several confirmed deaths in the United States. On July 17, 2015, Acetylfentanyl was temporarily placed into Schedule I of the CSA for 2 years upon finding that it posed an imminent hazard to the public safety. The Attorney General, though, may extend this temporary scheduling for up to 1 year.

α-Pyrrolidinovalerophenone (α-PVP or alpha-PVP) is a synthetic cathinone structurally and pharmacologically similar to amphetamine, 3,4-methylenedioxymethamphetamine (MDMA); cathinone; and other related substances. Effects reported by abusers of synthetic cathinone substances include euphoria; sense of well-being; and increased sociability, energy, empathy, alertness, and concentration and focus. Abusers also report experiencing unwanted effects such as tremor, vomiting, agitation, sweating, fever, and chest pain. Other adverse or toxic effects that have been reported with the abuse of synthetic cathinones include tachycardia, hypertension, hyperthermia, mydriasis, rhabdomyolysis, hyponatremia, seizures, altered mental status (*e.g.,* paranoia, hallucinations, or delusions), and even death. On March 7, 2014, alpha-PVP was temporarily placed into Schedule I of the CSA for 2 years upon finding that it posed an imminent hazard to the public safety. The Attorney General, though, may extend this temporary scheduling for up to 1 year.

4-Fluoroamphetamine (4–FA) is a psychoactive substance of the phenethylamine and substituted amphetamine chemical classes and produces stimulant effects. 4–FA is not currently controlled in the United States under the CSA.

Para-Methyl-4-methylaminorex (4,4'-DMAR) is a derivative of the stimulant drug 4-methylaminorex and has been involved in several deaths in the United States. 4,4'-DMAR is not currently controlled in the United States under the CSA.

Para-Methoxymethylamphetamine (PMMA) is a substituted amphetamine of the phenethylamine class, as well as a structural analog of para-methoxyamphetamine (PMA) which produces effects similar but not identical to that of MDMA. PMMA is not currently controlled in the United States under the CSA.

2-(ethylamino)-2-(3-methoxyphenyl)-cyclohexanone (Methoxetamine or MXE) is an arylcyclohexamine and is not currently controlled under the CSA in the United States. At its 36th meeting, the WHO Expert Committee on Drug Dependence noted the insufficiency of data regarding dependence, abuse, and risks to the public health, thereby recommending that Methoxetamine not be placed under international control but be kept under international surveillance.

IV. Opportunity To Submit Domestic Information

As required by section 201(d)(2)(A) of the CSA (21 U.S.C. 811(d)(2)(A)), FDA, on behalf of the Department of Health and Human Services (HHS), invites interested persons to submit comments regarding the 10 named drugs. Any comments received will be considered by HHS when it prepares a scientific and medical evaluation of these drugs. HHS will forward a scientific and medical evaluation of these drugs to WHO, through the Secretary of State, for WHO's consideration in deciding whether to recommend international control/decontrol of any of these drugs. Such control could limit, among other things, the manufacture and distribution (import/export) of these drugs and could impose certain recordkeeping requirements on them.

Although FDA is, through this notice, requesting comments from interested persons which will be considered by HHS when it prepares an evaluation of these drugs, HHS will not now make any recommendations to WHO regarding whether any of these drugs should be subjected to international controls. Instead, HHS will defer such consideration until WHO has made official recommendations to the Commission on Narcotic Drugs, which are expected to be made in early 2016. Any HHS position regarding international control of these drugs will be preceded by another **Federal Register** notice soliciting public comments, as required by section 201(d)(2)(B) of the CSA.

V. Electronic Access

Persons with access to the Internet may obtain the document at either *http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm* or *http://www.regulations.gov.*

Dated: September 29, 2015.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2015–25201 Filed 10–2–15; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2012–N–0559]

Agency Information Collection Activities; Proposed Collection; Comment Request; Public Health Service Guideline on Infectious Disease Issues in Xenotransplantation

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing an opportunity for public comment on the proposed collection of certain information by the Agency. Under the Paperwork Reduction Act of 1995 (the PRA), Federal Agencies are required to publish notice in the **Federal Register** concerning each proposed collection of information, including each proposed extension of an existing collection of information, and to allow 60 days for public comment in response to this notice. This notice solicits comments on the collection of information contained in the Public Health Service (PHS) guideline entitled ''PHS Guideline on Infectious Disease Issues in Xenotransplantation'' dated January 19, 2001.

DATES: Submit either electronic or written comments on the collection of information by December 4, 2015.

ADDRESSES: You may submit comments as follows:

Electronic Submissions

Submit electronic comments in the following way:

- *Federal eRulemaking Portal: http://www.regulations.gov.* Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to *http://www.regulations.gov* will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on *http://www.regulations.gov.*
- If you want to submit a comment with confidential information that you do not wish to be made available to the

public, submit the comment as a written/paper submission and in the manner detailed (see ''Written/Paper Submissions'' and ''Instructions'').

Written/Paper Submissions

Submit written/paper submissions as follows:

- *Mail/Hand delivery/Courier (for written/paper submissions):* Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Division of Dockets Management, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in ''Instructions.''

Instructions: All submissions received must include the Docket No. FDA–2012–N–0559 for ''Agency Information Collection Activities; Proposed Collection; Comment Request; Public Health Service Guideline on Infectious Disease Issues in Xenotransplantation.'' Received comments will be placed in the docket and, except for those submitted as ''Confidential Submissions,'' publicly viewable at *http://www.regulations.gov* or at the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

- *Confidential Submissions*—To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states ''THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION''. The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on *http://www.regulations.gov.* Submit both copies to the Division of Dockets Management. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as ''confidential.'' Any information marked as ''confidential'' will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: *http://www.fda.gov/regulatoryinformation/dockets/default.htm.*

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to *http://www.regulations.gov* and insert the docket number, found in brackets in the heading of this document, into the ''Search'' box and follow the prompts and/or go to the Division of Dockets Management, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: FDA PRA Staff, Office of Operations, Food and Drug Administration, 8455 Colesville Rd., COLE–14526, Silver Spring, MD 20993–0002, *PRAStaff@fda.hhs.gov.*

SUPPLEMENTARY INFORMATION: Under the PRA (44 U.S.C. 3501–3520), Federal Agencies must obtain approval from the Office of Management and Budget (OMB) for each collection of information they conduct or sponsor. ''Collection of information'' is defined in 44 U.S.C. 3502(3) and 5 CFR 1320.3(c) and includes Agency requests or requirements that members of the public submit reports, keep records, or provide information to a third party. Section 3506(c)(2)(A) of the PRA (44 U.S.C. 3506(c)(2)(A)) requires Federal Agencies to provide a 60-day notice in the **Federal Register** concerning each proposed collection of information, including each proposed extension of an existing collection of information, before submitting the collection to OMB for approval. To comply with this requirement, FDA is publishing notice of the proposed collection of information set forth in this document.

With respect to the following collection of information, FDA invites comments on: (1) Whether the proposed collection of information is necessary for the proper performance of FDA's functions, including whether the information will have practical utility; (2) the accuracy of FDA's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) ways to minimize the burden of the collection of information on respondents, including through the use of automated collection techniques when appropriate, and other forms of information technology.

PHS Guideline on Infectious Disease Issues in Xenotransplantation

OMB Control Number 0910–0456—Extension

The statutory authority to collect this information is provided under sections 351 and 361 of the PHS Act (42 U.S.C. 262 and 264) and the provisions of the Federal Food, Drug, and Cosmetic Act that apply to drugs (21 U.S.C. 301 *et seq.*). The PHS guideline recommends procedures to diminish the risk of transmission of infectious agents to the xenotransplantation product recipient and to the general public. The PHS guideline is intended to address public health issues raised by xenotransplantation, through identification of general principles of prevention and control of infectious diseases associated with xenotransplantation that may pose a hazard to the public health. The collection of information described in this guideline is intended to provide general guidance on the following topics: (1) The development of xenotransplantation clinical protocols; (2) the preparation of submissions to FDA; and (3) the conduct of xenotransplantation clinical trials. Also, the collection of information will help ensure that the sponsor maintains important information in a cross-referenced system that links the relevant records of the xenotransplantation product recipient, xenotransplantation product, source animal(s), animal procurement center, and significant nosocomial exposures. The PHS guideline describes an occupational health service program for the protection of health care workers involved in xenotransplantation procedures, caring for xenotransplantation product recipients, and performing associated laboratory testing. The PHS guideline is intended to protect the public health and to help ensure the safety of using xenotransplantation products in humans by preventing the introduction, transmission, and spread of infectious diseases associated with xenotransplantation.

The PHS guideline also recommends that certain specimens and records be maintained for 50 years beyond the date of the xenotransplantation. These include: (1) Records linking each xenotransplantation product recipient with relevant health records of the source animal, herd or colony, and the specific organ, tissue, or cell type included in or used in the manufacture of the product (section 3.2.7.1); (2) aliquots of serum samples from randomly selected animal and specific

disease investigations (section 3.4.3.1); (3) source animal biological specimens designated for PHS use (section 3.7.1); animal health records (section 3.7.2), including necropsy results (section 3.6.4); and (4) recipients' biological specimens (section 4.1.2). The retention period is intended to assist health care practitioners and officials in surveillance and in tracking the source of an infection, disease, or illness that might emerge in the recipient, the source animal, or the animal herd or colony after a xenotransplantation.

The recommendation for maintaining records for 50 years is based on clinical experience with several human viruses that have presented problems in human to human transplantation and are therefore thought to share certain characteristics with viruses that may pose potential risks in xenotransplantation. These characteristics include long latency periods and the ability to establish persistent infections. Several also share the possibility of transmission among individuals through intimate contact with human body fluids. Human immunodeficiency virus (HIV) and Human T-lymphotropic virus are human retroviruses. Retroviruses contain ribonucleic acid that is reverse-transcribed into deoxyribonucleic acid (DNA) using an enzyme provided by the virus and the human cell machinery. That viral DNA can then be integrated into the human cellular DNA. Both viruses establish persistent infections and have long latency periods before the onset of disease; 10 years and 40 to 60 years, respectively. The human hepatitis viruses are not retroviruses, but several share with HIV the characteristic that they can be transmitted through body fluids, can establish persistent infections, and have long latency periods, *e.g.,* approximately 30 years for hepatitis C.

In addition, the PHS guideline recommends that a record system be developed that allows easy, accurate, and rapid linkage of information among the specimen archive, the recipient's medical records, and the records of the source animal for 50 years. The development of such a record system is a one-time burden. Such a system is intended to cross-reference and locate relevant records of recipients, products, source animals, animal procurement centers, and nosocomial exposures.

Respondents to this collection of information are the sponsors of clinical studies of investigational xenotransplantation products under investigational new drug applications (INDs) and xenotransplantation product procurement centers, referred to as source animal facilities. There are an estimated three respondents who are sponsors of INDs that include protocols for xenotransplantation in humans and five clinical centers doing xenotransplantation procedures. Other respondents for this collection of information are an estimated four source animal facilities which provide source xenotransplantation product material to sponsors for use in human xenotransplantation procedures. These four source animal facilities keep medical records of the herds/colonies as well as the medical records of the individual source animal(s). The burden estimates are based on FDA's records of xenotransplantation-related INDs and estimates of time required to complete the various reporting, recordkeeping, and third-party disclosure tasks described in the PHS guideline.

FDA is requesting an extension of OMB approval for the following reporting, recordkeeping, and third-party disclosure recommendations in the PHS guideline:

TABLE 1—REPORTING RECOMMENDATIONS

PHS guideline Section	Description
3.2.7.2	Notify sponsor or FDA of new archive site when the source animal facility or sponsor ceases operations.

TABLE 2—RECORDKEEPING RECOMMENDATIONS

PHS guideline section	Description
3.2.7	Establish records linking each xenotransplantation product recipient with relevant records.
4.3	Sponsor to maintain cross-referenced system that links all relevant records (recipient, product, source animal, animal procurement center, and nosocomial exposures).
3.4.2	Document results of monitoring program used to detect introduction of infectious agents which may not be apparent clinically.
3.4.3.2	Document full necropsy investigations including evaluation for infectious etiologies.
3.5.1	Justify shortening a source animal's quarantine period of 3 weeks prior to xenotransplantation product procurement.
3.5.2	Document absence of infectious agent in xenotransplantation product if its presence elsewhere in source animal does not preclude using it.
3.5.4	Add summary of individual source animal record to permanent medical record of the xenotransplantation product recipient.
3.6.4	Document complete necropsy results on source animals (50-year record retention).
3.7	Link xenotransplantation product recipients to individual source animal records and archived biologic specimens.
4.2.3.2	Record baseline sera of xenotransplantation health care workers and specific nosocomial exposure.
4.2.3.3 and 4.3.2	Keep a log of health care workers' significant nosocomial exposure(s).
4.3.1	Document each xenotransplant procedure.
5.2	Document location and nature of archived PHS specimens in health care records of xenotransplantation product recipient and source animal.

TABLE 3—DISCLOSURE RECOMMENDATIONS

PHS Guideline Section	Description
3.2.7.2	Notify sponsor or FDA of new archive site when the source animal facility or sponsor ceases operations.
3.4	Standard operating procedures (SOPs) of source animal facility should be available to review bodies.
3.5.1	Include increased infectious risk in informed consent if source animal quarantine period of 3 weeks is shortened.
3.5.4	Sponsor to make linked records described in section 3.2.7 available for review.
3.5.5	Source animal facility to notify clinical center when infectious agent is identified in source animal or herd after xenotransplantation product procurement.

FDA estimates the burden for this collection of information as follows:

TABLE 4—ESTIMATED ANNUAL REPORTING BURDEN [1]

PHS guideline section	Number of respondents	Number of responses per respondent	Total annual responses	Average burden per response	Total hours
3.2.7.2 [2]	1	1	1	0.50 (30 minutes)	0.50

[1] There are no capital costs or operating and maintenance costs associated with this collection information.
[2] FDA is using 1 animal facility or sponsor for estimation purposes.

TABLE 5—ESTIMATED ANNUAL RECORDKEEPING BURDEN [1]

PHS guideline section	Number of recordkeepers	Number of records per recordkeeper	Total annual records	Average burden per recordkeeping	Total hours
3.2.7 [2]	1	1	1	16	16
4.3 [3]	3	1	3	0.75 (45 minutes)	2.25
3.4.2 [4]	3	10.67	32	0.25 (15 minutes)	8
3.4.3.2 [5]	3	2.67	8	0.25 (15 minutes)	2
3.5.1 [6]	3	0.33	1	0.50 (30 minutes)	0.50
3.5.2 [6]	3	0.33	1	0.25 (15 minutes)	0.25
3.5.4	3	1	3	0.17 (10 minutes)	0.51
3.6.4 [7]	3	2.67	8	0.25 (15 minutes)	2
3.7 [7]	4	2	8	0.08 (5 minutes)	0.64
4.2.3.2 [8]	5	25	125	0.17 (10 minutes)	21.25
4.2.3.2 [6]	5	0.20	1	0.17 (10 minutes)	0.17
4.2.3.3 and 4.3.2 [6]	5	0.20	1	0.17 (10 minutes)	0.17
4.3.1	3	1	3	0.25 (15 minutes)	0.75
5.2 [9]	3	4	12	0.08 (5 minutes)	0.96
Total					55.45

[1] There are no capital costs or operating and maintenance costs associated with this collection information.
[2] A one-time burden for new respondents to set up a recordkeeping system linking all relevant records. FDA is using one new sponsor for estimation purposes.
[3] FDA estimates there is minimal recordkeeping burden associated with maintaining the record system.
[4] Monitoring for sentinel animals (subset representative of herd) plus all source animals. There are approximately 6 sentinel animals per herd × 1 herd per facility × 4 facilities = 24 sentinel animals. There are approximately 8 source animals per year (see footnote 7 of this table); 24 + 8 = 32 monitoring records to document.
[5] Necropsy for animal deaths of unknown cause estimated to be approximately 2 per year × 1 herd per facility × 4 facilities = 8.
[6] Has not occurred in the past 3 years and is expected to continue to be a rare occurrence.
[7] On average 2 source animals are used for preparing xenotransplantation product material for one recipient. The average number of source animals is 2 source animals per recipients × 4 annually = 8 source animals per year. (See footnote 5 of table 6.)
[8] FDA estimates ther are 5 clinical centers doing xenotransplantation procedures × approximately 25 health care workers involved per center = 125 health care workers.
[9] Eight source animal records + 4 recipient records = 12 total records.

TABLE 6—ESTIMATED ANNUAL THIRD-PARTY DISCLOSURE BURDEN

PHS guideline section	Number of respondents	Number of disclosures per respondent	Total annual disclosures	Average burden per disclosure	Total hours
3.2.7.2 [2]	1	1	1	0.50 (30 minutes)	0.50
3.4 [3]	4	0.25	1	0.08 (5 minutes)	0.08
3.5.1 [4]	4	0.25	1	0.25 (15 minutes)	0.25
3.5.4 [5]	4	1	4	0.50 (30 minutes)	2
3.5.5 [4]	4	0.25	1	0.25 (15 minutes)	0.25
Total					3.08

[1] There are no capital costs or operating and maintenance costs associated with this collection of information.
[2] FDA is using one animal facility or sponsor for estimation purposes.
[3] FDA's records indicate that an average of 1 IND is expected to be submitted per year.
[4] To our knowledge, has not occurred in the past 3 years and is expected to continue to be a rare occurrence.
[5] Based on an estimate of 12 patients treated over a 3-year period, the average number of xenotransplantation product recipients per year is estimated to be 4.

Because of the potential risk for cross-species transmission of pathogenic persistent virus, the guideline recommends that health records be retained for 50 years. Since these records are medical records, the retention of such records for up to 50 years is not information subject to the PRA (5 CFR 1320.3(h)(5)). Also, because of the limited number of clinical studies with small patient populations, the number of records is expected to be insignificant at this time.

Information collections in this guideline not included in tables 1

through 6 can be found under existing regulations and approved under the OMB control numbers as follows: (1) ''Current Good Manufacturing Practice for Finished Pharmaceuticals,'' 21 CFR 211.1 through 211.208, approved under OMB control number 0910–0139; (2) ''Investigational New Drug Application,'' 21 CFR 312.1 through 312.160, approved under OMB control number 0910–0014; and (3) information included in a biologics license application, 21 CFR 601.2, approved under OMB control number 0910–0338. (Although it is possible that a xenotransplantation product may not be regulated as a biological product (*e.g.,* it may be regulated as a medical device), FDA believes, based on its knowledge and experience with xenotransplantation, that any xenotransplantation product subject to FDA regulation within the next 3 years will most likely be regulated as a biological product.) However, FDA recognized that some of the information collections go beyond approved collections; assessments for these burdens are included in tables 1 through 6.

In table 7, FDA identifies those collections of information activities that are already encompassed by existing regulations or are consistent with voluntary standards which reflect industry's usual and customary business practice.

TABLE 7—COLLECTION OF INFORMATION REQUIRED BY CURRENT REGULATIONS AND STANDARDS

PHS guideline section	Description of collection of information activity	21 CFR Section (unless otherwise stated)
2.2.1	Document offsite collaborations	312.52.
2.5	Sponsor ensures counseling patient + family + contacts	312.62(c).
3.1.1 and 3.1.6	Document well-characterized health history and lineage of source animals	312.23(a)(7)(a) and 211.84.
3.1.8	Registration with and import permit from the Centers for Disease Control and Prevention.	42 CFR 71.53.
3.2.2	Document collaboration with accredited microbiology labs	312.52.
3.2.3	Procedures to ensure the humane care of animals	9 CFR parts 1, 2, and 3 and PHS Policy.[1]
3.2.4	Procedures consistent for accreditation by the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC International) and consistent with the National Research Council's (NRC) Guide.	AAALAC International Rules of Accreditation[2] and NRC Guide.[3]
3.2.5, 3.4, and 3.4.1	Herd health maintenance and surveillance to be documented, available, and in accordance with documented procedures; record standard veterinary care.	211.100 and 211.122.
3.2.6	Animal facility SOPs	PHS Policy.[1]
3.3.3	Validate assay methods	211.160(a).
3.6.1	Procurement and processing of xenografts using documented aseptic conditions.	211.100 and 211.122.
3.6.2	Develop, implement, and enforce SOP's for procurement and screening processes.	211.84(d) and 211.122(c).
3.6.4	Communicate to FDA animal necropsy findings pertinent to health of recipient.	312.32(c).
3.7.1	PHS specimens to be linked to health records; provide to FDA justification for types of tissues, cells, and plasma, and quantities of plasma and leukocytes collected.	312.23(a)(6).
4.1.1	Surveillance of xenotransplant recipient; sponsor ensures documentation of surveillance program life-long (justify >2 yrs.); investigator case histories (2 yrs. after investigation is discontinued).	312.23(a)(6)(iii)(f) and (g), and 312.62(b) and (c).
4.1.2	Sponsor to justify amount and type of reserve samples	211.122.
4.1.2.2	System for prompt retrieval of PHS specimens and linkage to medical records (recipient and source animal).	312.57(a).
4.1.2.3	Notify FDA of a clinical episode potentially representing a xenogeneic infection.	312.32.
4.2.2.1	Document collaborations (transfer of obligation)	312.52.
4.2.3.1	Develop educational materials (sponsor provides investigators with information needed to conduct investigation properly).	312.50.
4.3	Sponsor to keep records of receipt, shipment, and disposition of investigative drug; investigator to keep records of case histories.	312.57 and 312.62(b).

[1] The ''Public Health Service Policy on Humane Care and Use of Laboratory Animals'' (*http://www.grants.nih.gov/grants/olaw/references/phspol.htm*).
[2] AAALAC International Rules of Accreditation (*http://www.aaalac.org/accreditation/rules.cfm*).
[3] The NRC's ''Guide for the Care and Use of Laboratory Animals.''

Dated: September 29, 2015.

Leslie Kux,

Associate Commissioner for Policy.

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