

4 p.m.–5 p.m., May 13, 2009.

Place: Holiday Inn Amarillo Hotel, 1911 I-40 East, Amarillo, TX 79102; Phone: (806) 372-8741; Fax: (806) 372-7045. Audio Conference Call via FTS Conferencing. The USA toll-free dial-in number is 1-866-659-0537 with a pass code of 9933701.

Status: Open to the public, limited only by the space available. The meeting space accommodates approximately 100 people.

Background: The Advisory Board was established under the Energy Employees Occupational Illness Compensation Program (EEOICP) Act of 2000 to advise the President on a variety of policy and technical functions required to implement and effectively manage the new compensation program. Key functions of the Advisory Board include providing advice on the development of probability of causation guidelines which have been promulgated by the Department of Health and Human Services (HHS) as a final rule; advice on methods of dose reconstruction which have also been promulgated by HHS as a final rule; advice on the scientific validity and quality of dose estimation and reconstruction efforts being performed for purposes of the compensation program, and advice on petitions to add classes of workers to the Special Exposure Cohort (SEC).

In December 2000, the President delegated responsibility for funding, staffing, and operating the Advisory Board to HHS, which subsequently delegated this authority to the CDC. NIOSH implements this responsibility for CDC. The charter was issued on August 3, 2001, renewed at appropriate intervals, and will expire on August 3, 2009.

Purpose: This Advisory Board is charged with (a) providing advice to the Secretary, HHS, on the development of guidelines under Executive Order 13179; (b) providing advice to the Secretary, HHS, on the scientific validity and quality of dose reconstruction efforts performed for this program; and (c) upon request by the Secretary, HHS, advise the Secretary on whether there is a class of employees at any Department of Energy facility who were exposed to radiation but for whom it is not feasible to estimate their radiation dose, and on whether there is reasonable likelihood that such radiation doses may have endangered the health of members of this class.

Matters To Be Discussed: The agenda for the Advisory Board meeting includes: NIOSH Program Status Update; Department of Labor (DOL) Update; Department of Energy (DOE) Update; Board Security Plan; Special Exposure Cohort (SEC) Petitions for: Linde Ceramics Plant (Residual Period); Standard Oil Development Company of New Jersey; Blockson Chemical Company (radon-related dose reconstruction); and Dow Chemical Company (Madison, Illinois); Special Exposure Cohort (SEC) Petition Status Updates; Work Group reports; Reports of the Subcommittees on Dose Reconstruction Reviews and Procedures Reviews; and Board Future Plans and Meetings.

The agenda is subject to change as priorities dictate.

In the event an individual cannot attend, written comments may be submitted

according to the policy provided below. Any written comments received will be provided at the meeting and should be submitted to the contact person below well in advance of the meeting.

Policy on Redaction of Board Meeting Transcripts (Public Comment), (1) if a person making a comment gives his or her name, no attempt will be made to redact that name. (2) NIOSH will take reasonable steps to ensure that individuals making public comment are aware of the fact that their comments (including their name, if provided) will appear in a transcript of the meeting posted on a public Web site. Such reasonable steps include: (a) A statement read at the start of each public comment period stating that transcripts will be posted and names of speakers will not be redacted; (b) A printed copy of the statement mentioned in (a) above will be displayed on the table where individuals sign up to make public comment; (c) A statement such as outlined in (a) above will also appear with the agenda for a Board Meeting when it is posted on the NIOSH Web site; (d) A statement such as in (a) above will appear in the **Federal Register** Notice that announces Board and Subcommittee meetings. (3) If an individual in making a statement reveals personal information (*e.g.*, medical information) about themselves that information will not usually be redacted. The NIOSH FOIA coordinator will, however, review such revelations in accordance with the Freedom of Information Act and the Federal Advisory Committee Act and if deemed appropriate, will redact such information. (4) All disclosures of information concerning third parties will be redacted. (5) If it comes to the attention of the Designated Federal Officer (DFO) that an individual wishes to share information with the Board but objects to doing so in a public forum, the DFO will work with that individual, in accordance with the Federal Advisory Committee Act, to find a way that the Board can hear such comments.

Contact Person for More Information:
Theodore Katz, M.P.A., Executive Secretary,
NIOSH, CDC, 1600 Clifton Road, MS E-20,
Atlanta, GA 30333, Telephone (513)533-
6800, Toll Free 1(800) CDC-INFO, e-mail
ocas@cdc.gov.

The Director, Management Analysis and Services Office, has been delegated the authority to sign **Federal Register** notices pertaining to announcements of meetings and other committee management activities, for both CDC and the Agency for Toxic Substances and Disease Registry.

Dated: April 16, 2009.

Elaine L. Baker,

Director, Management Analysis and Services Office, Centers for Disease Control and Prevention.

[FR Doc. E9-9332 Filed 4-22-09; 8:45 am]

BILLING CODE 4163-18-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Public Teleconference Regarding Licensing and Collaborative Research Opportunities for: A Double-Barreled Attack: Azatoxins, A New Hope for Treating Cancer

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

ACTION: Notice.

Technology Summary

This technology describes a novel class of Topoisomerase II (top2) inhibitors that are useful in treating cancer. Drugs that inhibit the top2 enzyme are among the most active anticancer agents discovered. However, many of the currently available inhibitors produce toxic side effects, have poor pharmacokinetics, or eventually become ineffective because malignant cells readily acquire resistance. Therefore, there is a need for developing new top2 inhibitor drugs that will overcome these limitations.

Azatoxin and its derivatives, which are derived by combining two parent compounds etoposide and ellipticine, are the first compounds rationally designed as inhibitors of top2. Azatoxins are also potent inhibitors of tubulin polymerization. These two anti-cancer activities can be successfully separated by synthesizing azatoxin derivatives to yield compounds which can be pharmacologically advantageous against tumor proliferation. The azatoxin platform represents an unexploited class of top2 inhibitors that could be developed into especially potent chemotherapeutics.

Competitive Advantage of Our Technology

Currently, several top2 inhibitors are approved for clinical use; however, they produce serious side effects. Etoposide, for example, causes problems with myelosuppression, drug resistance, and has poor bioavailability. Moreover, it appears to have carcinogenic properties as it has been linked to the development of acute myelogenous leukemia—an effect also observed with mitoxantrone. Anthracyclines, like doxorubicin, have the same limitations as etoposide, but they also possess cardiotoxic effects. Azatoxins have the potential to be developed into chemotherapeutics that outperform these currently used top2 inhibitors.

Azatoxins have been substantially characterized through years of pre-clinical research demonstrating that

they possess properties from both of its parental compounds, etoposide and ellipticine. They act by stabilizing the top2-DNA cleavage complex, like etoposide does, instead of inhibiting top2 catalytic activity, the mechanism by which ellipticine acts. With regard to DNA cleavage activity, azatoxins show similar activity to etoposide. In addition to acting as a top2 inhibitor, azatoxin is also a potent inhibitor of tubulin polymerization.

The anti-cancer activity of azatoxins has been validated by cell line screening. The Developmental Therapeutics Program (DTP) of the National Cancer Institute (NCI) has tested azatoxins in its tumor cell panel and established their effectiveness against disseminated leukemia and localized tumors, such as non-small cell lung and colon cancer. These results are very encouraging showing that certain azatoxin derivatives are 100 times more active than etoposide, which is the common top2 inhibitor used in chemotherapy. Azatoxins are a novel class of potent top2 and/or tubulin inhibitors that could outperform current chemotherapeutic agents.

Technology Description

Topoisomerase enzymes are critical for normal cell division because they prevent tangles and knots from forming during DNA replication by cleaving and religating DNA. Several compounds have been discovered that block topoisomerases and stop its ability to religate DNA resulting in an increased number of double strand DNA breaks that kill the cell. These inhibitors are especially effective against rapidly dividing malignant cells that express high levels of top2, which represents a main reason these top2 enzymes have become an important therapeutic target. The problem is that currently used drugs are limited by their toxicity, insolubility, and their susceptibility to induce drug resistance.

In an effort to produce top2 inhibitors with increased therapeutic efficiency, well established top2 inhibitors were compared by molecular modeling to produce a composite top2 inhibitor pharmacophore of the diverse inhibitors. Based on this model, azatoxin was designed as an analogue hybrid of etoposide and ellipticine. Subsequently, several modifications of azatoxin have been synthesized to generate derivatives, such as anilinoazatoxins, which have improved pharmacological profiles.

Market

Despite further discoveries leading to a greater understanding and treating of

cancer, it continues to be a burden to the public health. After heart disease, cancer is the most common cause of death in the United States. In 2008, it was estimated that about 565,650 Americans were expected to die of cancer. Although, the incidence of cancer has been dropping over the years, it was estimated that over 1.4 million Americans would be diagnosed with cancer in 2008.

Cancer is not only a health burden but also a financial burden to the country. The NIH estimated the overall cost of cancer in 2007 to be \$219.2 billion dollars with \$89 billion attributable to direct medical costs. It is expected that cancer will continue to be a public health problem for the foreseeable future which prompts the need for the development of new therapeutics.

Chemotherapy is still the standard approach for treating cancers even though there were high expectations that targeted therapeutics would become the preferred drugs in cancer treatment. Current topoisomerase inhibitors have demonstrated to be effective chemotherapy drugs and they continue being developed for use in combination therapy with targeted therapeutics. However, top2 inhibitors need to be improved in order to overcome their limitations. A next-generation top2 inhibitor like azatoxins has potential in meeting this need.

Patent Estate

The National Institutes of Health holds a substantial portfolio of patents in U.S., Europe, Canada, and Australia which claim compositions of azatoxin and its derivatives, pharmaceutical formulations, and methods of use for chemotherapy.

The portfolio includes the following issued patents:

I. United States Patent No. 5,622,960 entitled "Topoisomerase II inhibitors and therapeutic uses therefor" issued April 22, 1997 (HHS Ref. No. E-119-1992/1-US-01).

II. United States Patent No. 5,747,520 entitled "Topoisomerase II inhibitors and therapeutic uses therefor" issued May 5, 1998 (HHS Ref. No. E-119-1992/1-US-17).

III. European Patent No. 0665846 entitled "Topoisomerase II inhibitors and therapeutic uses therefor" issued July 29, 1998 (HHS Ref. No. E-119-1992/1-EP-10) validated in Austria, Belgium, Denmark, France, Germany, Great Britain, Ireland, Italy, Luxembourg, Switzerland, and The Netherlands.

IV. Canadian Patent No. 2147608 entitled "Topoisomerase II inhibitors and therapeutic uses therefor" issued

December 12, 2006 (HHS Ref. No. E-119-1992/1-CA-06).

V. Australian Patent No. 676511 entitled "Topoisomerase II inhibitors and therapeutic uses therefor" issued June 13, 1997 (HHS Ref. No. E-119-1992/1-AU-04).

Next Step: Teleconference

There will be a teleconference where the principal investigator, Dr. Yves Pommier, will explain this technology. Licensing and collaborative research opportunities will also be discussed. If you are interested in participating in this teleconference please call or e-mail Samuel Bish; (301) 435-5282; bishse@mail.nih.gov. The NIH Office of Technology Transfer (OTT) will then e-mail you the date, time, and number for the teleconference.

Dated: April 16, 2009.

Richard U. Rodriguez,

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

[FR Doc. E9-9344 Filed 4-22-09; 8:45 am]

BILLING CODE 4140-01-P

DEPARTMENT OF HOMELAND SECURITY

U.S. Customs and Border Protection

[Docket No. USCBP-2006-0037]

Expansion of Global Entry Pilot Program

AGENCY: U.S. Customs and Border Protection; Department of Homeland Security.

ACTION: General notice.

SUMMARY: U.S. Customs and Border Protection (CBP) is currently conducting an international trusted traveler pilot program, referred to as Global Entry, at seven U.S. airports. This document announces that pursuant to an arrangement between the United States and the Netherlands, CBP is expanding eligibility for participation in the Global Entry pilot to include citizens of the Netherlands who participate in Privium, an expedited travel program in the Netherlands, and who otherwise satisfy the requirements for participation in Global Entry. Currently, eligibility is limited to U.S. citizens, U.S. nationals, and U.S. lawful permanent residents (LPRs). Pursuant to this same arrangement, U.S. citizens who participate in the Global Entry pilot will have the option to also apply for participation in Privium.

DATES: *Effective Dates:* Applications for the Global Entry pilot are currently