TABLE 1.—LIST OF SAFETY AND EFFECTIVENESS SUMMARIES FOR APPROVED PMAS MADE AVAILABLE FROM JANUARY 1, 2008, THROUGH MARCH 31, 2008—Continued

| PMA No. Docket No. | Applicant | TRADE NAME | Approval Date |
|---|---|---|---|
| P070001 FDA–2008–M–0100 (formerly 2008M–0013) | Synthes Spine, Inc. | PRODISC–C TOTAL DISC PEPLACEMENT | December 17, 2007 |
| P050045 FDA–2008–M–0182 | Dako Denmark a/s | DAKO TOP2A FISH PHARM DX KIT | January 11, 2008 |
| P060033 FDA–2008–M–0109 | Medtronic Vascular | ENDEAVOR ZOTAROLIMUS-ELUTING CORONARY STENT ON THE OVER THE WIRE (OTW), RAPID EXCHANGE (RX), OR MULTI-EXHANGE II ($MX^2$) STENT DELIVERY SYSTEM | February 1, 2008 |

## II. Electronic Access

Persons with access to the Internet may obtain the documents at *http://www.fda.gov/cdrh/pmapage.html*.

Dated: August 14, 2008.

**Daniel G. Schultz,**

*Director, Center for Devices and Radiological Health.*

[FR Doc. E8–19907 Filed 8–27–08; 8:45 am]

**BILLING CODE 4160–01–S**

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### National Institutes of Health

### Government-Owned Inventions; Availability for Licensing

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

**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.

**Identification and Characterization of Folliculin-Interacting Protein 2, FNIP2**

*Description of Technology:* The invention describes the identification and characterization of a FNIP1 homolog, folliculin-interacting protein 2 (FNIP2), that interacts with folliculin, the protein encoded by the FLCN gene, which is responsible for the Birt-Hogg-Dube' (BHD) syndrome. BHD is a dermatologic disorder associated with an increased risk for developing renal cancer, spontaneous pneumothorax and lung cysts. FNIP2 binds to the C-terminus of folliculin and to AMPK. Importantly, FNIP2 expression was elevated in renal tumors seen in BDH patients. This finding suggests that FNIP2 may serve as a biomarker for BHD.

*Applications:* Research tool; Diagnostic applications.

*Advantages:* Could facilitate the development of therapeutic drugs to treat the skin lesions and renal tumors that develop in BHD patients.

*Development Status:* Early stage of development.

*Market:* Dermatologic products; Diagnostic applications.

*Inventors:* Laura S. Schmidt *et al.* (NCI).

*Relevant Publication:* H Hasumi *et al.* Identification and characterization of a novel folliculin-interacting protein FNIP2. (2008) Gene, in press.

*Patent Status:* HHS Reference No. E–213–2008/0—Research Tool. Patent protection is not being pursued for this technology.

*Licensing Status:* Available for biological materials licensing only.

*Licensing Contact:* John Stansberry, Ph.D.; 301–435–5236; *stansbej@mail.nih.gov*.

*Collaborative Research Opportunity:* The Urologic Oncology Branch at the National Cancer Institute is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize detection methods specific for FNIP2 to be used to screen FNIP2 as a biomarker for renal cancer. This may include development of an efficient FNIP2 antibody which does not cross react with FNIP1 for immunhistochemical screening of renal tumors for FNIP2 expression. Please contact John D. Hewes, Ph.D. at 301–435–3121 or *hewesj@mail.nih.gov* for more information.

**Immunotoxins Made With Modified Cholix Toxin and Uses Thereof**

*Description of Technology:* Immunotoxins are chimeric molecules comprising an antibody targeting moiety and a toxin domain capable of killing a cell. Immunotoxins represent an important therapeutic tool for the treatment of cancer because they are able to specifically target cancer cells while ignoring healthy cells. The major drawback to immunotoxins is the development of neutralizing antibodies against the toxin portion of the immunotoxin. Many patients treated with *Pseudomonas* exotoxin A (PE) based immunotoxins develop neutralizing antibodies after the first administration. As a result, only one effective administration of a PE-based immunotoxin is often possible.

NIH inventors have created a novel immunotoxin, where the toxin portion is a truncated Cholera exotoxin (cholix toxin). Although cholix toxin retains strong functional and structural similarity to PE, neutralizing antibodies to PE do not affect the truncated cholix toxin. As a result, cholix toxin-based immunotoxins are of potential utility after a patient has developed neutralizing antibodies to PE. The ability to deliver two rounds of immunotoxins to a patient will increase the successful treatment of various diseases, including cancer.

*Application:*

• Used as an alternative toxin moiety in immunotoxins.

• Immunotoxins can be used for the treatment of various cancers, depending on the targeting antibody.

• Can be used in tandem immunotoxin therapy with immunotoxins having distinct toxin moiety, such as PE-based immunotoxins.

*Advantages:*

• Cholix toxin-based immunotoxins are not affected by neutralizing antibodies to by PE-based immunotoxins, permitting multiple rounds of immunotoxin therapy.

• Ability to target specific cells by choosing specific targeting antibodies.

*Inventors:* David J. FitzGerald and Robert J. Sarnovsky (NCI).

*Patent Status:* U.S. Provisional Application No. 61/058,872 filed 04 Jun 2008 (HHS Reference No. E–194–2008/0–US–01).

*Licensing Status:* Available for licensing.

*Licensing Contact:* David A. Lambertson, Ph.D.; 301–435–4632; *lambertsond@mail.nih.gov.*

*Collaborative Research Opportunity:* The National Cancer Institute, CCR, Laboratory of Molecular Biology is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize immunotoxins composed of cholera exotoxin. Please contact John D. Hewes, Ph.D. at 301–435–3121 or *hewesj@mail.nih.gov* for more information.

**Large Semi-Synthetic Human Antibody Domain Fragment Library**

*Description of Technology:* Human monoclonal antibodies are important for the development of inhibitors, vaccines, diagnostic and research tools. Previously a large non-immune human antibody library (15 billion ($15 \times 10^9$) clones) was constructed from the lymph nodes, spleen and peripheral blood lymphocytes of 50 donors. One antibody, isolated from this library, includes a stop codon in the light chain but was still expressed and included a functional heavy chain. The VH domain exhibits high levels of expression and high solubility even in the absence of a light chain variable domain. This VH domain was used as a framework to construct a large human VH domain library (25 billion clones) by grafting naturally occurring complementarity determining regions (CDRs) from other human antibody libraries and randomly mutating one of the CDRs. This library has been used internally for selecting anti-HIV antibodies, viruses of biodefense interest and cancer-related antigens and is available for licensing as a biological material. Several high-affinity binders have already been identified.

The antibodies generated from this library are small (e.g., about more than 14 kDa), highly stable and can be expressed at high levels as monomers. The library permits the isolation of antibodies with favorable properties: affinity, stability, solubility, high levels of expression (at low cost), low rejection rates and low toxicity.

*Applications:* Antibody discovery; Therapeutics; Diagnostics; Research Materials.

*Inventors:* Dimiter S. Dimitrov and Weizao Chen (NCI).

*Relevant Publications:*

1. W Chen, Z Zhu, Y Feng, X Xiao, DS Dimitrov. Construction of a large phage-displayed human antibody domain library with a scaffold based on a newly identified highly soluble, stable heavy chain variable domain. J Mol Biol (2008), in press.

2. P Jirholt *et al.* Exploiting sequence space: Shuffling *in vivo* formed complementarity determining regions into a master framework. Gene. 1998 Jul 30;215(2):471–476.

3. Y Reiter *et al.* An antibody single-domain phage display library of a native heavy chain variable region: Isolation of functional single-domain VH molecules with a unique interface. J Mol Biol. 1999 Jul 16;290(3):685–698.

4. E Söderlind *et al.* Recombining germline-derived CDR sequences for creating diverse single framework antibody libraries. Nat Biotechnol. 2000 Aug 18;18(8):852–856.

5. LJ Holt *et al.* Domain antibodies: Proteins for therapy. Trends Biotechnol. 2003 Nov;21(11):484–490.

6. L Riechmann and S Muyldermans. Single domain antibodies: Comparison of camel VH and camelised human VH domains. J Immunol Methods. 1999 Dec 10;231(1–2)25–38.

*Patent Status:* HHS Reference No. E–037–2008/0—Research Tool. Patent protection is not being pursued for this technology.

*Licensing Status:* Available for licensing.

*Licensing Contact:* Michael A. Shmilovich, Esq.; 301/435–5019; *shmilovm@mail.nih.gov.*

*Collaborative Research Opportunity:* The National Cancer Institute's Nanobiology Program is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize Large Semi-Synthetic Human Antibody Domain Library. Please contact John D. Hewes, PhD at 301–435–3121 or *hewesj@mail.nih.gov* for more information.

**Methods of Preventing Tissue Ischemia**

*Description of Technology:* Nitric oxide (NO) plays an important role as a major intrinsic vasodilator, and increases blood flow to tissues and organs. Disruption of this process leads to peripheral vascular disease, ischemic heart disease, stroke, diabetes, and many more significant diseases.

Researchers at the NIH have discovered that the matrix protein thrombospondin-1 blocks the beneficial effects of NO, and prevents it from dilating blood vessels and increasing blood flow to organs and tissues. Additionally, the inventors discovered that this regulation requires interaction with thrombospondin-1's cell receptor CD47. Murine studies revealed that, in the presence of NO, genetically altered mice, lacking either thrombospondin-1 or CD47, showed dramatically improved blood flow and tissue oxygenation. The inventors have also shown in both mice and pigs that by targeting thrombospondin-1 and/or CD47, blood flow can be dramatically increased to ischemic tissues. The same therapeutics also were found to protect tissues from ischemia/reperfusion injury.

Available for licensing and commercial development are:

• Compositions and methods of treating tissue ischemia and/or tissue damage due to ischemia, increasing blood vessel diameter, blood flow and tissue perfusion in the presence of vascular disease including peripheral vascular disease, atherosclerotic vascular disease and stroke.

• Compositions and methods for decreasing blood flow as in the case of cancer through mimicking the effects of thrombospondin-1 and CD47 on blood vessel diameter and blood flow.

*Applications:*

• Potential therapeutics for precise regulation of blood flow to tissues and organs.

• Efficient methods to increase tissue survival under conditions of trauma and surgery.

• Efficient methods for the treatment of elderly subjects using agents that affect thrombospondin-1 and CD47 and thereby affect tissue perfusion.

• Methods for treatment of ischemia/reperfusion injury as associated with transplant surgery.

*Market:*

• People with ischemic disease are at increased risk of heart attack (myocardial infarction), stroke and peripheral vascular disease (PVD). Ischemic heart disease attributes to

more deaths, with 24 percent in the U.S., than any other cause.

• Cerebral ischemia is the third leading cause of death after heart diseases and cancer.

• Decreased blood flow underlies a significant number of chronic diseases that account for the majority of morbidity and mortality for elderly adults in this country.

• Cancer patients and traumatic injury victims requiring reconstructive surgery.

• Burn patients requiring skin transplants.

• Organ transplant patients.

*Development Status:* Early-stage of development (*in vivo* data available in mice and pigs).

*Inventors:* Jeff S. Isenberg *et al.* (NCI).

*Patent Status:* PCT Application No. PCT/US2007/080647 filed 5 Oct 2007, which published as WO 2008/060785 on 22 May 2008 (HHS Reference No. E–227–2006/5–PCT–01).

*Licensing Status:* Available for licensing.

*Licensing Contact:* Charlene A. Sydnor, PhD; 301–435–4689; *sydnorc@mail.nih.gov.*

*Collaborative Research Opportunity:* The National Cancer Institute Center for Cancer Research, Laboratory of Pathology is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize therapeutics targeting CD47 or thrombospondin-1. Please contact John D. Hewes, PhD at 301–435–3121 or *hewesj@mail.nih.gov* for more information.

**Total Synthesis of Northebaine, Normorphine, Noroxymorphone Enantiomers and Derivatives via N-Nor Intermediates**

*Description of Technology:* A new synthetic process has been found in which nordihydrocodeinone, an early intermediate in the total synthesis of codeine and related compounds, is easily formed into a number of N-nor compounds. These N-nor compounds can be used as precursors in the formation of narcotics, narcotic antagonists, or narcotic agonist-antagonists.

The manufacture of drugs of this type, such as northebaine or normorphine, can now be done without the use of thebaine as starting material. The syntheses have fewer steps than previous methods, and also have high yields. In addition, very significant simplification of existing thebaine based processes for the manufacture of opiates can be expected.

*Applications:* Potential new methodology for the synthesis of intermediates for drugs including naloxone, naltrexone, percodan and nalbuphine.

*Market:*

• More than a quarter of Americans suffer daily pain, a condition that costs the U.S. about $60 billion a year in lost productivity.

• Americans spent about $2.6 billion in over-the-counter pain medications and another nearly $14 billion on outpatient analgesics in 2004.

• Worldwide, nearly 300 million people are believed to suffer from chronic pain.

*Inventors:* Kenner C. Rice *et al.* (NIDDK)

*Patent Status:*

HHS Reference No. E–012–1986/1—

• Australian Patent 642447 issued 15 Feb 1994.

• Japanese Patent 2694156 issued 12 Sept 1997.

• Canadian Patent 2067200 issued 30 Jun 1998.

• European Patent 0496830 issued 31 Mar 1999 in Austria, Switzerland, Germany, Denmark, Greece, Luxembourg, Spain, Belgium, The Netherlands, Sweden, France, Italy and United Kingdom.

HHS Reference No. E–012–1986/2—

• United States Patent 5,668,285 issued 16 Sept 1997.

*Licensing Status:* Available for licensing.

*Licensing Contact:* Charlene A. Sydnor, PhD; 301–435–4689; *sydnorc@mail.nih.gov.*

Dated: August 18, 2008.

**Richard U. Rodriguez,**

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

[FR Doc. E8–19914 Filed 8–27–08; 8:45 am]

**BILLING CODE 4140–01–P**

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### National Institutes of Health

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**Botulinum Toxoid**

*Description of Technology:* Vaccination is the only approach that can be used to prevent botulism. A pentavalent botulinum toxoid comprised of formalin-detoxified botulinum neurotoxin (BoNT) BoNT/A, B, C, D and E hemagglutinin (Hmg) complexes has been used to immunize laboratory and military personnel since 1961, but this has never been licensed by the United States Food and Drug Administration (FDA). Vaccination immediately after toxin exposure has no protective benefit because the immune response is relatively slow compared to the rate of intoxication. The only treatment that is available upon intoxication is antibody therapy, which entails the injection of equine-derived botulinum antitoxin (BAT) or human-derived botulinum immunoglobulin (BIG) to remove toxin from the blood. Antibody therapy does not alleviate symptoms of botulism, but can limit the amount of toxin that enters nerve terminals and thus may lessen the severity and shorten the duration of paralysis.

Since a vaccine can be used to either protect a human population or produce a BAT or BIG product, it is important to have reliable methods to evaluate the antigenic integrity of botulinum vaccines. An *in vitro* assay that can serve in this capacity would be useful for evaluating the consistency of the antigen throughout the manufacturing process, as well as generating data that may reduce *in vivo* testing.

Available for licensing are a variety of new toxoids useful as botulinum vaccine antigens, for BAT or BIG production, or for development of tests to evaluate antigenicity of botulinum vaccines. The toxoids of the invention are derived from the Serotype A and B 150 kDa neurotoxin proteins. The resulting toxoids are antigenically identical to the native toxin as measured by inhibition ELISA in spite of showing