powder substances are smuggled via common carrier into the United States and find their way to clandestine designer drug product manufacturing operations located in residential neighborhoods, garages, warehouses, and other similar destinations throughout the country. According to online discussion boards and law enforcement encounters, applying by spraying or mixing the SCs with plant material provides a vehicle for the most common route of administration--smoking (using a pipe, a water pipe, or rolling the drug-laced plant material in cigarette papers).

5F-ADB, 5F-AMB, 5F-APINACA, ADB-FUBINACA, MDMB-CHMICA, and MDMB- FUBINACA have no accepted medical use in the United States. Use of these specific SCs has been reported to result in adverse effects in humans including deaths (see 3-Factor document in "Supporting and Related Material" section). Use of other SCs has resulted in signs of addiction and withdrawal, and based on the similar pharmacological profile of these six substances, it is believed that there will be similar observed adverse effects.

5F-ADB, 5F-AMB, 5F-APINACA, ADB-FUBINACA, MDMB-CHMICA and MDMB- FUBINACA are SCs that have pharmacological effects similar to the schedule I hallucinogen delta-[Delta]-tetrahydrocannabinol (THC) and temporarily and permanently controlled schedule I synthetic cannabinoid substances. In addition, the misuse of 5F-ADB, 5F-AMB, 5F-APINACA, ADB- FUBINACA, MDMB-CHMICA and/or MDMB-FUBINACA have been associated with either overdoses requiring emergency medical intervention or death (see factor 6). With no approved medical use and limited safety or toxicological information, 5F-ADB, 5F-AMB, 5F-APINACA, ADB-FUBINACA, MDMB-CHMICA and MDMB-FUBINACA have emerged on the designer drug market, and the abuse of these substances for their psychoactive properties is concerning. The DEA's analysis is available in its entirety under "Supporting and Related Material" of the public docket for this action at www.regulations.gov under docket number DEA-443.

Factor 4. History and Current Pattern of Abuse

Synthetic cannabinoids have been developed over the last 30 years as tools for investigating the endocannabinoid system (e.g. determining CB1 and CB2 receptor activity). The first encounter of SCs within the United States occurred in November 2008 by CBP. Since then the popularity of SCs and their

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associated products has increased steadily as evidenced by law enforcement seizures, public health information, and media reports. 5F- ADB, 5F-AMB, 5F-APINACA, ADB-FUBINACA, MDMB-CHMICA and MDMB-FUBINACA are SCs that have been recently encountered (see "Supporting and Related Material," Factor 5). Multiple overdoses involving emergency medical intervention or deaths have been associated with 5F-ADB, 5F- AMB, 5F-APINACA, ADB-FUBINACA, MDMB-CHMICA and MDMB-FUBINACA.

Research and clinical reports have demonstrated that SCs are applied onto plant material so that the material may be smoked as users attempt to obtain a euphoric and/or psychoactive "high," believed to be similar to marijuana. Data gathered from published studies, supplemented by discussions on Internet discussion Web sites, demonstrate that these products are being abused mainly by smoking for their psychoactive properties. The adulterated products are marketed as "legal" alternatives to marijuana. In recent overdoses, 5F-ADB, 5F- AMB, 5F-APINACA, ADB-FUBINACA, MDMB-CHMICA and MDMB-FUBINACA have been shown to be applied onto plant material, similar to the SCs that have been previously available.

Law enforcement personnel have encountered various application methods including buckets or cement mixers in which plant material and one or more SCs (including 5F-ADB, 5F-AMB, 5F-APINACA, ADB-FUBINACA, MDMB-CHMICA and/or MDMB-FUBINACA) are mixed together, as well as large areas where the plant material is spread out so that a dissolved SC mixture can be applied directly. Once mixed, the SC plant material is then allowed to dry before manufacturers package the product for distribution, ignoring any control mechanisms to prevent contamination or to ensure a consistent, uniform concentration of the substance in each package. Adverse health consequences may also occur from directly ingesting the substance(s) during the manufacturing process. 5F-ADB, 5F-AMB, 5F-APINACA, ADB-FUBINACA, MDMB-CHMICA and MDMB-FUBINACA, similar to other SCs, have been encountered in form of dried leaves or herbal blends.

The designer drug products laced with SCs, including 5F-ADB, 5F- AMB, 5F-APINACA, ADB-FUBINACA, MDMB-CHMICA and MDMB-FUBINACA, are often sold under the guise of "herbal incense" or "potpourri," use various product names, and are routinely labeled "not for human consumption." Additionally, these products are marketed as a "legal high" or "legal alternative to marijuana" and are readily available over the Internet, in head shops, or sold in convenience stores. There is an incorrect assumption that these products are safe, that they are a synthetic form of marijuana, and that labeling these products as "not for human consumption" is a legal defense to criminal prosecution.

A major concern, as reiterated by public health officials and medical professionals, is the targeting and direct marketing of SCs and SC-containing products to adolescents and youth. This is supported by law enforcement encounters and reports from emergency departments; however, all age groups have been reported by media as abusing these substances and related products. Individuals, including minors, are purchasing SCs from Internet Web sites, gas stations, convenience stores, and head shops.

Factor 5. Scope, Duration and Significance of Abuse

SCs, including 5F-ADB, 5F-AMB, 5F-APINACA, ADB-FUBINACA, MDMB- CHMICA and MDMB-FUBINACA, continue to be encountered on the illicit market regardless of scheduling actions that attempt to safeguard the public from the adverse effects and safety issues associated with these substances. Numerous substances are encountered each month, differing only by small modifications intended to avoid prosecution while maintaining the pharmacological effects. Law enforcement and health care professionals continue to report abuse of these substances and their associated products.

As described by the National Institute on Drug Abuse (NIDA), many substances being encountered in the illicit market, specifically SCs, have been available for ye but have reentered the marketplace due to a renewed popularity.

The threat of serious injury to the individual following the ingestion of 5F-ADB, 5F-AMB, 5F-APINACA, ADB-FUBINACA, MDMB-CHMICA and MDMB-FUBINACA and oth SCs persists. Numerous calls have been received by poison centers regarding the abuse of products potentially laced with SCs that have resulted in visits to emergency departments. Law enforcement continues to encounter novel SCs on the illicit market, including 5F-ADB, 5F-AMB, 5F-APINACA, ADB-FUBINACA, MDMB-CHMICA and MDMB-FUBINACA (see factor 5 in "Supporting and Related Material").

The following information details information obtained through NFLIS \2\ (queried on November 7, 2016), including dates of first encounter, exhibits/reports, and locations.

\2\ The National Forensic Laboratory Information System (NFLIS) is a national drug forensic laboratory reporting system that systematically collects results from drug chemistry analyses conducted by state and local forensic laboratories in the United States.

5F-ADB: NFLIS--2,311 reports, first encountered in September 2014, locations include: Arizona, Arkansas, California, Florida, Georgia, Idaho, Indiana, Iowa, Kansas, Kentucky, Louisiana, Missouri, New Jersey, North Dakota, Ohio, Oklahoma, Pennsylvania, South Carolina, Texas, Virginia, and Wisconsin.

5F-AMB: NFLIS--3,349 reports, first encountered in January 2014, locations include: Arizona, Arkansas, California, Colorado, Florida, Georgia, Hawaii, Idaho, Illinois, Indiana, Iowa, Kansas, Kentucky, Louisiana, Maryland, Massachusetts, Minnesota, Mississippi, Missouri, Nebraska, New Hampshire, New Jersey, New Mexico, New York, North Dakota, Ohio, Oklahoma, Oregon, Pennsylvania, South Carolina, Tennessee, Texas, Utah, Virginia, Wisconsin, and Wyoming.

5F-APINACA: NFLIS--1,936 reports, first encountered in August 2012, locations include: Alabama, Arizona, Arkansas, California, Colorado, Connecticut, Florida, Georgia, Idaho, Illinois, Indiana, Iowa, Kansas, Kentucky, Louisiana, Maryland, Minnesota, Mississippi, Missouri, Nebraska, New Hampshire, New Jersey, North Dakota, Ohio, Oklahoma, Pennsylvania, Puerto Rico, South Carolina, Tennessee, Texas, Utah, Virginia, West Virginia, Wisconsin, and Wyoming.

ADB-FUBINACA: NFLIS--942 reports, first encountered in March 2014, locations include: Arkansas, California, Colorado, Florida, Georgia, Illinois, Indiana, Iowa, Kansas, Kentucky, Louisiana, Maryland, Mississippi, Missouri, New Jersey, New Mexico, New York, North Dakota, Ohio, Pennsylvania, Texas, Utah, Virginia, and Wyoming.

MDMB-CHMICA: NFLIS--227 reports, first encountered in March 2015, locations include: Arkansas, Georgia, Indiana, Kentucky, Louisiana, Nevada, Ohio, Oklahoma, South Carolina, and Texas.

MDMB-FUBINACA: NFLIS--507 reports, first encountered in July 2015, locations include: Arkansas, California, Colorado, Connecticut, Georgia, Idaho,

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Indiana, Kansas, Kentucky, Louisiana, Missouri, Nevada, New Jersey, New Mexico, North Dakota, Ohio, Oklahoma, Pennsylvania, Texas, Virginia, Wisconsin, and West Virginia.

Factor 6. What, if Any, Risk There Is to the Public Health

5F-ADB, 5F-AMB, 5F-APINACA, ADB-FUBINACA, MDMB-CHMICA and MDMB- FUBINACA have all been identified in overdose and/or cases involving death attributed their abuse. Adverse health effects reported from these incidents involving 5F-ADB, 5F-AMB, 5F-APINACA, ADB-FUBINACA, MDMB-CHMICA and/or MDMB-FUBINACA have included: Nausea, persistent vomiting, agitation, altered mental status, seizures, convulsions, loss of consciousness and/or cardio toxicity. Large clusters of overdoses requiring medical care have been reported involving 5F-AMB, MDMB- FUBINACA, MDMB-CHMICA and 5F-ADB. Reported deaths involving these SCs have included 5F-ADB (8); 5F-AMB (6); 5F-APINACA (1); ADB-FUBINACA (2); MDMB-CHMICA (4), European Monitoring Centre for Drugs and Drug Addiction has reported an additional 12 deaths involving MDMB-CHMICA; and MDMB-FUBINACA (1) (see factor 6 in "Supporting and Related Material").

Finding of Necessity of Schedule I Placement to Avoid Imminent Hazard to Public Safety

In accordance with 21 U.S.C. 811 (h)(3), based on the available data and information summarized above, the continued uncontrolled manufacture, distribution, importation, exportation, conduct of research and chemical analysis, possession, and abuse of 5F-ADB, 5F- AMB, 5F-APINACA, ADB-FUBINACA, MDMB-CHMICA and MDMB-FUBINACA pose an imminent hazard to the public safety. The DEA is not aware of any currently accepted medical uses for these substances in the United States. A substance meeting the statutory requirements for temporary scheduling, 21 U.S.C. 811(h)(1), may only be placed in schedule I. Substances in schedule I are those that have a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. Available data and information for 5F-ADB, 5F-AMB, 5F- APINACA, ADB-FUBINACA, MDMB-CHMICA and MDMB-FUBINACA indicate that these SCs have a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. As required by section 201(h)(4) of the CSA, 21 U.S.C. 811(h)(4), the Administrator, through a letter dated April 22, 2016, notified the Assistant Secretary of the DEA's intention to temporarily place these six substances in schedule I.

Conclusion

This notice of intent initiates a temporary scheduling action and provides the 30-day notice pursuant to section 201(h) of the CSA, 21 U.S.C. 811(h). In accordance with the provisions of section 201(h) of the CSA, 21 U.S.C. 811(h), the Administrator considered available data and information, herein sets forth the grounds for his determination that it is necessary to temporarily schedule methyl 2-(1-(5- fluoropentyl)-1H-indazole-3-carboxamido)-3,3-dimethylbutanoate [5F-ADB; 5F-MDMB-PINACA]; methyl 2-(1-(5-fluoropentyl)-1H-indazole-3- carboxamido)-3-methylbutanoate [5F-AMB]; N-(adamantan-1-yl)-1-(5- fluoropentyl)-1H-indazole-3-carboxamide [5F-APINACA, 5F-AKB48]; N-(1- amino-3,3-dimethyl-1-oxobutan-2-yl)-1-(4-fluorobenzyl)-1H-indazole-3- carboxamide [ADB-FUBINACA]; methyl 2-(1-(cyclohexylmethyl)-1H-indole-3- carboxamido)-3,3-dimethylbutanoate [MDMB-CHMICA, MMB-CHMINACA] and methyl 2-(1-(4-fluorobenzyl)-1H-indazole-3-carboxamido)-3,3- dimethylbutanoate [MDMB-FUBINACA] in schedule I of the CSA, and finds that the placement of these substances into schedule I of the CSA on a temporary basis is necessary to avoid an imminent hazard to the public safety.

Because the Administrator hereby finds that it is necessary to temporarily place these SCs into schedule I to avoid an imminent hazard to the public safety, any subsequent final order temporarily scheduling these substances will be effective on the date of publication in the Federal Register, and will be in effect for a period of two years, with a possible extension of one additional year, pending completion of the regular (permanent) scheduling process. 21 U.S.C. 811(h)(1) and (2). It is the intention of the Administrator to issue such a final order as soon as possible after the expiration of 30 days from the date of publication of this notice. 5F-ADB, 5F-AMB, 5F-APINACA, ADB-FUBINACA, MDMB-CHMICA and MDMB-FUBINACA will then be subject to the regulatory controls and administrative, civil, and criminal sanctions applicable to the manufacture, distribution, importation, exportation, research, conduct of instructional activities, and chemical analysis and possession of a schedule I controlled substance.

The CSA sets forth specific criteria for scheduling a drug or other substance. Regular scheduling actions in accordance with 21 U.S.C. 811(a) are subject to formal rulemaking procedures done "on the record after opportunity for a hearing" conducted pursuant to the provisions of 5 U.S.C. 556 and 557. 21 U.S.C. 811. The reg scheduling process of formal rulemaking affords interested parties with appropriate process and the government with any additional relevant information needed to make a determination. Final decisions that conclude the regular scheduling process of formal rulemaking are subject to judicial review. 21 U.S.C. 877. Temporary scheduling orders are not subject to judicial review. 21 U.S.C. 811(h)(6).

Regulatory Matters

Section 201(h) of the CSA, 21 U.S.C. 811(h), provides for an expedited temporary scheduling action where such action is necessary to avoid an imminent hazard to the public safety. As provided in this subsection, the Attorney General may, by order, schedule a substance in schedule I on a temporary basis. Such an order may not be issued before the expiration of 30 days from (1) the publication of a notice in the Federal Register of the intention to issue such order and the grounds upon which such order is to be issued, and (2) the date that notice of the proposed temporary scheduling order is transmitted to the Assistant Secretary. 21 U.S.C. 811(h)(1).

Inasmuch as section 201(h) of the CSA directs that temporary scheduling actions be issued by order and sets forth the procedures by which such orders are to be issued, the DEA believes that the notice and comment requirements of section 553 of the Administrative Procedure Act (APA), 5 U.S.C. 553, do not apply to this notice of intent. In the alternative, even assuming that this notice of intent might be subject to section 553 of the APA, the Administrator finds that there is good cause to forgo the notice and comment requirements of section 553, as any further delays in the process for issuance of temporary scheduling orders would be impracticable and contrary to the public interest in view of the manifest urgency to avoid an imminent hazard to the public safety.

Although the DEA believes this notice of intent to issue a temporary scheduling order is not subject to the notice and comment requirements of section 553 of the APA, the DEA notes

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that in accordance with 21 U.S.C. 811(h)(4), the Administrator will take into consideration any comments submitted by the Assistant Secretary with regard to the proposed temporary scheduling order.

Further, the DEA believes that this temporary scheduling action is not a "rule" as defined by 5 U.S.C. 601(2), and, accordingly, is not subject to the requirements of the Regulatory Flexibility Act (RFA). The requirements for the preparation of an initial regulatory flexibility analysis in 5 U.S.C. 603(a) are not applicable where, as here, the DEA is not required by section 553 of the APA or any other law to publish a general notice of proposed rulemaking. Additionally, this action is not a significant regulatory action as defined by Executive Order 12866 (Regulatory Planning and Review), section 3(f), and, accordingly, this action has not been reviewed by the Office of Management and Budget.

This action will not have substantial direct effects on the States, on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government. Therefore, in accordance with Executive Order 13132 (Federalism) it is determined that this action does not have sufficient federalism implications to warrant the preparation of a Federalism Assessment.

List of Subjects in 21 CFR Part 1308

Administrative practice and procedure, Drug traffic control, Reporting and recordkeeping requirements.

For the reasons set out above, the DEA amends 21 CFR part 1308 as follows:

PART 1308--SCHEDULES OF CONTROLLED SUBSTANCES

0 1. The authority citation for part 1308 continues to read as follows:

Authority: 21 U.S.C. 811, 812, 871(b), unless otherwise noted.

0 2. In Sec. 1308.11, add paragraphs (h)(23) through (28) to read as follows:

Sec. 1308.11 Schedule I

* * * * *

(h) * * *

(23) methyl 2-(1-(5-fluoropentyl)-1H-indazole-3-carboxamido)-3,3-dimethylbutanoate, its optical, positional, and geometric isomers, salts and salts of isomers (Other names: 5F-ADB; 5F-MDMB-PINACA).....(7034)

(24) methyl 2-(1-(5-fluoropentyl)-1H-indazole-3-carboxamido)-3-methylbutanoate, its optical, positional, and geometric isomers, salts and salts of isomers (Other names: 5F-AMB).....(7033)

(25) N-(adamantan-1-yl)-1-(5-fluoropentyl)-1H-indazole-3-carboxamide, its optical, positional, and geometric isomers, salts and salts of isomers (Other names: 5F-APINACA, 5F-AKB48).....(7049)

(26) N-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-(4-fluorobenzyl)-1H-indazole-3-carboxamide, its optical, positional, and geometric isomers, salts and salts of isomers (Other names: ADB-FUBINACA).....(7010)

(27) methyl 2-(1-(cyclohexylmethyl)-1H-indole-3-carboxamido)-3,3-dimethylbutanoate, its optical, positional, and geometric isomers, salts and salts of isomers (Other names: MDMB-CHMICA, MMB-CHMINACA).....(7042)

(28) methyl 2-(1-(4-fluorobenzyl)-1H-indazole-3-carboxamido)-3,3-dimethylbutanoate, its optical, positional, and geometric isomers, salts and salts of isomers (Other names: MDMB-FUBINACA).....(7020)

Dated: December 13, 2016.

Chuck Rosenberg,
Acting Administrator.

[FR Doc. 2016-30595 Filed 12-20-16; 8:45 am]
BILLING CODE 4410-09-P

How FDA Reviews Proposed Drug Names

During the past two decades, the Food and Drug Administration (FDA) has worked to increase the safe use of drug products by minimizing user errors attributed to unclear nomenclature, labels, labeling, and packaging design of drug products. CDER has received approximately 126,000 reports of medication error is from 2000 to 2009, some of which are directly related to the similar sound and appearance of drug name pairs. Due to these postmarketing nomenclature-related events, the Center for Drug Evaluation and Research (CDER) has developed and refined internal procedures for evaluating, prior to the marketing of a drug, the potential for a proposed proprietary name (i.e., "brand name") to cause or contribute to medication errors as part of the Center's focus on the safe use of drug and therapeutic biologic products.

CDER considers the potential for confusion between an Applicant's proposed proprietary name and the proprietary and established names of drug products existing in the marketplace and pending products currently under review by the Center for Drug Evaluation and Research (CDER). The review of proposed proprietary names is conducted by the Division of Medication Error Prevention and Analysis (DMEPA) in CDER's Office of Surveillance and Epidemiology (OSE). DMEPA, in consultation with the Division of Drug Marketing, Advertising, and Communications (DDMAC) and with input from pertinent disciplines involved with the review of the application, determines the acceptability of proposed proprietary names for products marketed under an application (i.e., IND, NDA, BLA, and ANDA). DMEPA does not review proprietary names of products marketed under an OTC monograph or those of a distributor or repacker. DMEPA completes over five-hundred proprietary name reviews annually.

In addition, established names (i.e., nonproprietary or generic name) do not undergo review by CDER. The United States Adopted Names Council (USAN) is responsible for selecting a United States Adopted Name (USAN) for drugs marketed in the U.S. Unlike proprietary names, established names have a common, simple word element (a "stem") incorporated in the names of all members of a group of related drugs, and are thus designed to have some similarity to one another.

It is important for CDER to screen proposed proprietary names before marketing because accurate interpretation of a product's name is essential to ensure that the correct product is procured, prescribed, prepared, dispensed, and administered to the patient. In the U.S. healthcare system, healthcare practitioners rely on a product's name as a critical identifier of the appropriate therapy in a market of thousands of products. Therefore, product names that look or sound-alike can lead to medication errors and, potentially, to patient harm by increasing the risk of a healthcare practitioner's misprescribing or misinterpreting the correct product name, dispensing and/or administering the wrong product, or dispensing it incorrectly.

CDER review of proprietary names includes consideration of both safety and promotional aspects of a name. If a proposed proprietary name is determined to be promotional or represent a source of medication error, the name is found unacceptable for

use. The following sections provide a snapshot of elements used in the Agency's proprietary name review process.

Promotional Review

CDER's Division of Drug Marketing, Advertising, and Communications (DDMAC) evaluates proposed proprietary names to determine if they are overly fanciful, so as to misleadingly imply unique effectiveness or composition, as well as to assess whether they contribute to overstatement of product efficacy, minimization of risk, broadening of product indications, or making of unsubstantiated superiority claims.

Safety Review

CDER's Division of Medication Error Prevention and Analysis (DMEPA) conducts the safety review of a proprietary name. This evaluation involves methods that generate a list of names that could be confused with the proposed proprietary name as well as methods to test the likelihood of confusion between these names and the proposed proprietary name.

When reviewing a proposed proprietary name, DMEPA considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted throughout the medication use system (e.g., prescribing, dispensing, administering). The spelling of the proposed proprietary name is compared with the proprietary and established names of existing and proposed drug products because similarly spelled names may have greater likelihood to sound similar to one another when spoken, or look similar to one another when scripted.

In addition, DMEPA examines the orthographic appearance of the proposed name using a number of different legible handwriting samples. Handwritten communication of product names has a long-standing association with product name confusion, often leading to medication errors.

The expertise gained from DMEPA's root-cause analysis of postmarketing medication errors is applied to identify sources of ambiguity within the name that could be introduced when scripting (e.g., "A" may look like "C"), along with other orthographic attributes that determine the overall appearance of the product name when scripted. Additionally, since spoken communication of medication names is common in clinical settings, the pronunciation of the proposed proprietary name is compared with the pronunciation of other product names, accounting for the potential for phonological error due to predictable phonological variance.

DMEPA not only considers the potential for a name to be spelled similarly and/or sound similar to the name of a currently marketed product or one that is in the approval pipeline, but also considers the potential for the proposed proprietary name to inadvertently function as a source of error for other reasons, such as by suggesting a dosage form or route of administration or contains a USAN stem. Consideration is given

to the proposed product's characteristics (including its intended use, dosage form, strength, and route of administration) because the product characteristics provide a context for communication of the product name and ultimately determine the use of the product in the usual clinical practice setting.

The following techniques are used in the analysis of a proposed proprietary name.

Computational Methods

The majority of names with similarity to a proposed proprietary name are identified through database searches. A variety of publicly available databases and resources containing product names are used to identify similar names. In addition, DMEPA identifies other potentially similar names using a computerized method of identifying phonetic and orthographic similarities between product names using Phonetic and Orthographic Computer Analysis (POCA). This software uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Under PDUFA IV, FDA has made the source code for POCA available to public parties for further development (pocasourcecoderequest@fda.hhs.gov).

Medication Error Data

If a proposed name is for an active ingredient(s) is already marketed domestically or abroad, DMEPA searches databases containing medication error reports with the goal of identifying relevant information that might help to inform the analysis of the proposed name.

Name Simulation Studies

DMEPA performs simulation studies, which are limited to healthcare providers employed by the FDA, to test the response of healthcare practitioners to proposed names. FDA health professionals (nurses, pharmacists, physicians, etc.) are presented with written and verbal prescriptions to interpret in an attempt to simulate the prescription ordering process.

Name Assessments Conducted or Commissioned by the Applicant

Independent name assessments are sometimes submitted by Applicants. DMEPA reviews and considers these assessments when evaluating proprietary names. DMEPA compares its proprietary name risk assessment with the findings of the risk assessment submitted by the Applicant. When DMEPA's conclusion regarding the acceptability of the proposed name differs from the conclusion of external assessment, an explanation of the differences is provided to the Applicant.

Failure Mode and Effects Analysis (FMEA)

DMEPA uses FMEA, a systematic prospective method, to examine the nomenclature of a product for possible ways in which a failure (i.e., an error) can occur once a comprehensive list of potentially similar names is developed.[1] To identify potential failure modes, the proposed proprietary name is compared to all of the names gathered during the safety review. Because product name confusion can occur at any point in the medication use process, DMEPA considers the potential for confusion throughout the entire U.S. medication use process, including product procurement, prescribing/ordering, dispensing, administration, and monitoring the effects of a medication.[2] If the FMEA determines that the proposed proprietary name could be a source of confusion that could cause medication errors under the proposed prescribing conditions, the proposed proprietary name is found unacceptable.

Additional Information

Although FDA strives to identify potentially confusing names prior to marketing, there are cases in which the potential for name confusion is not predicted prior to approval and a name is marketed that leads to errors. In these situations, changing a proprietary name while the product is marketed may be necessary to address medication errors resulting from the name confusion. Therefore, we continue to encourage you to report all medication errors to MedWatch so that FDA can be made aware of potential problems early on and the agency can provide effective interventions that will minimize further errors.

The documents accessed through the following links provide additional information on the proprietary name review process.

www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072229.pdf

http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm075068.pdf

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[1] Joint Commission Resources, Root Cause Analysis in Healthcare 201 (3rdEd, 2005).

[2] Institute of Medicine, *Preventing Medication Errors*.

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Mark J. Hardy, PharmD, R.Ph.
Executive Director

Senate Bill No 2096 – Controlled Substances Rescheduling
House Judiciary Committee – Prairie Room
3:15 PM - Wednesday – March 1, 2017

Chairman Koppelman, members of the House Judiciary Committee, for the record I am Mark J. Hardy, PharmD, Executive Director of the North Dakota State Board of Pharmacy. I appreciate the opportunity to be here to speak to you today.

Senate Bill 2096 is the biennial bill introduced by State Board of Pharmacy to bring the Controlled Substances scheduling up-to-date with what the Food and Drug Administration [FDA] and Drug Enforcement Administration [DEA] have done over the past two years. This bill also adds a new category for derivatives of Fentanyl within the Schedule I controlled substances. The drafting of this bill, specifically the Schedule I substances was done in conjunction with the ND Crime Lab. A representative with the ND Crime Lab is here and will present testimony to explain much of the chemistry and reasons for the new category listed in this proposed legislation. The intention for these changes is to try to be proactive and ensure that we have future chemical modifications that can be made to these substances, identified as controlled substances. This bill is very lengthy and, we feel, as comprehensive as possible with the information that we have at this time.

I would like to highlight each provision of the bill to ensure you have an understanding of the changes we have in the drafting of this bill.

On page 4, line 1 – we have added the previously mentioned new category for derivatives of Fentanyl compounds, as schedule I opioids.

In the previous pages 1-3 you will notice multiply compounds that were struck from schedule I and were specifically added under the Fentanyl derivatives section as compounds which would chemically fall under that new section. Of course, these compounds have recently garnished a great deal of attention, specifically, furanyl fentanyl which is specifically listed on page 4 line 26 of this bill. The intention is to have the core structure listed with future illicit modifications considered a schedule I substance while still having the statement that Fentanyl derivatives which are FDA approved and listed in another schedule would be exempted.

On page 3, starting on line 27-31 are three opioid compounds separate from Fentanyl derivatives, which the DEA has scheduled since our last legislative session and we are adding as well.

On page 11, line 5-20 is the addition of new Indole Carboxamide compounds which were also scheduled by DEA. Other similar compounds were also made Schedule I compounds by DEA at the same time but, have already been specifically identified in past legislative sessions.

On page 18, beginning on line 30 through page 20 line 14 we made some modifications to the other known names of substituted cathinones and made the addition of Pentylone and 4-MePPP consistent with the DEA's scheduling.

Again, the attempt in the Schedule I Controlled Substances list is for the core chemical compounds as well as the individual compound to be listed in an attempt to be proactive in the complex nature of modifying these dangers drugs by chemists in foreign countries to circumvent laws. This is our best approach for protecting our citizens and of being proactive in assisting the legal system, by specifically listing the known chemicals for their legal cases.

On page 23, line 14 the addition of Thiafentanil which is a new controlled substance which has been scheduled by DEA since our last legislative session, into Schedule II.

On page 24, lines 30-31 is the addition of the chemical name for Tramadol as a Schedule IV substance to mirror that of DEA. The 2013 Legislative Session was proactive in scheduling Tramadol in North Dakota prior to the DEA scheduling it as we had such large abuse reports.

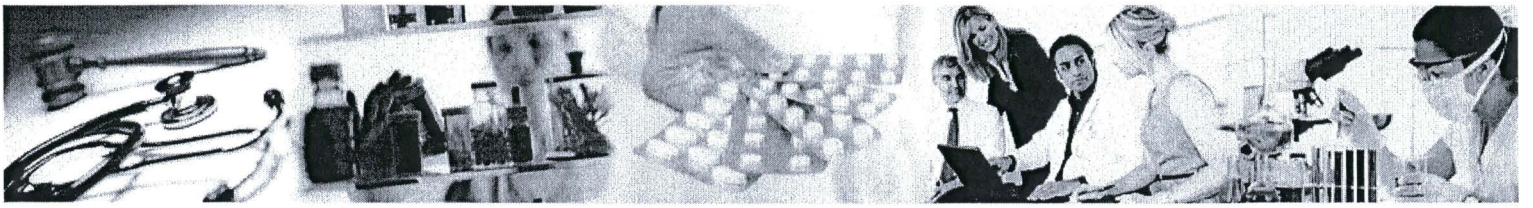
On Page 25, line 28 the addition of Flunitrazepam as a Schedule IV controlled substance to be consistent with DEA scheduling.

On page 27, starting with line 26 the addition of Eluxadone as a Schedule IV controlled substance to be consistent with DEA scheduling.

Also on page 27, line 30 we are proposing the addition of Epidiolex as a Schedule IV controlled substance to be consistent with DEA scheduling. This medication is a drug currently in phase 3 trials and is a cannabidiol derived medication. Cannabidiol is one of the compounds in the marijuana plant. This product will specifically be utilized to treat epilepsy conditions in children. The reason for the language offered in the amendments is due to Epidiolex as it currently stands would now fall as a Schedule I compound without this specific addition. The request for the amendment is to address the circumstances that the FDA would change the brand name of the drug in it's approval process. It is likely to be brought to market in late 2017

Page 29, line 8 Brivaracetam is added as a Schedule IV controlled substance to be consistent with DEA scheduling.

We respectfully request that this legislation be considered an emergency measure to put these changes into effect as soon as possible. I do appreciate your time and consideration on this legislation and am available for any questions you may have.



Rules - 2015

Drug Scheduling Actions

Final Rule: Placement of Eluxadoline Into Schedule IV; Correction (December 17, 2015)

Final Rule: Placement of Eluxadoline Into Schedule IV; Correction (November 16, 2015)

Proposed Rule: Placement of Three Synthetic Phenethylamines Into Schedule I (November 13, 2015)

Final Order: Extension of Temporary Placement of Three Synthetic Phenethylamines in Schedule I (November 13, 2015)

Final Rule: Placement of Eluxadoline Into Schedule IV (November 12, 2015)

Notice of Intent: Temporary Placement of the Synthetic Cannabinoid MAB-CHMINACA Into Schedule I (September 16, 2015)

Final Rule: Removal of [^{123}I]Ioflupane From Schedule II of the Controlled Substances Act (September 11, 2015)

Proposed Rule: Placement of Eluxadoline Into Schedule IV (August 11, 2015)

Final Order: Temporary Placement of Acetyl Fentanyl Into Schedule I (July 17, 2015)

Proposed Rule: Removal of [^{123}I]Ioflupane From Schedule II of the Controlled Substances Act (June 3, 2015)

Notice of Intent: Temporary Placement of Acetyl Fentanyl into Schedule I (May 21, 2015)

Final Order: Extension of Temporary Placement of UR-144, XLR11, and AKB48 in Schedule I of the Controlled Substances Act (May 15, 2015)

Proposed Rule: Placement of UR-144, XLR11, and AKB48 Into Schedule I (May 14, 2015)

Final Rule: Substances Temporarily Controlled Under Schedule I of the Controlled Substances Act (March 20, 2015)

Final Order: Temporary Placement of Three Synthetic Cannabinoids Into Schedule I (January 30, 2015)

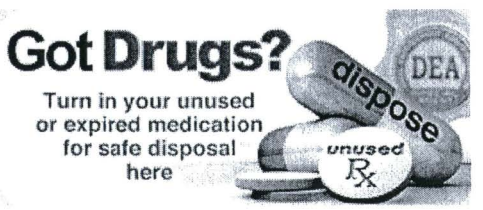
Final Rule: Removal of Naloxegol From Control (January 23, 2015)

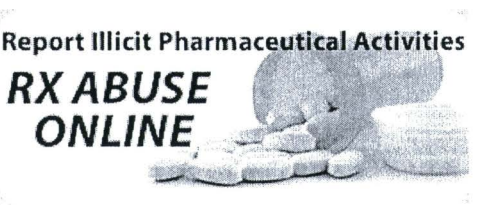
Excluded Nonnarcotic Products

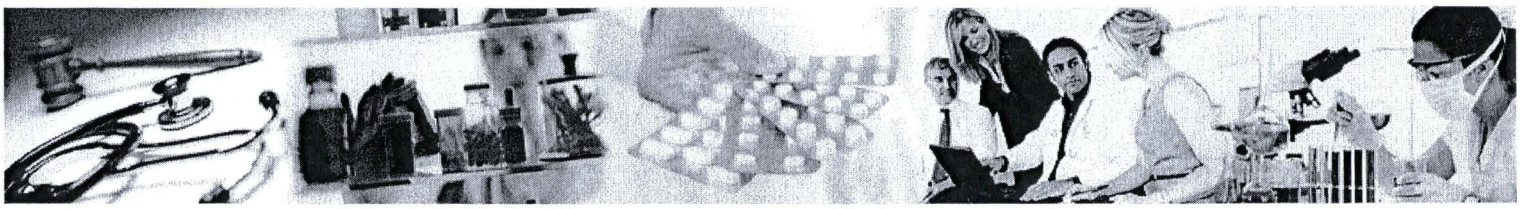
Interim Final Rule: Table of Excluded Nonnarcotic Products: Nasal Decongestant Inhaler/Vapor Inhaler (October 27, 2015)

Interim Final Rule: Table of Excluded Nonnarcotic Products: Vicks® VapoInhaler® (October 27, 2015)

Cases Against Doctors
Chemical Control Program
CMEA (Combat Meth Epidemic Act)
Controlled Substance Schedules
DATA Waived Physicians
Drug Disposal Information
Drug and Chemical Information
E-commerce Initiatives
Federal Agencies & Related Links
Federal Register Notices
National Take-Back Initiative
NFLIS
Publications & Manuals
Questions & Answers
Significant Guidance Documents
Synthetic Drugs
Title 21 Code of Federal Regulations
Title 21 USC Codified CSA







Rules - 2016

Combat Methamphetamine Enhancement Act of 2010 (MEA)

Final Rule: Self-Certification and Employee Training of Mail-Order Distributors of Scheduled Listed Chemical Products (January 25, 2016)

Drug Scheduling Actions

Notice of Intent: Temporary Placement of Six Synthetic Cannabinoids (5F-ADB, 5F-AMB, 5F-APINACA, ADB-FUBINACA, MDMB-CHMICA and MDMB-FUBINACA) Into Schedule I (December 21, 2016)

Final Rule : Establishment of a New Drug Code for Marihuana Extract (December 14, 2016)

Proposed Rule : Designation of Alpha-Phenylacetoacetonitrile (APAAN), a Precursor Chemical Used in the Illicit Manufacture of Phenylacetone, Methamphetamine, and Amphetamine, as a List I Chemical (December 12, 2016)

Final Order: Temporary Placement of Furanyl Fentanyl Into Schedule I (November 29, 2016)

Final Order: Temporary Placement of U-47700 Into Schedule I (November 14, 2016)

Withdrawal of Notice of Intent to Temporarily Place Mitragynine and 7-Hydroxymitragynine Into Schedule I (October 13, 2016)

Notice of Intent: Temporary Placement of Furanyl Fentanyl Into Schedule I (September 27, 2016)

Final Rule: Placement of Three Synthetic Phenethylamines Into Schedule I (September 27, 2016)

Notice of Intent: Temporary Placement of U-47700 Into Schedule I (September 7, 2016)

Final Rule: Placement of PB-22, 5F-PB-22, AB-FUBINACA and ADB-PINACA into Schedule I (September 6, 2016)

Notice of Intent: Temporary Placement of Mitragynine and 7-Hydroxymitragynine Into Schedule I (August 31, 2016)

Interim Final Rule: Placement of Thiafentanil Into Schedule II (August 26, 2016)

Interim Final Rule: Placement of Brivaracetam Into Schedule V (May 12, 2016)

Final Order: Temporary Placement of Butyryl Fentanyl and Beta-Hydroxythiofentanyl Into Schedule I (May 12, 2016)

Final Rule: Placement of UR-144, XLR11, and AKB48 into Schedule I (May 11, 2016)

Final Order: Placement of AH-7921 Into Schedule I (April 14, 2016)

Notice of Intent: Temporary Placement of Butyryl Fentanyl and Beta-Hydroxythiofentanyl Into Schedule I (March 23, 2016)

Proposed Rule: Placement of UR-144, XLR11, and AKB48 Into Schedule I; Correction (March 22, 2016)

Proposed Rule: Placement of 10 Synthetic Cathinones Into Schedule I (March 4, 2016)

Final Order: Extension of Temporary Placement of 10 Synthetic Cathinones in Schedule I of the Controlled Substances Act (March 4, 2016)

Proposed Rule: Placement of PB-22, 5F-PB-22, AB-FUBINACA and ADB-PINACA into Schedule I (February 5, 2016)

Final Order: Temporary Placement of the Synthetic Cannabinoid MAB-CHMINACA Into Schedule I (February 5, 2016)

Final Order: Extension of Temporary Placement of PB-22, 5F-PB-22, AB-FUBINACA and ADB-PINACA in Schedule I of the Controlled Substances Act (February 5, 2016)

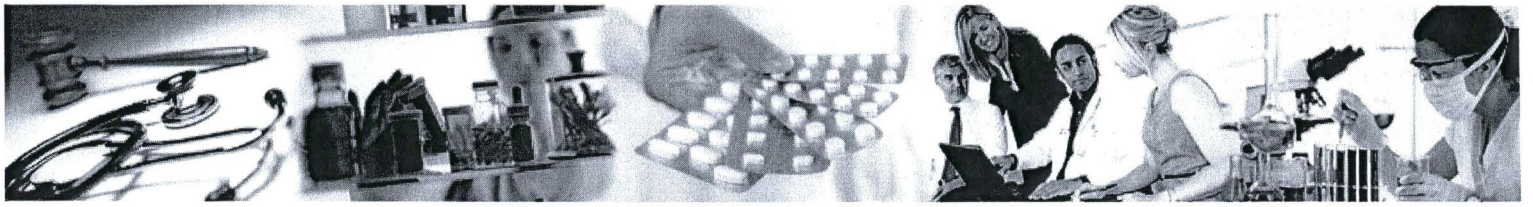
Excluded Nonnarcotic Products

Final Rule: Table of Excluded Nonnarcotic Products: Vicks® VapoInhaler® (February 8, 2016)

Final Rule: Table of Excluded Nonnarcotic Products: Nasal Decongestant Inhaler/Vapor Inhaler (February 8, 2016)

Exempt Chemical Preparations Under the Controlled Substances Act

Cases Against Doctors
Chemical Control Program
CMEA (Combat Meth Epidemic Act)
Controlled Substance Schedules
DATA Waived Physicians
Drug Disposal Information
Drug and Chemical Information
E-commerce Initiatives
Federal Agencies & Related Links
Federal Register Notices
National Take-Back Initiative
NFLIS
Publications & Manuals
Questions & Answers
Significant Guidance Docume
Synthetic Drugs
Title 21 Code of Federal Regulations
Title 21 USC Codified CSA



Rules - 2015

[Federal Register Volume 80, Number 242 (Thursday, December 17, 2015)]
[Rules and Regulations]
[Page 78657]
From the Federal Register Online via the Government Publishing Office [www.gpo.gov]
[FR Doc No: 2015-31843]

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA-419F]

Schedules of Controlled Substances: Placement of Eluxadoline Into Schedule IV; Correction

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Final rule; correction.

SUMMARY: The Drug Enforcement Administration (DEA) is correcting a final rule that appeared in the Federal Register of November 12, 2015 (80 FR 69861). The document issued an action placing the substance 5-[[[(2S)-2-amino-3-[4-aminocarbonyl)-2,6-dimethylphenyl]-1-oxopropyl][(1S)-1-(4-phenyl-1H-imidazol-2-yl)ethyl] amino]methyl]-2-methoxybenzoic acid (eluxadoline), including its salts, isomers, and salts of isomers, into schedule IV of the Controlled Substances Act. This document inadvertently included a paragraph in the regulatory text that was not intended for publication, and was unable to be removed before being placed on public inspection. This document corrects the final rule by removing this paragraph.

DATES: Effective December 17, 2015.

FOR FURTHER INFORMATION CONTACT: John R. Scherbenske, Office of Diversion Control, Drug Enforcement Administration; Mailing Address: 8701 Morrissette Drive, Springfield, Virginia 22152, Telephone: (202) 598-6812.

SUPPLEMENTARY INFORMATION: In **FR Doc. 2015-28718** appearing on page 69864 in the Federal Register of Thursday, November 12, 2015, the following correction is made:

Administrative Procedure Act [Corrected]

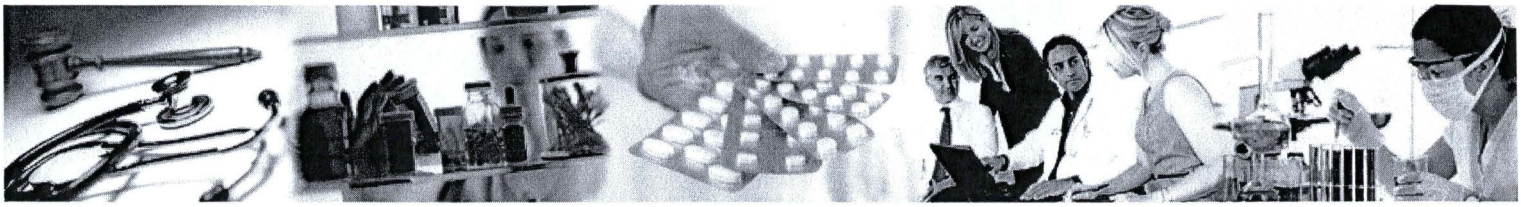
1. On page 69864, in the preamble, at the bottom of the first and top of the second columns, the section titled *Administrative Procedure Act* is removed entirely.

Dated: December 11, 2015.

Chuck Rosenberg,
Acting Administrator.

[FR Doc. 2015-31843 Filed 12-16-15; 8:45 am]

BILLING CODE 4410-09-P



Rules - 2016

[Federal Register Volume 81, Number 166 (Friday, August 26, 2016)]
[Rules and Regulations]
[Pages 58834-58840]
From the Federal Register Online via the Government Publishing Office [www.gpo.gov]
[FR Doc No: 2016-20463]

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Parts 1301, 1305, and 1308

[Docket No. DEA-375]

Schedules of Controlled Substances: Placement of Thiafentanil Into Schedule II

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Interim final rule with request for comments.

SUMMARY: The Drug Enforcement Administration is placing the substance thiafentanil (4-(methoxycarbonyl)-4-(N-phenmethoxyacetamido)-1-[2-(thienyl)ethyl] piperidine), including its isomers, esters, ethers, salts and salts of isomers, esters and ethers as possible, into schedule II of the Controlled Substances Act. This scheduling action is pursuant to the Controlled Substances Act, as revised by the Improving Regulatory Transparency for New Medical Therapies Act which was signed into law on November 25, 2015.

DATES: The effective date of this rule is August 26, 2016. Interested persons may file written comments on this rule in accordance with **21 U.S.C. 811**(j)(3) and **21 CFR 1308.43**(g). Electronic comments must be submitted, and written comments must be postmarked, on or before September 26, 2016. Commenters should be aware that the electronic Federal Docket Management System will not accept comments after 11:59 p.m. Eastern Time on the last day of the comment period.

Interested persons, defined at **21 CFR 1300.01** as those "adversely affected or aggrieved by any rule or proposed rule issuable pursuant to section 201 of the Act (**21 U.S.C. 811**)," may file a request for hearing or waiver of hearing pursuant to **21 CFR 1308.44** and in accordance with **21 CFR 1316.45** and/or **1316.47**, as applicable. Requests for hearing and waivers of an opportunity for a hearing or to participate in a hearing must be received on or before September 26, 2016.

ADDRESSES: To ensure proper handling of comments, please reference "Docket No. DEA-375" on all correspondence, including any attachments.

- *Electronic comments:* The Drug Enforcement Administration encourages that all comments be submitted electronically through the Federal eRulemaking Portal, which provides the ability to type short comments directly into the comment field on the Web page or attach a file for lengthier comments. Please go to http://www.regulations.gov and follow the online instructions at that site for submitting comments. Upon completion of your submission, you will receive a Comment Tracking Number for your comment. Please be aware that submitted comments are not instantaneously available for public view on Regulations.gov. If you have received a Comment Tracking Number, your comment has been successfully submitted and there is no need to resubmit the same comment.
- *Paper comments:* Paper comments that duplicate the electronic submission are not necessary and are discouraged. Should you wish to mail a paper comment in lieu of an electronic comment, it should be sent via regular or express mail to: Drug Enforcement Administration, Attn: DEA Federal Register Representative/ODW, 8701 Morrissette Drive, Springfield, Virginia 22152.
- *Hearing requests:* All requests for hearing and waivers of participation must be sent to: Drug Enforcement Administration, Attn: Administrator, 8701 Morrissette Drive, Springfield, Virginia 22152. All requests for hearing and waivers of participation should also be sent to: (1) Drug Enforcement Administration, Attn: Hearing Clerk/LJ, 8701 Morrissette Drive, Springfield, Virginia 22152; and (2) Drug Enforcement Administration, Attn: DEA Federal Register Representative/ ODW, 8701 Morrissette Drive, Springfield, Virginia 22152.

FOR FURTHER INFORMATION CONTACT: Michael J. Lewis, Office of Diversion Control, Drug Enforcement Administration; Mailing Address: 8701 Morrissette Drive, Springfield, Virginia 22152; Telephone: (202) 598-6812.

SUPPLEMENTARY INFORMATION:

Posting of Public Comments

Please note that all comments received are considered part of the public record. They will, unless reasonable cause is given, be made available by the Drug Enforcement

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Administration (DEA) for public inspection online at http://www.regulations.gov. Such information includes personal identifying information (such as your name, address, etc.) voluntarily submitted by the commenter. The Freedom of Information Act (FOIA) applies to all comments received. If you want to submit personal identifying information (such as your name, address, etc.) as part of your comment, but do not want it to be made publicly available, you must include the phrase

"PERSONAL IDENTIFYING INFORMATION" in the first paragraph of your comment. You must also place all of the personal identifying information you do not want made publicly available in the first paragraph of your comment and identify what information you want redacted.

If you want to submit confidential business information as part of your comment, but do not want it to be made publicly available, you must include the phrase "CONFIDENTIAL BUSINESS INFORMATION" in the first paragraph of your comment. You must also prominently identify the confidential business information to be redacted within the comment.

[redacted]ments containing personal identifying information and confidential business information identified as directed above will generally be made publicly available in [redacted]cted form. If a comment has so much confidential business information or personal identifying information that it cannot be effectively redacted, all or part of that [redacted]mment may not be made publicly available. Comments posted to http://www.regulations.gov may include any personal identifying information (such as name, address, and phone number) included in the text of your electronic submission that is not identified as directed above as confidential.

An electronic copy of this document and supplemental information, including the complete Department of Health and Human Services and Drug Enforcement Administration eight-factor analyses, to this interim final rule are available at http://www.regulations.gov for easy reference.

Request for Hearing, Notice of Appearance at Hearing, or Waiver of Participation in Hearing

Pursuant to **21 U.S.C. 811**(a), this action is a formal rulemaking "on the record after opportunity for a hearing." Such proceedings are conducted pursuant to the provisions of the Administrative Procedure Act (APA), 5 U.S.C. 551-559. **21 CFR 1308.41-1308.45**; **21 CFR part 1316**, subpart D. In accordance with **21 CFR 1308.44**(a)-(c), requests for a hearing, notices of appearance, and waivers of an opportunity for a hearing or to participate in a hearing may be submitted only by interested persons, defined as those "adversely affected or aggrieved by any rule or proposed rule issuable pursuant to section 201 of the Act (21 U.S.C. 811)." **21 CFR 1300.01**. Requests for a hearing and notices of participation must conform to the requirements of **21 CFR 1308.44**(a) or (b), as applicable, and include a statement of the interest of the person in the proceeding and the objections or issues, if any, concerning which the person desires to be heard. Any waiver of an opportunity for a hearing must conform to the requirements of 21 CFR 1308.44(c), including a written statement regarding the interested person's position on the matters of fact and law involved in any hearing.

Please note that pursuant to **21 U.S.C. 811**(a), the purpose and subject matter of the hearing are restricted to "(A) find[ing] that such drug or other substance has a potential for abuse, and (B) mak[ing] with respect to such drug or other substance the findings prescribed by subsection (b) of **section 812** of this title for the schedule in which such drug is to be placed . . . ." Requests for a hearing and waivers of participation in the hearing should be submitted to the DEA on or before the deadline specified above, using the address information provided therein.

Background, Legal Authority, and Basis for This Scheduling Action

Thiafentanil, known chemically as 4-(methoxycarbonyl)-4-(N-phenylmethoxyacetamido)-1-[2-(2-thienyl)ethyl]piperidine, a potent opioid, is an analogue of fentanyl. The product Thianil (thiafentanil oxalate, a salt form of thiafentanil) was reviewed by the Food and Drug Administration (FDA) to determine whether it meets the requirements for addition to the Index of Legally Marketed Unapproved New Animal Drugs for Minor Species (the Index) (21 U.S.C. 360ccc-1) as set forth by the Minor Use and Minor Species Animal Health Act of 2004 (MUMS Act, 2004). The MUMS Act amended the Federal Food, Drug, and Cosmetic Act (FDCA) to allow for the legal marketing of unapproved new animal drugs intended for use in minor species. In a letter from the Department of Health and Human Services (HHS) dated June 20, 2016, the DEA received notification that HHS/FDA added Thianil (thiafentanil oxalate) to the Index under section 572 of the FDCA. In this same notification, HHS/FDA stated that on June 16, 2016, HHS/FDA granted the request for the addition of Thianil to the Index under Minor Species Index File (MIF) 900000. Thianil is indicated for use in the immobilization of non-domestic, non-food-producing minor species hoofstock.

Thiafentanil will be marketed as thiafentanil oxalate, 4-(methoxycarbonyl)-4-(N-phenylmethoxyacetamido)-1-[2-(2-thienyl)ethyl]piperidinium oxalate. Thiafentanil should not be confused with thiofentanyl (N-phenyl-N-(1-(2-(thiophen-2-yl)ethyl)piperidin-4-yl)propionamide), which is currently listed as a controlled schedule I substance.

Under the Controlled Substances Act (CSA), as amended in 2015 by the Improving Regulatory Transparency for New Medical Therapies Act (Pub. L. 114-89), where the DEA receives notification from HHS that the Secretary has indexed a drug under section 572 of the FDCA, the DEA is required to issue an interim final rule [redacted]ntrolling the drug not later than 90 days after receiving such notification from HHS. **21 U.S.C. 811**(j). Accordingly, the DEA is issuing this interim final rule [redacted]ntrolling thiafentanil.

When controlling a drug pursuant to **section 811**(j), the DEA must apply the scheduling criteria of subsections 811(b), (c), and (d) and **section 812**(b). 21 U.S.C. 811(j)(3). In accordance with these criteria, the DEA has reviewed the scientific and medical evaluation and scheduling recommendation provided by the HHS, along with all other relevant data, and completed its own eight-factor review document on thiafentanil pursuant to 21 U.S.C. 811(c). As explained below, based on these considerations, the DEA concludes that thiafentanil meets the criteria for placement in schedule II of the CSA.

On November 28, 2011, the HHS provided the DEA with its initial scientific and medical evaluation and scheduling recommendation regarding thiafentanil. Pursuant to **21 U.S.C. 811**(b), this document contained an eight-factor analysis of the abuse potential of thiafentanil as a new drug, along with the HHS' recommendation to control thiafentanil and its salts under schedule II of the CSA. Subsequently, on March 23, 2016, the HHS provided the DEA with a supplement to its 2011 analysis, which indicated that the HHS/FDA planned to add Thianil (thiafentanil oxalate) to the Index for use in the immobilization of non-domestic, non-food-producing minor species hoofstock and reiterated their recommendation that thiafentanil be placed in schedule II of the CSA. By

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letter dated June 20, 2016, the DEA received notification from the HHS that the FDA had granted the request on June 16, 2016, for Thianil (thiafentanil oxalate) to be added to the Index.

Pursuant to **21 U.S.C. 811**(j), and based on the HHS recommendation, MUMS Act indication by the HHS/FDA, and the DEA's determination, the DEA finds that thiafentanil has a high potential for abuse, a currently accepted medical use with severe restrictions, and that abuse of thiafentanil may lead to severe psychological or physical dependence. Accordingly, the DEA is issuing this interim final rule to add thiafentanil (4-(methoxycarbonyl)-4-(N-phenylmethoxyacetamido)-1-[2-(2-thienyl) ethyl]piperidine) and its isomers, esters, ethers, salts and salts of isomers, esters and ethers, whenever the existence of such, to schedule II of the CSA.

Included below is a brief summary of each factor as analyzed by the HHS and the DEA, and as considered by the DEA in its scheduling action. Please note that the DEA and HHS analyses, along with the HHS supplement, are available in their entirety under "Supporting Documents" in the public docket for this interim final rule at http://www.regulations.gov, under Docket Number "DEA-375." Full analysis of, and citations to, the information referenced in the summary may also be found in the supporting and related material.

1. *The Drug's Actual or Relative Potential for Abuse:* Thiafentanil is a chemical substance that has not been marketed in the United States, however, it is approved and marketed in the Republic of South Africa as a salt form under the brand name Thianil (thiafentanil oxalate). There is no information available which details actual abuse of thiafentanil.

According to the HHS, thiafentanil is a synthetic analogue of fentanyl and is structurally related to other fentanyl-like opioids such as sufentanil (schedule II) and carfentanil (schedule II). It acts as a potent [micro]-opioid receptor agonist and produces strong morphine-like effects in animals. It is only intended for the immobilization of non-domestic, non-food-producing minor species hoofstock. Thiafentanil has been used in a manner similar to other opioid immobilizing agents such as etorphine hydrochloride (schedule II) and carfentanil (schedule II), which are approved only for veterinary use as animal immobilization agents. The abuse potential of thiafentanil has not been evaluated in humans or in animal behavioral models that are predictors of abuse by humans. Because thiafentanil shares chemical and pharmacological similarities with schedule II fentanyl and its analogues, the abuse potential of thiafentanil is considered similar to that of schedule II opioid substances such as sufentanil and carfentanil.

[redacted]Pharmacologically, as a potent [micro] opioid receptor agonist, thiafentanil is slightly less potent than carfentanil, which is 100 times more potent than fentanyl and [redacted],000 times more potent than morphine. Thiafentanil is a potent fentanyl analogue. Thus, it is reasonable to assume that there will be potentially significant diversion [redacted] thiafentanil from legitimate channels by people who have access to it, and that thiafentanil would be used without medical advice, therefore causing substantial hazards to the users or to the safety of the community if not controlled. The chemical and potent opioid-like pharmacological properties of thiafentanil predict that its risk to the public health is likely to be similar to fentanyl (schedule II) and its analogues such as carfentanil (schedule II), sufentanil (schedule II) and alpha-methylfentanyl (schedule I).

2. *Scientific Evidence of the Drug's Pharmacological Effects, if Known:* According to HHS' scientific and medical review, there are no data on the effects of thiafentanil in humans. Thiafentanil's effects in humans are predicted from its effects in animals and its chemical and pharmacological similarity to other schedule II potent opioids such as fentanyl and carfentanil.

The HHS eight-factor review document described a study directly comparing the immobilizing effects of thiafentanil (15 mg) and carfentanil (2 or 4 mg) in elk in which thiafentanil produced a faster immobilization effect (0.7 to 2.2 minutes) than carfentanil. In addition, the elk returned to standing 0.9 to 1.4 minutes faster under the thiafentanil condition. This study appears to support a faster immobilization and recovery time with thiafentanil relative to carfentanil. However, the authors st[redacted] that the role of the increased dose of thiafentanil is unknown.

Animal studies described by the HHS demonstrated that the effects of thiafentanil and carfentanil are completely reversed by naltrexone. As a [micro]-opioid receptor antagonist, naltrexone can reverse the effects of a variety of opioid drugs including thiafentanil and carfentanil. Those studies suggest that thiafentanil possesses a neuro-pharmacological mechanism of action similar to other schedule II opioid drugs with a high abuse potential.

According to HHS' review, Thianil (thiafentanil) is currently approved and registered for use in the Republic of South Africa. Thiafentanil oxalate is suggested as a drug of choice in the capture of exotic and ungulate wildlife species.

3. *The State of Current Scientific Knowledge Regarding Thiafentanil:* The chemical name of free base thiafentanil is 4-(methoxycarbonyl) -4-(N-phenylmethoxyacetamido)-1-[2-(2-thienyl)ethyl]piperidine. It has a molecular formula of C22H28N2O4S and a molecular weight of 416.52 g/mol with a Chemical Abstract Registry Number (CAS) of 101345-60-2. Thiafentanil oxalate is also known as A3080 with a CAS number of 101365-73-5 and has a molecular formula of C24H30N2O8S with a molecular weight of 506.57 g/mol. Thiafentanil oxalate is a white crystalline powder with a melting point of 190-192 [deg]C and its salt crystalizes from absolute alcohol. Thiafentanil should not be confused with thiofentanyl (N-phenyl-N-(1-(2-(thiophen-2-yl)ethyl)piperidin-4-yl)propionamide), which is currently listed as a schedule I substance.

4. *Its History and Current Pattern of Abuse:* According to the HHS' review, there are no reports of actual abuse and misuse of thiafentanil. This may be due to the limited use of thiafentanil as an immobilizing agent by trained veterinarians.

Current data from the National Forensic Laboratory System (NFLIS),\1\ the System to Retrieve Information from Drug Evidence (STRIDE),\2\ and the STARLiMS databases show that there is no evidence of law enforcement encounters of thiafentanil in the United States. However, thiafentanil's pharmacological and structural properties suggest that its pattern of abuse would be similar to other potent

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schedule II [micro]-opioid receptor agonists such as fentanyl and carfentanil.

\1\ The National Forensic Laboratory System (NFLIS) is a program of the DEA, Office of Diversion Control. NFLIS systematically collects drug identification results and associated information from drug cases submitted to and analyzed by State and local forensic laboratories. NFLIS represents an important resource in monitoring illicit drug abuse and trafficking, including the diversion of legally manufactured pharmaceuticals into illegal markets. NFLIS is a comprehensive information system that includes data from forensic laboratories that handle approximately 90% of an estimated 1.0 million distinct annual State and local drug analysis cases. NFLIS includes drug chemistry results from completed analyses only. While NFLIS data is not direct evidence of abuse, it can lead to an inference that a drug has been diverted and abused. See 76 FR 77330, 77332, Dec. 12, 2011.

\2\ The System to Retrieve Information from Drug Evidence (STRIDE) is a database of drug exhibits sent to DEA laboratories for analysis. Exhibits from the database are from the DEA, other federal agencies, and local law enforcement agencies. Reporting via STRIDE ceased on September 30, 2014. STRIDE was succeeded by STARLiMS.

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5. *The Scope, Duration, and Significance of Abuse:* An assessment of the scope, duration, and significance of thiafentanil abuse is not available since it has only bee[redacted] used in a limited market. However, as stated in the HHS review, the structural and pharmacological properties of thiafentanil suggest that it could lead to an ab[redacted] pattern with a scope, duration, and significance of abuse similar to that observed with other opioid drugs and opioid analogues if it were marketed in a non-cont[redacted] status or were the subject of clandestine synthesis. The HHS and DEA note that thiafentanil is not known to be or to have been the subject of abuse in the Unite[redacted] States.

6. *What, if any, Risk There is to the Public Health:* The HHS review indicates that thiafentanil presents a significant risk to the public health and, in this vein, that thiafentanil should only be used in certain animals for very limited purposes and with extreme caution. Based on the review of the structural and pharmacological properties of thiafentanil, the HHS concluded that the abuse of thiafentanil is likely to pose a similar risk to public health as that of other potent opioid drugs such as sufentanil (schedule II), fentanyl (schedule II), carfentanil (schedule II) and clandestinely synthesized alpha-methylfentanyl (schedule I). Thus, inappropriate use of thiafentanil poses a high risk to the public health. Among other things, HHS noted that as a fentanyl derivative, and assuming that thiafentanil can be aerosolized, the use of thiafentanil presents a significant risk to the public health.

HHS described that thiafentanil's labeling indicates that it is solely intended for use by zoologic, wildlife, or exotic animal veterinarians or field biologists who have received training and are supervised by veterinarians. The sponsor recommends the use of handling protocols similar to those in place for other scheduled potent opioids such as carfentanil. HHS further indicated that thiafentanil should be handled in teams consisting of at least two individuals knowledgeable about the hazards of working with potent [mu]-opioid agonist substances. Personal protective equipment such as latex gloves and protective eyewear should be used and syringes must be disposed of properly. If exposure to thiafentanil occurs in a remote or distant environment, veterinary naltrexone is recommended for use as a reversal agent. The label information will further state that thiafentanil must never be used unless an adequate amount of reversal agent (naltrexone hydrochloride) is immediately available.

HHS also describes the risk of thiafentanil intoxication upon ingestion of animals immobilized with thiafentanil. The label information states that thiafentanil is not intended for human or animal consumption or in non-food producing minor species that become eligible for consumption by humans or food-producing animals. Because thiafentanil, similar to carfentanil, etorphine hydrochloride and diprenorphine, is a potent [mu]-opioid receptor agonist, it will be subject to specialized handling, distribution and storage procedures similar to those applicable for carfentanil, etorphine hydrochloride and diprenorphine as set forth in **21 CFR parts 1301** and **1305**. As a result, this interim final rule revises **21 CFR 1301.74**(g), **1301.75**(e), **1305.07** introductory text and paragraph (a), and **1305.17**(d) to include "thiafentanil."

7. *Its Psychic or Physiological Dependence Liability:* HHS' review states that the structural and pharmacological properties of thiafentanil suggest that it possesses a psychic and physiological dependence liability that is similar to other schedule II related [micro]-opioid receptor agonist drugs such as sufentanil, fentanyl and carfentanil.

As cited by the HHS review, a double-blind abuse liability study examining intravenous fentanyl, buprenorphine, heroin, morphine, and oxycodone in methadone-maintained patients reported that fentanyl produced subjective effects similar to heroin (schedule I) on several outcome measures indicating that the two drugs produce similar subjective effects. It also demonstrates the psychic dependence liability of fentanyl, and thiafentanil is expected to produce effects similar to fentanyl and to present a similar risk of psychic and physiological dependence. There has been a major increase in abuse of opioids analgesics in the United States (HHS review document, 2011; Compton and Volkow, 2006). Thiafentanil, similar to these opioid analgesics, presents a risk of severe psychic and physiological dependence.

8. *Whether the Substance is an Immediate Precursor of a Substance Already Controlled under the CSA:* Thiafentanil is not considered an immediate precursor of any controlled substance.

Determination of Appropriate Schedule

The CSA lists the findings required to place a drug or other substance in any particular schedule (I, II, III, IV, or V). **21 U.S.C. 812**(b). After consideration of th[redacted] analysis and recommendation of the Assistant Secretary for Health of the HHS and review of all available data, the Acting Administrator of the DEA, pursuant to U.S.C. 812(b)(2), finds that:

1. Thiafentanil has a high potential for abuse. Based on its structural and pharmacological properties, thiafentanil has an abuse potential that is comparable to other schedule II opioid drugs such as fentanyl, carfentanil, and sufentanil;

2. FDA determined that Thianil (thiafentanil oxalate) meets the requirements for addition to the Index as set forth by the MUMS Act, 2004 and accordingly added Thianil (thiafentanil oxalate) to the Index of Legally Marketed Unapproved New Animal Drugs for Minor Species (the Index) under section 572 of the Federal Food, Drug, and Cosmetic Act. Thianil (thiafentanil oxalate) will be legally marketed in the United States and will have an accepted medical use with severe restrictions; \3\ and

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\3\ According to the HHS analysis, "[u]se of a new animal indexed drug is subject to significant restrictions. For example, use of an indexed new animal drug for minor species is limited to a minor species for which there is a reasonable certainty that the animal or edible products from the animal will not be consumed by humans or food producing animals. 21 U.S.C. Sec. 360ccc-l(a)(1). The requester must label, distribute, and promote the new animal drug in accordance with the Index entry, and the FDA may remove a new animal drug from the Index if the conditions and limitations of use have not been followed. 21 U.S.C. 360ccc-l(d)(l)(G); (f)(l)(F). The labeling of an indexed new animal drug must prominently state that the extra-label use of the product is prohibited. 21 U.S.C. 360ccc-l(h). Such restrictions are not imposed upon approved human or animal drugs."

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3. Due to the chemical and pharmacological similarities of thiafentanil to other schedule II fentanyl derivatives, abuse of thiafentanil may lead to severe psychological or physical dependence.

Based on these findings, the Acting Administrator of the DEA concludes that thiafentanil, including its isomers, esters, ethers, salts and salts of isomers, esters and ethers whenever the existences of such isomers, esters, ethers, and salts is possible warrants control in schedule II of the CSA. **21 U.S.C. 812**(b)(2).

Requirements for Handling Thiafentanil

Thiafentanil is subject to the CSA's schedule II regulatory controls and administrative, civil, and criminal sanctions applicable to the manufacture, distribution, reverse distribution, dispensing, importing, exporting, research, and conduct of instructional

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activities and chemical analysis with, and possession involving schedule II substances, including the following:

1. *Registration.* Any person who desires to handle thiafentanil (manufacture, distribute, reverse distribute, dispense, import, export, engage in research, or conduct instructional activities or chemical analysis with, or possess), must be registered with the DEA to conduct such activities pursuant to **21 U.S.C. 822**, **823**, **957**, and **958** and in accordance with **21 CFR parts 1301** and **1312**.

2. *Quota.* Only registered manufacturers are permitted to manufacture thiafentanil in accordance with a quota assigned pursuant to **21 U.S.C. 826** and in accordance with **21 CFR part 1303**.

3. *Disposal of stocks.* Upon obtaining a schedule II registration to handle thiafentanil, and if subsequently, any person who does not desire or is not able to maintain a schedule II registration must surrender all quantities of currently held thiafentanil, or may transfer all quantities of currently held thiafentanil to a person registered with the DEA in accordance with **21 CFR part 1317**, in addition to all other applicable federal, state, local, and tribal laws.

4. *Security.* Thiafentanil is subject to schedule II security requirements and must be handled and stored pursuant to **21 U.S.C. 821** and **823**, and in accordance with **21 CFR 1301.71-1301.93**.

5. *Labeling and Packaging.* All labels, labeling, and packaging for commercial containers of thiafentanil must comply with **21 U.S.C. 825** and **958**(e), and be in accordance with **21 CFR part 1302**. In addition, thiafentanil is subject to additional labeling requirements provided by FDA. Thiafentanil must be labeled, distributed, and promoted in accordance with the Index entry of the new animal drug and the FDA may remove a new animal drug from the Index if the conditions and limitations of use have not been followed. 21 U.S.C. 360ccc-l(d)(l)(G); (f)(l)(F). The labeling of an indexed new animal drug must prominently state that the extra-label use of the product is prohibited. 21 U.S.C. 360ccc-l(h).

[redacted]*Inventory.* Every DEA registrant who desires to possess any quantity of thiafentanil must take an inventory of thiafentanil on hand, pursuant to **21 U.S.C. 827** and **8**, and in accordance with **21 CFR 1304.03**, **1304.04**, and **1304.11**.

Any person who becomes registered with the DEA to handle thiafentanil must take an initial inventory of all stocks of controlled substances (including thiafentanil) on hand on the date the registrant first engages in the handling of controlled substances, pursuant to **21 U.S.C. 827** and **958**, and in accordance with **21 CFR 1304.03**, **1304.04**, and **1304.11**.

After the initial inventory, every DEA registrant must take a new inventory of all stocks of controlled substances (including thiafentanil) on hand every two years, pursuant to **21 U.S.C. 827** and **958**, and in accordance with **21 CFR 1304.03**, **1304.04**, and **1304.11**.

7. *Records and Reports.* Every DEA registrant must maintain records and submit reports for thiafentanil, or products containing thiafentanil, pursuant to **21 U.S.C. 827** and **958**(e), and in accordance with **21 CFR parts 1304**, **1312**, and **1317**.

8. *Orders for thiafentanil.* Every DEA registrant who distributes thiafentanil is required to comply with order form requirements, pursuant to **21 U.S.C. 828**, and in accordance with **21 CFR part 1305**.

9. *Prescriptions and other dispensing.* All prescriptions for thiafentanil or products containing thiafentanil must comply with **21 U.S.C. 829**, and be issued in accordance with **21 CFR parts 1306** and **1311**, subpart C. Moreover, given that thiafentanil is not the subject of an approved new drug application under the FDCA, and that it is only allowed under the MUMS Act amendments to the FDCA to be marketed for extremely limited use in minor species, DEA would not consider any dispensing of thiafentanil for human use to be for a legitimate medical purpose within the meaning of the CSA. Likewise, DEA would not consider any dispensing of thiafentanil for animal use beyond the scope of the drug's labeling authorized under the MUMS Act amendments to the FDCA to be for a legitimate medical purpose within the meaning of the CSA.

10. *Manufacturing and Distributing.* In addition to the general requirements of the CSA and DEA regulations that are applicable to manufacturers and distributors of schedule II controlled substances, such registrants should be advised that (consistent with the foregoing considerations) any manufacturing or distribution of thiafentanil may only be for the legitimate purposes consistent with the drug's labeling authorized under the MUMS Act, or for research activities authorized by the FDCA and CSA.

11. *Importation and Exportation.* All importation and exportation of thiafentanil must be in compliance with **21 U.S.C. 952**, **953**, **957**, and **958**, and in accordance with **21 CFR part 1312**.

12. *Liability.* Any activity involving thiafentanil not authorized by, or in violation of, the CSA or its implementing regulations, is unlawful, and may subject the person to administrative, civil, and/or criminal sanctions.

Regulatory Analyses

Administrative Procedure Act

Public Law 114-89 was signed into law, amending **21 U.S.C. 811**. This amendment provides that in cases where a new drug is (1) approved or indexed by the Department of Health and Human Services (HHS) and (2) HHS recommends control in CSA schedule II-V, the DEA shall issue an interim final rule scheduling the drug within 90 days. Additionally, the law specifies that the rulemaking shall become immediately effective as an interim final rule without requiring the DEA to demonstrate good cause. Therefore, the DEA has determined that the notice and comment requirements of section 553 of the APA, 5 U.S.C. 553, do not apply to this scheduling [redacted]tion.

[redacted]*ecutive Orders 12866, Regulatory Planning and Review, and 13563, Improving Regulation and Regulatory Review*

In accordance with Public Law 114-89, this scheduling action is subject to formal rulemaking procedures performed "on the record after opportunity for a hearing," which are conducted pursuant to the provisions of 5 U.S.C. 556 and 557. The CSA sets forth the procedures and criteria for scheduling a drug or other substance. Such actions are exempt from review by the Office of Management and Budget (OMB) pursuant to section 3(d)(1) of Executive Order 12866 and the principles reaffirmed in Executive Order 13563.

Executive Order 12988, Civil Justice Reform

This regulation meets the applicable standards set forth in sections 3(a) and 3(b)(2) of Executive Order 12988 to eliminate drafting errors and ambiguity, minimize litigation, provide a clear legal standard for affected conduct, and promote simplification and burden reduction.

Executive Order 13132, Federalism

This rulemaking does not have federalism implications warranting the application of Executive Order 13132. The rule does not have substantial direct effects or States, on the relationship between the national government and the States, or on the distribution of power and

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responsibilities among the various levels of government.

Executive Order 13175, Consultation and Coordination With Indian Tribal Governments

This rule does not have tribal implications warranting the application of Executive Order 13175. It does not have substantial direct effects on one or more Indian tribes, on the relationship between the Federal government and Indian tribes, or on the distribution of power and responsibilities between the Federal government and Indian tribes.

Regulatory Flexibility Act

In accordance with 5 U.S.C. 603(a), "[w]henever an agency is required by [5 U.S.C. 553], or any other law, to publish general notice of proposed rulemaking for any proposed rule, or publishes a notice of proposed rulemaking for an interpretive rule involving the internal revenue laws of the United States, the agency shall prepare and make available for public comment an initial regulatory flexibility analysis." As noted in the above discussion regarding applicability of the Administrative Procedure Act, the DEA has determined that the notice and comment requirements of section 553 of the APA, 5 U.S.C. 553, do not apply to this scheduling action. Consequently, the RFA does not apply to this interim final rule.

Unfunded Mandates Reform Act of 1995

In accordance with the Unfunded Mandates Reform Act (UMRA) of 1995, 2 U.S.C. 1501 et seq., the DEA has determined and certifies that this action would not result in any Federal mandate that may result "in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted for inflation) in any one year." Therefore, neither a Small Government Agency Plan nor any other action is required under UMRA of 1995.

Paperwork Reduction Act of 1995

This action does not impose a new collection of information requirement under the Paperwork Reduction Act of 1995. 44 U.S.C. 3501-3521. This action would not impose recordkeeping or reporting requirements on State or local governments, individuals, businesses, or organizations. An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Congressional Review Act

This rule is not a major rule as defined by section 804 of the Small Business Regulatory Enforcement Fairness Act of 1996 (Congressional Review Act (CRA)). This rule will not result in: An annual effect on the economy of $100,000,000 or more; a major increase in costs or prices for consumers, individual industries, Federal, State, or local government agencies, or geographic regions; or significant adverse effects on competition, employment, investment, productivity, innovation, or on the ability of U.S.-based companies to compete with foreign based companies in domestic and export markets. However, pursuant to the CRA, the DEA has submitted a copy of this interim final rule to both Houses of Congress and to the Comptroller General.

List of Subjects

21 CFR Part 1301

Administrative practice and procedure, Drug traffic control, Security measures.

21 CFR Part 1305

Drug traffic control, Reporting and recordkeeping requirements.

21 CFR Part 1308

Administrative practice and procedure, Drug traffic control, Reporting and recordkeeping requirements.

For the reasons set out above, the DEA amends **21 CFR parts 1301**, **1305** and **1308** as follows:

PART 1301--REGISTRATION OF MANUFACTURERS, DISTRIBUTORS, AND DISPENSERS OF CONTROLLED SUBSTANCES

- 1. The authority citation for 21 CFR part 1301 continues to read as follows:

  Authority: 21 U.S.C. 821, 822, 823, 824, 831, 871(b), **875, 877, 886a, 951, 952, 953, 956, 957, 958, 965**.

- 2. In **Sec. 1301.74**, revise paragraph (g) to read as follows:

Sec. 1301.74 Other security controls for non-practitioners; narcotic treatment programs and compounders for narcotic treatment programs.

* * * * *

(g) Before the initial distribution of thiafentanil, carfentanil, etorphine hydrochloride and/or diprenorphine to any person, the registrant must verify that the person is authorized to handle the substance(s) by contacting the Drug Enforcement Administration.

* * * * *

- 3. In **Sec. 1301.75**, revise paragraph (e) to read as follows:

Sec. 1301.75 Physical security controls for practitioners.

* * * * *

(e) Thiafentanil, carfentanil, etorphine hydrochloride and diprenorphine shall be stored in a safe or steel cabinet equivalent to a U.S. Government Class V security container.

PART 1305--ORDERS FOR SCHEDULE I AND II CONTROLLED SUBSTANCES

- 4. The authority citation for 21 CFR part 1305 continues to read as follows:

  Authority: **21 U.S.C. 821, 828, 871**(b), unless otherwise noted.

- 5. In **Sec. 1305.07**, revise the introductory text and paragraph (a) to read as follows:

Sec. 1305.07 Special procedure for filling certain orders.

A supplier of thiafentanil, carfentanil, etorphine hydrochloride, or diprenorphine, if he or she determines that the purchaser is a veterinarian engaged in zoo and exotic animal practice, wildlife management programs, or research, and is authorized by the Administrator to handle these substances, may fill the order in accordance with the procedures set forth in **Sec. 1305.17** except that:

[redacted] DEA Form 222 or an electronic order for thiafentanil, carfentanil, etorphine hydrochloride, and diprenorphine must contain only these substances in reasonable [redacted]tities.

* * * * *

- 6. In **Sec. 1305.17**, revise paragraph (d) to read as follows:

Sec. 1305.17 Preservation of DEA Forms 222.

* * * * *

(d) The supplier of thiafentanil, carfentanil, etorphine hydrochloride, and diprenorphine must maintain DEA Forms 222 for these substances separately from all other DEA Forms 222 and records required to be maintained by the registrant.

PART 1308--SCHEDULES OF CONTROLLED SUBSTANCES

- 7. The authority citation for 21 CFR part 1308 continues to read as follows:

  Authority: **21 U.S.C. 811, 812, 871**(b), unless otherwise noted.

- 8. In **Sec. 1308.12**, add paragraph (c)(29) to read as follows:

Sec. 1308.12 Schedule II.

* * * * *

(c) * * *

(29) Thiafentanil 9729

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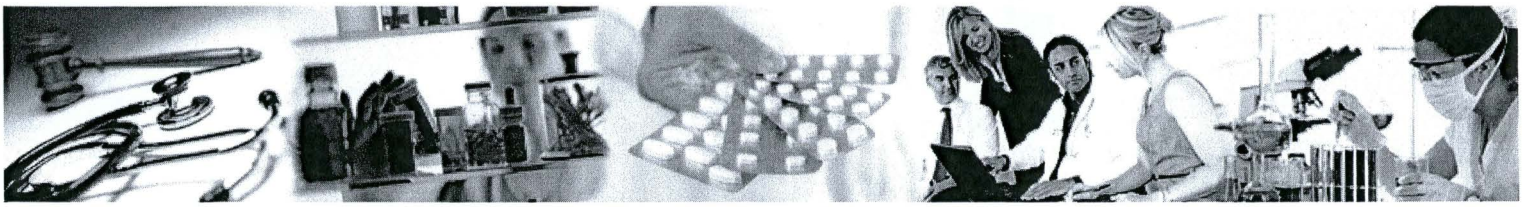
Dated: August 18, 2016.

Chuck Rosenberg,
Acting Administrator.

[FR Doc. 2016-20463 Filed 8-25-16; 8:45 am]

[redacted]LING CODE 4410-09-P



Rules - 2016

[Federal Register Volume 81, Number 43 (Friday, March 4, 2016)]
[Proposed Rules]
[Pages 11479-11486]
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[FR Doc No: 2016-05002]

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA-436]

Schedules of Controlled Substances: Placement of 10 Synthetic Cathinones Into Schedule I

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Notice of proposed rulemaking.

SUMMARY: The Drug Enforcement Administration proposes placing 10 synthetic cathinones: 4-methyl-N-ethylcathinone (4-MEC); 4-methyl-alpha-pyrrolidinopropiophenone (4-MePPP); alpha-pyrrolidinopentiophenone (α-PVP); 1-(1,3-benzodioxol-5-yl)-2-(methylamino)butan-1-one (butylone); 2-(methylamino)-1-phenylpentan-1-one (pentedrone); 1-(1,3-benzodioxol-5-yl)-2-(methylamino)pentan-1-one (pentylone); 4-fluoro-N-methylcathinone (4-FMC); 3-fluoro-N-methylcathinone (3-FMC); 1-(naphthalen-2-yl)-2-(pyrrolidin-1-yl)pentan-1-one (naphyrone); alpha-pyrrolidinobutiophenone (α-PBP) and their optical, positional, and geometric isomers, salts and salts of isomers into schedule I of the Controlled Substances Act. This proposed scheduling action is pursuant to the Controlled Substances Act which requires that such actions be made on the record after opportunity for a hearing through formal rulemaking. If finalized, this action would impose the regulatory controls and administrative, civil, and criminal sanctions applicable to schedule I controlled substances on persons who handle (manufacture, distribute, import, export, engage in research, conduct instructional activities or chemical analysis, or possess), or propose to handle 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, or α-PBP.

DATES: Interested persons may file written comments on this proposal in accordance with **21 CFR 1308.43**(g). Comments must be submitted electronically or postmarked on or before April 4, 2016. Commenters should be aware that the electronic Federal Docket Management System will not accept comments after 11:59 p.m. Eastern Time on the last day of the comment period.

Interested persons, defined at **21 CFR 1300.01** as those "adversely affected or aggrieved by any rule or proposed rule issuable pursuant to section 201 of the Act (**21 U.S.C. 811**)," may file a request

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for hearing or waiver of hearing pursuant to **21 CFR 1308.44** and in accordance with **21 CFR 1316.45** and/or **1316.47**, as applicable. Requests for hearing and waivers of an opportunity for a hearing or to participate in a hearing must be received on or before April 4, 2016.

ADDRESSES: To ensure proper handling of comments, please reference "Docket No. DEA-436" on all correspondence, including any attachments.

- *Electronic comments:* The Drug Enforcement Administration encourages that all comments be submitted electronically through the Federal eRulemaking Portal which provides the ability to type short comments directly into the comment field on the Web page or to attach a file for lengthier comments. Please go to http://www.regulations.gov and follow the online instructions at that site for submitting comments. Upon completion of your submission you will receive a Comment Tracking Number for your comment. Please be aware that submitted comments are not instantaneously available for public view on Regulations.gov. If you have received a Comment Tracking Number, your comment has been successfully submitted and there is no need to resubmit the same comment.
- *Paper comments:* Paper comments that duplicate the electronic submission are not necessary. Should you wish to mail a paper comment in lieu of an electronic comment, it should be sent via regular or express mail to: Drug Enforcement Administration, Attn: DEA Federal Register Representative/ODW, 8701 Morrissette Drive, Springfield, Virginia 22152.
- *Hearing requests:* All requests for hearing and waivers of participation must be sent to: Drug Enforcement Administration, Attn: Administrator, 8701 Morrissette Drive, Springfield, Virginia 22152. All requests for hearing and waivers of participation should also be sent to: Drug Enforcement Administration, Attn: Hearing Clerk/LJ, 8701 Morrissette Drive, Springfield, Virginia 22152; and (2) Drug Enforcement Administration, Attn: DEA Federal Register Representative/ ODW, 8701 Morrissette Drive, Springfield, Virginia 22152.

FOR FURTHER INFORMATION CONTACT: Barbara J. Boockholdt, Office of Diversion Control, Drug Enforcement Administration; Mailing Address: 8701 Morrissette Drive, Springfield, Virginia 22152; Telephone: (202) 598-6812.

SUPPLEMENTARY INFORMATION:

Posting of Public Comments

Please note that all comments received in response to this docket are considered part of the public record. They will, unless reasonable cause is given, be made available by the Drug Enforcement Administration (DEA) for public inspection online at http://www.regulations.gov. Such information includes personal identifying information (such as your name, address, etc.) voluntarily submitted by the commenter. The Freedom of Information Act (FOIA) applies to all comments received. If you want to submit personal identifying information (such as your name, address, etc.) as part of your comment, but do not want it to be made publicly available, you must include the phrase "PERSONAL IDENTIFYING INFORMATION" in the first paragraph of your comment. You must also place all of the personal identifying information you do not want made publicly available in the first paragraph of your comment and identify what information you want redacted.

[redacted]u want to submit confidential business information as part of your comment, but do not want it to be made publicly available, you must include the phrase [redacted]NFIDENTIAL BUSINESS INFORMATION" in the first paragraph of your comment. You must also prominently identify confidential business information to be [redacted]dacted within the comment.

Comments containing personal identifying information and confidential business information identified as directed above will generally be made publicly available in redacted form. If a comment has so much confidential business information or personal identifying information that it cannot be effectively redacted, all or part of that comment may not be made publicly available. Comments posted to http://www.regulations.gov may include any personal identifying information (such as name, address, and phone number) included in the text of your electronic submission that is not identified as directed above as confidential.

An electronic copy of this document and supplemental information to this proposed rule are available at http://www.regulations.gov for easy reference.

Request for Hearing or Waiver of Participation in a Hearing

Pursuant to **21 U.S.C. 811**(a), this action is a formal rulemaking "on the record after opportunity for a hearing." Such proceedings are conducted pursuant to the provisions of the Administrative Procedure Act (APA), 5 U.S.C. 551-559. **21 CFR 1308.41-1308.45**; **21 CFR part 1316**, subpart D. In accordance with **21 CFR 1308.44** (a)-(c), requests for hearing, notices of appearance, and waivers of an opportunity for a hearing or to participate in a hearing may be submitted only by interested persons, defined as those "adversely affected or aggrieved by any rule or proposed rule issuable pursuant to section 201 of the Act (21 U.S.C. 811)." **21 CFR 1300.01**. Such requests or notices must conform to the requirements of 21 CFR 1308.44 (a) or (b), and **1316.47** or **1316.48**, as applicable, and include a statement of interest of the person in the proceeding and the objections or issues, if any, concerning which the person desires to be heard. Any waiver must conform to the requirements of 21 CFR 1308.44(c) and may include a written statement regarding the interested person's position on the matters of fact and law involved in any hearing.

Please note that pursuant to **21 U.S.C. 811**(a), the purpose and subject matter of a hearing held in relation to this rulemaking are restricted to: "(A) find[ing] that such drug or other substance has a potential for abuse, and (B) mak[ing] with respect to such drug or other substance the findings prescribed by subsection (b) of **section 812** of this title for the schedule in which such drug is to be placed . . ." All requests for hearing and waivers of participation must be sent to the DEA using the address information provided above.

Legal Authority

The DEA implements and enforces Titles II and III of the Comprehensive Drug Abuse Prevention and Control Act of 1970, as amended. Titles II and III are referred to as the "Controlled Substances Act" and the "Controlled Substances Import and Export Act," respectively, and are collectively referred to as the "Controlled Substances Act" or the "CSA" for the purposes of this action. **21 U.S.C. 801-971**. The DEA publishes the implementing regulations for these statutes in title 21 of the Code of Federal Regulations (CFR), chapter II. The CSA and its implementing regulations are designed to prevent, detect, and eliminate the diversion of controlled substances and listed chemicals into the illicit market while providing for the legitimate medical, scientific, research, and industrial needs of the United States. Controlled substances have the potential for abuse and dependence and are controlled to protect the public health and safety.

Under the CSA, controlled substances are classified into one of five schedules

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based upon their potential for abuse, their currently accepted medical use in treatment in the United States, and the degree of dependence the substance may cause. [redacted]**1 U.S.C. 812**. The initial schedules of controlled substances established by Congress are found at 21 U.S.C. 812(c), and the current list of scheduled substances is [redacted]blished at **21 CFR part 1308**.

[redacted]ursuant to **21 U.S.C. 811**(a)(1), the Attorney General may, by rule, "add to such a schedule or transfer between such schedules any drug or other substance if he (A) finds that such drug or other substance has a potential for abuse, and (B) makes with respect to such drug or other substance the findings prescribed by subsection (b) of **section 812** of this title for the schedule in which such drug is to be placed . . ." The Attorney General has delegated scheduling authority under 21 U.S.C. 811 to the Administrator of the DEA. 28 CFR 0.100.

The CSA provides that proceedings for the issuance, amendment, or repeal of the scheduling of any drug or other substance may be initiated by the Attorney General (1) on her own motion; (2) at the request of the Secretary of the Department of Health and Human Services (HHS); \1\ or (3) on the petition of any interested party. **21 U.S.C. 811**(a). This proposed action is supported by a recommendation from the Assistant Secretary of the HHS and an evaluation of all other relevant data by the DEA. If finalized, this action would impose the regulatory controls and administrative, civil, and criminal sanctions of schedule I controlled substances on any person who handles or proposes to handle 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-;FMC, 3-FMC, naphyrone, or α-PBP.

\1\ As discussed in a memorandum of understanding entered into by the Food and Drug Administration (FDA) and the National Institute on Drug Abuse (NIDA), the FDA acts as the lead agency within the HHS in carrying out the Secretary's scheduling responsibilities under the CSA, with the concurrence of NIDA. 50 FR 9518, Mar. 8, 1985. The Secretary of the HHS has delegated to the Assistant Secretary for Health of the HHS the authority to make domestic drug scheduling recommendations. 58 FR 35460, July 1, 1993.

Background

On March 7, 2014, the DEA published a final order in the Federal Register amending **21 CFR 1308.11**(h) to temporarily place 4-methyl-N-ethylcathinone (4-MEC); 4-methyl-alpha-pyrrolidinopropiophenone (4-MePPP); alpha-pyrrolidinopentiophenone (α-PVP); 1-(1,3-benzodioxol-5-yl)-2-(methylamino)butan-1-one (butylone); 2-(methylamino)-1-phenylpentan-1-one (pentedrone); 1-(1,3-benzodioxol-5-yl)-2-(methylamino)pentan-1-one (pentylone); 4-fluoro-N-methylcathinone (4-FMC); 3-fluoro-N-methylcathinone (3-FMC); 1-(naphthalen-2-yl)-2-(pyrrolidin-1-yl)pentan-1-one (naphyrone); and alpha-pyrrolidinobutiophenone (α-PBP) into schedule I of the CSA pursuant to the temporary scheduling provisions of **21 U.S.C. 811**(h). 79 FR 12938. That final order, which became effective on the date of publication, was based on findings by the Deputy Administrator of the DEA that the temporary scheduling of these 10 synthetic cathinones was necessary to avoid an imminent hazard to public safety pursuant to 21 U.S.C. 811(h)(1). At the time the final order took effect, section 201(h)(2) of the CSA (21 U.S.C. 811(h)(2)), required that the temporary scheduling of a substance expire at the end of two years from the date of issuance of the scheduling order, and it provided that, during the pendency of proceedings under 21 U.S.C. 811(a)(1) with respect to the substance, temporary scheduling of that substance could be extended for up to 1 year. Pursuant to 21 U.S.C. 811(h)(2), the temporary scheduling of 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP expires on March 6, 2016, unless extended. An extension of the temporary order is being ordered by the DEA Administrator in a separate action.

As described in the final order published on March 7, 2014, 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP are structurally and pharmacologically similar to amphetamine, 3,4-methylenedioxymethamphetamine (MDMA), cathinone, and other related substances. While 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP have been used as research chemicals and/or studied due to their misuse and abuse, based on the review of the scientific literature, there are no known currently accepted medical uses for these substances. The Assistant Secretary of Health for the U.S. Department of Health and Human Services (HHS) has advised that there are no exemptions or approvals in effect for 4-MEC, 4-MePPP, α-PVP, butylone, [redacted]entedrone, pentylone, 4-FMC, 3-FMC, naphyrone, or α-PBP under section 505 (21 U.S.C. 355) of the Federal Food, Drug and Cosmetic Act. As stated by the HHS, [redacted]MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP have no known accepted medical use. They are not the subject of [redacted]y approved new drug applications (NDAs) or investigational new drug applications (INDs), and are not currently marketed as approved drug products. The HHS [redacted]ecommends that 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP and their salts be placed into schedule I of the Controlled Substances Act (CSA).

Proposed Determination To Schedule 4-MEC, 4-MePPP, α-PVP, Butylone, Pentedrone, Pentylone, 4-FMC, 3-FMC, Naphyrone, and α-PBP

Pursuant to **21 U.S.C. 811**(a)(1), proceedings to add a drug or substance to those controlled under the CSA may be initiated by the Attorney General, or her delegate, the DEA Administrator. On December 30, 2014, the DEA requested scientific and medical evaluations and scheduling recommendations from the Assistant Secretary of Health for the HHS for 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP pursuant to 21 U.S.C. 811(b). Upon receipt of the scientific and medical evaluation and scheduling recommendations from the HHS on March 2, 2016, the DEA reviewed the documents and all other relevant data, and conducted its own eight-factor analysis of the abuse potential of 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP pursuant to 21 U.S.C. 811(c). Included below is a brief summary of each of the eight factors as analyzed by the HHS and the DEA, and as considered by the DEA in its proposed scheduling action. Please note that both the DEA 8-Factor and the HHS 8-Factor analyses are available in their entirety in the tab "Supporting Documents" of the public docket for this action at http://www.regulations.gov under Docket Number "DEA-436."

1. *The Drug's Actual or Relative Potential for Abuse:* The term "abuse" is not defined in the CSA. However, the legislative history of the CSA suggests that the DEA consider the following criteria when determining whether a particular drug or substance has a potential for abuse: \2\

\2\ Comprehensive Drug Abuse Prevention and Control Act of 1970, H.R. Rep. No. 91-1444, 91st Cong., Sess. 1 (1970); reprinted in 1970 U.S.C.C.A.N. 4566, 4603.

(a) There is evidence that individuals are taking the drug or drugs containing such a substance in amounts sufficient to create a hazard to their health or to the safety of other individuals or of the community; or

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(b) There is significant diversion of the drug or drugs containing such a substance from legitimate drug channels; or

(c) Individuals are taking the drug or drugs containing such a substance on their own initiative rather than on the basis of medical advice from a practitioner licensed by law to administer such drugs in the course of his professional practice; or

(d) The drug or drugs containing such a substance are new drugs so related in their action to a drug or drugs already listed as having a potential for abuse to make it likely that the drug will have the same potentiality for abuse as such drugs, thus making it reasonable to assume that there may be significant diversions from legitimate channels, significant use contrary to or without medical advice, or that it has a substantial capability of creating hazards to the health of the user or to the safety of the community.

As described by the HHS, the abuse potentials of 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP are associated with their abilities to produce psychoactive effects that are similar to those produced by mephedrone, methylone, MDPV, and other schedule I and II substances such as amphetamine, methamphetamine, cocaine, methcathinone, and MDMA that have a high potential for abuse.

The substances 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP have no approved medical uses in the United States and they have been encountered on the illicit market with adverse outcomes on the public health and safety. Because these substances are not approved drug products, a practitioner may not legally prescribe them, and they cannot be dispensed to an individual. Therefore, the use of these substances is without medical advice, leading to the conclusion that the 10 synthetic cathinones are being abused for their psychoactive properties. There are no legitimate drug channels for these synthetic cathinones as marketed drugs but the DEA notes that the 10 synthetic cathinones have use in scientific research. However, despite the limited legitimate use of these substances, reports from public health and law enforcement communicate that these substances are being abused and taken in amounts sufficient to create a hazard to an individual's health. This misuse is evidenced by emergency department admissions and deaths, representing a significant safety issue for those in the community. Papers published in the medical literature (e.g., case reports) related to 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, or α-PBP describe the effects of these substances to be similar to those of the schedule I cathinone substances MDPV, mephedrone, and methylone and other stimulant and hallucinogenic substances to include methamphetamine, cocaine and MDMA. In particular, the responses in humans to the 10 synthetic cathinones are stimulant-like and include paranoia, agitation, palpitations, tachycardia, hypertension, hyperthermia, and seizures. Data from forensic databases are used as indicators of illicit activity with drugs and abuse \3\ within the United States and include data from the System to Retrieve Information from Drug Evidence (STRIDE),\4\ STARLiMS, and the National Forensic Laboratory Information System (NFLIS).\5\ From January 2010 through December 2015 (query dates: Febru & 11, 2016), STRIDE, STARLiMS and NFLIS databases registered a total of 20,090 reports pertaining to the 10 synthetic cathinones (4-MEC--2,820 reports; 4-M 438 reports; α-PVP--13,295 reports; butylone--789 reports; pentedrone--1,645 reports; pentylone--411 reports; FMC--375 reports; naphyrone--84 reports; α-PB 233 reports). These drug reports represent all of the 10 synthetic cathinones reported to these databases by participating DEA, State, local, and other forensic laboratories. Consequently, the data indicate that these substances are being abused, and they present safety hazards to the health of individuals who consume them due to their stimulant properties, making them a hazard to the safety of the community.

\3\ While law enforcement data is not direct evidence of abuse, it can lead to an inference that a drug has been diverted and abused. See 76 FR 77330, 77332, Dec. 12, 2011.

\4\ STRIDE was a database that collected analyses of results from drug evidence sent to DEA laboratories. Evidence was submitted by the DEA, other Federal agencies, and select local law enforcement agencies. On October 1, 2014, STARLiMS replaced STRIDE as the DEA system of record for forensic laboratory drug evidence data.

\5\ NFLIS is a DEA program and a national forensic laboratory reporting system that systematically collects results from drug chemistry analyses conducted by state and local forensic laboratories in the United States. The NFLIS database also contains Federal data from U.S. Customs and Border Protection (CBP). NFLIS only includes drug chemistry results from completed analyses.

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2. *Scientific Evidence of the Drug's Pharmacological Effects, if Known:* Studies show that 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP produce pharmacological effects that are similar to those produced by schedule I and II substances such as methamphetamine, cocaine, MDMA, mephedrone, MDPV, and methylone. Similar to schedule I and II stimulants, the 10 synthetic cathinone substances affect monoamine transmission. The 10 synthetic cathinones, similar to methamphetamine, cocaine, MDMA, mephedrone, MDPV, methylone, and other related schedule I and II substances, bind to transporters for the dopamine, serotonin, and/or norephinephrine neurotransmitters and are uptake inhibitors of these neurotransmitters. Additionally, behavioral studies in animals demonstrate that the 10 synthetic cathinones produce locomotor behavior and discriminative stimulus effects that are similar to those of the schedule I and II substances methamphetamine and cocaine. Furthermore, the 10 synthetic cathinone produce rewarding properties as demonstrated in self-administration and conditioned place preference (CPP) studies. Drugs that have rewarding effects in animals are likely to produce rewarding effects in humans, which is indicative of abuse potential. Overall, these data indicate that the 10 synthetic cathinones produce pharmacological effects and stimulant-like behaviors that are similar to those of the schedule I substances (MDMA, mephedrone, MDPV, methylone), as well as the schedule II stimulants (methamphetamine and cocaine).

3. *The State of Current Scientific Knowledge Regarding the Drug or Other Substance:* 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP are synthetic cathinones (β-keto-phenethylamines) of the larger phenethylamine structural class (amphetamines, cathinones, 2C compounds, aminoindanes, etc.). These substances share the core phenethylamine structure with a keto functional group [carbonyl (C=O)] at the β-position and substitutions at the α-position and on the phenyl ring and nitrogen atom. Available data demonstrate that 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP are β-ketophenethylamines (i.e., synthetic cathinones) and are structurally and pharmacologically similar to amphetamine, MDMA, cathinone, mephedrone, methylone, MDPV, and other related substances. Metabolism studies demonstrate that humans metabolize synthetic cathinones to their corresponding amphetamines followed by reduction of the beta-keto group to the corresponding alcohol. According to the HHS, 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone,

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and α-PBP have no known accepted medical use. They are not the subject of any approved new drug applications (NDAs) or investigational new drug application (INDs), and are not currently marketed as approved drug products in the U.S or in any other country. The HHS also states that there are no reported clinical trials with the 10 synthetic cathinones. Accordingly, the DEA is not aware of any accepted medical use for 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP in the United States. In addition, although the chemistry of 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP is known and has been reproduced, no studies have been undertaken to evaluate the efficacy, toxicology, and safety of these substances in humans.

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4. *Its History and Current Pattern of Abuse:* 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP are synthetic cathinones that emerged on the U.S. illicit drug market around the time of the scheduling of mephedrone, methylone, and MDPV on October 21, 2011. These synthetic cathinone substances, like the schedule I synthetic cathinones (mephedrone, methylone, and MDPV), are promoted as being 'legal' alternatives to cocaine, methamphetamine, and MDMA. As reported in the medical literature, synthetic cathinones can induce stimulant effects, especially under high dose conditions, including tachycardia, palpitations, hypertension, tremor, seizures, hallucinations, paranoia, delusions, hyperthermia, sweating, headache, hyponatremia, and rhabdomyolysis. Products that contain 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP are falsely marketed as "research chemicals," "jewelry cleaner," "stain remover," "plant food or fertilizer," "insect repellants," or "bath salts" and are sold at smoke shops, head shops, convenience stores, adult book stores, and gas stations. They can also be purchased on the Internet under a variety of product names (e.g., "White Dove," "Explosion," "Tranquility"). They are commonly encountered in the form of powders, crystals, resins, tablets, and capsules. The packages of these commercial products usually contain the warning "not for human consumption." Information from published scientific studies indicate that the most common routes of administration for synthetic cathinone substances is ingestion by swallowing capsules or tablets, or nasal insufflation by snorting the powder tablets. Evidence from poison centers and published reports suggest that the main users of methylone are young adults. There is evidence that these synthetic cathinone substances are ingested with other substances including other synthetic cathinones, common cutting agents, or other recreational substances.

5. *The Scope, Duration, and Significance of Abuse:* 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP, like mephedrone, methylone, and MDPV, are popular recreational drugs. Evidence that these synthetic cathinone substances are being abused and trafficked is confirmed by law enforcement encounters of these substances and reports from national databases. Forensic laboratories have analyzed drug exhibits received from state, local, or Federal law enforcement agencies that were found to contain 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, or α-PBP. NFLIS registered over 17,000 reports from State, local, and other forensic laboratories identifying these substances in drug-related reports for the period from January 2010 to December 2015 from 47 states. STRIDE & STARLiMS registered over 2,000 reports from DEA forensic laboratories from January 2010 to December 2015. Encounters of 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP by law enforcement have occurred in several states. Additionally, large seizures of these substances have occurred by the U.S. Customs and Border Protection (CBP). Concerns over the abuse of these synthetic cathinone substances have prompted many States to regulate them. These data demonstrate that 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP have a scope, duration, and significance of abuse that supports scheduling under the CSA.

6. *What, if Any, Risk There is to the Public Health:* Available evidence on the overall public health risks associated with the use of synthetic cathinones indicates that 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP can cause acute health problems leading to emergency department (ED) admissions, violent behaviors causing harm to self or others, or death. Law enforcement, forensic laboratories, case reports, and public health officials have reported toxic exposure to some of the 10 synthetic cathinones that demonstrate the public health risks associated with these substances. Serious adverse effects have resulted in documented hospital ED admissions from the ingestion of butylone, 4-FMC, or naphyrone. Individuals under the influence of 4-MEC or α-PVP have acted violently and unpredictably causing harm, or even death, to themselves or others. Butylone has been directly implicated in two fatalities reported in the medical literature. Other synthetic cathinones, such as α-PVP, pentedrone, and pentylone, have also been implicated in the deaths of individuals. Acute effects of these substances are those typical of a sympathomimeticagent (e.g., cocaine, methamphetamine, amphetamine) and include among other effects tachycardia, headache, palpitations, agitation, anxiety, mydriasis, tremor, fever or sweating, and hypertension. Other effects, with possible public health risk implications, that have been reported from the use of synthetic cathinone substances include psychological effects such as psychosis, paranoia, hallucinations, and agitation. Finally, the possibility of death for individuals abusing 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP also indicates that these substances pose a serious public health threat. In addition to the recognized harm from ingesting and abusing synthetic cathinones, abusers risk harm when they obtain these drugs through unknown sources. Products containing these synthetic cathinone substances often do not bear labeling information regarding their ingredients and if they do, they may not contain the expected active ingredients or identify the health risks and potential hazards associated with these products. Thus, the limited knowledge about product contents, its purity and lack of information about its effects may pose another level of risk to users.

7. *Its Psychic or Physiological Dependence Liability:* The DEA is unaware of any clinical studies that have evaluated the dependence potential of 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, or α-PBP; however, according to the HHS, synthetic cathinones have rewarding properties in rodents similar to those of schedule II stimulants. Generally, there is a strong correlation between drugs that serve as reinforcers in animals, and drugs associated with problems of addiction, dependence, or abuse by humans. In a self-administration study,

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α-PVP and pentedrone were self-administered by rodents. In the intracranial self-stimulation (ICSS) assay, α-PVP and 4-MEC significantly reduced the ICSS threshold compared to vehicle control. In drug discrimination studies, all 10 synthetic cathinone substances fully generalize to the discriminative stimulus effects produced by the schedule II stimulants--cocaine and methamphetamine. In conditioned place preference (CPP) studies, α-PBP, α-PVP, and pentedrone produce CPP in rodents. Thus, these data indicate that 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP have behavioral and rewarding properties in rodents similar to those of schedule II stimulants and, consequently, psychic dependence on these substances can develop and may contribute to the continued use among individuals who abuse them despite their adverse consequences.

8. *Whether the Substance is an Immediate Precursor of a Substance Already Controlled Under the CSA:* 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP are not considered immediate precursors of any controlled substance of the CSA.

Conclusion: After considering the scientific and medical evaluation conducted by the HHS, the HHS's recommendation, and the DEA's own eight-factor analysis, the DEA finds that the facts and all relevant data constitute substantial evidence of the potential for abuse of 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP. As such, the DEA hereby proposes to schedule 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP as controlled substances under the CSA.

Proposed Determination of Appropriate Schedule

The CSA establishes five schedules of controlled substances known as schedules I, II, III, IV, and V. The CSA also outlines the findings required to place a drug or other substance in any particular schedule. **21 U.S.C. 812**(b). After consideration of the analysis and recommendation of the Assistant Secretary for the HHS and review of all other available data, the Administrator of the DEA, pursuant to **21 U.S.C. 811**(a) and 21 U.S.C. 812(b)(1), finds that:

1. 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP have a high potential for abuse that is comparable to other schedule I and schedule II substances such as mephedrone, methylone, MDPV, methcathinone, MDMA, amphetamine, methamphetamine, and cocaine;

2. 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP have no currently accepted medical use in treatment in the United States; and

3. There is a lack of accepted safety for use of 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP under medical supervision.

Based on these findings, the Administrator of the DEA concludes that 4-methyl-N-ethylcathinone (4-MEC); 4-methyl-alpha-pyrrolidinopropiophenone (4-MePPP); alpha-pyrrolidinopentiophenone (α-PVP); 1-(1,3-benzodioxol-5-yl)-2-(methylamino)butan-1-one (butylone); 2-(methylamino)-1-phenylpentan-1-one (pentedrone); 1-(1,3-benzodioxol-5-yl)-2-(methylamino)pentan-1-one (pentylone); 4-fluoro-N-methylcathinone (4-FMC); 3-fluoro-N-methylcathinone (3-FMC); 1-(naphthalen-2-yl) -2-(pyrrolidin-1-yl)pentan-1-one (naphyrone); alpha-pyrrolidinobutiophenone (α-PBP) and their optical, positional, and geometric isomers, salts and salts of isomers, warrant control in schedule I of the CSA. **21 U.S.C. 812**(b)(1).

Requirements for Handling 4-MEC, 4-MePPP, α-PVP, Butylone, Pentedrone, Pentylone, 4-FMC, 3-FMC, Naphyrone, and α-PBP

If this rule is finalized as proposed, 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP would continue \6\ to be subject to the regulatory controls and administrative, civil, and criminal sanctions applicable to the manufacture, distribution, possession, importing, research, conduct of instructional activities, and exporting of schedule I controlled substances, including the following:

\6\ 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, or α-PBP are currently subject to schedule I controls on a temporary basis, pursuant to **21 U.S.C. 811**(h). 79 FR 12938, Mar. 7, 2014.

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1. *Registration.* Any person who handles (manufactures, distributes, dispenses, imports, exports, engages in research, conducts instructional activities or chemical analysis with, or possesses) 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, or α-PBP, or who desires to handle 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, or α-PBP would be required to be registered with the DEA to conduct such activities pursuant to **21 U.S.C. 822**, **823**, **957**, and **958**, and in accordance with **21 CFR parts 1301** and **1312**.

2. *Security.* 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, or α-PBP would be subject to schedule I security requirements and would need to be handled and stored pursuant to **21 U.S.C. 821** and **823**, and in accordance with **21 CFR 1301.71-1301.93**.

3. *Labeling and Packaging.* All labels, labeling, and packaging for commercial containers of 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, or α-PBP would need to be in compliance with **21 U.S.C. 825** and **958**(e), and be in accordance with **21 CFR part 1302**.

4. *Quota.* Only registered manufacturers would be permitted to manufacture 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, or α-PBP in accordance with a quota assigned pursuant to **21 U.S.C. 826**, and in accordance with **21 CFR part 1303**.

5. *Inventory.* Any person who becomes registered with the DEA on or after the effective date of the final rule must take an initial inventory of all stocks of controlled substances (including 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP) on hand on the date the registrant first engages in the handling of controlled substances pursuant to **21 U.S.C. 827** and **958**, and in accordance with **21 CFR 1304.03**, **1304.04**, and **1304.11**.

After the initial inventory, every DEA registrant must take a new inventory of all stocks of controlled substances (including 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP) on hand every two years pursuant to **21 U.S.C. 827** and **958**, and in accordance with **21 CFR 1304.03**, **1304.04**, and **1304.11**.

6. *Records and Reports.* Every DEA registrant would be required to maintain records and submit reports with respect to 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and/ or α-PBP pursuant to **21 U.S.C. 827** and **958**(e), and in accordance with **21 CFR parts 1304** and **1312**.

7. *Order Forms.* Every DEA registrant who distributes 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, or α-PBP would be required to comply with the order form requirements, pursuant to **21 U.S.C. 828**, and **21 CFR part 1305**.

8. *Importation and Exportation.* All importation and exportation of 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC,

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naphyrone, or α-PBP would need to be in compliance with **21 U.S.C. 952**, **953**, **957**, and **958**, and in accordance with **21 CFR part 1312**.

9. *Liability.* Any activity involving 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, or α-PBP not authorized by, or in violation of, the CSA or its implementing regulations would be unlawful, and could subject the person to administrative, civil, and/ or criminal sanctions.

Regulatory Analyses

Executive Orders 12866 and 13563

In accordance with **21 U.S.C. 811**(a), this proposed scheduling action is subject to formal rulemaking procedures done "on the record after opportunity for a hearing," which are conducted pursuant to the provisions of 5 U.S.C. 556 and 557. The CSA sets forth the criteria for scheduling a drug or other substance. Such actions are exempt from review by the Office of Management and Budget (OMB) pursuant to section 3(d)(1) of Executive Order 12866 and the principles reaffirmed in Executive Order 13563.

Executive Order 12988

This proposed regulation meets the applicable standards set forth in sections 3(a) and 3(b)(2) of Executive Order 12988 to eliminate drafting errors and ambiguity, minimize litigation, provide a clear legal standard for affected conduct, and promote simplification and burden reduction.

Executive Order 13132

This proposed rulemaking does not have federalism implications warranting the application of Executive Order 13132. The proposed rule does not have substantial direct effects on the States, on the relationship between the national government and the States, or the distribution of power and responsibilities among the various levels of government.

Executive Order 13175

This proposed rule does not have tribal implications warranting the application of Executive Order 13175. It does not have substantial direct effects on one or more Indian tribes, on the relationship between the Federal Government and Indian tribes, or on the distribution of power and responsibilities between the Federal Government and Indian tribes.

Regulatory Flexibility Act

The Administrator, in accordance with the Regulatory Flexibility Act (RFA), 5 U.S.C. 601-602, has reviewed this proposed rule and by approving it, certifies that it will not have a significant economic impact on a substantial number of small entities. On March 7, 2014, the DEA published a final order to temporarily place 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP into schedule I of the CSA pursuant to the temporary scheduling provisions of **21 U.S.C. 811**(h). The DEA estimates that all entities handling or planning to handle 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, or α-PBP are currently registered to handle these substances. There are currently 43 registrations authorized to handle 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, or α-PBP, as well as a number of registered analytical labs that are authorized to handle schedule I controlled substances generally. These 43 registrations represent 31 entities, of which 11 are small entities. Therefore, the DEA estimates that 11 small entities are affected by this proposed rule.

A review of the 43 registrations indicates that all entities that currently handle 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, or α-PBP also handle other schedule I controlled substances, and have established and implemented (or currently maintain) the systems and processes required to handle 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, or α-PBP. Therefore, the DEA anticipates that this proposed rule will impose minimal or no economic impact on any affected entities; and thus, will not have a significant economic impact on any of the 11 affected small entities. Therefore, the DEA has concluded that this proposed rule will not have a significant effect on the small entities.

Unfunded Mandates Reform Act of 1995

In accordance with the Unfunded Mandates Reform Act (UMRA) of 1995, 2 U.S.C. 1501 et seq., the DEA has determined and certifies that this action would not result in any Federal mandate that may result "in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted for inflation) in any one year . . ." Therefore, neither a Small Government Agency Plan nor any other action is required under UMRA of 1995.

Paperwork Reduction Act of 1995

This action does not impose a new collection of information under the Paperwork Reduction Act of 1995. 44 U.S.C. 3501-3521. This action would not impose recordkeeping or reporting requirements on State or local governments, individuals, businesses, or organizations. An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

List of Subjects in 21 CFR Part 1308

Administrative practice and procedure, Drug traffic control, Reporting and recordkeeping requirements.

For the reasons set out above, 21 CFR part 1308 is proposed to be amended to read as follows:

PART 1308--SCHEDULES OF CONTROLLED SUBSTANCES

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- 1. The authority citation for 21 CFR part 1308 continues to read as follows:

Authority: 21 U.S.C. 811, 812, 871(b), unless otherwise noted. 2. In Sec. 1308.11:

- a. Add paragraphs (d)(58) through (d)(67);
- b. Remove paragraphs (h)(11) through (h)(20),
- c. Redesignate paragraphs (h)(21) through (h)(25) as (h)(11) through (h)(15);

The additions to read as follows:

Sec. 1308.11 Schedule I.

* * * * *

(d) * * *

(58) 4-methyl-*N*-ethylcathinone (4MEC)	(1249)
(59) 4-methyl-*alpha*-pyrrolidinopropiophenone (4-MePPP)	(7498)
(60) *alpha*-pyrrolidinopentiophenone (α-PVP)	(7545)
(61) 1-(1,3-benzodioxol-5-yl)-2-(methylamino)butan-1-one (butylone, bk-MB	(7541)
(62) 2-(methylamino)-1-phenylpentan-1-one (pentedrone)	(1246)
(63) 1-(1,3-benzodioxol-5-yl)-2-(methylamino)pentan-1-one (pentylone, bk-MBDP)	(7542)
(64) 4-fluoro-*N*-methylcathinone (4-FMC; flephedrone)	(1238)
(65) 3-fluoro-*N*-methylcathinone (3-FMC)	(1233)
(66) 1-(naphthalen-2-yl)-2-(pyrrolidin-1-yl)pentan-1-one (naphyrone)	(1258)
(67) *alpha*-pyrrolidinobutiophenone	(7546)

* * * * *

[[Page 11486]]

Dated: March 2, 2016.

Chuck Rosenberg,
Acting Administrator.

[FR Doc. 2016-05002 Filed 3-3-16; 8:45 am]

BILLING CODE 4410-09-P

NOTICE: This is an unofficial version. An official version of this publication may be obtained directly from the Government Printing Office (GPO).

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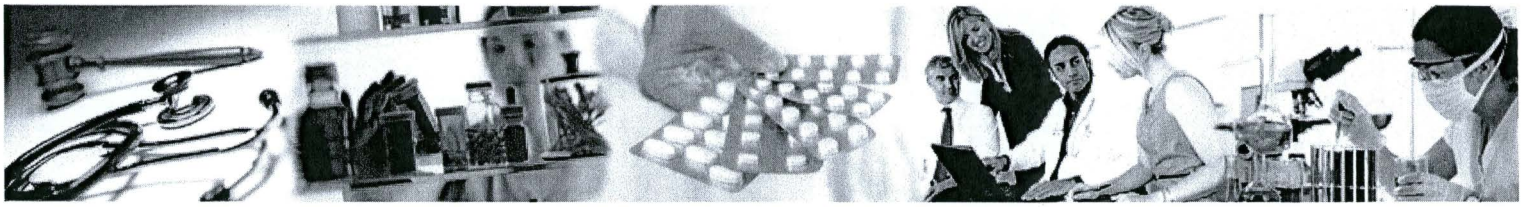

Rules - 2015

[Federal Register Volume 80, Number 179 (Wednesday, September 16, 2015)]
[Proposed Rules]
[Pages 55565-55568]
From the Federal Register Online via the Government Publishing Office [www.gpo.gov]
[FR Doc No: 2015-23198]

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA-421N]

Schedules of Controlled Substances: Temporary Placement of the Synthetic Cannabinoid MAB-CHMINACA Into Schedule I

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Notice of intent.

SUMMARY: The Administrator of the Drug Enforcement Administration is issuing this notice of intent to temporarily schedule the synthetic cannabinoid N-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-(cyclohexylmethyl)-1H-indazole-3-carboxamide (common names, MAB-CHMINACA and ADB-CHMINACA) into schedule I pursuant to the temporary scheduling provisions of the Controlled Substances Act. This action is based on a finding by the Administrator that the placement of this synthetic cannabinoid into schedule I of the Controlled Substances Act is necessary to avoid an imminent hazard to the public safety. Any final order will impose the administrative, civil, and criminal sanctions and regulatory controls applicable to schedule I controlled substances under the Controlled Substances Act on the manufacture, distribution, possession, importation, exportation, research, and conduct of instructional activities of this synthetic cannabinoid.

DATES: September 16, 2015.

FOR FURTHER INFORMATION CONTACT: John R. Scherbenske, Office of Diversion Control, Drug Enforcement Administration; Mailing Address: 8701 Morrissette Drive, Springfield, Virginia 22152; Telephone: (202) 598-6812.

SUPPLEMENTARY INFORMATION: Any final order will be published in the Federal Register and may not be effective prior to October 16, 2015.

Legal Authority

The Drug Enforcement Administration (DEA) implements and enforces titles II and III of the Comprehensive Drug Abuse Prevention and Control Act of 1970, as amended. Titles II and III are referred to as the "Controlled Substances Act" and the "Controlled Substances Import and Export Act," respectively, and are collectively referred to as the "Controlled Substances Act" or the "CSA" for the purpose of this action. The DEA publishes the implementing regulations for these statutes in title 21 of the Code of Federal Regulations (CFR), chapter II. The CSA and its implementing regulations are designed to prevent, detect, and eliminate the diversion of controlled substances and listed chemicals into the illicit market while ensuring an adequate supply is available for the legitimate medical, scientific, research, and industrial needs of the United States. Controlled substances have the potential for abuse and dependence and are controlled to protect the public health and safety.

Under the CSA, every controlled substance is classified into one of five schedules based upon its potential for abuse, its currently accepted medical use in treatment in the United States, and the degree of dependence the drug or other substance may cause. **21 U.S.C. 812**. The initial schedules of controlled substances established by Congress are found at 21 U.S.C. 812(c), and the current list of all scheduled substances is published at **21 CFR part 1308**.

Section 201 of the CSA, **21 U.S.C. 811**, provides the Attorney General with the authority to temporarily place a substance into schedule I of the CSA for two years without regard to the requirements of 21 U.S.C. 811(b) if she finds that such action is necessary to avoid imminent hazard to the public safety. 21 U.S.C. 811(h)(1). In addition, if proceedings to control a substance are initiated under 21 U.S.C. 811(a)(1), the Attorney General may extend the temporary scheduling for up to one year. 21 U.S.C. 811(h)(2).

Where the necessary findings are made, a substance may be temporarily scheduled if it is not listed in any other schedule under section 202 of the CSA, **21 U.S.C. 812**, or if there is no exemption or approval in effect for the substance under section 505 of the Federal Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. 355. **21 U.S.C. 811**(h)(1). The Attorney General has delegated her scheduling authority under 21 U.S.C. 811 to the Administrator of the DEA. 28 CFR 0.100.

Background

Section 201(h)(4) of the CSA, **21 U.S.C. 811**(h)(4), requires the Administrator to notify the Secretary of the Department of Health and Human Services (HHS) of the Administrator's intention to temporarily place a substance into schedule I of the CSA.\1\ The Administrator transmitted notice of intent to place N-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-(cyclohexylmethyl)-1H-indazole-3-carboxamide (hereinafter referred to as MAB-CHMINACA) into schedule I on a temporary basis to the Assistant Secretary by letter dated May 14, 2015. The Assistant Secretary responded to this notice by letter dated June 3, 2015, and advised that based on review by the Food and Drug Administration (FDA), there are currently no investigational new drug applications or approved new drug applications for MAB-CHMINACA. The Assistant Secretary also stated that HHS has no objection to the temporary placement of MAB-CHMINACA into schedule I of the CSA. The DEA has taken into consideration the Assistant Secretary's comments. MAB-CHMINACA is not currently listed in any schedule under the CSA, and no exemptions or

approvals are in effect for MAB-CHMINACA under section 505 of the FDCA, 21 U.S.C. 355. The DEA has found that the control of MAB-CHMINACA in schedule I on a temporary basis is necessary to avoid an imminent hazard to public safety.

\1\ Because the Secretary of the HHS has delegated to the Assistant Secretary for Health of the HHS the authority to make domestic drug scheduling recommendations, for purposes of this notice of intent, all subsequent references to "Secretary" have been replaced with "Assistant Secretary." As set forth in a memorandum of understanding entered into by the HHS, the Food and Drug Administration (FDA), and the National Institute on Drug Abuse (NIDA), the FDA acts as the lead agency within the HHS in carrying out the Assistant Secretary's scheduling responsibilities under the CSA, with the concurrence of NIDA. 50 FR 9518, Mar. 8, 1985.

To find that placing a substance temporarily into schedule I of the CSA is necessary to avoid an imminent hazard to the public safety, the Administrator is required to consider three of the eight factors set forth in section 201(c) of the CSA, **21 U.S.C. 811**(c): the substance's history and current pattern of abuse; the scope, duration and significance of abuse; and what, if any, risk there is to the public health. 21 U.S.C. 811(h)(3). Consideration of these factors includes actual abuse, diversion from legitimate channels, and clandestine importation, manufacture, or distribution. 21 U.S.C. 811(h)(3).

A substance meeting the statutory requirements for temporary scheduling may only be placed in schedule I. **21 U.S.C. 811**(h)(1). Substances in schedule I are those that have a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. **21 U.S.C. 812**(b)(1).

MAB-CHMINACA

Available data and information for MAB-CHMINACA, summarized below,

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indicate that this synthetic cannabinoid (SC) has a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. The DEA analysis is available in its entirety under the tab "Supporting and Related Material" of the public docket of this action at www.regulations.gov under Docket Number DEA-421N.

Synthetic Cannabinoids

Synthetic cannabinoids are substances synthesized in laboratories that mimic the biological effects of delta-9-tetrahydrocannabinol (THC), the main psychoactive ingredient in marijuana. It is believed SCs were first introduced on the designer drug market in several European countries as "herbal incense" before the initial encounter in the United States by U.S. Customs and Border Protection (CBP) in November 2008. From 2009 to present, misuse of SCs has increased in the United States with law enforcement encounters describing plant material laced with SCs intended for human consumption. It has been demonstrated that the substances and the associated designer products are abused for their psychoactive properties. With many generations of SCs being encountered since 2009, MAB-CHMINACA is one of the latest, and based upon reports from public health and law enforcement, the misuse and abuse of this substance is negatively impacting the public health and communities.

The designer drug products laced with SCs, including MAB-CHMINACA, are often sold under the guise of "herbal incense" or "potpourri," use various product names, and are routinely labeled "not for human consumption." Additionally, these products are marketed as a "legal high" or "legal alternative to marijuana" and are readily available over the Internet, in head shops, or sold in convenience stores. There is an incorrect assumption that these products are safe, and that labeling these products as "not for human consumption" is a legal defense to criminal prosecution.

MAB-CHMINACA is a SC that has pharmacological effects similar to the schedule I hallucinogen THC and other temporarily and permanently controlled schedule I substances. MAB-CHMINACA has been shown to cause severe toxicity and adverse health effects following ingestion, including seizures, excited delirium, cardiotoxicity and death. With no approved medical use and limited safety or toxicological information, MAB-CHMINACA has emerged on the illicit drug market and is being abused its psychoactive properties.

ctor 4. History and Current Pattern of Abuse

SCs have been developed over the last 30 years as tools for investigating the cannabinoid system. SCs were first encountered by CBP within the United States in November 2008. Since then, the popularity of SCs and their associated products has increased steadily as evidenced by law enforcement seizures, public health information, and media reports. Amidst multiple administrative and legislative actions to place SCs found on the illicit market into schedule I of the CSA, new versions of SCs intended to circumvent current law continue to be encountered. MAB-CHMINACA is a SC that was encountered following the hospitalization of 125 individuals around the Baton Rouge, Louisiana area in October 2014 (see factor 6 of supporting materials). Since that time, multiple overdoses and deaths involving MAB-CHMINACA have been reported. For example, overdose clusters attributed to MAB-CHMINACA have been reported in Shreveport, Louisiana; Bryan, Texas; Beaumont, Texas; multiple cities in the State of Mississippi; Hampton, Virginia; and Hagerstown, Maryland (see factor 6 of supporting materials). Specifically, in April 2015, the largest nationwide outbreak involving SCs was reported by multiple news outlets. In addition, State public health entities have collectively reported over 2,000 overdoses and at least 33 deaths across at least 11 States attributed to the misuse of SCs. Of these overdoses and deaths, currently available toxicology results have determined that a number of overdoses from this most recent cluster were connected to ingestion of MAB-CHMINACA (see factor 6 of supporting materials).

On April 29, 2015, the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) reported multiple outbreaks of intoxications within the United States resulting from the ingestion of products believed to contain SCs. EMCDDA further reported that MAB-CHMINACA had been implicated in at least some of those cases. EMCDDA also reported on two deaths involving MAB-CHMINACA, one in Hungary and the other in Japan.

A major concern, as reiterated by public health officials and medical professionals, remains the targeting and direct marketing of SCs and SC-containing products to adolescents and youth. This is supported by law enforcement encounters and reports from emergency departments: however, all age groups have been reported by the media as abusing these substances and related products. Individuals, including minors, are purchasing SCs from the Internet, gas stations, convenience stores, and head shops.

Smoking mixtures of these substances for the purpose of achieving intoxication have resulted in numerous emergency department visits and calls to poison control centers. As reported by the American Association of Poison Control Centers (AAPCC), adverse effects including severe agitation, anxiety, racing heartbeat, high blood pressure, nausea, vomiting, seizures, tremors, intense hallucinations, psychotic episodes, suicide, and other harmful thoughts and/or actions can occur following ingestion of SCs. Presentations at emergency departments directly linked to the abuse of MAB-CHMINACA have resulted in similar symptoms, including severe agitation, seizures and/or death (see factor 6).

As discussed previously, it is believed most abusers of SCs or SC-related products smoke the product following application to plant material. Until recently, this was the preferred route of administration. Law enforcement has also begun to encounter new variations of SCs in liquid form. It is believed abusers have been applying the liquid to hookahs or "e-cigarettes," which allows the user to administer a vaporized liquid that can be inhaled.

Factor 5. Scope, Duration and Significance of Abuse

Following multiple scheduling actions designed to safeguard the public from the adverse effects and safety issues associated with SCs, encounters by law enforcement and health care professionals indicate the continued abuse of these substances and their associated products. With each action to control SCs, drug manufacturers and suppliers are adapting at an alarmingly quick pace to design new SCs that circumvent regulatory controls. Even before DEA temporarily controlled the latest group of SCs, AB-CHMINACA, AB-PINACA, and THJ-2201, on January 30, 2015, MAB-CHMINACA was already available on the illicit market and responsible for overdoses and deaths (see factor 6 of supporting materials). From October 2014 to the present, multiple overdoses and deaths have been attributed to the abuse of MAB-CHMINACA.

October 29, 2014, the State of Louisiana issued an emergency rule adding N-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-(cyclohexylmethyl)-1H-indazole-3-rboxamide (MAB-

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CHMINACA) to the list of schedule I Controlled Dangerous Substances section of the Louisiana Administrative Code (La. Admin. Code tit. 46, section 2704 (2014)), upon the determination that it had a high potential for abuse and should be scheduled as a controlled substance to avoid an imminent peril to the public health, safety, and welfare.

Poison control centers continue to report the abuse of SCs and their associated products. These substances remain a threat to both the short- and long-term public health and safety. Exposures to SCs were first reported to the AAPCC in 2011. The most alarming report via the AAPCC was published on April 23, 2015. The AAPCC reported a dramatic spike in poison center exposure calls throughout the United States in 2015. The AAPCC reported 1,512 exposure calls in April 2015, representing an almost three-fold increase in exposures to SCs as compared to the previous largest monthly tally (657 exposures in January 2012) since reporting began in 2011. It is likely that many of the calls are directly attributable to the abuse of MAB-CHMINACA based on its high prevalence in drug seizure reports and specimen test reports (see factor 6 and table 3 of supporting materials). Further, exposure calls to the AAPCC from within the first five months of 2015 (January 1 to June 1) are greater than the total exposure calls involving SCs from all of 2014. In addition, a majority of exposure incidents from 2011 to the present resulted in individu[redacted] seeking medical attention at health care facilities.

The following information regarding MAB-CHMINACA was obtained through NFLIS \2\ (queried on May 27, 2015):

\2\ National Forensic Laboratory Information System (NFLIS) is a national drug forensic laboratory reporting system that systematically collects results from drug chemistry analyses conducted by state and local forensic laboratories in the United States.

MAB-CHMINACA: NFLIS-451 reports; first encountered in September 2014; locations include Arkansas, Indiana, Kansas, Louisiana, Missouri, Oklahoma, Texas, Virginia, and Wisconsin.

Factor 6. What, if Any, Risk There Is to the Public Health

MAB-CHMINACA was identified in a cluster of 125 subjects that presented to emergency facilities within the Baton Rouge and Shreveport, Louisiana areas in October 2014. On October 29, 2014, the Louisiana Secretary of the Department of Health and Hospitals announced the addition of MAB-CHMINACA into schedule I of the Controlled Dangerous Substances section of the Louisiana Administrative Code (La. Admin. Code tit. 46, section 2704 (2014)). From October 2014 to the present, multiple clusters of overdoses involving MAB-CHMINACA and at least four deaths attributed to the misuse and abuse of MAB-CHMINACA have been reported. (see factor 6 and table 3 of supporting materials). Adverse health effects reported from use of MAB-CHMINACA have included: seizures, coma, severe agitation, loss of motor control, loss of consciousness, difficulty breathing, altered mental status, and convulsions that in some cases resulted in death.

Since abusers obtain these drugs through unknown sources, the identity, purity, and quantity of these substances is uncertain and inconsistent, thus posing significant adverse health risks to users. The SCs encountered on the illicit drug market have no accepted medical use within the United States. Regardless, SC products continue to be easily available and abused by diverse populations. Unknown factors including detailed product analysis and dosage variations between various packages and batches present a significant danger to an abusing individual. Designer drug products have been found to vary in the amount and type of SC that plant material is laced with, which could be one explanation for the numerous emergency department admissions that have been connected to these substances. Similar to previous SCs, MAB-CHMINACA has been found on plant material.

Finding of Necessity of Schedule I Placement To Avoid Imminent Hazard to Public Safety

Based on the data and information summarized above, the continued uncontrolled manufacture, distribution, importation, exportation, and abuse of MAB-CHMINACA poses an imminent hazard to the public safety. The DEA is not aware of any currently accepted medical uses for MAB-CHMINACA in the United States. A substance meeting the statutory requirements for temporary scheduling, **21 U.S.C. 811**(h)(1), may only be placed in schedule I. Substances in schedule I are those that have a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. Available data and information for MAB-CHMINACA indicate that this substance has a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. As required by section 201(h)(4) of the CSA, 21 U.S.C. 811(h)(4), the DEA, through a letter dated May 14, 2015, notified the Assistant Secretary of the DEA's intention to temporarily this substance in schedule I.

Conclusion

This notice of intent initiates an expedited temporary scheduling action and provides the 30-day notice pursuant to section 201(h) of the CSA, **21 U.S.C. 811**(h[redacted] accordance with the provisions of section 201(h) of the CSA, 21 U.S.C. 811(h), the Administrator considered available data and information, herein set forth th[redacted] grounds for his determination that it is necessary to temporarily schedule MAB-CHMINACA in schedule I of the CSA, and finds that placement of this SC into sch[redacted] of the CSA is necessary to avoid an imminent hazard to the public safety.

Because the Administrator hereby finds that it is necessary to temporarily place this SC into schedule I to avoid an imminent hazard to the public safety, any subsequent final order temporarily scheduling these substances will be effective on the date of publication in the Federal Register, and will be in effect for a period of two years, with a possible extension of one additional year, pending completion of the regular (permanent) scheduling process. **21 U.S.C. 811**(h) (1) and (2). It is the intention of the Administrator to issue such a final order as soon as possible after the expiration of 30 days from the date of publication of this document. MAB-CHMINACA will then be subject to the regulatory controls and administrative, civil, and criminal sanctions applicable to the manufacture, distribution, possession, importation, exportation, research, and conduct of instructional activities of a schedule I controlled substance.

The CSA sets forth specific criteria for scheduling a drug or other substance. Regular scheduling actions in accordance with **21 U.S.C. 811**(a) are subject to formal rulemaking procedures done "on the record after opportunity for a hearing" conducted pursuant to the provisions of 5 U.S.C. 556 and 557. 21 U.S.C. 811. The regular scheduling process of formal rulemaking affords interested parties with appropriate process and the government with any additional relevant information needed to make a determination. Final decisions that conclude the regular scheduling process of formal rulemaking are subject to judicial review. **21 U.S.C. 877**. Temporary

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scheduling orders are not subject to judicial review. **21 U.S.C. 811**(h)(6).

Regulatory Matters

Section 201(h) of the CSA, **21 U.S.C. 811**(h), provides for an expedited temporary scheduling action where such action is necessary to avoid an imminent hazard to the public safety. As provided in this subsection, the Attorney General may, by order, schedule a substance in schedule I on a temporary basis. Such an order may not be issued before the expiration of 30 days from (1) the publication of a notice in the Federal Register of the intention to issue such order and the grounds upon which such order is to be issued, and (2) the date that notice of the proposed temporary scheduling order is transmitted to the Assistant Secretary. 21 U.S.C. 811(h)(1).

Inasmuch as section 201(h) of the CSA directs that temporary scheduling actions be issued by order and sets forth the procedures by which such orders are to be issued, the DEA believes that the notice and comment requirements of the Administrative Procedure Act (APA) at 5 U.S.C. 553, do not apply to this notice of intent. In the alternative, even assuming that this notice of intent might be subject to section 5 U.S.C. 553, the Administrator finds that there is good cause to forgo the notice and comment requirements of section 553, as any further delays in the process for issuance of temporary scheduling orders would be impracticable and contrary to the public interest in view of the manifest urgency to avoid an imminent hazard to the public safety.

Although the DEA believes this notice of intent to issue a temporary scheduling order is not subject to the notice and comment requirements of the APA, the DEA notes that in accordance with **21 U.S.C. 811**(h)(4), the Administrator will take into consideration any comments submitted by the Assistant Secretary with regard to the proposed temporary scheduling order.

Further, the DEA believes that this temporary scheduling action is not a "rule" as defined by 5 U.S.C. 601(2), and, accordingly, is not subject to the requirements of the Regulatory Flexibility Act. The requirements for the preparation of an initial regulatory flexibility analysis in 5 U.S.C. 603(a) are not applicable where, as here, the DEA is not required by the APA or any other law to publish a general notice of proposed rulemaking.

Additionally, this action is not a significant regulatory action as defined by Executive Order 12866 (Regulatory Planning and Review), section 3(f), and, accordin[redacted] this action has not been reviewed by the Office of Management and Budget.

This action will not have substantial direct effects on the States, on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government. Therefore, in accordance with Executive Order 13132 (Federalism), it is determined that this action does not have sufficient federalism implications to warrant the preparation of a Federalism Assessment.

List of Subjects in 21 CFR Part 1308

Administrative practice and procedure, Drug traffic control, Reporting and recordkeeping requirements.

For the reasons set out above, the DEA proposes to amend 21 CFR part 1308 as follows:

PART 1308--SCHEDULES OF CONTROLLED SUBSTANCES

- 1. The authority citation for part 1308 continues to read as follows:

Authority: 21 U.S.C. 811, 812, 871(b), unless otherwise noted.

- 2. In **Sec. 1308.11**, add paragraph (h)(25) to read as follows:

Sec. 1308.11 Schedule I.

* * * * *

(h) * * *

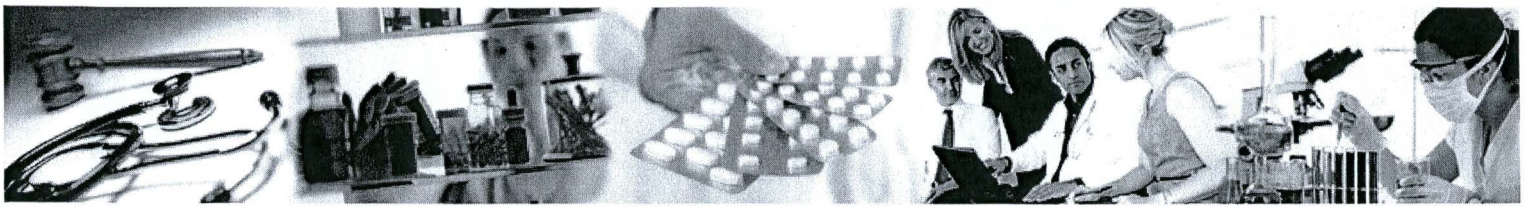
(25) N-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-(cyclohexylmethyl)-1H-indazole-3-carboxamide, its optical, positional, and geometric isomers, salts and salts of isomers—7032 (Other names: MAB-CHMINACA; ADB-CHMINACA)

Dated: September 10, 2015.

Chuck Rosenberg,
Acting Administrator.

[FR Doc. 2015-23198 Filed 9-15-15; 8:45 am]

BILLING CODE 4410-09-P



Rules - 2016

[Federal Register Volume 81, Number 92 (Thursday, May 12, 2016)]
[Rules and Regulations]
[Pages 29492-29496]
From the Federal Register Online via the Government Publishing Office [www.gpo.gov]
[FR Doc No: 2016-11219]

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA-434F]

Schedules of Controlled Substances: Temporary Placement of Butyryl Fentanyl and Beta-Hydroxythiofentanyl Into Schedule I

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Final order.

SUMMARY: The Administrator of the Drug Enforcement Administration is issuing this final order to temporarily schedule the synthetic opioids, N-(1-phenethylpiperidin-4-yl)-N-phenylbutyramide, also known as N-(1-phenethylpiperidin-4-yl)-N-phenylbutanamide, (butyryl fentanyl) and N-[1-[2-hydroxy-2-(thiophen-2-yl)ethyl]piperidin-4-yl]-N-phenylpropionamide, also known as N-[1-[2-hydroxy-2-(2-thienyl)ethyl]-4-piperidinyl]-N-phenylpropanamide, (beta-hydroxythiofentanyl), and their isomers, esters, ethers, salts and salts of isomers, esters and ethers, into schedule I pursuant to the temporary scheduling provisions of the Controlled Substances Act. This action is based on a finding by the Administrator that the placement of butyryl fentanyl and beta-hydroxythiofentanyl into schedule I of the Controlled Substances Act is necessary to avoid an imminent hazard to the public safety. As a result of this order, the regulatory controls and administrative, civil, and criminal sanctions applicable to schedule I controlled substances will be imposed on persons who handle (manufacture, distribute, reverse distribute, import, export, engage in research, conduct instructional activities or chemical analysis, or possess), or propose to handle, butyryl fentanyl and beta-hydroxythiofentanyl.

DATES: This final order is effective on May 12, 2016.

FOR FURTHER INFORMATION CONTACT: Barbara J. Boockholdt, Office of Diversion Control, Drug Enforcement Administration; Mailing Address: 8701 Morrissette Drive, Springfield, Virginia 22152; Telephone: (202) 598-6812.

SUPPLEMENTARY INFORMATION:

Legal Authority

The Drug Enforcement Administration (DEA) implements and enforces titles II and III of the Comprehensive Drug Abuse Prevention and Control Act of 1970, as amended. **21 U.S.C. 801-971**. Titles II and III are referred to as the "Controlled Substances Act" and the "Controlled Substances Import and Export Act," respectively, and are collectively referred to as the "Controlled Substances Act" or the "CSA" for the purpose of this action. The DEA publishes the implementing regulations for these statutes in title 21 of the Code of Federal Regulations (CFR), chapter II. The CSA and its implementing regulations are designed to prevent, detect, and eliminate the diversion of controlled substances and listed chemicals into the illicit market while ensuring an adequate supply is available for the legitimate medical, scientific, research, and industrial needs of the United States. Controlled substances have the potential for abuse and dependence and are controlled to protect the public health and safety.

Under the CSA, every controlled substance is classified into one of five schedules based upon its potential for abuse, its currently accepted medical use in treatment in the United States, and the degree of dependence the drug or other substance may cause. **21 U.S.C. 812**. The initial schedules of controlled substances established by Congress are found at 21 U.S.C. 812(c), and the current list of all scheduled substances is published at **21 CFR part 1308**.

Section 201 of the CSA, **21 U.S.C. 811**, provides the Attorney General with the authority to temporarily place a substance into schedule I of the CSA for two years without regard to the requirements of 21 U.S.C. 811(b) if she finds that such action is necessary to avoid an imminent hazard to the public safety. 21 U.S.C. 811(h)(1). In addition, if proceedings to control a substance are initiated under 21 U.S.C. 811(a)(1), the Attorney General may extend the temporary scheduling for up to one year. 21 U.S.C. 811(h)(2).

Where the necessary findings are made, a substance may be temporarily scheduled if it is not listed in any other schedule under section 202 of the CSA, **21 U.S.C. 812**, or if there is no exemption or approval in effect for the substance under section 505 of the Federal Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. 355. **21 U.S.C. 811**(h)(1). The Attorney General has delegated her scheduling authority under 21 U.S.C. 811 to the Administrator of the DEA. 28 CFR 0.100.

Background

Section 201(h)(4) of the CSA, **21 U.S.C. 811**(h)(4), requires the Administrator to notify the Secretary of the Department of Health and Human Services (HHS) of his intention to temporarily place a substance into schedule I of the CSA.\1\ The Administrator transmitted the notice of intent to place butyryl fentanyl and beta-hydroxythiofentanyl into schedule I on a temporary basis to the Assistant Secretary by letter dated December 21, 2015. The Assistant Secretary responded to this notice by letter dated January 13, 2016, and advised that based on review by the Food and Drug Administration (FDA), there are currently no investigational new drug

applications or approved new drug applications for butryl fentanyl or beta-hydroxythiofentanyl. The Assistant Secretary also stated that the HHS has no objection to the temporary placement of butryl fentanyl or beta-hydroxythiofentanyl into schedule I of the CSA. The DEA has taken into consideration the Assistant Secretary's comments as required by **21 U.S.C. 811**(h)(4). Neither butryl fentanyl nor beta-hydroxythiofentanyl is currently listed in any schedule under the CSA, and no exemptions or approvals are in effect for butryl fentanyl or beta-hydroxythiofentanyl under section 505 of the FDCA, 21 U.S.C. 355. The DEA has found that the control of butryl fentanyl and beta-hydroxythiofentanyl in schedule I on a temporary basis is necessary to avoid an imminent hazard to public safety, and as required by 21 U.S.C. 811(h)(1)(A), a notice of intent to temporarily schedule butryl fentanyl and beta-hydroxythiofentanyl was published in the Federal Register on March 23, 2016. 81 FR 15485.

\1\ As discussed in a memorandum of understanding entered into by the Food and Drug Administration (FDA) and the National Institute on Drug Abuse (NIDA), the FDA acts as the lead agency within the HHS in carrying out the Secretary's scheduling responsibilities under the CSA, with the concurrence of NIDA. 50 FR 9518, Mar. 8, 1985. The Secretary of the HHS has delegated to the Assistant Secretary for Health of the HHS the authority to make domestic drug scheduling recommendations. 58 FR 35460, July 1, 1993.

To find that placing a substance temporarily into schedule I of the CSA is necessary to avoid an imminent hazard to the public safety, the

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Administrator is required to consider three of the eight factors set forth in section 201(c) of the CSA, **21 U.S.C. 811**(c): The substance's history and current pattern of abuse; the scope, duration and significance of abuse; and what, if any, risk there is to the public health. 21 U.S.C. 811(h)(3). Consideration of these factors includes actual abuse, diversion from legitimate channels, and clandestine importation, manufacture, or distribution. 21 U.S.C. 811(h)(3).

A substance meeting the statutory requirements for temporary scheduling may only be placed into schedule I. **21 U.S.C. 811**(h)(1). Substances in schedule I are those that have a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. **21 U.S.C. 812**(b)(1). Available data and information for butryl fentanyl and beta-hydroxythiofentanyl, summarized below, indicate that these synthetic opioids have a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. The DEA's three-factor analysis, and the Assistant Secretary's January 13, 2016, letter, are available in their entirety under the tab "Supporting Documents" of the public docket of this action at www.regulations.gov under FDMS Docket ID: DEA-2016-0005 (Docket Number DEA-434).

Factor 4. History and Current Pattern of Abuse

Clandestinely produced substances structurally related to the schedule II opioid analgesic fentanyl were trafficked and abused on the West Coast in the late 1970s and 1980s. These clandestinely produced fentanyl-like substances were commonly known as designer drugs, and recently there has been a reemergence in the trafficking and abuse of designer drug substances, including fentanyl-like substances. Alpha-methylfentanyl, the first fentanyl analogue identified in California, was placed into schedule I of the CSA in September 1981. 46 FR 46799. Following the control of alpha-methylfentanyl, the DEA identified several other fentanyl analogues (3-methylthiofentanyl, acetyl-alpha-methylfentanyl, beta-hydroxy-3-methylfentanyl, alpha-methylthiofentanyl, thiofentanyl, beta-hydroxyfentanyl, para-fluorofentanyl, and 3-methylfentanyl) in submissions to forensic laboratories. These substances were temporarily controlled \2\ in 1985-1987 under schedule I of the CSA after finding that they posed an imminent hazard to public safety and were subsequently permanently placed in schedule I of the CSA. On July 17, 2015, acetyl fentanyl was temporarily controlled under schedule I of the CSA after a finding by the Administrator that it posed an imminent hazard to public safety. 80 FR 42381.

\2\ 50 FR 43698, 51 FR 42834, 50 FR 11690, 51 FR 15474, and 51 FR 4722. [The temporary scheduling of para-fluorofentanyl was extended in 1987, at 52 FR 7270.

Prior to October 1, 2014, the System to Retrieve Information from Drug Evidence (STRIDE) collected the results of drug evidence analyzed at DEA laboratories and selected evidence submitted by the DEA, other federal law enforcement agencies, and some local law enforcement agencies. STRIDE data were queried through September 30, 2014, by date submitted to federal forensic laboratories. Since October 1, 2014, STARLiMS (a web-based, commercial laboratory information management system) has replaced STRIDE as the DEA laboratory drug evidence data system of record. DEA laboratory data submitted after September 30, 2014, are deposited in STARLiMS. Data from STRIDE and STARLiMS were queried on December 21, 2015. The National Forensic Laboratory Information System (NFLIS) is a program of the DEA that collects drug identification results from drug cases analyzed by other federal, state, and local forensic laboratories. NFLIS reports from other federal, state, and local forensic laboratories were queried on December 22, 2015.\3\

\3\ Data are still being reported for September-November 2015 due to normal lag time for laboratories to report to NFLIS.

The first laboratory submission of butyryl fentanyl was recorded in Kansas in March 2014 according to NFLIS. STRIDE, STARLiMS, and NFLIS registered seven reports containing butyryl fentanyl in 2014 in Illinois, Kansas, Minnesota, and Pennsylvania; 81 reports of butyryl fentanyl were recorded in 2015 in California, Connecticut, Florida, Indiana, North Dakota, New York, Ohio, Oregon, Tennessee, Virginia, and Wisconsin. A total of three reports of beta-hydroxythiofentanyl were recorded by STARLiMS, all of which were reported in 2015 from Florida. As of December 22, 2015, beta-hydroxythiofentanyl had not been reported in NFLIS; however, this substance was identified in June 2015 by a forensic laboratory in Oregon.

Evidence also suggests that the pattern of abuse of fentanyl analogues, including butyryl fentanyl and beta-hydroxythiofentanyl, parallels that of heroin and prescription opioid analgesics. Seizures of butyryl fentanyl have been encountered in tablet and powder form. Butyryl fentanyl was identified on bottle caps and spoons and residue was detected within glassine bags, on digital scales, and on sifters which demonstrates the abuse of this substance as a replacement for heroin or other opioids, either knowingly or unknowingly. Butyryl fentanyl has been encountered as a single substance as well as in combination with other illicit substances, such as acetyl fentanyl, heroin, cocaine, or methamphetamine. Like butyryl fentanyl, beta-hydroxythiofentanyl has been encountered in both tablet and powder form. Both butyryl fentanyl and beta-hydroxythiofentanyl have caused fatal overdoses, in which intravenous routes of administration are documented.

Factor 5. Scope, Duration and Significance of Abuse

The DEA is currently aware of at least 40 confirmed fatalities associated with butyryl fentanyl and 7 confirmed fatalities associated with beta-hydroxythiofentanyl. The information on these deaths occurring in 2015 was collected from toxicology and medical examiner reports and was reported from four states--Florida (7, beta-hydroxythiofentanyl), Maryland (1, butyryl fentanyl), New York (38, butyryl fentanyl), and Oregon (1, butyryl fentanyl). STRIDE, STARLiMS, and NFLIS have a total of 88 drug reports in which butyryl fentanyl was identified in drug exhibits submitted in 2014 and 2015 from California, Connecticut, Florida, Illinois, Indiana, Kansas, Minnesota, North Dakota, New York, Ohio, Oregon, Pennsylvania, Tennessee, Virginia, and Wisconsin. STARLiMS has a total of three drug reports in which beta-hydroxythiofentanyl was identified in drug exhibits submitted in 2015 from Florida. It is likely that the prevalence of butyryl fentanyl and beta-hydroxythiofentanyl in opioid analgesic-related emergency room admissions and deaths is underreported as standard immunoassays cannot differentiate these substances from fentanyl.

The population likely to abuse butyryl fentanyl and beta-hydroxythiofentanyl overlaps with the populations abusing prescription opioid analgesics and heroin. This is evidenced by the routes of administration and drug use history documented in butyryl fentanyl and beta-hydroxythiofentanyl fatal overdose cases. Because abusers of these fentanyl analogues are likely to obtain these

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substances through illicit sources, the identity, purity, and quantity is uncertain and inconsistent, thus posing significant adverse health risks to abusers of butyryl fentanyl and beta-hydroxythiofentanyl. Individuals who initiate (i.e., use an illicit drug for the first time) butyryl fentanyl or beta-hydroxythiofentanyl abuse are likely to be at risk of developing substance use disorder, overdose, and death similar to that of other opioid analgesics (e.g., fentanyl, morphine, etc.).

Factor 6. What, if Any, Risk There Is to the Public Health

Butyryl fentanyl and beta-hydroxythiofentanyl exhibit pharmacological profiles similar to that of fentanyl and other mu-opioid receptor agonists. Due to limited scientific data, their potency and toxicity are not known; however, the toxic effects of both butyryl fentanyl and beta-hydroxythiofentanyl in humans are demonstrated

by overdose fatalities involving these substances. Abusers of these fentanyl analogues may not know the origin, identity, or purity of these substances, thus posing significant adverse health risks when compared to abuse of pharmaceutical preparations of opioid analgesics, such as morphine and oxycodone.

Based on the documented case reports of overdose fatalities, the abuse of butyryl fentanyl and beta-hydroxythiofentanyl leads to the same qualitative public health risks as heroin, fentanyl and other opioid analgesic substances. The public health risks attendant to the abuse of heroin and opioid analgesics are well established and have resulted in large numbers of drug treatment admissions, emergency department visits, and fatal overdoses.

Butyryl fentanyl and beta-hydroxythiofentanyl have been associated with numerous fatalities. At least 40 confirmed overdose deaths involving butyryl fentanyl have been reported in Maryland (1), New York (38), and Oregon (1) in 2015. At least seven confirmed overdose fatalities involving beta-hydroxythiofentanyl have been reported in Florida in 2015. This indicates that both butyryl fentanyl and beta-hydroxythiofentanyl pose an imminent hazard to the public safety.

Finding of Necessity of Schedule I Placement To Avoid Imminent Hazard to Public Safety

In accordance with **21 U.S.C. 811**(h)(3), based on the data and information summarized above, the continued uncontrolled manufacture, distribution, importation, exportation, and abuse of butyryl fentanyl and beta-hydroxythiofentanyl pose an imminent hazard to the public safety. The DEA is not aware of any currently accepted medical uses for these substances in the United States. A substance meeting the statutory requirements for temporary scheduling, 21 U.S.C. 811(h)(1), may only be placed into schedule I. Substances in schedule I are those that have a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. Available data and information for butyryl fentanyl and beta-hydroxythiofentanyl indicate that these substances have a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. As required by section 201(h)(4) of the CSA, 21 U.S.C. 811(h)(4), the Administrator, through a letter dated December 21, 2015, notified the Assistant Secretary of the DEA's intention to temporarily place these substances into schedule I.

Conclusion

In accordance with the provisions of section 201(h) of the CSA, **21 U.S.C. 811**(h), the Administrator considered available data and information, herein sets forth the grounds for his determination that it is necessary to temporarily schedule butyryl fentanyl and beta-hydroxythiofentanyl into schedule I of the CSA, and finds that placement of these synthetic opioids into schedule I of the CSA is necessary to avoid an imminent hazard to the public safety. Because the Administrator hereby finds it necessary to temporarily place these synthetic opioids into schedule I to avoid an imminent hazard to the public safety, this final order temporarily scheduling butyryl fentanyl and beta-hydroxythiofentanyl will be effective on the date of publication in the Federal Register, and will be in effect for a period of two years, with a possible extension of one additional year, pending completion of the regular (permanent) scheduling process. 21 U.S.C. 811(h)(1) and (2).

The CSA sets forth specific criteria for scheduling a drug or other substance. Permanent scheduling actions in accordance with **21 U.S.C. 811**(a) are subject to formal rulemaking procedures done "on the record after opportunity for a hearing" conducted pursuant to the provisions of 5 U.S.C. 556 and 557. 21 U.S.C. 811. The permanent scheduling process of formal rulemaking affords interested parties with appropriate process and the government with any additional relevant information needed to make a determination. Final decisions that conclude the permanent scheduling process of formal rulemaking are subject to judicial review. **21 U.S.C. 877**. Temporary scheduling orders are not subject to judicial review. 21 U.S.C. 811(h)(6).

Requirements for Handling

Upon the effective date of this final order, butyryl fentanyl and beta-hydroxythiofentanyl will become subject to the regulatory controls and administrative, civil, and criminal sanctions applicable to the manufacture, distribution, reverse distribution, importation, exportation, engagement in research, and conduct of instructional activities or chemical analysis with, and possession of schedule I controlled substances including the following:

1. *Registration.* Any person who handles (manufactures, distributes, reverse distributes, imports, exports, engages in research, or conducts instructional activities or chemical analysis with, or possesses), or who desires to handle, butyryl fentanyl and beta-hydroxythiofentanyl must be registered with the DEA to conduct such activities pursuant to **21 U.S.C. 822**, **823**, **957**, and **958** and in accordance with **21 CFR parts 1301** and **1312**, as of May 12, 2016. Any person who currently handles butyryl fentanyl and beta-hydroxythiofentanyl, and is not registered with the DEA, must submit an application for registration and may not continue to handle butyryl fentanyl or beta-hydroxythiofentanyl as of May 12, 2016, unless the DEA has approved that application for registration pursuant to 21 U.S.C. 822, 823, 957, 958, and in accordance with 21 CFR parts 1301 and 1312. Retail sales of schedule I controlled substances to the general public are not allowed under the CSA. Possession of any quantity of this substance in a manner not authorized by the CSA on or after May 12, 2016 is unlawful and those in possession of any quantity of this substance may be subject to prosecution pursuant to the CSA.

2. *Disposal of stocks.* Any person who does not desire or is not able to obtain a schedule I registration to handle butyryl fentanyl and beta-hydroxythiofentanyl, must surrender all quantities of currently held butyryl fentanyl and beta-hydroxythiofentanyl.

3. *Security.* Butyryl fentanyl and beta-hydroxythiofentanyl are subject to schedule I security requirements and must be handled and stored pursuant to **21 U.S.C. 821**, **823**, **871**(b), and in accordance with **21 CFR 1301.71-1301.93**, as of May 12, 2016.

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4. *Labeling and packaging.* All labels, labeling, and packaging for commercial containers of butyryl fentanyl and beta-hydroxythiofentanyl must be in compliance with **21 U.S.C. 825**, **958**(e), and be in accordance with **21 CFR part 1302**. Current DEA registrants shall have 30 calendar days from May 12, 2016, to comply with all labeling and packaging requirements.

5. *Inventory.* Every DEA registrant who possesses any quantity of butyryl fentanyl and beta-hydroxythiofentanyl on the effective date of this order must take an inventory of all stocks of this substance on hand, pursuant to **21 U.S.C. 827** and **958**, and in accordance with **21 CFR 1304.03**, **1304.04**, and **1304.11**. Current DEA registrants shall have 30 calendar days from the effective date of this order to be in compliance with all inventory requirements. After the initial inventory, every DEA registrant must take an inventory of all controlled substances (including butyryl fentanyl and beta-hydroxythiofentanyl) on hand on a biennial basis, pursuant to 21 U.S.C. 827 and **958**, and in accordance with **21 CFR 1304.03**, **1304.04**, and **1304.11**.

6. *Records.* All DEA registrants must maintain records with respect to butyryl fentanyl and beta-hydroxythiofentanyl pursuant to **21 U.S.C. 827** and **958**, and in accordance with **21 CFR parts 1304**, and **1312**, **1317** and **Sec. 1307.11**. Current DEA registrants authorized to handle butyryl fentanyl and beta-hydroxythiofentanyl shall have 30 calendar days from the effective date of this order to be in compliance with all recordkeeping requirements.

7. *Reports.* All DEA registrants who manufacture or distribute butyryl fentanyl and beta-hydroxythiofentanyl must submit reports pursuant to **21 U.S.C. 827** and in accordance with **21 CFR parts 1304**, and **1312** as of May 12, 2016.

8. *Order Forms.* All DEA registrants who distribute butyryl fentanyl and beta-hydroxythiofentanyl must comply with order form requirements pursuant to **21 U.S.C. 828** and in accordance with **21 CFR part 1305** as of May 12, 2016.

9. *Importation and Exportation.* All importation and exportation of butyryl fentanyl and beta-hydroxythiofentanyl must be in compliance with **21 U.S.C. 952**, **953**, **957**, **958**, and in accordance with **21 CFR part 1312** as of May 12, 2016.

10. *Quota.* Only DEA registered manufacturers may manufacture butyryl fentanyl and beta-hydroxythiofentanyl in accordance with a quota assigned pursuant to **21 U.S.C. 826** and in accordance with **21 CFR part 1303** as of May 12, 2016.

11. *Liability.* Any activity involving butyryl fentanyl and beta-hydroxythiofentanyl not authorized by, or in violation of the CSA, occurring as of May 12, 2016, is unlawful, and may subject the person to administrative, civil, and/or criminal sanctions.

Regulatory Matters

Section 201(h) of the CSA, **21 U.S.C. 811**(h), provides for an expedited temporary scheduling action where such action is necessary to avoid an imminent hazard to the public safety. As provided in this subsection, the Attorney General may, by order, schedule a substance in schedule I on a temporary basis. Such an order may be issued before the expiration of 30 days from (1) the publication of a notice in the Federal Register of the intention to issue such order and the grounds upon which such order is to be issued, and (2) the date that notice of the proposed temporary scheduling order is transmitted to the Assistant Secretary. 21 U.S.C. 811(h)(1).

Inasmuch as section 201(h) of the CSA directs that temporary scheduling actions be issued by order and sets forth the procedures by which such orders are to be issued, the DEA believes that the notice and comment requirements of the Administrative Procedure Act (APA) at 5 U.S.C. 553, do not apply to this temporary scheduling action. In the alternative, even assuming that this action might be subject to 5 U.S.C. 553, the Administrator finds that there is good cause to forgo the

notice and comment requirements of 5 U.S.C. 553, as any further delays in the process for issuance of temporary scheduling orders would be impracticable and contrary to the public interest in view of the manifest urgency to avoid an imminent hazard to the public safety.

Further, the DEA believes that this temporary scheduling action is not a "rule" as defined by 5 U.S.C. 601(2), and, accordingly, is not subject to the requirements of the Regulatory Flexibility Act. The requirements for the preparation of an initial regulatory flexibility analysis in 5 U.S.C. 603(a) are not applicable where, as here, the DEA is not required by the APA or any other law to publish a general notice of proposed rulemaking.

[redacted]itionally, this action is not a significant regulatory action as defined by Executive Order 12866 (Regulatory Planning and Review), section 3(f), and, accordingly, [redacted]action has not been reviewed by the Office of Management and Budget (OMB).

This action will not have substantial direct effects on the States, on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government. Therefore, in accordance with Executive Order 13132 (Federalism) it is determined that this action does not have sufficient federalism implications to warrant the preparation of a Federalism Assessment.

As noted above, this action is an order, not a rule. Accordingly, the Congressional Review Act (CRA) is inapplicable, as it applies only to rules. However, if this were a rule, pursuant to the Congressional Review Act, "any rule for which an agency for good cause finds that notice and public procedure thereon are impracticable, unnecessary, or contrary to the public interest, shall take effect at such time as the federal agency promulgating the rule determines." 5 U.S.C. 808(2). It is in the public interest to schedule these substances immediately because they pose a public health risk. This temporary scheduling action is taken pursuant to **21 U.S.C. 811** (h), which is specifically designed to enable the DEA to act in an expeditious manner to avoid an imminent hazard to the public safety. 21 U.S.C. 811(h) exempts the temporary scheduling order from standard notice and comment rulemaking procedures to ensure that the process moves swiftly. For the same reasons that underlie 21 U.S.C. 811(h), that is, the DEA's need to move quickly to place these substances into schedule I because they pose an imminent hazard to public safety, it would be contrary to the public interest to delay implementation of the temporary scheduling order. Therefore, this order shall take effect immediately upon its publication. The DEA has submitted a copy of this final order to both Houses of Congress and to the Comptroller General, although such filing is not required under the Small Business Regulatory Enforcement Fairness Act of 1996 (Congressional Review Act), 5 U.S.C. 801-808 because, as noted above, this action is an order, not a rule.

List of Subjects in 21 CFR Part 1308

Administrative practice and procedure, Drug traffic control, Reporting and recordkeeping requirements.

For the reasons set out above, the DEA amends 21 CFR part 1308 as follows:

PART 1308--SCHEDULES OF CONTROLLED SUBSTANCES

- 1. The authority citation for part 1308 continues to read as follows:

  Authority: 21 U.S.C. 811, **812**, **871**(b), unless otherwise noted.

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- 2. Amend **Sec. 1308.11** by adding paragraphs (h)(26) and (27) to read as follows:

Sec. 1308.11 Schedule I.

* * * * *

(h) * * *

[redacted]6) *N*-(1-phenethylpiperidin-4-yl)-*N*-phenylbutyramide, its isomers, esters, ethers, salts and salts of isomers, esters and ethers (Other names: Butyryl [redacted]anyl) ..... (9822)

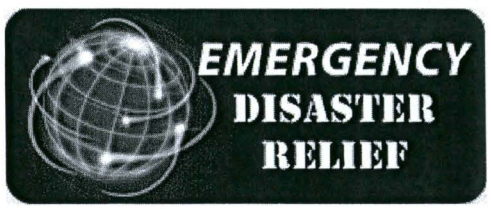
[redacted]27) *N*-[1-[2-hydroxy-2-(thiophen-2-yl)ethyl]piperidin-4-yl]-*N*-phenylpropionamide, its isomers, esters, ethers, salts and salts of isomers, esters and ethers (Other names: beta-hydroxythiofentanyl) ..... (9836)

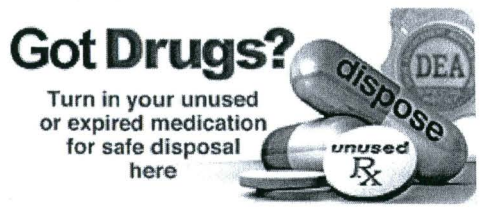
Dated: May 6, 2016.

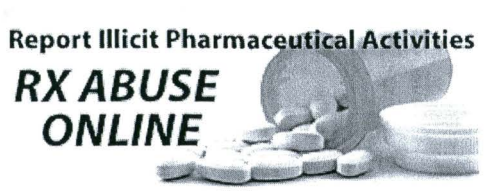
Chuck Rosenberg,
Acting Administrator.

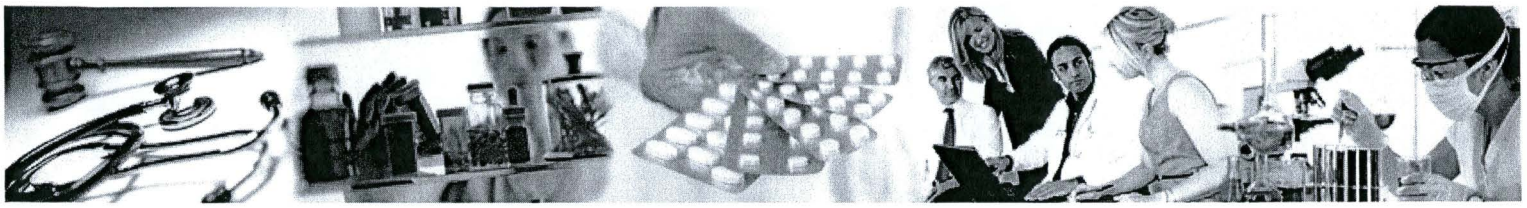
[FR Doc. 2016-11219 Filed 5-11-16; 8:45 am]

BILLING CODE 4410-09-P









Rules - 2016

[Federal Register Volume 81, Number 72 (Thursday, April 14, 2016)]
[Rules and Regulations]
[Pages 22023-22025]
From the Federal Register Online via the Government Publishing Office [www.gpo.gov]
[FR Doc No: 2016-08566]

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA-432]

Schedules of Controlled Substances: Placement of AH-7921 Into Schedule I

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Final order.

SUMMARY: With the issuance of this final order, the Administrator of the Drug Enforcement Administration places the substance AH-7921 (Systematic IUPAC Name: 3,4-dichloro-N-[(1dimethylamino)cyclohexylmethyl]benzamide), including its isomers, esters, ethers, salts, and salts of isomers, esters and ethers, into schedule I of the Controlled Substances Act. This scheduling action is pursuant to the Controlled Substances Act and is required in order for the United States to discharge its obligations under the Single Convention on Narcotic Drugs, 1961. This action imposes the regulatory controls and administrative, civil, and criminal sanctions applicable to schedule I controlled substances on persons who handle (manufacture, distribute, import, export, engage in research or conduct instructional activities with, or possess), or propose to handle, AH-7921.

DATES: Effective May 16, 2016.

FOR FURTHER INFORMATION CONTACT: Barbara J. Boockholdt, Office of Diversion Control, Drug Enforcement Administration; Mailing Address: 8701 Morrissette Drive, Springfield, Virginia 22152; Telephone: (202) 598-6812.

SUPPLEMENTARY INFORMATION:

Legal Authority

The Drug Enforcement Administration (DEA) implements and enforces titles II and III of the Comprehensive Drug Abuse Prevention and Control Act of 1970, as amended. Titles II and III are referred to as the "Controlled Substances Act" and the "Controlled Substances Import and Export Act," respectively, and are collectively referred to as the "Controlled Substances Act" or the "CSA" for the purpose of this action. **21 U.S.C. 801-971**. The DEA publishes the implementing regulations for these statutes in title 21 of the Code of Federal Regulations (CFR), chapter II. The CSA and its implementing regulations are designed to prevent, detect, and eliminate the diversion of controlled substances and listed chemicals into the illicit market while providing for the legitimate medical, scientific, research, and industrial needs of the United States. Controlled substances have the potential for abuse and dependence and are controlled to protect the public health and safety.

Under the CSA, controlled substances are classified into one of five schedules based upon their potential for abuse, their currently accepted medical use in treatment in the United States, and the degree of dependence the substance may cause. **21 U.S.C. 812**. The initial schedules of controlled substances established by Congress are found at 21 U.S.C. 812(c), and the current list of scheduled substances is published at **21 CFR part 1308**.

Section 201(d)(1) of the CSA (**21 U.S.C. 811**(d)(1)) states that, if control of a substance is required "by United States obligations under international treaties, conventions, or protocols in effect on October 27, 1970, the Attorney General shall issue an order controlling such drug under the schedule he deems most appropriate to carry out such obligations, without regard to the findings and procedures required by section 201(a) and (b) (21 U.S.C. 811(a) and (b)) and section 202(b) (**21 U.S.C. 812**(b)) of the Act." 21 U.S.C. 811(d)(1), **21 CFR 1308.46**. If a substance is added to one of the schedules of the Single Convention on Narcotic Drugs, 1961, then, in accordance with article 3, paragraph 7 of the Convention, as a signatory Member State, the United States is obligated to control that substance under its national drug control legislation, the CSA. The Attorney General has delegated scheduling authority under 21 U.S.C. 811 to the Administrator of the DEA. 28 CFR 0.100.

Background

On May 8, 2015, the Secretary-General of the United Nations advised the Secretary of State of the United States, that during the 58th session of the Commission on Narcotic Drugs, AH-7921 was added to schedule I of the Single Convention on Narcotic Drugs, 1961. This letter was prompted by a decision at the 58th session of the Commission on Narcotic Drugs in March 2015 to schedule AH-7921 under schedule I of the Single Convention on Narcotic Drugs. As a signatory Member State to the Single Convention on Narcotic Drugs, the United States is obligated to control AH-7921 under its national drug control legislation, the CSA, in the schedule deemed most appropriate to carry out its international obligations. **21 U.S.C. 811**(d)(1).

AH-7921

AH-7921 is an N-substituted cyclohexylmethyl benzamide developed in 1962 by Allen and Hanbury's, Ltd., a pharmaceutical company in the United Kingdom. AH-7921 is a [micro]-opioid receptor agonist with analgesic activity similar to that of morphine. The DEA is not aware of any commercial or medical uses for this substance. In animals, withdrawal symptoms are observed following repeated administration of AH-7921. Currently, clinical studies evaluating the safety and pharmacological effects of AH-7921 in humans have not been reported in the scientific literature. Usage of AH-7921 for eliciting euphoria and relaxation has been documented. There have been several reports of overdoses and deaths from AH-7921 reported worldwide including at least one published case report of a death resulting from AH-7921 in the United States. Given the increasing abuse of opioid prescription drugs (e.g., oxycodone, hydrocodone and fentanyl) and increased use of heroin in the United States, [redacted] are legitimate concerns about an increased potential of abuse of AH-7921.

[redacted] is not aware of any claims or any medical or scientific literature suggesting that AH-7921 has a currently accepted medical use in treatment in the United States. Accordingly, DEA has not requested that HHS conduct a scientific and medical evaluation of the substance's medical utility.

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Furthermore, DEA is not required under **21 U.S.C. 811**(d)(1) to make any findings required by 21 U.S.C. 811(a) or **812**(b), and is not required to follow the procedures prescribed by 21 U.S.C. 811(a) and (b). Therefore, consistent with the framework of 21 U.S.C. 811(d), DEA concludes that AH-7921 has no currently accepted medical use in treatment in the United States and is most appropriately placed in schedule I of the CSA.

Conclusion

In order to meet the obligations of the Single Convention on Narcotic Drugs, 1961 and because AH-7921 has no currently accepted medical use in treatment in the United States, the Administrator of the Drug Enforcement Administration has determined that this substance should be placed in schedule I of the Controlled Substances Act.

Requirements for Handling

Upon the effective date of this final order, AH-7921 is subject to the CSA's schedule I regulatory controls and administrative, civil, and criminal sanctions applicable to the manufacture, distribution, importation, exportation, engagement in research, and conduct of instructional activities with, and possession of schedule I controlled substances including the following:

1. *Registration.* Any person who handles (manufactures, distributes, imports, exports, engages in research or conducts instructional activities with, or possesses), or who desires to handle, AH-7921 must be registered with the DEA to conduct such activities pursuant to **21 U.S.C. 822**, **823**, **957**, and **958** and in accordance with **21 CFR parts 1301** and **1312**, as of May 16, 2016. Any person who currently handles AH-7921, and is not registered with the DEA, must submit an application for registration and may not continue to handle AH-7921 as of May 16, 2016, unless the DEA has approved that application for registration pursuant to 21 U.S.C. 822, 823, 957, 958, and in accordance with 21 CFR parts 1301 and 1312.

2. *Disposal of stocks.* Any person who does not desire or is not able to obtain a schedule I registration must surrender all quantities of currently held AH-7921, or may transfer all quantities of currently held AH-7921 to a person registered with the DEA on or before May 16, 2016 in accordance with all applicable federal, state, local, and tribal laws. As of May 16, 2016, controlled substances must be disposed of in accordance with **21 CFR part 1317**, in additional to all other applicable federal, state, local, and tribal laws.

3. *Security.* AH-7921 is subject to schedule I security requirements and must be handled and stored pursuant to **21 U.S.C. 821**, **823**, **871**(b), and in accordance with **21 CFR 1301.71-1301.93**, as of May 16, 2016.

4. *Labeling and packaging.* All labels, labeling, and packaging for commercial containers of AH-7921 must be in compliance with **21 U.S.C. 825**, **958**(e), and be in accordance with **21 CFR part 1302** as of May 16, 2016.

5. *Quota.* A quota assigned pursuant to **21 U.S.C. 826** and in accordance with **21 CFR part 1303** is required in order to manufacture AH-7921 as of May 16, 2016.

6. *Inventory.* Every DEA registrant who possesses any quantity of AH-7921 on the effective date of this order must take an inventory of all stocks of this substance on hand as of May 16, 2016, pursuant to **21 U.S.C. 827** and **958**, and in accordance with **Sec. Sec. 1304.03**, **1304.04**, and **1304.11**.

Every person who becomes registered with the DEA after May 16, 2016 must take an initial inventory of all stocks of controlled substances (including AH-7921) on hand on the date the registrant first engages in the handling of controlled substances, pursuant to **21 U.S.C. 827** and **958** and in accordance with **21 CFR 1304.03**, **1304.04**, and **1304.11**.

After the initial inventory, every DEA registrant must take an inventory of all controlled substances (including AH-7921) on hand on a biennial basis, pursuant to **21 U.S.C. 827** and **958**, and in accordance with **Sec. Sec. 1304.03**, **1304.04**, and **1304.11**.

7. *Records and Reports.* Every DEA registrant would be required to maintain records and submit reports with respect to AH-7921 pursuant to **21 U.S.C. 827** and **958**, and in accordance with **21 CFR parts 1304** and **1312**.

8. *Order Forms.* All DEA registrants who distribute AH-7921 must comply with order form requirements pursuant to **21 U.S.C. 828** and in accordance with **21 CFR part 1305** as of May 16, 2016.

9. *Importation and Exportation.* All importation and exportation of AH-7921 must be in compliance with **21 U.S.C. 952**, **953**, **957**, **958**, and in accordance with **21 CFR part 1312** as of May 16, 2016.

10. *Liability.* Any activity involving AH-7921 not authorized by, or in violation of the CSA, occurring as of May 16, 2016, is unlawful, and may subject the person to administrative, civil, and/or criminal sanctions.

Regulatory Analyses

Administrative Procedure Act

The CSA provides for an expedited scheduling action where control is required by the United States obligations under international treaties, conventions, or protocols. **21 U.S.C. 811**(d)(1). If control is required pursuant to such international treaty, convention, or protocol, the Attorney General must issue an order controlling such drug under the schedule he deems most appropriate to carry out such obligations, without regard to the findings or procedures otherwise required for scheduling actions. Id.

To the extent that **21 U.S.C. 811**(d)(1) directs that if control is required by the United States obligations under international treaties, conventions, or protocols in effect on October 27, 1970, scheduling actions shall be issued by order (as compared to scheduling pursuant to 21 U.S.C. 811(a) by rule), the DEA believes that the notice and comment requirements of section 553 of the Administrative Procedure Act (APA), 5 U.S.C. 553, do not apply to this scheduling action. In the alternative, even if this action does constitute "rule making" under 5 U.S.C. 551(5), this action is exempt from the notice and comment requirements of 5 U.S.C. 553 pursuant to 21 U.S.C. 553(a)(1) as an action involving a foreign affairs function of the United States given that this action is being done in accordance with 21 U.S.C. 811(d)(1)'s requirement that such action be taken to comply with the United States obligations under the specified international agreements.

Executive Order 12866

This action is not a significant regulatory action as defined by Executive Order 12866 (Regulatory Planning and Review), section 3(f), and, accordingly, this action has not been reviewed by the Office of Management and Budget (OMB).

Executive Order 13132

[redacted]s action does not have federalism implications warranting the application of Executive Order 13132. This action will not have substantial direct effects on the States, on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government. Therefore, in accordance with Executive Order 13132 (Federalism) it is determined that this action does not have sufficient federalism implications to warrant the preparation of a Federalism Assessment.

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Executive Order 13175

This action does not have tribal implications warranting the application of Executive Order 13175. The action does not have substantial direct effects on one or more Indian tribes, on the relationship between the Federal government and Indian tribes, or on the distribution of power and responsibilities between the Federal government and Indian tribes.

Regulatory Flexibility Act

The Regulatory Flexibility Act (RFA) (5 U.S.C. 601-612) applies to rules that are subject to notice and comment under section 553(b) of the APA or any other l[redacted] explained above, the CSA exempts this final order from notice and comment. Consequently, the RFA does not apply to this action.

Paperwork Reduction Act of 1995

This action does not impose a new collection of information requirement under the Paperwork Reduction Act of 1995. 44 U.S.C. 3501-3521. An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Congressional Review Act

This action is not a major rule as defined by section 804 of the Small Business Regulatory Enforcement Fairness Act of 1996 (Congressional Review Act). However, the DEA has submitted a copy of this final order to both Houses of Congress and to the Comptroller General.

List of Subjects in 21 CFR Part 1308

Administrative practice and procedure, Drug traffic control, Narcotics, Prescription drugs.

For the reasons set out above, the DEA amends 21 CFR part 1308 as follows:

PART 1308--SCHEDULES OF CONTROLLED SUBSTANCES

- 1. The authority citation for part 1308 continues to read as follows:

  Authority: 21 U.S.C. 811, 812, 871(b), unless otherwise noted.

- 2. Amend **Sec. 1308.11** by redesignating paragraphs (b)(3) through (55) as (b)(4) through (56) and adding a new (b)(3)to read as follows:

Sec. 1308.11 Schedule I.

* * * * *

(b) * * *

(3) AH-7921 (3,4-dichloro-*N*-[(1-dimethylamino) cyclohexylmethyl]benzamide 9551

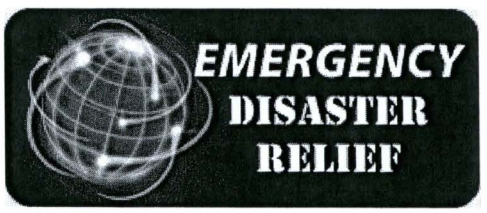
* * * * *

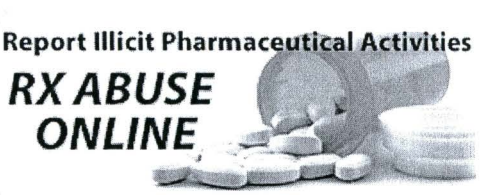
Dated: April 8, 2016

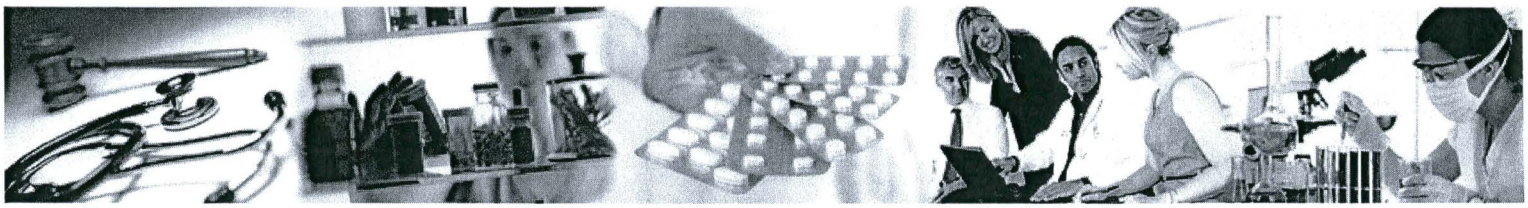
Chuck Rosenberg,
Acting Administrator.

[FR Doc. 2016-08566 Filed 4-13-16; 8:45 am]

BILLING CODE 4410-09-P







Rules - 2016

[Federal Register Volume 81, Number 219 (Monday, November 14, 2016)]
[Rules and Regulations]
[Pages 79389-79393]
From the Federal Register Online via the Government Publishing Office [www.gpo.gov]
[FR Doc No: 2016-27357]

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA-440]

Schedules of Controlled Substances: Temporary Placement of U-47700 Into Schedule I

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Final Order

SUMMARY: The Administrator of the Drug Enforcement Administration is issuing this final order to temporarily schedule the synthetic opioid, 3,4-dichloro-N-[2-(dimethylamino)cyclohexyl]-N-methylbenzamide (also known as U-47700), and its isomers, esters, ethers, salts and salts of isomers, esters and ethers, into schedule I pursuant to the temporary scheduling provisions of the Controlled Substances Act. This action is based on a finding by the Administrator that the placement of U-47700 into schedule I of the Controlled Substances Act is necessary to avoid an imminent hazard to the public safety. As a result of this order, the regulatory controls and administrative, civil, and criminal sanctions applicable to schedule I controlled substances will be imposed on persons who handle (manufacture, distribute, reverse distribute, import, export, engage in research, conduct instructional activities or chemical analysis, or possess), or propose to handle, U-47700.

DATES: This final order is effective on November 14, 2016.

FOR FURTHER INFORMATION CONTACT: Michael J. Lewis, Diversion Control Division, Drug Enforcement Administration; Mailing Address: 8701 Morrissette Drive, Springfield, Virginia 22152; Telephone: (202) 598- 6812.

SUPPLEMENTARY INFORMATION:

Legal Authority

The Drug Enforcement Administration (DEA) implements and enforces titles II and III of the Comprehensive Drug Abuse Prevention and Control Act of 1970, as amended. **21 U.S.C. 801-971**. Titles II and III are referred to as the "Controlled Substances Act" and the "Controlled Substances Import and Export Act," respectively, and are collectively referred to as the "Controlled Substances Act" or the "CSA" for the purpose of this action. The DEA publishes the implementing regulations

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for these statutes in title 21 of the Code of Federal Regulations (CFR), chapter II. The CSA and its implementing regulations are designed to prevent, detect, and eliminate the diversion of controlled substances and listed chemicals into the illicit market while ensuring an adequate supply is available for the legitimate medical, scientific, research, and industrial needs of the United States. Controlled substances have the potential for abuse and dependence and are controlled to protect the public health and safety.

Under the CSA, every controlled substance is classified into one of five schedules based upon its potential for abuse, its currently accepted medical use in treatment in the United States, and the degree of dependence the drug or other substance may cause. 21 U.S.C. 812. The initial schedules of controlled substances established by Congress are found at **21 U.S.C. 812**(c), and the current list of all scheduled substances is published at **21 CFR part 1308.**

Section 201 of the CSA, **21 U.S.C. 811**, provides the Attorney General with the authority to temporarily place a substance into schedule I of the CSA for two years without regard to the requirements of 21 U.S.C. 811(b) if she finds that such action is necessary to avoid an imminent hazard to the public safety. 21 U.S.C. 811(h)(1). In addition, if proceedings to control a substance are initiated under 21 U.S.C. 811(a)(1), the Attorney General may extend the temporary scheduling for up to one year. 21 U.S.C. 811(h)(2).

Where the necessary findings are made, a substance may be temporarily scheduled if it is not listed in any other schedule under section 202 of the CSA, 21 U.S.C. 812, or if there is no exemption or approval in effect for the substance under section 505 of the Federal Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. 355. 21 U.S.C. 811(h)(1). The Attorney General has delegated her scheduling authority under 21 U.S.C. 811 to the Administrator of the DEA. 28 CFR 0.100.

Background

Section 201(h)(4) of the CSA, 21 U.S.C. 811(h)(4), requires the Administrator to notify the Secretary of the Department of Health and Human Services (HHS) of his intention to temporarily place a substance into schedule I of the CSA.\1\ The Administrator transmitted the notice of intent to place U-47700 into schedule I on a temporary basis to the Assistant Secretary by letter dated April 18, 2016. The Assistant Secretary responded to this notice by letter dated April 28, 2016, and advised

that based on review by the Food and Drug Administration (FDA), there are currently no investigational new drug applications or approved new drug applications for U-47700. The Assistant Secretary also stated that the HHS has no objection to the temporary placement of U-47700 into schedule I of the CSA. The DEA has taken into consideration the Assistant Secretary's comments as required by 21 U.S.C. 811(h)(4). U-47700 is not currently listed in any schedule under the CSA, and no exemptions or approvals are in effect for U-47700 under section 505 of the FDCA, 21 U.S.C. 355. The DEA has found that the control of U-47700 in schedule I on a temporary basis is necessary to avoid an imminent hazard to the public safety, and as required by 21 U.S.C. 811(h)(1)(A), a notice of intent to temporarily schedule U-47700 was published in the Federal Register on September 7, 2016. 81 FR 61636.

\1\ As discussed in a memorandum of understanding entered into by the Food and Drug Administration (FDA) and the National Institute on Drug Abuse (NIDA), the FDA acts as the lead agency within the HHS in carrying out the Secretary's scheduling responsibilities under the CSA, with the concurrence of NIDA. 50 FR 9518, Mar. 8, 1985. The Secretary of the HHS has delegated to the Assistant Secretary for Health of the HHS the authority to make domestic drug scheduling recommendations. 58 FR 35460, July 1, 1993.

To find that placing a substance temporarily into schedule I of the CSA is necessary to avoid an imminent hazard to the public safety, the Administrator is required to consider three of the eight factors set forth in section 201(c) of the CSA, 21 U.S.C. 811(c): The substance's history and current pattern of abuse; the scope, duration and significance of abuse; and what, if any, risk there is to the public health. 21 U.S.C. 811(h)(3). Consideration of these factors includes actual abuse, diversion from legitimate channels, and clandestine importation, manufacture, or distribution. 21 U.S.C. 811(h)(3).

A substance meeting the statutory requirements for temporary scheduling may only be placed into schedule I. 21 U.S.C. 811(h)(1). Substances in schedule I are those that have a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. 21 U.S.C. 812(b)(1). Available data and information for U- 47700, summarized below, indicate that this synthetic opioid has a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. The DEA's updated three-factor analysis, and the Assistant Secretary's April 28, 2016, letter, are available in their entirety under the tab "Supporting Documents" of the public docket of this action at www.regulations.gov under FDMS Docket ID: DEA-2016-0016 (Docket Number DEA-440).

Factor 4. History and Current Pattern of Abuse

The recreational abuse of novel opioids continues to be a significant concern. These substances are distributed to users with often unpredictable outcomes. The novel synthetic opioid U-47700 has recently been encountered by law enforcement and public health officials and the adverse health effects and outcomes are documented in the scientific literature. Self-reporting by users describes the effects of U-47700 to be similar to other opioids. The negative effects documented in the scientific literature are also consistent with other opioids. The National Forensic Laboratory Information System (NFLIS) is a national drug forensic laboratory reporting system that systematically collects results from drug chemistry analyses conducted by participating Federal, State, and local forensic laboratories across the country. The DEA utilizes NFLIS to monitor for drug trends. The first laboratory submission of U-47700 was recorded in October 2015; a total of 88 records were reported from State and local forensic laboratories between October 2015--September 2016 according to NFLIS (query date: October 24, 2016).

On October 1, 2014, the DEA implemented STARLiMS (a web-based, commercial laboratory information management system) as its laboratory drug evidence data system of record. DEA laboratory data submitted after September 30, 2014, are reposited in STARLiMS; data from STARLiMS were queried on November 1, 2016. STARLiMS registered 45 reports containing U-47700 in 2016 from California, Connecticut, Florida, Maryland, Montana, North Dakota, New Jersey, New York, Tennessee, Texas, Virginia, West Virginia, and the District of Columbia. Through information collected from NFLIS, law enforcement reports, and email communications, the DEA is aware of the identification of U-47700 from toxicology reports and submitted evidence to forensic laboratories in several states, including Arkansas, California, Colorado, Connecticut, Florida, Georgia, Iowa, Kentucky, Missouri, Montana, New

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Hampshire, New Jersey, New York, North Carolina, North Dakota, Ohio, Oklahoma, Oregon, Pennsylvania, Texas, and Wisconsin. These identifications occurred in 2015 and 2016.

Evidence suggests that the pattern of abuse of U-47700 parallels that of heroin, prescription opioid analgesics, and other novel opioids. Seizures of U-47700 have been encountered in powder form and in counterfeit tablets that mimic pharmaceutical opioids. U-47700 has also been encountered in glassine bags and envelopes and knotted corners of plastic bags. These clandestine forms of distribution demonstrate the abuse of this substance as a replacement for heroin or other opioids, either knowingly or unknowingly. Further, U-47700 has been encountered as a single substance as well as in combination with other substances, including heroin, fentanyl, and furanyl fentanyl in drug exhibits.

The scientific literature and information collected by DEA demonstrate U-47700 is being abused for its opioid properties. The distribution of U-47700 and the increased prevalence of abuse remain deeply concerning to the DEA.

Factor 5. Scope, Duration and Significance of Abuse

The scientific literature and reports collected by the DEA demonstrate U-47700 is being abused for its opioid properties. This abuse of U-47700 has resulted in morbidity and mortality (see updated DEA 3-Factor Analysis for full discussion). The DEA has received reports for at least 46 confirmed fatalities \2\ associated with U-47700. The information on these deaths occurring in 2015 and 2016 was collected from email communications and toxicology and medical examiner reports and was reported from New Hampshire (1), New York (31), North Carolina (10), Ohio (1), Texas (2), and Wisconsin (1). The scientific literature notes additional fatal overdoses connected to U-47700. The population likely to abuse U-47700 appears to overlap with the populations abusing prescription opioid analgesics, other "designer opioids," and heroin, as evidenced by drug use history documented in U-47700 fatal overdose cases. This observation is further supported by U-47700 being sold on the illicit market in glassine bags, some of which are marked with stamped logos, imitating the sale of heroin. Additionally, U-47700 has been found in counterfeit pills. Because abusers of U-47700 are likely to obtain this substance through non- regulated sources (i.e., on-line purchases or drug dealers), the identity, purity, and quantity are uncertain and inconsistent, thus posing significant adverse health risks to the end user. Individuals who initiate (i.e., use a drug for the first time) U-47700 abuse are likely to be at risk of developing substance use disorder, overdose, and death similar to that of other opioid analgesics (e.g., fentanyl, morphine, etc.).

\2\ Due to a proofreading error, the number of fatalities listed in the U-47700 NOI, which was 15, is incorrect. The correct number, 46, has been added to this Final Order.

STARLiMS contains 45 reports in which U-47700 was identified in drug exhibits submitted in 2016. A query of NFLIS returned 88 records of U-47700 being identified in exhibits submitted to State and local forensic laboratories between October 2015--September 2016. The DEA is not aware of any laboratory analyses of drug evidence identifying U- 47700 prior to 2015, indicating that this synthetic opioid only recently became available as a replacement for other opioids that are commonly abused (i.e. oxycodone, heroin, fentanyl). U-47700 is available over the Internet and is marketed as a "research chemical." The on-line sale and marketing of U-47700 are similar to other new psychoactive substances that have rapidly appeared on the recreational drug market and also resulted in negative consequences for the user.

Factor 6. What, if Any, Risk There Is to the Public Health

U-47700 exhibits pharmacological profiles similar to that of morphine and other mu-opioid receptor agonists. Cases of intoxication are reported in the literature with morbidity and mortality associated with U-47700 use. The toxic effects of U-47700 in humans are demonstrated by overdoses and overdose fatalities associated this substance, as reported in the scientific literature. Abusers of U-47700 may not know the origin, identity, or purity of this substance, thus posing significant adverse health risks when compared to abuse of pharmaceutical preparations of opioid analgesics, such as morphine and oxycodone. Additionally, the potent opi U-47700 may serve as a precursor to problematic opioid use and dependence.

Based on reports in the scientific literature and information received by the DEA, the abuse of U-47700 leads to the same qualitative public health risks as heroin, fentanyl and other opioid analgesic substances. As with any non-medically approved opioid, the health and safety risks for users are great. The public health risks

attendant to the abuse of heroin and opioid analgesics are well established and have resulted in large numbers of drug treatment admissions, emergency department visits, and fatal overdoses.

U-47700 has been associated with a number of fatalities and non- fatal overdoses as detailed in the scientific literature. The DEA has received information connecting U-47700 to at least 46 confirmed overdose deaths, occurring in 2015 and 2016 in New Hampshire (1), New York (31), North Carolina (10), Ohio (1), Texas (2), and Wisconsin (1).

[redacted]ing of Necessity of Schedule I Placement To Avoid Imminent Hazard to Public Safety

[redacted]ccordance with **21 U.S.C. 811**(h)(3), based on the data and information summarized above, the continued uncontrolled manufacture, distribution, importation, exportation, and abuse of U-47700 pose an imminent hazard to the public safety. The DEA is not aware of any currently accepted medical uses for this substance in the United States. A substance meeting the statutory requirements for temporary scheduling, 21 U.S.C. 811(h)(1), may only be placed into schedule I. Substances in schedule I are those that have a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. Available data and information for U-47700 indicate that this substance has a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. As required by section 201(h)(4) of the CSA, 21 U.S.C. 811(h)(4), the Administrator, through a letter dated April 18, 2016, notified the Assistant Secretary of the DEA's intention to temporarily place this substance into schedule I.

Conclusion

In accordance with the provisions of section 201(h) of the CSA, 21 U.S.C. 811(h), the Administrator considered available data and information, herein sets forth the grounds for his determination that it is necessary to temporarily schedule U-47700 into schedule I of the CSA, and finds that placement of this synthetic opioid into schedule I of the CSA is necessary to avoid an imminent hazard to the public safety. Because the Administrator hereby finds it necessary to temporarily place this synthetic opioid into schedule I to avoid an imminent hazard

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to the public safety, this final order temporarily scheduling U-47700 will be effective on the date of publication in the Federal Register, and will be in effect for a period of two years, with a possible extension of one additional year, pending completion of the regular (permanent) scheduling process. 21 U.S.C. 811(h) (1) and (2).

The CSA sets forth specific criteria for scheduling a drug or other substance. Permanent scheduling actions in accordance with 21 U.S.C. 811(a) are subject to formal rulemaking procedures done "on the record after opportunity for a hearing" conducted pursuant to the provisions of 5 U.S.C. 556 and 557. 21 U.S.C. 811. The permanent scheduling process of formal rulemaking affords interested parties with appropriate process and the government with any additional relevant information needed to make a determination. Final decisions that conclude the permanent scheduling process of formal rulemaking are subject to judicial review. 21 U.S.C. 877. Temporary scheduling orders are not subject to judicial review. 21 U.S.C. 811(h)(6).

Requirements for Handling

Upon the effective date of this final order, U-47700 will become subject to the regulatory controls and administrative, civil, and criminal sanctions applicable to the manufacture, distribution, reverse distribution, importation, exportation, engagement in research, and conduct of instructional activities or chemical analysis with, and possession of schedule I controlled substances including the following:

1. Registration. Any person who handles (manufactures, distributes, reverse distributes, imports, exports, engages in research, or conducts instructional activities or chemical analysis with, or possesses), or who desires to handle, U-47700 must be registered with the DEA to conduct such activities pursuant to 21 U.S.C. 822, 823, 957, and 958 and in accordance with 21 CFR parts 1301 and 1312, as of November 14, 2016. Any person who currently handles U-47700, and is not registered with the DEA, must submit an application for registration and may not continue to handle U-47700 as of November 14, 2016, unless the DEA has approved that application for registration pursuant to 21 U.S.C. 822, 823, 957, 958, and in accordance with 21 CFR parts 1301 and 1312. Retail sales of schedule I controlled substances to the general public are not allowed under the CSA. Possession of any quantity of this substance in a manner not authorized by the CSA on or after November 14, 2016 is unlawful and those in possession of any quantity of this substance may be subject to prosecution pursuant to the CSA.

[redacted]Disposal of stocks. Any person who does not desire or is not able to obtain a schedule I registration to handle U-47700, must surrender all quantities of currently [redacted]d U-47700.

3. Security. U-47700 is subject to schedule I security requirements and must be handled and stored pursuant to **21 U.S.C. 821**, **823**, **871**(b), and in accordance with **21 CFR 1301.71-1301.93**, as of November 14, 2016.

4. Labeling and packaging. All labels, labeling, and packaging for commercial containers of U-47700 must be in compliance with **21 U.S.C. 825**, **958**(e), and be in accordance with **21 CFR part 1302**. Current DEA registrants shall have 30 calendar days from November 14, 2016, to comply with all labeling and packaging requirements.

5. Inventory. Every DEA registrant who possesses any quantity of U- 47700 on the effective date of this order must take an inventory of all stocks of this substance on hand, pursuant to **21 U.S.C. 827** and **958**, and in accordance with **21 CFR 1304.03, 1304.04, and 1304.11**. Current DEA registrants shall have 30 calendar days from the effective date of this order to be in compliance with all inventory requirements. After the initial inventory, every DEA registrant must take an inventory of all controlled substances (including U-47700) on hand on a biennial basis, pursuant to 21 U.S.C. 827 and 958, and in accordance with **21 CFR 1304.03, 1304.04, and 1304.11.**

6. Records. All DEA registrants must maintain records with respect to U-47700 pursuant to 21 U.S.C. 827 and 958, and in accordance with **21 CFR parts 1304**, and **1312**, **1317** and **Sec. 1307.11**. Current DEA registrants shall have 30 calendar days from the effective date of this order to be in compliance with all recordkeeping requirements.

7. Reports. All DEA registrants who manufacture or distribute U- 47700 must submit reports pursuant to 21 U.S.C. 827 and in accordance with 21 CFR parts 1304, and 1312 as of November 14, 2016.

8. Order Forms. All DEA registrants who distribute U-47700 must comply with order form requirements pursuant to 21 U.S.C. 828 and in accordance with **21 CFR part 1305** as of November 14, 2016.

9. Importation and Exportation. All importation and exportation of U-47700 must be in compliance with 21 U.S.C. 952, 953, 957, 958, and in accordance with **21 CFR part 1312** as of November 14, 2016.

10. Quota. Only DEA registered manufacturers may manufacture U- 47700 in accordance with a quota assigned pursuant to 21 U.S.C. 826 and in accordance with **21 CFR part 1303** as of November 14, 2016.

11. Liability. Any activity involving U-47700 not authorized by, or in violation of the CSA, occurring as of November 14, 2016, is unlawful, and may subject the person to administrative, civil, and/or criminal sanctions.

Regulatory Matters

Section 201(h) of the CSA, 21 U.S.C. 811(h), provides for a temporary scheduling action where such action is necessary to avoid an imminent hazard to the public safety. As provided in this subsection, the Attorney General may, by order, schedule a substance in schedule I on a temporary basis. Such an order may not be issued before the expiration of 30 days from (1) the publication of a notice in the Federal Register of the intention to issue such order and the grounds upon which such order is to be issued, and (2) the date that notice of the proposed temporary scheduling order is transmitted to the Assistant Secretary. 21 U.S.C. 811(h)(1).

[redacted]asmuch as section 201(h) of the CSA directs that temporary scheduling actions be issued by order and sets forth the procedures by which such orders are to be [redacted]ued, the DEA believes that the notice and comment requirements of the Administrative Procedure Act (APA) at 5 U.S.C. 553, do not apply to this temporary [redacted]cheduling action. In the alternative, even assuming that this action might be subject to 5 U.S.C. 553, the Administrator finds that there is good cause to forgo the notice and comment requirements of 5 U.S.C. 553, as any further delays in the process for issuance of temporary scheduling orders would be impracticable and contrary to the public interest in view of the manifest urgency to avoid an imminent hazard to the public safety.

Further, the DEA believes that this temporary scheduling action is not a "rule" as defined by 5 U.S.C. 601(2), and, accordingly, is not subject to the requirements of the Regulatory Flexibility Act. The requirements for the preparation of an initial regulatory flexibility analysis in 5 U.S.C. 603(a) are not applicable where, as here, the DEA is not required by the APA or any other law to publish a general notice of proposed rulemaking.

Additionally, this action is not a significant regulatory action as defined by Executive Order 12866 (Regulatory Planning and Review), section 3(f), and, accordingly, this action has not been

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reviewed by the Office of Management and Budget (OMB). This action will not have substantial direct effects on the States, on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government. Therefore, in accordance with Executive Order 13132 (Federalism) it is determined that this action does not have sufficient federalism implications to warrant the preparation of a Federalism Assessment.

As noted above, this action is an order, not a rule. Accordingly, the Congressional Review Act (CRA) is inapplicable, as it applies only to rules. However, if this were a rule, pursuant to the Congressional Review Act, "any rule for which an agency for good cause finds that notice and public procedure thereon are impracticable, unnecessary, or contrary to the public interest, shall take effect at such time as the federal agency promulgating the rule determines." 5 U.S.C. 808(2). It is in the public interest to schedule this substance immediately because it poses a public health risk. This temporary scheduling action is taken pursuant to 21 U.S.C. 811(h), which is specifically designed to enable the DEA to act in an expeditious manner to avoid an imminent hazard to the public safety. 21 U.S.C. 811(h) exempts the temporary scheduling order from standard notice and comment rulemaking procedures to ensure that the process moves swiftly. For the same reasons that underlie 21 U.S.C. 811(h), that is, the DEA's need to move quickly to place this substance into schedule I because it poses an imminent hazard to the public safety and it would be contrary to the public interest to delay implementation of the temporary scheduling order. Therefore, this order shall take effect immediately upon its publication. The DEA has submitted a copy of this final order to both Houses of Congress and to the Comptroller General, although such filing is not required under the Small Business Regulatory Enforcement Fairness Act of 1996 (Congressional Review Act), 5 U.S.C. 801-808, because, as noted above, this action is an order, not a rule.

List of Subjects in 21 CFR Part 1308

Administrative practice and procedure, Drug traffic control, Reporting and recordkeeping requirements.

For the reasons set out above, the DEA amends 21 CFR part 1308 as follows:

PART 1308--SCHEDULES OF CONTROLLED SUBSTANCES

1. The authority citation for part 1308 continues to read as follows:

Authority: 21 U.S.C. 811, 812, 871(b), unless otherwise noted.

2. Amend Sec. 1308.11 by adding paragraph (h)(18) to read as follows:

Sec. 1308.11 Schedule I.

* * * * *

(h) * * *

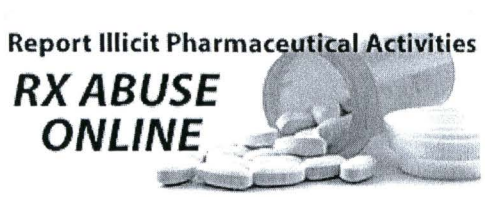
(18) 3,4-Dichloro-N-[2-(dimethylamino)cyclohexyl]-N-methylbenzamide, its isomers, esters, ethers, salts and salts of isomers, esters and ethers (Other name: U-47700).....(9547)

* * * * *

Dated: November 7, 2016.

Chuck Rosenberg,
Acting Administrator.

[FR Doc. 2016-27357 Filed 11-10-16; 8:45 am]
BILLING CODE 4410-09-P



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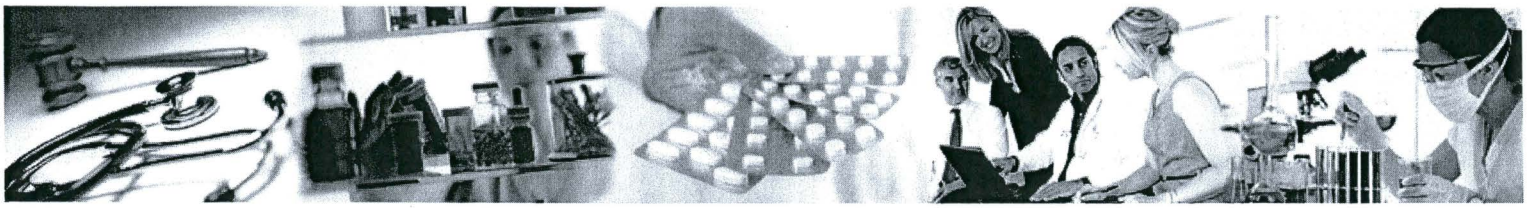

Rules - 2016

[Federal Register Volume 81, Number 229 (Tuesday, November 29, 2016)]
[Rules and Regulations]
[Pages 85873-85877]
From the Federal Register Online via the Government Publishing Office [www.gpo.gov]
[FR Doc No: 2016-28693]

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA-448]

Schedules of Controlled Substances: Temporary Placement of Furanyl Fentanyl Into Schedule I

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Final Order

SUMMARY: The Administrator of the Drug Enforcement Administration is issuing this final order to temporarily schedule the synthetic opioid, N-(1-phenethylpiperidin-4-yl)-N-phenylfuran-2-carboxamide (furanyl fentanyl), and its isomers, esters, ethers, salts and salts of isomers, esters and ethers, into schedule I pursuant to the temporary scheduling provisions of the Controlled Substances Act. This action is based on a finding by the Administrator that the placement of furanyl fentanyl into schedule I of the Controlled Substances Act is necessary to avoid an imminent hazard to the public safety. As a result of this order, the regulatory controls and administrative, civil, and criminal sanctions applicable to schedule I controlled substances will be imposed

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on persons who handle (manufacture, distribute, reverse distribute, import, export, engage in research, conduct instructional activities or chemical analysis, or possess), or propose to handle, furanyl fentanyl.

DATES: This final order is effective on November 29, 2016.

FOR FURTHER INFORMATION CONTACT: Michael J. Lewis, Diversion Control Division, Drug Enforcement Administration; Mailing Address: 8701 Morrissette Drive, Springfield, Virginia 22152; Telephone: (202) 598-6812.

SUPPLEMENTARY INFORMATION:

Legal Authority

The Drug Enforcement Administration (DEA) implements and enforces titles II and III of the Comprehensive Drug Abuse Prevention and Control Act of 1970, as amended. 21 U.S.C. 801-971. Titles II and III are referred to as the "Controlled Substances Act" and the "Controlled Substances Import and Export Act," respectively, and are collectively referred to as the "Controlled Substances Act" or the "CSA" for the purpose of this action. The DEA publishes the implementing regulations for these statutes in title 21 of the Code of Federal Regulations (CFR), chapter II. The CSA and its implementing regulations are designed to prevent, detect, and eliminate the diversion of controlled substances and listed chemicals into the illicit market while ensuring an adequate supply is available for the legitimate medical, scientific, research, and industrial needs of the United States. Controlled substances have the potential for abuse and dependence and are controlled to protect the public health and safety. Under the CSA, every controlled substance is classified into one of five schedules based upon its potential for abuse, its currently accepted medical use in treatment in the United States, and the degree of dependence the drug or other substance may cause. 21 U.S.C. 812. The initial schedules of controlled substances established by Congress are found at 21 U.S.C. 812(c), and the current list of all scheduled substances is published at 21 CFR part 1308.

Section 201 of the CSA, **21 U.S.C. 811**, provides the Attorney General with the authority to temporarily place a substance into schedule I of the CSA for two years without regard to the requirements of 21 U.S.C. 811(b) if she finds that such action is necessary to avoid an imminent hazard to the public safety. 21 U.S.C. 811(h)(1). In addition, if proceedings to control a substance are initiated under 21 U.S.C. 811(a)(1), the Attorney General may extend the temporary scheduling for up to one year. 21 U.S.C. 811(h)(2).

Where the necessary findings are made, a substance may be temporarily scheduled if it is not listed in any other schedule under section 202 of the CSA, 21 U.S.C. 812, or if there is no exemption or approval in effect for the substance under section 505 of the Federal Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. 355. 21 U.S.C. 811(h)(1). The Attorney General has delegated her scheduling authority under 21 U.S.C. 811 to the Administrator of the DEA. 28 CFR 0.100.

Background

Section 201(h)(4) of the CSA, 21 U.S.C. 811(h)(4), requires the Administrator to notify the Secretary of the Department of Health and Human Services (HHS) of his intention to temporarily place a substance into schedule I of the CSA.\1\ The Administrator transmitted the notice of intent to place furanyl fentanyl into schedule I on a temporary basis to the Assistant Secretary by letter dated June 22, 2016. The Assistant Secretary responded to this notice by letter dated July 8, 2016, and advised that based on review by the Food and Drug Administration (FDA), there are currently no investigational new drug applications or approved new drug applications for furanyl fentanyl. The Assistant Secretary also stated that the HHS has no objection to the temporary placement of furanyl fentanyl into schedule I of the CSA. The DEA

has taken into consideration the Assistant Secretary's comments as required by 21 U.S.C. 811(h)(4). Furanyl fentanyl is not currently listed in any schedule under the CSA, and no exemptions or approvals are in effect for furanyl fentanyl under section 505 of the FDCA, 21 U.S.C. 355. The DEA has found that the control of furanyl fentanyl in schedule I on a temporary basis is necessary to avoid an imminent hazard to the public safety, and as required by 21 U.S.C. 811(h)(1)(A), a notice of intent to temporarily schedule furanyl fentanyl was published in the Federal Register on September 27, 2016. 81 FR 66224.

\1\ As discussed in a memorandum of understanding entered into by the Food and Drug Administration (FDA) and the National Institute on Drug Abuse (NIDA), the FDA acts as the lead agency within the HHS in carrying out the Secretary's scheduling responsibilities under the CSA, with the concurrence of NIDA. 50 FR 9518, Mar. 8, 1985. The Secretary of the HHS has delegated to the Assistant Secretary for Health of the HHS the authority to make domestic drug scheduling recommendations. 58 FR 35460, July 1, 1993.

To find that placing a substance temporarily into schedule I of the CSA is necessary to avoid an imminent hazard to the public safety, the Administrator is required to consider three of the eight factors set forth in section 201(c) of the CSA, 21 U.S.C. 811(c): The substance's history and current pattern of abuse; the scope, duration and significance of abuse; and what, if any, risk there is to the public health. 21 U.S.C. 811(h)(3). Consideration of these factors includes actual abuse, diversion from legitimate channels, and clandestine importation, manufacture, or distribution. 21 U.S.C. 811(h)(3).

A substance meeting the statutory requirements for temporary scheduling may only be placed into schedule I. 21 U.S.C. 811(h)(1). Substances in schedule I are those that have a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. **21 U.S.C. 812**(b)(1). Available data and information for furanyl fentanyl, summarized below, indicate that this synthetic opioid has a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. The DEA's updated three-factor analysis, and the Assistant Secretary's July 8, 2016, letter, are available in their entirety under the tab "Supporting Documents" of the public docket of this action at www.regulations.gov under FDMS Docket ID: DEA-2016-0018 (Docket Number DEA-448).

Factor 4. History and Current Pattern of Abuse

The recreational abuse of fentanyl-like substances continues to be a significant concern. These substances are distributed to users with often unpredictable outcomes. Furanyl fentanyl has recently been encountered by law enforcement and public health officials and the adverse health effects and outcomes are documented in the scientific literature. The documented negative effects of furanyl fentanyl are consistent with those of other opioids. On October 1, 2014, the DEA implemented STARLiMS (a Web-based, commercial laboratory information management system) to replace the System to Retrieve Information from Drug Evidence (STRIDE) as its laboratory drug evidence data system of record. DEA laboratory data submitted after September 30, 2014, are reposited in STARLiMS; data from STRIDE and STARLiMS were queried on November 2, 2016. STARLiMS registered 113

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reports containing furanyl fentanyl, all reported in 2016, from Alabama, California, Connecticut, Delaware, Florida, Georgia, Illinois, Maryland, Mississippi, Missouri, Montana, New Jersey, New York, North Carolina, North Dakota, Rhode Island, Tennessee, Texas, Utah, Virginia, Wisconsin, West Virginia, and the District of Columbia.

The National Forensic Laboratory Information System (NFLIS) is a national drug forensic laboratory reporting system that systematically collects results from drug chemistry analyses conducted by participating Federal, State and local forensic laboratories across the country. According to NFLIS, the first report of furanyl fentanyl was recorded in December 2015 in Oregon. From December 2015 through September 2016, a total of 494 submissions to state and local forensic laboratories identifying furanyl fentanyl were reported in NFLIS as a result of law enforcement encounters in California, Connecticut, Florida, Iowa, Kentucky, Massachusetts, Minnesota, Missouri, New Jersey, North Dakota, Ohio, Oklahoma, Oregon, Pennsylvania, Virginia, and Wisconsin (query date: November 2, 2016). The DEA is not aware of any laboratory identifications of furanyl fentanyl prior to 2015.

Evidence suggests that the pattern of abuse of fentanyl analogues, including furanyl fentanyl, parallels that of heroin and prescription opioid analgesics. Seizures of furanyl fentanyl have been encountered in powder form. Furanyl fentanyl has also been encountered in drug paraphernalia commonly associated with heroin or opioid abuse including glassine bags, and as a residue on spoons and bottle caps. Furanyl fentanyl has been encountered as a single substance as well as in combination with other substances of abuse, including heroin, fentanyl, butyryl fentanyl, and U-47700. Furanyl fentanyl has been connected to fatal overdoses, in which intravenous routes of administration are documented.

Factor 5. Scope, Duration and Significance of Abuse

The scientific literature and reports collected by the DEA demonstrate furanyl fentanyl is being abused for its opioid properties. This abuse of furanyl fentanyl has resulted in morbidity and mortality (see updated DEA 3-Factor Analysis for full discussion). The DEA has received reports for at least 128 confirmed fatalities associated with furanyl fentanyl. The information on these deaths occurring in 2015 and 2016 was collected from email communications or toxicology and medical examiner reports received by the DEA. These deaths were reported from five states--Illinois (36), Maryland (41), New Jersey (1), North Carolina (49), and Ohio (1). The scientific literature notes additional fatal overdoses connected to furanyl fentanyl. STARLiMS and NFLIS have a total of 607 drug reports in which furanyl fentanyl was identified in drug exhibits submitted to forensic laboratories from December 2015 through September 2016 from law enforcement encounters. It is likely that the prevalence of furanyl fentanyl in opioid analgesic-related emergency room admissions and deaths is underreported as standard immunoassays may not differentiate this substance from fentanyl.

The population likely to abuse furanyl fentanyl overlaps with the population abusing prescription opioid analgesics and heroin. This is evidenced by the routes of drug administration and drug use history documented in furanyl fentanyl fatal overdose cases. Because abusers of furanyl fentanyl are likely to obtain this substance through unregulated sources (i.e. on-line purchases or drug dealers), the identity, purity, and quantity are uncertain and inconsistent, thus posing significant adverse health risks to the end user. Individuals who initiate (i.e. use a drug for the first time) furanyl fentanyl abuse are likely to be at risk of developing substance use disorder, overdose, and death similar to that of other opioid analgesics (e.g., fentanyl, morphine, etc.).

Factor 6. What, if Any, Risk There Is to the Public Health

Furanyl fentanyl exhibits pharmacological profiles similar to that of fentanyl and other [micro]-opioid receptor agonists. The toxic effects of furanyl fentanyl in humans are demonstrated by overdose fatalities involving this substance. Abusers of furanyl fentanyl may not know the origin, identity, or purity of this substance, thus posing significant adverse health risks when compared to abuse of pharmaceutical preparations of opioid analgesics, such as morphine and oxycodone.

Based on reports in the scientific literature and information received by the DEA, the abuse of furanyl fentanyl leads to the same qualitative public health risks as heroin, fentanyl and other opioid analgesic substances. As with any non-medically approved opioid, the health and safety risks for users are great. The public health risks attendant to the abuse of heroin and opioid analgesics are well established and have resulted in large numbers of drug treatment admissions, emergency department visits, and fatal overdoses. Furanyl fentanyl has been associated with a number of fatalities and non-fatal overdoses as detailed in the scientific literature. The DEA has received information connecting furanyl fentanyl to at least 128 confirmed overdose deaths occurring in 2015 and 2016 in Illinois (36), Maryland (41), New Jersey (1), North Carolina (49), and Ohio (1).

Finding of Necessity of Schedule I Placement To Avoid Imminent Hazard to Public Safety

In accordance with **21 U.S.C. 811**(h)(3), based on the data and information summarized above, the continued uncontrolled manufacture, distribution, importation, exportation, and abuse of furanyl fentanyl pose an imminent hazard to the public safety. The DEA is not aware of any currently accepted medical uses for this substance in treatment in the United States. A substance meeting the statutory requirements for temporary scheduling, 21 U.S.C. 811(h)(1), may only be placed into schedule I. Substances in schedule I are those that have a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. Available data and information for furanyl fentanyl indicate that this substance has a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. As required by section 201(h) of the CSA, 21 U.S.C. 811(h)(4), the Administrator, through a letter dated June 22, 2016, notified the Assistant Secretary of the DEA's intention to temporarily place this substance into schedule I.

Conclusion

In accordance with the provisions of section 201(h) of the CSA, 21 U.S.C. 811(h), the Administrator considered available data and information, herein sets forth the grounds for his determination that it is necessary to temporarily schedule furanyl fentanyl into schedule I of the CSA, and finds that placement of this synthetic opioid into schedule I of the CSA is necessary to avoid an imminent hazard to the public safety. Because the Administrator hereby finds it necessary to temporarily place this synthetic opioid into schedule I to avoid an imminent hazard to the public safety, this final order temporarily scheduling furanyl fentanyl will be effective on the date of publication in the Federal Register, and will be in effect for a period of two

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years, with a possible extension of one additional year, pending completion of the regular (permanent) scheduling process. 21 U.S.C. 811(h) (1) and (2).

The CSA sets forth specific criteria for scheduling a drug or other substance. Permanent scheduling actions in accordance with **21 U.S.C. 811**(a) are subject to formal rulemaking procedures done "on the record after opportunity for a hearing" conducted pursuant to the provisions of 5 U.S.C. 556 and 557. 21 U.S.C. 811. The permanent scheduling process of formal rulemaking affords interested parties with appropriate process and the government with any additional relevant information needed to make a determination. Final decisions that conclude the permanent scheduling process of formal rulemaking are subject to judicial review. 21 U.S.C. 877. Temporary scheduling orders are not subject to judicial review. 21 U.S.C. 811(h)(6).

Requirements for Handling

Upon the effective date of this final order, furanyl fentanyl will become subject to the regulatory controls and administrative, civil, and criminal sanctions applicable to the manufacture, distribution, reverse distribution, importation, exportation, engagement in research, and conduct of instructional activities or chemical analysis with, and possession of schedule I controlled substances including the following:

1. *Registration*. Any person who handles (manufactures, distributes, reverse distributes, imports, exports, engages in research, or conducts instructional activities or chemical analysis with, or possesses), or who desires to handle, furanyl fentanyl must be registered with the DEA to conduct such activities pursuant to 21 U.S.C. 822, 823, 957, and 958 and in accordance with 21 CFR parts 1301 and 1312, as of November 29, 2016. Any person who currently handles furanyl fentanyl, and is not registered with the DEA, must submit an application for registration and may not continue to handle furanyl fentanyl as of November 29, 2016, unless the DEA has approved that application for registration pursuant to 21 U.S.C. 822, 823, 957, 958, and in accordance with 21 CFR parts 1301 and 1312. Retail sales of schedule I controlled substances to the general public are not allowed under the CSA. Possession of any quantity of this substance in a manner not authorized by the CSA on or after November 29, 2016 is unlawful and those in possession of any quantity of this substance may be subject to prosecution pursuant to the CSA.

2. *Disposal of stocks*. Any person who does not desire or is not able to obtain a schedule I registration to handle furanyl fentanyl, must surrender all quantities of currently held furanyl fentanyl.

3. *Security*. Furanyl fentanyl is subject to schedule I security requirements and must be handled and stored pursuant to **21 U.S.C. 821**, **823**, **871**(b), and in accordance with **21 CFR 1301.71-1301.93**, as of November 29, 2016.

4. *Labeling and packaging*. All labels, labeling, and packaging for commercial containers of furanyl fentanyl must be in compliance with 21 U.S.C. 825, 958(e), and be in accordance with **21 CFR part 1302**. Current DEA registrants shall have 30 calendar days from November 29, 2016, to comply with all labeling and packaging requirements.

5. *Inventory*. Every DEA registrant who possesses any quantity of furanyl fentanyl on the effective date of this order must take an inventory of all stocks of this substance on hand, pursuant to 21 U.S.C. 827 and 958, and in accordance with 21 CFR 1304.03, 1304.04, and 1304.11. Current DEA registrants shall have 30 calendar days from the effective date of this order to be in compliance with all inventory requirements. After the initial inventory, every DEA registrant must take an inventory of all controlled substances (including furanyl fentanyl) on hand on a biennial basis, pursuant to **21 U.S.C. 827** and **958**, and in accordance with **21 CFR 1304.03, 1304.04, and 1304.11.**

6. *Records*. All DEA registrants must maintain records with respect to furanyl fentanyl pursuant to 21 U.S.C. 827 and 958, and in accordance with **21 CFR parts 1304**, and **1312**, **1317** and Sec. **1307.11**. Current DEA registrants shall have 30 calendar days from the effective date of this order to be in compliance with all recordkeeping requirements.

7. *Reports*. All DEA registrants who manufacture or distribute furanyl fentanyl must submit reports pursuant to 21 U.S.C. 827 and in accordance with 21 CFR parts 1304, and 1312 as of November 29, 2016.

8. *Order Forms*. All DEA registrants who distribute furanyl fentanyl must comply with order form requirements pursuant to **21 U.S.C. 828** and in accordance with 21 CFR part 1305 as of November 29, 2016.

9. *Importation and Exportation*. All importation and exportation of furanyl fentanyl must be in compliance with **21 U.S.C. 952**, **953**, **957**, **958**, and in accordance with **21 CFR part 1312** as of November 29, 2016.

10. *Quota*. Only DEA registered manufacturers may manufacture furanyl fentanyl in accordance with a quota assigned pursuant to **21 U.S.C. 826** and in accordance with **21 CFR part 1303** as of November 29, 2016.

11. *Liability*. Any activity involving furanyl fentanyl not authorized by, or in violation of the CSA, occurring as of November 29, 2016, is unlawful, and may subject the person to administrative, civil, and/or criminal sanctions.

Regulatory Matters

Section 201(h) of the CSA, 2**1 U.S.C. 811**(h), provides for a temporary scheduling action where such action is necessary to avoid an imminent hazard to the public safety. As provided in this subsection, the Attorney General may, by order, schedule a substance in schedule I on a temporary basis. Such an order may not be issued before the expiration of 30 days from (1) the publication of a notice in the Federal Register of the intention to issue such order and the grounds upon which such order is to be issued, and (2) the date that notice of the proposed temporary scheduling order is transmitted to the Assistant Secretary. 21 U.S.C. 811(h)(1).

Inasmuch as section 201(h) of the CSA directs that temporary scheduling actions be issued by order and sets forth the procedures by which such orders are to be issued, the DEA believes that the notice and comment requirements of the Administrative Procedure Act (APA) at 5 U.S.C. 553, do not apply to this temporary scheduling action. In the alternative, even assuming that this action might be subject to 5 U.S.C. 553, the Administrator finds that there is good cause to forgo the notice and comment requirements of 5 U.S.C. 553, as any further delays in the process for issuance of temporary scheduling orders would be impracticable and contrary to the public interest in view of the manifest urgency to avoid an imminent hazard to the public safety.

Further, the DEA believes that this temporary scheduling action is not a "rule" as defined by 5 U.S.C. 601(2), and, accordingly, is not subject to the requirements of the Regulatory Flexibility Act. The requirements for the preparation of an initial regulatory flexibility analysis in 5 U.S.C. 603(a) are not applicable where, as here, the DEA is not required by the APA or any other law to publish a general notice of proposed rulemaking.

Additionally, this action is not a significant regulatory action as defined by Executive Order 12866 (Regulatory Planning and Review), section 3(f), and, accordingly, this action has not been reviewed by the Office of Management and Budget (OMB).

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This action will not have substantial direct effects on the States, on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government. Therefore, in accordance with Executive Order 13132 (Federalism) it is determined that this action does not have sufficient federalism implications to warrant the preparation of a Federalism Assessment.

As noted above, this action is an order, not a rule. Accordingly, the Congressional Review Act (CRA) is inapplicable, as it applies only to rules. However, if this were a rule, pursuant to the Congressional Review Act, "any rule for which an agency for good cause finds that notice and public procedure thereon are impracticable, unnecessary, or contrary to the public interest, shall take effect at such time as the federal agency promulgating the rule determines." 5 U.S.C. 808(2). It is in the public interest to schedule this substance immediately to avoid an imminent hazard to the public safety. This temporary scheduling action is taken pursuant to 21 U.S.C. 811(h), which is specifically designed to enable the DEA to act in an expeditious manner to avoid an imminent hazard to the public safety. 21 U.S.C. 811(h) exempts the temporary scheduling order from standard notice and comment rulemaking procedures to ensure that the process moves swiftly. For the same reasons that underlie 21 U.S.C. 811(h), that is, the DEA's need to move quickly to place this substance into schedule I because it poses an imminent hazard to the public safety, it would be contrary to the public interest to delay implementation of the temporary scheduling order. Therefore, this order shall take effect immediately upon

its publication. The DEA has submitted a copy of this final order to both Houses of Congress and to the Comptroller General, although such filing is not required under the Small Business Regulatory Enforcement Fairness Act of 1996 (Congressional Review Act), 5 U.S.C. 801-808 because, as noted above, this action is an order, not a rule.

List of Subjects in 21 CFR Part 1308

Administrative practice and procedure, Drug traffic control, Reporting and recordkeeping requirements.

- For the reasons set out above, the DEA amends 21 CFR Part 1308 as follows:

PART 1308--SCHEDULES OF CONTROLLED SUBSTANCES

- 1. The authority citation for part 1308 continues to read as follows:

Authority: 21 U.S.C. 811, 812, 871(b), unless otherwise noted.

- 2. Amend Sec. 1308.11 by adding paragraph (h)(19) to read as follows:

Sec. 1308.11 Schedule I.

* * * * *

(h) * * *

(19) N-(1-phenethylpiperidin-4-yl)-N-phenylfuran-2-carboxamide, its isomers, esters, ethers, salts and salts of isomers, esters and ethers (Other name: Furanyl fentanyl) (9834).

Dated: November 22, 2016

Chuck Rosenberg,
Acting Administrator.

[FR Doc. 2016-28693 Filed 11-28-16; 8:45 am]
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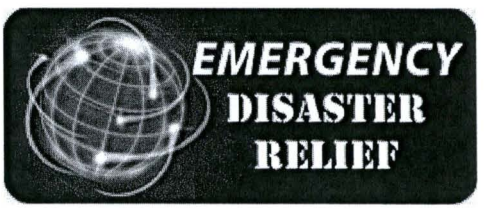

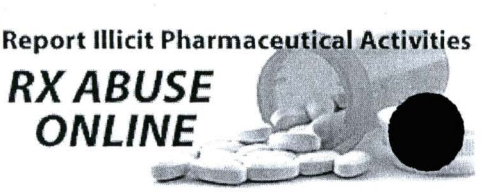

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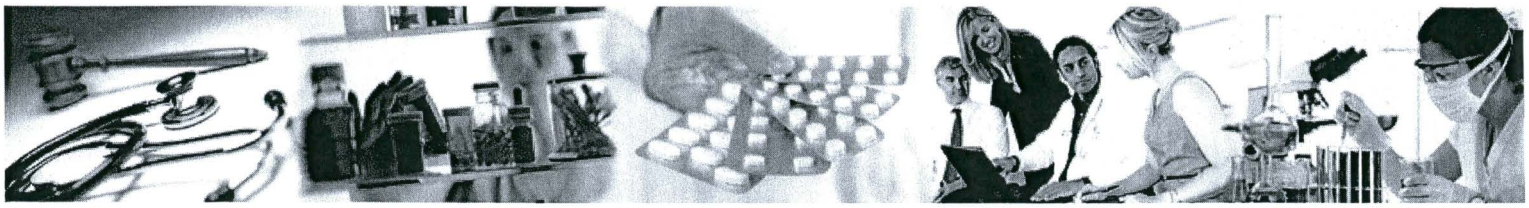

Rules - 2016

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DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA-435]

Schedules of Controlled Substances: Placement of Brivaracetam Into Schedule V

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Interim final rule, with request for comments.

SUMMARY: The Drug Enforcement Administration is placing the substance brivaracetam ((2S)-2-[(4R)-2-oxo-4-propylpyrrolidin-1-yl] butanamide) (also referred to as BRV; UCB-34714; Briviact) (including its salts) into schedule V of the Controlled Substances Act. This scheduling action is pursuant to the Controlled Substances Act, as revised by the Improving Regulatory Transparency for New Medical Therapies Act which was signed into law on November 25, 2015.

DATES: The effective date of this rulemaking is May 12, 2016. Interested persons may file written comments on this rulemaking in accordance with **21 CFR 1308.43** (g). Electronic comments must be submitted, and written comments must be postmarked, on or before June 13, 2016. Commenters should be aware that the electronic Federal Docket Management System will not accept comments after 11:59 p.m. Eastern Time on the last day of the comment period.

Interested persons, defined at **21 CFR 1300.01** as those "adversely affected or aggrieved by any rule or proposed rule issuable pursuant to section 201 of the Act (**21 U.S.C. 811**)," may file a request for hearing or waiver of hearing pursuant to **21 CFR 1308.44**. Requests for hearing and waivers of an opportunity for a hearing or to participate in a hearing must be received on or before June 13, 2016.

ADDRESSES: To ensure proper handling of comments, please reference "Docket No. DEA-435" on all correspondence, including any attachments.

- *Electronic comments:* The Drug Enforcement Administration encourages that all comments be submitted electronically through the Federal eRulemaking Portal, which provides the ability to type short comments directly into the comment field on the Web page or attach a file for lengthier comments. Please go to http://www.regulations.gov and follow the online instructions at that site for submitting comments. Upon completion of your submission, you will receive a Comment Tracking Number for your comment. Please be aware that submitted comments are not instantaneously available for public view on Regulations.gov. If you have received a Comment Tracking Number, your comment has been successfully submitted and there is no need to resubmit the same comment.
- *Paper comments:* Paper comments that duplicate the electronic submission are not necessary and are discouraged. Should you wish to mail a paper comment in lieu of an electronic comment, it should be sent via regular or express mail to: Drug Enforcement Administration, Attn: DEA Federal Register Representative/ODW, 8701 Morrissette Drive, Springfield, VA 22152.
- *Hearing requests:* All requests for hearing and waivers of participation must be sent to: Drug Enforcement Administration, Attn: Administrator, 8701 Morrissette Drive, Springfield, Virginia 22152. All requests for hearing and waivers of participation should also be sent to: (1) Drug Enforcement Administration, Attn: Hearing Clerk/LJ, 8701 Morrissette Drive, Springfield, Virginia 22152; and (2) Drug Enforcement Administration, Attn: DEA Federal Register Representative/ ODW, 8701 Morrissette Drive, Springfield, Virginia 22152.

FOR FURTHER INFORMATION CONTACT: Barbara J. Boockholdt, Office of Diversion Control, Drug Enforcement Administration; Mailing Address: 8701 Morrissette Drive, Springfield, Virginia 22152; Telephone: (202) 598-6812.

SUPPLEMENTARY INFORMATION:

Posting of Public Comments

Please note that all comments received are considered part of the public record. They will, unless reasonable cause is given, be made available by the Drug Enforcement Administration (DEA) for public inspection online at http://www.regulations.gov. Such information includes personal identifying information (such as your name, address, etc.) voluntarily submitted by the commenter. The Freedom of Information Act (FOIA) applies to all comments received. If you want to submit personal identifying information (such as your name, address, etc.) as part of your comment, but do not want it to be made publicly available, you must include the phrase "PERSONAL IDENTIFYING INFORMATION" in the first paragraph of your comment. You must also place all of the personal identifying information you do not want made publicly available in the first paragraph of your comment and identify what information you want redacted.

If you want to submit confidential business information as part of your comment, but do not want it to be made publicly available, you must include the phrase "CONFIDENTIAL BUSINESS INFORMATION" in the first paragraph of your comment. You must also prominently identify the confidential business information to be redacted within the comment.

Comments containing personal identifying information and confidential business information identified as directed above will generally be made publicly available in redacted form. If a comment has so much confidential business information or personal identifying information that it cannot be effectively redacted, all or part of that comment may not be made publicly available. Comments posted to http://www.regulations.gov may include any personal identifying information (such as name, address, and phone number) included in the text of your electronic submission that is not identified as directed above as confidential.

An electronic copy of this document and supplemental information, including the complete Department of Health and Human Services and Drug Enforcement Administration eight-factor analyses, to this interim final rule are available at http://www.regulations.gov for easy reference.

Request for Hearing, Notice of Appearance at Hearing, or Waiver of Participation in Hearing

Pursuant to **21 U.S.C. 811**(a), this action is a formal rulemaking "on the record after opportunity for a hearing." Such proceedings are conducted pursuant to the provisions of the Administrative Procedure Act (APA), 5 U.S.C. 551-559. **21 CFR 1308.41-1308.45**; **21 CFR part 1316**, subpart D. In accordance with **21 CFR 1308.44**(a)-

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(c), requests for a hearing, notices of appearance, and waivers of an opportunity for a hearing or to participate in a hearing may be submitted only by interested persons, defined as those "adversely affected or aggrieved by any rule or proposed rule issuable pursuant to section 201 of the Act (**21 U.S.C. 811**)." **21 CFR 1300.01**. Requests for a hearing and notices of participation must conform to the requirements of **21 CFR 1308.44**(a) or (b), as applicable, and include a statement of the interest of the person in the proceeding and the objections or issues, if any, concerning which the person desires to be heard. Any waiver of an opportunity for a hearing must conform to the requirements of **21 CFR 1308.44**(c) including a written statement regarding the interested person's position on the matters of fact and law involved in any hearing.

Please note that pursuant to **21 U.S.C. 811**(a), the purpose and subject matter of the hearing are restricted to "(A) find[ing] that such drug or other substance has a potential for abuse, and (B) mak[ing] with respect to such drug or other substance the findings prescribed by subsection (b) of **section 812** of this title for the schedule in which such drug is to be placed. * * *" Requests for a hearing and waivers of participation in the hearing should be submitted to DEA using the address information provided above.

Legal Authority

The DEA implements and enforces titles II and III of the Comprehensive Drug Abuse Prevention and Control Act of 1970, as amended. **21 U.S.C. 801-971**. Titles II and III are referred to as the "Controlled Substances Act" and the "Controlled Substances Import and Export Act," respectively, and are collectively referred to as the "Controlled Substances Act" or the "CSA" for the purpose of this action. The DEA publishes the implementing regulations for these statutes in title 21 of the Code of Federal Regulations (CFR), chapter II. The CSA and its implementing regulations are designed to prevent, detect, and eliminate the diversion of controlled substances and listed chemicals into the illicit market while providing for the legitimate medical, scientific, research, and industrial needs of the United States. Controlled substances have the potential for abuse and dependence and are controlled to protect the public health and safety.

Under the CSA, controlled substances are classified into one of five schedules based upon their potential for abuse, their currently accepted medical use in treatment in the United States, and the degree of dependence the substance may cause. **21 U.S.C. 812**. The initial schedules of controlled substances established by Congress are found at 21 U.S.C. 812(c), and the current list of all scheduled substances is published at **21 CFR part 1308**.

Pursuant to **21 U.S.C. 811**(a)(1), the Attorney General may, by rule, "add to such a schedule or transfer between such schedules any drug or other substance if he * * * finds that such drug or other substance has a potential for abuse, and * * * makes with respect to such drug or other substance the findings prescribed by subsection (b) of **section 812** of this title for the schedule in which such drug is to be placed * * *" The Attorney General has delegated this scheduling authority under 21 U.S.C. 811 to the Administrator of the DEA. 28 CFR 0.100.

The CSA provides that scheduling of any drug or other substance may be initiated by the Attorney General (1) on her own motion; (2) at the request of the Secretary of Health and Human Services (HHS); or (3) on the petition of any interested party. **21 U.S.C. 811**(a). This action imposes the regulatory controls and administrative, civil, and criminal sanctions of schedule V controlled substances for any person who handles or proposes to handle BRV.

The Improving Regulatory Transparency for New Medical Therapies Act (Pub. L. 114-89) was signed into law on November 25, 2015. This law amended **21 U.S.C. 811** and states that in cases where a new drug is (1) approved by the Department of Health and Human Services (HHS) and (2) HHS recommends control in CSA schedule II-V, DEA shall issue an interim final rule scheduling the drug, within 90 days.

The law further states that the 90-day timeframe starts the later of (1) the date DEA receives the HHS scientific and medical evaluation/ scheduling recommendation or (2) the date DEA receives notice of drug approval by HHS. In addition, the law specifies that the rulemaking shall become immediately effective as an interim final rule without requiring the DEA to demonstrate good cause therefor.

Specifically, Public Law 114-89 revised section 201 of the CSA (**21 U.S.C. 811**) by inserting after subsection (i) a new paragraph (j), which requires that with respect to a drug referred to in subsection (f), if the Secretary recommends that the Attorney General control the drug in schedule II, III, IV, or V pursuant to subsections (a) and (b), the Attorney General is required to, within 90 days, issue an interim final rule controlling the drug in accordance with such subsections and **21 U.S.C. 812**(b) using the specified procedures. For purposes of calculating the 90 days, Public Law 114-89 states that such date shall be the later of the date on which the Attorney General receives the scientific and medical evaluation and the scheduling recommendation from the Secretary in accordance with subsection (b), or the date on which the Attorney General receives notification from the Secretary that the Secretary has approved an application under section 505(c), 512, or 571 of the Federal Food, Drug, and Cosmetic Act or section 351(a) of the Public Health Service Act, or indexed a drug under section 572 of the Federal Food, Drug, and Cosmetic Act, with respect to the drug described in paragraph (1). Public Law 114-89 further stipulates that a rule issued by the Attorney General under paragraph (1) becomes immediately effective as an interim final rule without requiring the Attorney General to demonstrate good cause and requires that the interim final rule give interested persons the opportunity to comment and to request a hearing. After the conclusion of such proceedings, the Attorney General must issue a final rule in accordance with the scheduling criteria of subsections **21 U.S.C. 811**(b), (c), and (d) of this section and 21 U.S.C. 812(b).

Background

Brivaracetam ((2S)-2-[(4R)-2-oxo-4-propylpyrrolidin-1-yl] butanamide) (also referred to as BRV; UCB-34714; Briviact) is a new molecular entity with central nervous system (CNS) depressant properties. BRV is known to be a high affinity ligand for the synaptic vesicle protein, SV2A, which is found on excitatory synapses in the brain. On November 22, 2014, UCB Inc. (Sponsor) submitted three New Drug Applications (NDAs) to the U.S. Food and Drug Administration (FDA) for the tablet, oral, and intravenous formulations of BRV. The FDA accepted the NDA filings for BRV on January 21, 2015.

On March 28, 2016 the DEA received notification that HHS/FDA approved BRV as an add-on treatment to other medications to treat partial onset seizures in patients age 16 years and older with epilepsy.

Determination to Schedule BRV

Pursuant to **21 U.S.C. 811**(a)(1), proceedings to add a drug or substance to those controlled under the CSA may be initiated by request of the Secretary

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of the HHS.\1\ On September 8, 2015, the HHS provided the DEA with a scientific and medical evaluation document prepared by the FDA entitled "Basis for the Recommendation to Place Brivaracetam in Schedule V of the Controlled Substances Act." Pursuant to **21 U.S.C. 811**(b), this document contained an eight-factor analysis of the abuse potential of BRV as a new drug, along with the HHS' recommendation to control BRV under schedule V of the CSA.

\1\ As set forth in a memorandum of understanding entered into by the HHS, the FDA, and the National Institute on Drug Abuse (NIDA), the FDA acts as the lead agency within the HHS in carrying out the Secretary's scheduling responsibilities under the CSA, with the concurrence of the NIDA. 50 FR 9518, Mar. 8, 1985. The

Secretary of the HHS has delegated to the Assistant Secretary for Health of the HHS the authority to make domestic drug scheduling recommendations. 58 FR 35460, July 1, 1993.

In response, in December 2015, the DEA reviewed the scientific and medical evaluation and scheduling recommendation provided by the HHS, along with all other relevant data, and completed its own eight-factor review document pursuant to **21 U.S.C. 811**(c). The DEA concluded that BRV met the **21 U.S.C. 812**(b)(5) criteria for placement in schedule V of the CSA. Subsequently, on March 28, 2016, the DEA received notification that HHS/FDA approved three NDAs for BRV (see Background section).

Pursuant to the provisions of the Improving Regulatory Transparency for New Medical Therapies Act (Pub. L. 114-89), and based on the HHS recommendation, NDA approvals by HHS/FDA, and DEA's determination, DEA is issuing this interim final rule to schedule brivaracetam ((2S)-2-[(4R)-2-oxo-4-propylpyrrolidin-1-yl] butanamide) (including its salts) as a controlled substance under the CSA.

Included below is a brief summary of each factor as analyzed by the HHS and the DEA, and as considered by the DEA in its scheduling action. Please note that both the DEA and HHS analyses are available in their entirety under "Supporting Documents" in the public docket for this interim final rule at http://www.regulations.gov, under Docket Number "DEA-435." Full analysis of, and citations to, the information referenced in the summary may also be found in the supporting and related material.

1. *The Drug's Actual or Relative Potential for Abuse:* BRV is a new chemical entity and has not been marketed in the United States or in any other country; information on actual abuse of BRV is not available. The HHS characterized BRV as related in its action to lacasamide and ezogabine, which are both schedule V CNS depressant anti-epileptics (AEDs). Based on data submitted by the Sponsor in their NDAs, the HHS indicated that administration of BRV in mice, rats, and dogs resulted in CNS depressant effects, including decreased locomotor activity and reactivity, motor incoordination, and ataxia.

BRV is not self-administered in animals and, unlike schedule IV benzodiazepines and the schedule III AED perampanel, lacks pentobarbital-like (schedule II) discriminative stimulus and reinforcing effects (HHS review, 2015). In humans, BRV is most similar to the schedule V AEDs lacosamide, ezogabine, and pregabalin in producing positive subjective effects without producing sedation and withdrawal following drug discontinuation that is observed with schedule IV benzodiazepines. Based on this collective evidence, the HHS concluded that BRV has an abuse potential that is most similar to AEDs in schedule V.

2. *Scientific Evidence of the Drug's Pharmacological Effects, if Known:* BRV selectively binds with high affinity to synaptic vesicle protein 2A (SV2A). It produces reverse inhibition caused by negative modulators of gamma aminobutyric acid (GABA) and glycine and inhibits sodium (Na+) channels. These sites appear to underlie pharmacological activity of BRV.

In rats, BRV at high doses partially generalizes to the schedule IV benzodiazepine chlordiazepoxide. BRV, across a wide range of doses, neither initiates nor maintains self-administration in rats trained to self-administer cocaine. Human studies have reported that healthy individuals may experience euphoria, sedation, and a drunken-like feeling following BRV administration. When treatment-emergent adverse events (TEAEs) \2\ were pooled across several clinical BRV studies, the most common TEAEs were dizziness and sedative-related events such as fatigue, extreme drowsiness, and extreme weakness. In a human abuse potential study, the oral abuse potential, safety, tolerability, and pharmacokinetics of BRV (50 mg, 200 mg, and 1000 mg) were compared to 1.5 and 3.0 mg of the schedule IV CNS depressant alprazolam (ALP) and placebo. When surveyed, for all doses of BRV, there was an increase of drug likability, feeling of a high, and taking the drug again in comparison to placebo. The HHS mentioned that individuals who took BRV had fewer sedative, euphoric, stimulant, dizziness, and overall negative subjective effects compared to ALP.

\2\ Treatment-emergent adverse event (TEAE): An event or unexpected medical occurrence (e.g. adverse event) which first appears during treatment with a drug or substance. TEAEs are typically absent prior to the onset of treatment or would have been exacerbated relative to pre-treatment conditions.

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3. *The State of Current Scientific Knowledge Regarding Brivaracetam:* The chemical name for brivaracetam is (2S)-2-[(4R)-2-oxo-4-propylpyrrolidin-1-yl] butanamide. Other names include BRV and UCB-34714. The Chemical Abstract Services number (CAS #) of BRV is: 357336-20-0. BRV is a racetam derivative.\3\ As the HHS noted, BRV does not have structural similarities to any other scheduled AED or to any major classes of abused sedative drugs with noted euphoric effects. Chemical synthesis of BRV is considered highly complex and includes several steps, reagents and specialized equipment.

\3\ Racetams are a class of drugs that have a pyrrolidoline center.

BRV is readily soluble in water at up to 700 mg/mL. In an in vitro oral tablet dissolution evaluation, BRV oral tablets were placed in a buffer (pH 6.4) for 16 hours. Approximately 86-96% of BRV was released after 16 hours in the buffer; 14-30% of BRV was released following 1 hour and 40-66% BRV was released after 4 hours.

Following oral ingestion, BRV is rapidly and completely absorbed. In healthy young males, the half-life of BRV was determined to be approximately 9 hours. According to the HHS, the half-life of BRV is decreased to 6 hours when a repeated oral dose of 800 mg/day BRV is administered. The HHS noted that BRV binds weakly to plasma proteins and is extensively metabolized through several pathways. Clearance through the kidneys represents 5-10% of the total clearance and only 3-7% of the parent compound (BRV) was detected in the urine. The three main metabolites of BRV were detected in urine and according to the HHS, these metabolites are relatively inactive. One BRV metabolite was characterized as having a potency that was 20 times less than BRV, and this metabolite was not detected in human plasma and represented less than 3% of the dose in urine.

4. *Its History and Current Pattern of Abuse:* As noted by the HHS, information on the history and current pattern of abuse of BRV is not available since this drug is currently not marketed in any country. A review of the animal and human data indicates that BRV has an abuse potential similar to other schedule V AEDs. If BRV were to be

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approved for medical use, the HHS indicated that BRV would be abused for its euphoric properties and other abuse-related TEAEs that were reported in human clinical studies. Based on the available information, the HHS concluded that the history and pattern of abuse of BRV will be similar to other schedule V CNS depressants.

5. *The Scope, Duration, and Significance of Abuse:* As noted by the HHS, information on the scope, duration, and significance of abuse of BRV is not available since this drug is currently not marketed in any country. Results from animal and human studies suggest that there is abuse potential associated with BRV and if marketed in the United States, it is likely that BRV will be abused similar to other AEDs that are CNS depressants. The HHS stated that it is unlikely that epileptic individuals (the population expected to take this drug) will abuse BRV. The HHS concluded that based on abuse potential similarities between BRV and other schedule V AEDs, it is likely that the scope, duration, and significance of abuse of BRV will be similar to these compounds.

6. *What, if any, Risk There is to the Public Health:* The HHS characterized BRV's drug abuse potential to be similar to schedule V AEDs. As such, the public health risk with BRV will also be similar to other schedule V AEDs. The HHS noted that if BRV were approved for medical use, it would be abused for its rewarding properties. In healthy volunteers administered 600 mg or higher of BRV, cognitive and motor impairment and sedation were observed. It is unknown how BRV would interact in combination with other CNS depressants and if the sedative effects would be additive or even a lethal combination. In an interaction study with BRV and intravenous ethanol in healthy individuals, it was determined that BRV enhanced the effects of ethanol.

7. *Its Psychic or Physiological Dependence Liability:* BRV has limited psychological dependence and does not appear to have physical dependence. When rats were administered BRV for 30 days, no signs of physical dependence were noted in comparison to the schedule IV comparator, chlordiazepoxide. Similarly, in human clinical studies with healthy volunteers, there were no reports or adverse events that noted physical dependence or a withdrawal syndrome associated with BRV use. The low potential for physical dependence observed with BRV is consistent with other schedule V AEDs. There is limited evidence for psychological dependence with BRV. Clinical studies have reported individuals experiencing increasing euphoria with increasing doses of BRV. Tolerance does not appear to develop with respect to BRV treatment on epileptic seizure reduction.

8. *Whether the Substance is an Immediate Precursor of a Substance Already Controlled under the CSA:* BRV is not an immediate precursor of any controlled substance.

Conclusion: After considering the scientific and medical evaluation conducted by the HHS, the HHS' recommendation, and its own eight-factor analysis, the DEA has determined that these facts and all relevant data constitute substantial evidence of a potential for abuse of BRV. As such, the DEA hereby schedules BRV as a controlled substance under the CSA.

Determination of Appropriate Schedule

The CSA outlines the findings required to place a drug or other substance in any particular schedule (I, II, III, IV, or V). **21 U.S.C. 812**(b). After consideration of analysis and recommendation of the Assistant Secretary for Health of the HHS and review of all available data, the Acting Administrator of the DEA, pursuant to 21 U.S.C. 812(b)(5), finds that:

1. BRV has a low potential for abuse relative to the drugs or other substances in schedule IV. The overall abuse potential of BRV is comparable to schedule V controlled substances such as ezogabalin, pregabalin, and lacosamide;

2. With FDA's approval of the new drug applications, BRV has a currently accepted medical use in the United States as adjunctive treatment of partial onset seizures in epileptic individuals ages 16 and older; and

3. Human and animal studies demonstrate that BRV has limited psychological dependence and does not appear to have physical dependence. There was no evidence of physical dependence associated with BRV in human and animal studies since there have been no reports of withdrawal syndromes or other physical dependence effects. Based on these data, abuse of BRV may lead to limited psychological dependence similar to schedule V AEDs but less than that of drugs in schedule IV.

Based on these findings, the Acting Administrator of the DEA concludes that brivaracetam ((2S)-2-[(4R)-2-oxo-4-propylpyrrolidin-1-yl] butanamide) (also referred to as BRV; UCB-34714; Briviact), including its salts, warrants control in schedule V of the CSA. **21 U.S.C. 812**(b)(5).

Requirements for Handling Brivaracetam

BRV is subject to the CSA's schedule V regulatory controls and administrative, civil, and criminal sanctions applicable to the manufacture, distribution, reverse distribution, dispensing, importing, exporting, research, and conduct of instructional activities and chemical analysis with, and possession involving schedule V substances, including the following:

1. *Registration.* Any person who handles (manufactures, distributes, reverse distributes, dispenses, imports, exports, engages in research, or conducts instructional activities or chemical analysis with, or possesses) BRV, or who desires to handle BRV, must be registered with the DEA to conduct such activities pursuant to **21 U.S.C. 822**, **823**, **957**, and **958** and in accordance with **21 CFR parts 1301** and **1312**. Any person who currently handles BRV, and is not registered with the DEA, must submit an application for registration and may not continue to handle BRV, unless the DEA has approved that application for registration, pursuant to 21 U.S.C. 822, 823, 957, and 958, and in accordance with 21 CFR parts 1301 and 1312.

2. *Disposal of stocks.* Any person who does not desire or is not able to obtain a schedule V registration must surrender all quantities of currently held BRV, or may transfer all quantities of currently held BRV to a person registered with the DEA in accordance with **21 CFR part 1317**, in additional to all other applicable federal, state, local, and tribal laws.

3. *Security.* BRV is subject to schedule III-V security requirements and must be handled and stored pursuant to **21 U.S.C. 821**, **823**, and **871**(b), and in accordance with **21 CFR 1301.71-1301.93**.

4. *Labeling and Packaging.* All labels, labeling, and packaging for commercial containers of BRV must comply with **21 U.S.C. 825** and **958**(e), and be in accordance with **21 CFR part 1302**.

5. *Inventory.* Every DEA registrant who possesses any quantity of BRV must take an inventory of BRV on hand, pursuant to **21 U.S.C. 827** and **958**, and in accordance with **21 CFR 1304.03**, **1304.04**, and **1304.11**.

Any person who becomes registered with the DEA must take an initial inventory of all stocks of controlled substances (including BRV) on hand on the date the registrant first engages in the handling of controlled substances, pursuant to **21 U.S.C. 827** and **958**, and in accordance with **21 CFR 1304.03**, **1304.04**, and **1304.11**.

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After the initial inventory, every DEA registrant must take a new inventory of all stocks of controlled substances (including BRV) on hand every two years, pursuant to **21 U.S.C. 827** and **958**, and in accordance with **21 CFR 1304.03**, **1304.04**, and **1304.11**.

6. *Records and Reports.* Every DEA registrant must maintain records and submit reports for BRV, or products containing BRV, pursuant to **21 U.S.C. 827** and **958**(e), and in accordance with **21 CFR parts 1304**, **1312**, and **1317**.

7. *Prescriptions.* All prescriptions for BRV or products containing BRV must comply with **21 U.S.C. 829**, and be issued in accordance with **21 CFR parts 1306** and **1311**, subpart C.

8. *Importation and Exportation.* All importation and exportation of BRV must be in compliance with **21 U.S.C. 952**, **953**, **957**, and **958**, and in accordance with **21 CFR part 1312**.

9. *Liability.* Any activity involving BRV not authorized by, or in violation of, the CSA or its implementing regulations, is unlawful, and may subject the person to administrative, civil, and/or criminal sanctions.

Regulatory Analyses

Administrative Procedure Act

Public Law 114-89 was signed into law, amending **21 U.S.C. 811**. This amendment provides that in cases where a new drug is (1) approved by the Department of Health and Human Services (HHS) and (2) HHS recommends control in CSA schedule II-V, the DEA shall issue an interim final rule scheduling the drug within 90 days. Additionally, the law specifies that the rulemaking shall become immediately effective as an interim final rule without requiring the DEA to demonstrate good cause. Therefore, the DEA has determined that the notice and comment requirements of section 553 of the APA, 5 U.S.C. 553, do not apply to this scheduling action.

Executive Orders 12866, Regulatory Planning and Review, and 13563, Improving Regulation and Regulatory Review

In accordance with Public Law 114-89, this scheduling action is subject to formal rulemaking procedures performed "on the record after opportunity for a hearing," which are conducted pursuant to the provisions of 5 U.S.C. 556 and 557. The CSA sets forth the procedures and criteria for scheduling a drug or other substance. Such actions are exempt from review by the Office of Management and Budget (OMB) pursuant to section 3(d)(1) of Executive Order 12866 and the principles reaffirmed in Executive Order 13563.

Executive Order 12988, Civil Justice Reform

This regulation meets the applicable standards set forth in sections 3(a) and 3(b)(2) of Executive Order 12988 to eliminate drafting errors and ambiguity, minimize litigation, provide a clear legal standard for affected conduct, and promote simplification and burden reduction.

Executive Order 13132, Federalism

This rulemaking does not have federalism implications warranting the application of Executive Order 13132. The rule does not have substantial direct effects on the States, on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government.

Executive Order 13175, Consultation and Coordination With Indian Tribal Governments

This rule does not have tribal implications warranting the application of Executive Order 13175. It does not have substantial direct effects on one or more Indian tribes, on the relationship between the Federal government and Indian tribes, or on the distribution of power and responsibilities between the Federal government and Indian tribes.

Regulatory Flexibility Act

In accordance with 5 U.S.C. 603(a), "[w]henever an agency is required by [5 U.S.C. 553], or any other law, to publish general notice of proposed rulemaking for any proposed rule, or publishes a notice of proposed rulemaking for an interpretive rule involving the internal revenue laws of the United States, the agency shall prepare and make available for public comment an initial regulatory flexibility analysis." As noted in the above discussion regarding applicability of the Administrative Procedure Act, the DEA has determined that the notice and comment requirements of section 553 of the APA, 5 U.S.C. 553, do not apply to this scheduling action. Consequently, the RFA does not apply to this interim final rule.

[redacted]nded Mandates Reform Act of 1995

In accordance with the Unfunded Mandates Reform Act (UMRA) of 1995, 2 U.S.C. 1501 et seq., the DEA has determined and certifies that this action would not result in any Federal mandate that may result "in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted for inflation) in any one year." Therefore, neither a Small Government Agency Plan nor any other action is required under UMRA of 1995.

Paperwork Reduction Act of 1995

This action does not impose a new collection of information requirement under the Paperwork Reduction Act of 1995. 44 U.S.C. 3501-3521. This action would not impose recordkeeping or reporting requirements on State or local governments, individuals, businesses, or organizations. An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Congressional Review Act

This rule is not a major rule as defined by section 804 of the Small Business Regulatory Enforcement Fairness Act of 1996 (Congressional Review Act (CRA)). This rule will not result in: An annual effect on the economy of $100,000,000 or more; a major increase in costs or prices for consumers, individual industries, Federal, State, or local government agencies, or geographic regions; or significant adverse effects on competition, employment, investment, productivity, innovation, or on the ability of U.S.-based companies to compete with foreign based companies in domestic and export markets. However, pursuant to the CRA, the DEA has submitted a copy of this interim final rule to both Houses of Congress and to the Comptroller General.

List of Subjects in 21 CFR Part 1308

Administrative practice and procedure, Drug traffic control, Reporting and recordkeeping requirements.

For the reasons set out above, the DEA amends 21 CFR part 1308:

PART 1308--SCHEDULES OF CONTROLLED SUBSTANCES

- 1. The authority citation for 21 CFR part 1308 continues to read as follows:

  Authority: 21 U.S.C. 811, 812, 871(b), unless otherwise noted.

- 2. Amend **Sec. 1308.15** by redesignating paragraphs (e)(1) through (e)(3) as paragraphs (e)(2) through (e)(4) and adding new paragraph (e)(1) to read as follows:

Sec. 1308.15 Schedule V.

* * * * *

(e) * * *

[redacted]ge 29492]]

Brivaracetam ((2S)-2-[(4R)-2-oxo-4-propylpyrrolidin-1-yl]butanamide) (also referred to as BRV; UCB–34714; Briviact) (including its salts) 2710

* * * * *

Dated: May 6, 2016.

Chuck Rosenberg,
Acting Administrator.

[FR Doc. 2016-11245 Filed 5-11-16; 8:45 am]

BILLING CODE 4410-09-P

GW pharmaceuticals

April 25, 2016

Mark Hardy
Executive Director
North Dakota State Board of Pharmacy
1906 E. Broadway Ave.
Bismarck, ND 58501-1354

Dear Mr. Hardy,

Please allow me to introduce myself. I am the Vice President of U.S. Professional Relations for GW Pharmaceuticals. GW is the developer of Epidiolex®, a pure cannabidiol (CBD) investigational product that is being studied as a potential anti-convulsive treatment for children with certain types of childhood-onset, medication-resistant epilepsies, including Dravet Syndrome and Lennox Gastaut Syndrome (LGS).

We have just announced that the results of our first study in Dravet Syndrome were highly statistically significant in favor of Epidiolex® over placebo. Epidiolex® achieved the primary endpoint of a significant reduction in convulsive seizures assessed over the entire treatment period compared with placebo (p=0.01). The results from our two trials in LGS will become available over the next few months, and the results from our second Dravet study will be available in the second half of the year. I include the press release announcing the first Dravet study results. Epidiolex® has both Orphan Drug Designation and Fast Track Designation from the U.S. Food and Drug Administration (FDA) in the treatment of Dravet syndrome and also Orphan designation for LGS.

Dravet Syndrome is a severe infantile-onset and highly treatment-resistant epileptic syndrome. Over time, people with Dravet Syndrome can develop multiple types of seizures and are prone to prolonged seizures called status epilepticus, which can be life threatening. Risk of premature death including SUDEP (sudden expected death in epilepsy) is elevated in people with Dravet Syndrome. Additionally, the majority will develop moderate to severe intellectual and development disabilities and require lifelong supervision and care. **There are currently no FDA-approved treatments**, and nearly all patients continue to have uncontrolled seizures and other medical needs throughout their lifetime.

Patients with Lennox Gastaut Syndrome commonly have frequent seizures of a wide variety, including convulsive, atonic seizures, which can cause abrupt falls and serious injury. LGS is also highly medication resistant. Most children with LGS experience some degree of impaired intellectual functioning or information processing, as well as developmental delays and behavioral disturbances.

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GW pharmaceuticals

As you can see, there is a pressing need for new treatment options for patients with Dravet Syndrome and LGS. These syndromes have serious consequences for both the patients and for their families.

GW intends to file a New Drug Application with the FDA as soon as possible within the next year. Since Epidiolex has Fast Track status, we hope that the FDA will afford it a Priority Review cycle, which could result in approval within eight months of submission. Because CBD is a purified derivative of the cannabis plant, it is currently classified in Schedule I of the U.S. Controlled Substances Act (CSA). If Epidiolex® were approved by FDA, it would then be rescheduled by DEA to a lower schedule so that it could be prescribed. Under recent federal legislation, that rescheduling should be accomplished within 90 days of FDA approval. Almost all states have their own state controlled drug laws, and CBD is a Schedule I substance under those laws. ***Therefore, despite being approved by FDA and rescheduled by DEA, Epidiolex® could not be made available to patients in your state until it is also rescheduled under state law.*** In summary:

- Late 2016/beginning of 2017 - GW files a New Drug Application with FDA
- Potential FDA approval within 8 months of submission - based on Fast Track status and Priority Review Cycle
- 90 days after FDA approval - DEA reschedules Epidiolex® from Schedule I to lower schedule.
- Subsequently, the state reschedules Epidiolex® under state law similarly to DEA rescheduling.

We understand that your agency is responsible for implementing the administrative process that must occur in order for such rescheduling to take place. Therefore, we are reaching out to you with this information in order to minimize any delays in patient access in your state to a much-needed treatment option.

We would very much like to speak with you in the very near future to provide you with additional information about our research and answer any questions you might have about the development path of Epidiolex®. Thank you so much for considering our request.

Best wishes,

Alice P. Mead

Alice P. Mead
Vice President, U.S. Professional Relations
GW Pharmaceuticals

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For Patients

GW's Epidiolex® Clinical Program

GW is committed to developing new medicines to treat rare, treatment-resistant epilepsy conditions where there are limited or in some cases, no approved treatment options.

Epidiolex is GW's lead cannabinoid product candidate and is a proprietary oral solution of pure plant-derived cannabidiol, or CBD. GW's Epidiolex development is initially concentrating on severe, orphan, early-onset, treatment-resistant epilepsy syndromes including Dravet syndrome, Lennox-Gastaut syndrome (LGS), Tuberous Sclerosis Complex (TSC) and Infantile Spasms (IS).

GW's Epidiolex development includes two distinct programs:

FDA-authorized clinical trials program

- We have commenced a series of clinical trials designed to obtain safety and efficacy data on Epidiolex to provide to the FDA and other regulatory authorities around the world, which is necessary to be considered for approval as a prescription medicine. Target indications currently include Dravet syndrome, Lennox-Gastaut syndrome, Tuberous Sclerosis Complex, and Infantile Spasms. In these trials, eligible patients are randomly assigned to receive Epidiolex or placebo added to their current treatment and evaluated over a specific period of time. These trials are "blinded" meaning that patients, families, and physicians do not know which treatment arm they have been assigned.
- GW's current Phase 3 pivotal trials program for Epidiolex includes two Phase 3 trials in Dravet syndrome, two in LGS, one in TSC, and one in IS. The first two of these Phase 3 trials, one in Dravet syndrome and one in LGS, have showed significantly greater reductions in specific seizure types for patients taking Epidiolex compared to those taking placebo. (see GW press releases: 14 March 2016 & 27 June 2016, 26 September 2016).
- To learn more about GW's Epidiolex clinical trials please see the ClinicalTrials.gov website here.
- Link to a form for your health care professional to fill out to reach GW's medical affairs group. Please note: You must be a health care professional (HCP) to fill out this form. By clicking submit, you are confirming you are a health care professional. Please do not include any patient-identifying information.

FDA-authorized, independent Physician-led program or Expanded Access (which are at times called Compassionate Use programs in some countries) and for which GW supplies Epidiolex*

- The FDA may authorize expanded access programs to facilitate access to investigational drugs for treatment use for patients with a serious or immediately life-threatening disease or condition who lack therapeutic alternatives. This is done through FDA granting Investigational New Drug (IND) applications.
- The FDA has granted individual patient emergency INDs to physicians as well as INDs to physicians and state programs to treat groups of patients suffering from intractable epilepsy with Epidiolex.
- The most recent physician-reported data from this Expanded Access Program was presented in December 2015 at the American Epilepsy Society's annual meeting. Results from 261 patients receiving Epidiolex under these INDs showed promising signals of clinical effect in reducing seizures (link to press release and poster).

Support and Advocacy Organizations

- There are a number of organizations which provide invaluable help, information, and support to people living with epilepsy. They are also a useful resource for caregivers, friends, and relatives. The following list includes links to some websites of patient organizations that may be useful.
  - **Epilepsy Foundation**
  - **Dravet syndrome**
  - **Lennox-Gastaut syndrome**
  - **Tuberous Sclerosis Complex**
  - **Infantile Spasms**

GW is committed to respecting the primary role of healthcare providers in the treatment of epilepsy disorders. Therefore, we cannot respond to medical questions about your personal health situation, nor can we accept private medical information. Please contact your healthcare provider with any questions pertaining to your or a family member's medical condition

If you are interested in participating in a GW-sponsored clinical trial, please have your physician contact GW at: medicalinformation@gwpharm.com

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SB 2096

House Judiciary Committee, March 1, 2017

Testimony of Charlene Rittenbach, Forensic Scientist

ND Crime Laboratory Division, Office of Attorney General

Mr. Chairman, members of the Judiciary Committee.

This is my fourth legislative session helping to update North Dakota's laws to extend to the new designer drug compounds being identified in forensic casework. The original concept of these designer drugs was to produce and sell drugs that are not regulated, but can give the same effects as drugs that are already controlled, thus producing legal highs. It started 8 years ago, with the surge of Synthetic Cannabinoid compounds – sold as incense or potpourri giving users a high similar to THC (Marijuana). Then six years ago, I was here explaining the Substituted Cathinones - sold as Bath Salts producing central nervous system stimulant effects and the potent synthetic hallucinogens (Substituted Phenethylamines and Substituted Tryptamines) that were groups of compounds that were being added to the law. I am happy to say that this legislation has proved to be sufficient, as new compounds emerging today are covered in this group language. Last legislative session, three additional Synthetic Cannabinoid groups were added that were more comprehensive therefore replacing four existing groups. I am pleased to say that these changes have been effective and all current synthetic cannabinoids that have been identified in casework thus far have fallen into one of these groups and been included under our law.

Today I will be talking about a different class of drugs – synthetic opioids. Recently synthetic opioid analgesics have been emerging that are extremely potent and are increasing the number of overdoses. One of the most abundant drugs being produced and abused is fentanyl, which is about 100 times more potent than morphine (30-50 times more potent than heroin) as an analgesic. Fentanyl is a schedule II controlled substance and has many legitimate uses to treat pain. It is used during surgical procedures, and also administered to patents via transdermal patches and transmucosal lozenges also known as lollipops. Prescription fentanyl medications have led to overdoses and fatalities in the past, but the large increase in fatal overdoses since 2013 is primarily due to clandestine produced fentanyl that is distributed in tablet, capsule, powder and liquid form. In addition to fentanyl, various analogs of fentanyl such as furanyl fentanyl, butyryl fentanyl and others are surfacing on the street and causing problems with user overdoses.

Fentanyl and fentanyl analogs are traditionally mixed into or sold as heroin, oftentimes without the customer's knowledge. The typical dosage (by IV) for fentanyl is 125 µg, which is roughly equivalent to 2 grains of salt. The average lethal dose for fentanyl is 2 mg, which is the average weight of a mosquito. This means the user taking fentanyl for its euphoric effects has a very small window

between a recreational dose and a lethal overdose. The United States is in the midst of a fentanyl crisis, with law enforcement reporting and public health data indicating higher availability of fentanyl and fentanyl analogs, increased seizures of fentanyl and fentanyl analogs and more known overdose deaths from fentanyl and fentanyl analogs than at any other time since the drugs were first created in 1959.

The DEA's data query system, NFLIS (National Forensic Laboratory Information System) collects drug chemistry analysis results from cases analyzed by state, local and federal forensic laboratories. The following national statistics from 2012 to 2016 show the dramatic rise in fentanyl and fentanyl analogue identifications from state, local and federal forensic laboratories throughout the United States:

2012 – 686
2013 – 787
2014 – 4,456
2015 – 14,953
2016 – 34,650

This legislative session, the proposed changes include adding a section called Fentanyl Derivatives. This group will account for the newer analog compounds which uses a chemical class approach that defines a core molecular structure (Fentanyl) and lists possible substitutions and modifications. Some compounds that would fall into this class are already specifically listed schedule I opiates so they would be moved under this class and listed as an example. The definition does state that unless specifically excepted, listed in another schedule or are not FDA approved drugs to account for legitimate fentanyl analogs already listed in Schedule II or new compounds that may be FDA approved in the future.

In addition to the fentanyl derivative language, three other synthetic opioids are being specifically listed as they are structurally different than the fentanyls. The potent synthetic opioids AH-7921, MT-45 and U-47700 are compounds that have been identified in forensic casework and numerous deaths associated with each have been reported.

I have stated in previous years that North Dakota has some of the best all inclusive laws encompassing hundreds of compounds when you compare our law to some other states. The addition of the fentanyl derivative section and the addition of some compounds specifically, will strengthen our laws to include potent synthetic opioids being identified in forensic casework which have the potential to cause overdose deaths. The opioid epidemic cannot simply be solved by controlling all the compounds but at least it is one step that will make obtaining these currently legal analogs harder to obtain and a tool to prosecute the sellers of these harmful substances.