

food effect. In its February 15, 1994, letter accompanying NDA 50-711, Pfizer explained that the tablets are bioequivalent to the capsule formulation and “* * * unlike the capsule, can be taken without regard to meals.” After NDA 50-711 was approved, Pfizer decided not to market the capsule formulation and ZITHROMAX (azithromycin) 250-mg oral capsules were moved from the prescription drug product list to the “Discontinued Drug Product List” section of the Orange Book. The “Discontinued Drug Product List” delineates, among other items, drug products that have been discontinued from marketing for reasons other than safety or effectiveness.

In a citizen petition submitted under 21 CFR 10.30 dated May 4, 2004 (Docket No. 2004P-0220), as amended by a letter dated May 17, 2004, Wapner, Newman, Wigrizer & Brecher requested that FDA determine whether ZITHROMAX (azithromycin) 250-mg oral capsules were withdrawn from sale for reasons of safety or effectiveness. The agency has determined that ZITHROMAX (azithromycin) 250-mg oral capsules were not withdrawn from sale for reasons of safety or effectiveness. The petitioners identified no data or other information suggesting that ZITHROMAX (azithromycin) 250-mg oral capsules were withdrawn from sale as a result of safety or effectiveness concerns. FDA has independently evaluated relevant literature and data and has found no information that would indicate this product was withdrawn for reasons of safety or effectiveness.

After considering the citizen petition and reviewing agency records, FDA determines that, for the reasons outlined in this document, ZITHROMAX (azithromycin) 250-mg oral capsules, approved under NDA 50-670, were not withdrawn from sale for reasons of safety or effectiveness. Accordingly, the agency will continue to list ZITHROMAX (azithromycin) 250-mg oral capsules in the “Discontinued Drug Product List” section of the Orange Book. As a result, ANDAs that refer to ZITHROMAX (azithromycin) 250-mg oral capsules may be approved by the agency.

Dated: May 12, 2005.

Jeffrey Shuren,

Assistant Commissioner for Policy.

[FR Doc. 05-10032 Filed 5-19-05; 8:45 am]

BILLING CODE 4160-01-S

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Health Resources and Services Administration

National Advisory Committee on Rural Health and Human Services; Notice of Meeting

In accordance with section 10(a)(2) of the Federal Advisory Committee Act (Pub. L. 92-463), notice is hereby given that the following committee will convene its fiftieth meeting:

Name: National Advisory Committee on Rural Health and Human Services.

Dates and Times: June 12, 2005, 1:30 p.m.–5:15 p.m., June 13, 2005, 8:45 a.m.–5 p.m., June 14, 2005, 9 a.m.–10:45 a.m.

Place: Carnegie Hotel, 1216 W State of Franklin Road, Johnson City, TN 37604, Phone: 423-979-6400, Fax: 423-979-6424.

Status: The meeting will be open to the public.

Purpose: The National Advisory Committee on Rural Health and Human Services provides advice and recommendations to the Secretary with respect to the delivery, research, development, and administration of health and human services in rural areas.

Agenda: Sunday afternoon, June 12, at 1:30 p.m., the Chairperson, the Honorable David Beasley, will open the meeting and welcome the Committee. There will be a brief discussion of Committee business and updates by Federal staff. The first session will open with an overview of East Tennessee by Dr. Paul Stanton, President of East Tennessee State University. The remainder of the day's meeting will be devoted to panel discussions on the three topics for the 2006 workplan: Pharmacy Access, Health Information Technology (HIT), and Elderly Caregiver Support. The Sunday meeting will close at 5:15 p.m.

Monday morning, June 13, at 8:45 a.m., the Committee will break into Subcommittees and conduct site visits to local health and human services facilities. Transportation to these sites will not be provided to the general public. The Pharmacy Access Subcommittee will visit Wilson Pharmacy in Johnson City; the HIT Subcommittee will visit Central Appalachian Health Information Partnership in Mountain City; and the Elderly Caregiver Support Subcommittee will visit the Mountain Empire Older Citizens Area Agency on Aging in Big Stone Gap. The Subcommittees will reconvene at 1:45 p.m. at the Carnegie Hotel to continue discussions on the workplan. The Committee of the whole will reconvene at 4:30 p.m. for a brief discussion of the workplan. The Monday meeting will close at 5 p.m.

The final session will be convened Tuesday morning, June 14, at 9 a.m. The Committee will review the discussion of the 2006 Workplan and have updates on the Subcommittees site visits. The meeting will conclude with a discussion of the September meeting. The meeting will be adjourned at 10:45 a.m.

For Further Information Contact: Anyone requiring information regarding the

Committee should contact Tom Morris, M.P.A., Executive Secretary, National Advisory Committee on Rural Health and Human Services, Health Resources and Services Administration, Parklawn Building, Room 9A-55, 5600 Fishers Lane, Rockville, MD 20857, telephone (301) 443-0835, Fax (301) 443-2803.

Persons interested in attending any portion of the meeting should contact Michele Pray-Gibson, Office of Rural Health Policy (ORHP), telephone (301) 443-0835. The Committee meeting agenda will be posted on ORHP's Web site <http://www.ruralhealth.hrsa.gov>.

Dated: May 13, 2005.

Tina M. Cheatham,

Director, Division of Policy Review and Coordination.

[FR Doc. 05-10098 Filed 5-19-05; 8:45 am]

BILLING CODE 4165-15-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Opportunity for a Cooperative Research and Development Agreement (CRADA) for Research and Development of Vigabatrin as a Potential Pharmacotherapy for the Treatment of Cocaine and Methamphetamine Dependence

AGENCY: National Institutes of Health, PHS, DHHS.

ACTION: Notice.

SUMMARY: The National Institute on Drug Abuse, a component of the National Institutes of Health, Department of Health and Human Services (DHHS) seeks an agreement with a pharmaceutical or biotechnology company to test the hypotheses that vigabatrin may be a safe and effective medication for the treatment of cocaine and methamphetamine dependence.

A body of literature relevant to preclinical studies of vigabatrin as a potential treatment agent for various types of substance dependence (including cocaine and methamphetamine) and a more limited body of literature concerning clinical results exists. As there are currently no medications approved by the U. S. Food and Drug Administration (FDA) for the treatment of cocaine and/or methamphetamine dependence, and cocaine and methamphetamine dependence have substantial negative public health impacts, the National Institute on Drug Abuse is interested in evaluating the safety and efficacy of vigabatrin for the treatment of cocaine and methamphetamine dependence.

Rationale for Studying Vigabatrin in Stimulant(s) Dependence

The dependence-producing properties of stimulants have been associated with their pharmacological actions on the mesolimbic dopamine reward pathways in the central nervous system (CNS). Gamma-amino butyric acid (GABA) inhibits striatal dopamine release, and attenuates cocaine-induced increases in extracellular dopamine in the striatum and nucleus accumbens (Molina *et al.*, 1999). Selective increases in GABAergic tone attenuate cocaine-induced dopamine release without the apparent side effects typically associated with GABA agonists. Therefore, targeting brain GABAergic systems is a potentially effective pharmacologic treatment strategy for cocaine and methamphetamine dependence (Molina *et al.*, 1999). Data from proof of concept clinical trials of similar GABAergic medications *e.g.* topiramate, baclofen, and tiagabine show efficacy in reducing cocaine use or in preventing relapse to use. These data suggest that vigabatrin, which possesses more potent GABAergic action, may be more efficacious than these medications. Preclinical studies in animal models have confirmed that dosing with vigabatrin can block the manifestations of consumption of cocaine typically seen in these models (Stromberg *et al.*, 2001), without impairing the usual dopamine mechanisms necessary to maintain a stable equilibrium. In rodent models, vigabatrin has been shown to reduce self-administration of cocaine and alcohol (Stromberg *et al.*, 2001; Kushner *et al.*, 1999), and to block conditioned place preference induced by cocaine (Dewey *et al.*, 1998), nicotine (Dewey *et al.*, 1999), and heroin (Paul, *et al.*, 2001). Further, vigabatrin can reduce the increases in nucleus accumbens dopamine induced by cocaine (Schiffer *et al.*, 2003), as well as methamphetamine, heroin, and ethanol (Gerasimov *et al.*, 1999).

Vigabatrin (GVG) is an irreversible gamma-amino butyric acid (GABA) transaminase inhibitor that produces a two to three fold rise in brain GABA concentrations (Guberman *et al.*, 2000). Following oral administration, vigabatrin readily crosses the blood-brain barrier and is active within the central nervous system. It has been shown to be effective, both as an add-on agent and in monotherapy in resistant and newly-diagnosed epilepsy (Guberman *et al.*, 2000) and as first line monotherapy in the treatment of infantile spasms (West syndrome) (Hancock *et al.*, 1999). After oral dosing, vigabatrin is well absorbed

(bioavailability c. 75%) and widely distributed. The drug is eliminated primarily by the renal route and is not significantly bound to plasma proteins. The elimination half-life is approximately 5–9 hours in healthy subjects and may be prolonged in elderly patients or those with impaired renal function (Rey *et al.*, 1992). The usual adult dose of vigabatrin for epilepsy is 1–3 g/day. There is no evidence that plasma concentrations of vigabatrin correlate closely with therapeutic effects (Brodie *et al.*, 2003).

There are anecdotal reports that dosing with vigabatrin prevents the “high” associated with cocaine intake in humans dependent on cocaine and can, therefore, result in decreased cocaine consumption. Two open label pilot studies suggest a therapeutic effect in most patients recruited in abstaining from cocaine or methamphetamine (Brodie *et al.*, 2005) use (Brodie *et al.*, 2003; Brodie *et al.*, 2005).

Therefore, it may be predicted that dosing with vigabatrin in a cocaine dependent population might prevent the cocaine “high” and the subsequent “craving”, and possibly reduce the perceived need for repeated use, and often higher, drug doses (Dewey *et al.*, 1999).

As an initial step in the clinical development of vigabatrin for stimulants dependence, it is important to assess the potential efficacy and safety of this compound in cocaine and methamphetamine dependent subjects.

References

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- Stromberg MF, Mackler SA, Volpicelli JR, O'Brien CP, Dewey SL (2001). The effect of gamma-vinyl-GABA on the consumption of concurrently available oral cocaine and ethanol in the rat. *Pharmacol Biochem Behav* 68:291–299.

DATES: NIDA will consider all proposals received within 45 days of the date of publication of this notice. This notice is active until July 5, 2005.

ADDRESSES: Proposals and questions about this opportunity may be addressed to Frank Vocci, Ph.D., Division of Pharmacotherapy and Medical Consequences of Drug Abuse, National Institute on Drug Abuse, 6001 Executive Blvd., MSC 9551, Bethesda, Maryland 20892–9551. For overnight mail service, 6001 Executive Blvd., Room 4123, Rockville, Maryland 20852. Tel: (301) 443–2711, Fax: (301) 443–2599.

SUPPLEMENTARY INFORMATION: NIDA will consider proposals from all qualified entities and will, subject to negotiation of the details of a mutually agreed upon Research Plan, provide the CRADA Collaborator access to its comprehensive preclinical and clinical trials resources with the understanding that the CRADA Collaborator will be able to utilize data derived from the CRADA to pursue regulatory filings in the U.S. and abroad. NIDA's Medications Development Program possesses the capacity to perform chemical synthesis, dosage form development, pharmacokinetics, pharmacodynamics, toxicology, regulatory management, and clinical testing (Phase I through Phase III) meeting FDA requirements for Good Manufacturing, Good Laboratory Procedures, and Good Clinical Practices standards. NIDA may apply these capacities in the assessment of vigabatrin, as may be warranted based

on NIDA's evaluation of the information, capacities, and plans provided by potential Collaborator(s).

NIDA follows stepwise development processes and procedures common to the medications development paradigm, *i.e.*, a candidate compound must successfully complete each necessary pre-requisite step prior to being advanced for further testing and development. It is NIDA's intention to provide, assuming pre-requisite preclinical and clinical safety, preclinical and clinical trials services sufficient to permit the completion of Phase II hypothesis testing trials for cocaine and methamphetamine dependence indications. Assuming demonstration and review of safety and efficacy at the conclusion of Phase II trials and subject to negotiation, NIDA will consider undertaking Phase III trials sufficient to permit Collaborator to seek a U.S. New Drug Application (NDA).

Please note that a CRADA is not a funding mechanism. No NIH funding may be provided to a Collaborator under a CRADA. All assistance is provided "in-kind". Therefore the Collaborator will bear the financial and organizational costs of meeting its share of obligations under any Research Plan that may be negotiated in connection with the CRADA.

"Cooperative Research and Development Agreement" or "CRADA" means the anticipated joint agreement to be entered into by NIDA pursuant to the Federal Technology Transfer Act of 1986 and Executive Order 12591 of October 10, 1987 to collaborate on the specific research project described below.

The National Institute on Drug Abuse seeks an agreement with a pharmaceutical or biotechnology company for joint research, development, evaluation, and potential commercialization of vigabatrin for the treatment of cocaine and methamphetamine dependence.

The CRADA aims include the rapid publication of research results and the timely exploitation of commercial opportunities. The CRADA partner will enjoy rights of first negotiation for licensing Government rights to any inventions arising under the agreement and will advance funds payable upon signing the CRADA to help defray Government expenses for patenting such inventions and other CRADA-related costs.

The expected duration of the CRADA will be 3 to 5 years.

Selection criteria for choosing the CRADA partner will include but not be limited to:

1. Ability to collaborate with NIDA on further research and development of this technology in Phase I and Phase II clinical studies. All such studies will occur in the United States and under FDA IND rules. Demonstration of experience and expertise in this or related areas of technology and the ability to provide intellectual contribution to the ongoing research and development. Ability to accomplish objectives according to an appropriate timetable to be outlined in the Collaborator's proposal. At an absolute minimum, Collaborator must be able to provide vigabatrin and placebo sufficient to complete all clinical and preclinical studies required in the Research Plan.

2. Demonstration of the resources (facilities, personnel and expertise) necessary to perform research, development and commercialization of this technology.

3. Commitment of reasonable effort and resources on research, development and commercialization of this technology.

4. Expertise in the commercial development, production, marketing and sales of products related to this area of technology.

5. The level of financial support, if any, the Collaborator will supply for CRADA-related Government activities.

6. A willingness to cooperate with the National Institute on Drug Abuse in the publication of research results.

7. An agreement to be bound by the DHHS rules involving human subjects, patent rights and ethical treatment of animals.

8. A willingness to accept the legal provisions and language of the CRADA with only minor modifications (if any).

9. Provisions for equitable distribution of patent rights to any inventions made during the course of the subject CRADA research. Generally, the rights of ownership are retained by the organization which is the employer of the inventor, with (1) an irrevocable, nonexclusive, royalty-free license to the Government (when a company employee is the sole inventor) or (2) an option to negotiate an exclusive or nonexclusive license to the company on terms that are appropriate (when a Government employee is an inventor).

Dated: May 11, 2005.

Steven M. Ferguson,

Director, Division of Technology Development and Transfer, Office of Technology Transfer, National Institutes of Health.

[FR Doc. 05-10066 Filed 5-19-05; 8:45 am]

BILLING CODE 4140-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Health, Public Health Service, DHHS.

ACTION: Notice.

SUMMARY: The inventions listed below are owned by an agency of the U.S. Government and are available for licensing in the U.S. in accordance with 35 U.S.C. 207 to achieve expeditious commercialization of results of federally-funded research and development. Foreign patent applications are filed on selected inventions to extend market coverage for companies and may also be available for licensing.

ADDRESSES: Licensing information and copies of the U.S. patent applications listed below may be obtained by writing to the indicated licensing contact at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852-3804; telephone: (301) 496-7057; fax: (301) 402-0220. A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

Synthesis of Phosphocholine Ester Derivatives and Conjugates Thereof

Louis J. Rezanka (NIA), U.S. Provisional Application No. 60/623,762 filed 29 Oct 2004 (DHHS Reference No. E-330-2004/0-US-01)

Licensing Contact: Michael Shmilovich; (301) 435-5019; shmilovm@mail.nih.gov.

Available for licensing and commercial development is a method of synthesizing EPC (4-Nitrophenyl-6-(O-phosphocholine) hydroxyhexanoate) and methods of synthesizing phosphocholine analogues and the phosphocholine conjugates formed therefrom. These molecules have clinical and research applications as anti-microbial agents. Specifically, EPC conjugated to protein carriers has been demonstrated to generate a protective immune response to *Streptococcus pneumoniae*. The invention provides a process for EPC synthesis as well as for its reaction intermediates for use in synthesis.

In addition to licensing, the technology is available for further development through collaborative research opportunities with the inventors.