publication of this document in the **Federal Register**. Therefore, a comment is best assured of having its full effect if OMB receives it within 30 days of publication. Written comments and recommendations for the proposed information collection should be sent directly to the following: Office of Management and Budget, Paperwork Reduction Project, 725 17th Street, NW., Washington, DC 20503, Attn: Desk Officer for ACF.

Dated: February 27, 2001.

Bob Sargis,

Reports Clearance Officer.

[FR Doc. 01–5234 Filed 3–2–01; 8:45 am]

BILLING CODE 4184–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 00N–1441]

Agency Information Collection Activities; Announcement of OMB Approval; Infant Formula Requirements

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing that a collection of information entitled ''Infant Formula Requirements'' has been approved by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995.

FOR FURTHER INFORMATION CONTACT: Peggy Schlosburg, Office of Information Resources Management (HFA–250), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–1223.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of November 9, 2000 (65 FR 67388), the agency announced that the proposed information collection had been submitted to OMB for review and clearance under 44 U.S.C. 3507. 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. OMB has now approved the information collection and has assigned OMB control number 0910–0256. The approval expires on February 29, 2004. A copy of the supporting statement for this information collection is available on the Internet at http://www.fda.gov/ohrms/dockets.

Dated: February 23, 2001.

William K. Hubbard,

Senior Associate Commissioner for Policy, Planning, and Legislation.

[FR Doc. 01–5158 Filed 3–2–01; 8:45 am]

BILLING CODE 4160–01–S

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 00N–1257]

International Drug Scheduling; Convention on Psychotropic Substances; Single Convention on Narcotic Drugs; World Health Organization Scheduling Recommendations for 4-Bromo-2,5-dimethoxyphenethylamine (2C–B); Gamma-hydroxybutyric acid (GHB); 4-Methylthioamphetamine (4-MTA); Zolpidem (INN)

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is providing interested persons with the opportunity to submit written comments concerning recommendations by the World Health Organization (WHO) to impose international manufacturing and distribution restrictions, under international treaties, on certain drug substances. The comments received in response to this notice will be considered in preparing the U.S. position on these proposals for a meeting of the United Nations Commission on Narcotic Drugs (CND) in Vienna, Austria, March 20 to 29, 2001. This notice is issued under the Controlled Substances Act.

DATES: Submit written comments by March 15, 2001.

ADDRESSES: Submit written comments to the Dockets Management Branch (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. To ensure expeditious review of written comments, send a copy by facsimile or e-mail to: James R. Hunter (address below).

FOR FURTHER INFORMATION CONTACT: James R. Hunter, Controlled Substances Staff (HFD–9), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–2098, Fax: 301–443–9222, e-mail: hunterj@cder.fda.gov.

SUPPLEMENTARY INFORMATION:

I. Background

The United States is a party to the 1971 Convention on Psychotropic Substances (the Convention). Section 201(d)(2)(B) of the Controlled Substances Act (the CSA) (21 U.S.C. 811(d)(2)(B)) provides that when the United States is notified under Article 2 of the Convention that CND proposes to decide whether to add a drug or other substance to one of the schedules of the Convention, transfer a drug or substance from one schedule to another, or delete it from the schedules, the Secretary of State must transmit notice of such information to the Secretary of Health and Human Services (HHS). The Secretary of HHS must then publish a summary of such information in the **Federal Register** and provide opportunity for interested persons to submit comments. The Secretary of HHS must then evaluate the proposal and furnish a recommendation to the Secretary of State that shall be binding on the representative of the United States in discussions and negotiations relating to the proposal.

As detailed below, the Secretary of State has received notification from the Secretary-General of the United Nations (the Secretary-General) regarding substances to be considered for control under the Convention. The notification reflects the recommendations from the 31st WHO Expert Committee for Drug Dependence (ECDD), which met in June 1998. In the **Federal Register** of April 28, 2000 (65 FR 24969), FDA announced the WHO ECDD review, and the agency invited interested persons to submit information for WHO's consideration.

The full text of the notification from the Secretary-General is provided in section II of this document. Section 201(d)(2)(B) of the CSA requires the Secretary of HHS, after receiving a notification proposing scheduling, to publish a notice in the **Federal Register** to provide the opportunity for interested persons to submit information and comments on the proposed scheduling action.

II. United Nations Notification

The formal United Nations notification that identifies the drug substances and explains the basis for the recommendations is reproduced below.

Notification on 2C-B, 4-MTA, GHB and Zolpidem: Reference: NAR/CL.26/2000 CU 2000/240.

C1971/WHO
UNDCP 42nd CND
TLACSB/CNDS–40/00

The Secretary-General of the United Nations presents his compliments to the Secretary of State of the United States of

America and has the honour to inform the Government that, pursuant to article 2, paragraphs 1 and 4, of the Convention on Psychotropic Substances, 1971, he has received a notification from the World Health Organization (WHO) concerning proposed recommendations for international control in respect of the following four substances: 2C-B, 4-MTA, GHB and zolpidem.

In accordance with the provisions of article 2, paragraph 2, of the 1971 Convention, the Secretary-General is transmitting the text of that notification as an annex to the present note.

As will be seen from the notification and the attached assessments and recommendations, WHO recommends that 2C-B be included in Schedule II, 4-MTA in Schedule I, and GHB and zolpidem in Schedule IV of that Convention.

Article 2, paragraph 1, of the Convention reads:

> If a Party or the World Health Organization has information relating to a substance not yet under international control which in its opinion may require the addition of that substance to any of the Schedules of this Convention, it shall notify the Secretary-General and furnish him with the information in support of that notification. The foregoing procedure shall also apply when a Party or the World Health Organization has information justifying the transfer of a substance from one Schedule to another among those Schedules, or the deletion of a substance from the Schedules.

Article 2, paragraph 4, reads:

> If the World Health Organization finds: (a) That the substance has the capacity to produce (i)(1) a state of dependence and (2) central nervous system stimulation or depression, resulting in hallucinations or disturbances in motor function or thinking or behaviour or perception or mood, or (ii) similar abuse and similar ill effects as a substance in Schedule I, II, III or IV, and (b) That there is sufficient evidence that the substance is being or is likely to be abused so as to constitute a public health and social problem warranting the placing of the substance under international control, the World Health Organization shall communicate to the Commission an assessment of the substance, including the extent or likelihood of abuse, the degree of seriousness of the public health and social problem and the degree of usefulness of the substance in medical therapy, together with recommendations on control measures, if any, that would be appropriate in the light of its assessment.

Pursuant to article 2, paragraph 2, of the Convention, the notification, together with the assessments and recommendations from WHO as well as any data received from Governments on any of these substances, will be brought to the attention of the Commission on Narcotic Drugs at its forty-fourth session in March 2001. Any action or decision taken by the Commission with respect to that notification, pursuant to article 2, paragraph 5, of the Convention, will be notified to States Parties in due course.

Article 2, paragraph 5, of the Convention reads:

> The Commission, taking into account the communication from the World Health Organization, whose assessments shall be determinative as to medical and scientific matters, and bearing in mind the economic, social, legal, administrative and other factors it may consider relevant, may add the substance to Schedule I, II, III or IV. The Commission may seek further information from the World Health Organization or from other appropriate sources.

The Secretary-General would appreciate it if the Government would submit data on seizures of any of these substances or on the existence of clandestine laboratories manufacturing them. Such data would assist the Commission in its consideration of possible international control of some or all of the substances under review.

In order to further assist the Commission in reaching a decision, it would be appreciated if any economic, social, legal, administrative or other factors the Government may consider relevant to the question of the possible scheduling of these four substances could be communicated by 12 December 2000 to the Executive Director of the United Nations International Drug Control Programme, c/o Commission on Narcotic Drugs Secretariat Section, P.O. Box 500, A–1400 Vienna, Austria, fax: 43–1–26060–5885.

2 November 2000
NAR/CL.26/2000

Annex—Note Dated 4 October 2000 Addressed to the Secretary-General by the Director-General of the World Health Organization

The Director-General of the World Health Organization presents her compliments to the Secretary-General of the United Nations and has the honour to submit, in accordance with Article 2, paragraphs 1 and 4, of the Convention on Psychotropic Substances, 1971, assessments and recommendations of the World Health Organization, as set forth on the annex hereto, concerning the proposed international control in respect of 2C-B, 4-MTA, GHB, and zolpidem.

The Director-General of the World Health Organization avails herself of this opportunity to renew to the Secretary-General of the United Nations the assurances of her highest consideration.

2C-B (4-Bromo-2,5-dimethoxyphenylethylamine) Substance identification

2C-B is chemically 4-bromo-2,5-dimethoxyphenylethylamine; 2-(4-bromo-2,5-dimethoxyphenyl) ethylamine (CAS 66142–81–2). Other names include: α-desmethyl DOB; BDMPEA; MFT; Erox; Nexus; Performax. There are no chiral centres; therefore, no stereoisomers or racemates are possible.

Similarity to Known Substances and Effects on the Central Nervous System

2C-B has structural and pharmacological similarities to brolamfetamine and mescaline. 2C–B is a selective partial agonist for 5-HT_{2A}- and 5-HT_{2C}-serotonin receptors. In humans, 2C–B is more potent than mescaline but less potent than brolamfetamine. In low doses it has sensory enhancing effects: skin sensitivity, heightened responsiveness to smells, tastes and sexual stimulation. In higher doses 2C-B is a strong hallucinogen. 2C-B produces particularly marked visual hallucinations with an intense colour play, intriguing patterns emerging on surfaces and distortions of objects and faces. It was reported to enhance sexual feelings, sexual perception and performance.

Dependence Potential

There are no animal or human studies about the dependence potential of 2C-B.

Actual Abuse and/or Evidence of Likelihood of Abuse

In the 1990s, 2C-B was sold as an aphrodisiac in several countries and some abuse of 2C-B has been reported by a number of countries. These suggest that 2C-B has modest abuse liability like other hallucinogens. Although hallucinogens are rarely associated with compulsive use or dependent use, they are known to have modest abuse potential, particularly in polydrug abusers.

Therapeutic Usefulness

Apart from the controversial experimental use to facilitate psychotherapy, hallucinogens, such as 2C-B, do not have any therapeutic usefulness.

Recommendation

Despite the limited availability of studies, the chemical and pharmacological similarity of 2C-B to the hallucinogen mescaline has been demonstrated. The altered state of mind induced by hallucinogens such as 2C-B may result in harm to the user and to

others. Based on its perceived aphrodisiac effects and known modest abuse potential of hallucinogenic drugs in general, it is estimated that 2C-B may be abused so as to constitute a public health and social problem warranting its placement under international control. However, hallucinogens are rarely associated with compulsive use and abuse of 2C-B has been infrequent, suggesting that abuse of 2C–B is likely to constitute a substantial, rather than an especially serious, risk to public health. On these bases, it is recommended that 2C-B be placed in Schedule II of the 1971 Convention on Psychotropic Substances.

4-MTA (4-methylthioamphetamine) Substance Identification

4-MTA is chemically 4-methylthioamphetamine (CAS 14116–06–4) Other names include: α-methyl 4-methylthiophenetylarnine, *p*-methylthioamphetamine; 4-MTA; *p–MTA;* MTA; MK; S5; S_5; Flatliner; The One and Only Dominator. 4-MTA has one chiral centre and can exist in two enatiomers and a racemate. Only the racemic mixture has been reported to have been synthesised.

Similarity to Known Substances and Effects on the Central Nervous System

4-MTA is a potent serotonin-releasing agent and reversible inhibitor of monoamine oxidase-A, and is structurally similar to 4-methoxyamphetamine. Pharmacologically, it is similar to MDA and MDMA; studies suggest that 4-MTA is six times more potent than MDMA and MDA in inhibiting 5-HT uptake.

Dependence Potential

Drug discrimination studies in rats suggest that 4-MTA produces discriminative stimulus effects similar to MDMA. 4-MTA did not substitute for amphetamine, LSD or phencyclidine. Reports from the United Kingdom indicate that 4-MTA is abused for its stimulant/euphoric effects similar to MDMA.

Actual Abuse and/or Evidence of Likelihood of Abuse

4-MTA is mainly abused in Europe. It appears that 4-MTA is part of the dance music culture although its use is relatively less widespread probably because of perceptions by users that the drug is stronger and more harmful than other ''club drugs'' such as MDMA. 4-MTA has resulted in a number of fatalities and hospital admissions. It appears that toxic effects can be produced directly from the drug and that the presence of other drugs or alcohol may exacerbate such effects.

Therapeutic Usefulness

4-MTA has no recognized therapeutic use.

Recommendation

4-MTA is chemically and pharmacologically similar to MDA and MDMA. 4-MTA is a new synthetic drug which was seized for the first time in 1997. Although evidence of its actual abuse is available only in several countries in Europe, seizures, including those of large quantities reported from a wider range of countries, suggest that the trafficking and abuse of 4-MTA are more widespread than have been reported. Based on this and its similarity to known MDA-type psychotropic substances, as well as data from drug discrimination studies in animals, it is estimated that 4-MTA is likely to be abused so as to constitute a public health and social problem warranting its placement under international control. Taking into consideration that 4-MTA has no recognized therapeutic use and that it has resulted in a number of fatalities, abuse of 4-MTA is estimated to constitute an especially serious risk to public health. It is therefore recommended that 4-MTA be placed in Schedule I of the 1971 Convention on Psychotropic Substance.

GHB (Gamma-hydroxybutyric acid) Substance Identification

GHB is chemically γ-hydroxybutyric acid; 4-hydroxybutyric acid (CAS 591–81–1). GHB usually exists as either the free acid or as the sodium salt. Sodium oxybate (CAS 502–85–2) is a national nonproprietary name for its sodium salt. There are no chiral centres; therefore, no stereoisomers or racemates are possible.

Similarity to Known Substances and Effects on the Central Nervous System

GHB is an endogenous compound and is structurally similar to the neurotransmitter GABA. Pharmacologically, it produces sedative and anaesthetic effects at high doses. Such depressant effects of GHB appear to be associated with its cataleptic effects and are different from those of barbiturates and benzodiazepines. GHB sedation possessed distinct excitatory properties, which may be due to its effect on the dopaminergic system (increase in intracellular neuronal dopamine). GHB has been found to induce anesthesia (but does not provide pain relief), (slow-wave) sleep, bradycardia, vomiting, random clonic movements, hypothermia, reduction in potassium levels, decrease in ventilatory rate and apnoea. However, the respiratory centre remains sensitive to an increase in carbon dioxide.

Dependence Potential

In drug discrimination studies in animals, none of the known abused drugs has the ability to fully substitute for GHB. Morphine, dexamphetamine, LSD and some benzodiazepines produced, at best, partial substitution. There have been few studies regarding the dependence/abuse potential of GHB. However, during the numerous studies involving administration of GHB to patients at varying concentrations, no dependence has been observed at low doses of GHB. At prolonged high doses, however, a withdrawal syndrome including insomnia, muscular cramping, tremor and anxiety has been noted upon discontinuation in some cases.

Actual Abuse and/or Evidence of Likelihood of Abuse

GHB abuse has been reported in Australia, USA and many countries in Europe. Precursors of GHB, such as γ-butyrolaztone and 1,4-butanediol, which are metabolized to GHB in the body, have also been abused. Although initially abused by body-builders for its apparent growth hormone promoting properties, the more recent primary mode of abuse worldwide has been the use of GHB for its subjective hypnotic, euphoric and hallucinogenic effects, especially in the context of the dance music culture (i.e. ''raves''). Some users have also claimed to use GHB as an alternative to alcohol (for relaxation), as a sexual adjunct, appetite suppressant, anti-aging product and has also been implicated in cases of sexual assault.

It appears that toxic effects can be produced directly from the drug and the presence of other depressant or sedative drugs (e.g. opiates, benzodiazepines, alcohol and barbiturates) and possibly other psychoactive compounds (e.g. amphetamine) may exacerbate the effects of GHB. Hospital admissions and deaths have been linked to GHB ingestion and generally involve the onset of coma and respiratory depression.

Therapeutic Usefulness

GHB has been used as an anaesthetic agent and as an aid to alcohol/opiate withdrawal, primarily in France, Germany and Italy, respectively. In USA and Canada it is currently under evaluation for the treatment of narcolepsy-associated cataplexy.

Recommendation

Although GHB is an endogenous compound that exists in the human body, GHB has psychoactive and toxic effects when administered. The pattern and consequences of its abuse in a number of countries in Europe and the USA seem to suggest that its liability to abuse constitutes a significant risk to public health. The current easy availability of GHB and some of its precursors has contributed to its recent abuse. The wide availability is likely to be reduced once GHB is placed under international control. On these bases, it is recommended that GHB be placed in Schedule IV of the 1971 Convention on Psychotropic Substances.

Zolpidem (INN) Substance Identification

Zolpidem is chemically N,N,6-trimethyl-2-p-tolylimidazo [1,2-a]pyridine-3-acetamide; N,N,6-trimethyl-2-(4-methylphenyl)imidazo[1,2-a]pyridine-3-acetamide (CAS 82626–48–0). Trade names include: Ambien, Bikalm, Niotal, Stilnoct, Stilnox.

Similarity to Known Substances and Effects on the Central Nervous System

Though chemically different from benzodiazepines, zolpidem produces benzodiazepine-like effects. It acts as an agonist binding with high and low affinity to BZ_1 and BZ_2 receptor subtypes, respectively. It is generally believed to produce relatively greater hypnotic effects than other benzodiazepine-like effects.

Dependence Potential

The results of human laboratory studies suggest that zolpidem and triazolam are generally similar in terms of producing subjective reinforcing effects. As with many of the benzodiazepines, there have been a number of case reports describing withdrawal symptoms after cessation of zolpidem administration. Though withdrawal discomfort does not necessarily lead to compulsory drug taking (drug dependence) in humans, there are reports of clinically diagnosed cases of drug dependence resulting from a prolonged use of zolpidem.

Actual Abuse and/or Evidence of Likelihood of Abuse

Epidemiological studies indicate that zolpidem is associated with relatively low incidence of abuse. Sporadic case reports in the scientific literature have indicated that zolpidem is abused, but these cases usually involved patients with histories of drug abuse or chronic psychiatric disorders. Cases of zolpidem overdose requiring emergency treatment have been reported. Death due to zolpidem overdose is rare. Rates of actual abuse and dependence of zolpidem appear to be similar to other hypnotic benzodiazepines in Schedule IV. In terms of the numbers of cases of abuse, dependence and withdrawal reported as adverse drug reactions to the WHO adverse drug reaction database, less than ten benzodiazepines are ranked higher than zolpidem.

Therapeutic Usefulness

Zolpidem is used for treatment of insomnia in more than 80 countries.

Recommendation

Although zolpidem has a somewhat novel neuropharmacological profile relative to classic benzodiazepines, studies of its abuse potential suggest that it may be comparable to that of many benzodiazepines. Furthermore, rates of actual abuse and dependence of zolpidem in medical use, as well as the risk to public health of its abuse, appear to be similar to hypnotic benzodiazepines presently placed in Schedule IV. On these bases, it is recommended that zolpidem be placed in Schedule IV of the 1971 Convention on Psychotropic Substances.

I. Discussion

Although WHO has made specific scheduling recommendations for each of the drug substances, the CND is not obliged to follow the WHO recommendations. Options available to the CND for substances considered for control under the Psychotropic Convention include: (1) Acceptance of the WHO recommendations; (2) acceptance of the recommendations to control, but control the drug substance in a schedule other than that recommended; or (3) rejection of the recommendations entirely.

4-Bromo-2,5-dimethoxyphenethylamine (2C-B) is a Schedule I controlled substance in the United States. The U.S. Drug Enforcement Administration (DEA) placed 2C-B (including salts, isomers, and salts of isomers: isomers include optical, positional, and geometric) in Schedule I of the Controlled Substance Act (CSA) in June 1995. 4-methylthioamphetamine (4-MTA) is not marketed in the United States and is not currently a controlled substance in the United States. Gamma hydroxybutyric acid (GHB) is a Schedule I controlled substance in the United States. GHB, including its salts, optical isomers, and salts of optical isomers, became a Schedule I controlled substance in March 2000. Registered manufacturers and distributors of GHB when it is manufactured, distributed, or possessed in accordance with an FDA authorized investigational new drug exemption under Section 505(i) of the Federal Food, Drug, and Cosmetic Act (21 USC 355(i)) are subject to Schedule III security requirements. If FDA approves a drug product containing GHB for marketing, the approved product will be placed into Schedule III under Public Law 106–172. Zolpidem, its salts, isomers, and salts of isomers, is a Schedule IV controlled substance in the United States. The DEA placed zolpidem in Schedule IV in February 1993. With the exception of 4-MTA, current controls in the United States on the substances under consideration for international control appear to meet the requirements of the recommended Psychotropic Convention schedules.

IV. Comments

Interested persons may, on or before March 15, 2001, submit to the Dockets Management Branch (address above) written comments regarding this notice. This abbreviated comment period is necessary to allow HHS to furnish a recommendation to the Secretary of State in time for the March 2001 meeting of the United Nations Commission on Narcotic Drugs. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the Dockets Management Branch (address above) between 9 a.m. and 4 p.m., Monday through Friday.

Dated: February 27, 2001.

Ann M. Witt,

Acting Associate Commissioner for Policy.

[FR Doc. 01–5218 Filed 2–28–01; 11:36 am]

BILLING CODE 4160–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

Blood Products Advisory Committee; Notice of Meeting

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

This notice announces a forthcoming meeting of a public advisory committee of the Food and Drug Administration (FDA). The meeting will be open to the public.

Name of Committee: Blood Products Advisory Committee.

General Function of the Committee: To provide advice and