site. Submit a single copy of electronic comments or two paper copies of any mailed comments, except that individuals may submit one paper copy. Comments are to be identified with the docket number found in brackets in the heading of this document. The guidance, notices, and received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

IV. Electronic Access

Persons with access to the Internet may obtain the document at either *http://www.fda.gov/cder/guidance/index.htm* or *http://www.regulations.gov*.

Dated: May 27, 2009.

Jeffrey Shuren,

Associate Commissioner for Policy and Planning.

[FR Doc. E9–13261 Filed 6–5–09; 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.

Interactive Venn Diagram Software Designed for Microarray Analysis

Description of Technology: Multiple conditions from any source, but designed for experiments involving microarrays, will produce (significant gene lists for arrays) lists from each condition, thus multiple lists. This Java® based software provides investigators with a method of displaying multiple conditions in a single graphic along with producing a text output of genes that are the product of these conditional intersections along with each conditions unique list. A standard Venn diagram is limited to only display three (3) comparisons; this software can display any number of comparisons and will automatically create lists from all intersections even if not able to be displayed along with each conditions unique list.

Applications:

- Microarray analysis.
- Genomics.
- Bioinformatics.
- Any environment creating multiple lists (Business, Accounting, Inventory Control, etc.).

Inventor: Daniel E. Sturdevant (NIAID).

Patent Status: HHS Reference No. E–189–2009/0—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.*

Axenically-Produced *Coxiella burnetii* and Methods for Producing Axenic *Coxiella burnetii*

Description of Technology: Coxiella burnetii is the causative agent of Q (Query) fever. Currently, there is a need for a safe Q fever vaccine. It is anticipated that axenically-produced *C. burnetii,* which is free of host cell related impurities, could provide either the basis for a whole-cell Q fever vaccine or advance the development of a safe recombinant Q fever vaccine. Currently, there are no licensed Q-fever vaccines except for a whole-cell, formalin inactivated, vaccine which is available in Australia (Q–Vax). Individuals with a previous exposure to *C. burnetii* may, however, have a severe allergic reaction to this vaccine and other individuals may experience a headache or flu-like symptoms after vaccination. It is anticipated that axenically-produced *C. burnetii* could provide the basis for a less reactogenic whole-cell vaccine or facilitate the development of a recombinant vaccine that does not cause an allergic reaction. Additionally, the inability to propagate obligate intracellular pathogens under axenic (host cell-free) culture conditions imposes severe experimental constraints that have negatively impacted progress in understanding pathogen virulence and disease mechanisms.

Q fever is a zoonotic disease and farm animals, pets, and rodents are significant reservoirs for *C. burnetii. C. burnetii* persists in the soil for a long time and typically humans are exposed to Q fever by the inhalation of the bacterium deposited with animal waste such as urine, feces, and amniotic fluid. The epidemiology of Q fever is diverse and the disease does not discriminate between developed and developing countries. Additionally, urban outbreaks have been known to occur due to windborne *C. burnetii. C. burnetii* is listed as a select agent by the Department of Health and Human Services (HHS) because of its potential as an agent of bioterrorism. Deployed military personnel are also at risk of contracting Q fever and thousands of cases of Q fever have been reported among military personnel since the disease was first reported in the 1930s.

Advantages:

- The ability to propagate, previously unpropagatable, *C. burnetii* without a hostcell.
- The ability to study *C. burnetii* virulence using axenic conditions or conditions free of host cell-related impurities.
- This technology is ready for use in drug/vaccine discovery, production, and development.
- Potential licensees of this invention include companies that are: 1) seeking vaccine production platforms based on host cell-free (axenic) media, 2) seeking to develop recombinant vaccines for obligate, intracellular, bacteria; or 3) seeking to lower costs and ease scale-up would be potential licensees of this technology.

Development Status: This technology has been demonstrated with *C. burnetii.* Currently, the inventors are testing this technology for support of axenic growth of other obligate, intracellular, bacteria of public health significance.

Inventors: Robert A. Heinzen, Anders Omsland, Diane C. Cockrell, Dale Howe (NIAID).

Publication: A Omsland et al. Host cell-free growth of the Q fever bacterium *Coxiella burnetii*. Proc Natl Acad Sci USA. 2009 Mar 17;106(11):4430–4434.

Patent Status: U.S. Provisional Application No. 61/154,330 filed 20 Feb 2009 (HHS Reference No. E–114–2009/0–US–01).

Licensing Status: Available for licensing.

Licensing Contact: Peter A. Soukas, J.D.; 301–435–4646; *soukasp@mail.nih.gov.*

Self-Expanding Stent for Valve Replacement

Description of Technology: Aortic stenosis and aortic regurgitation are the most common types of aortic valvular diseases. Such diseased aortic valves in the body are traditionally replaced with valve prosthesis by an open surgical implantation. Available for licensing and commercial development is intellectual property covering stents for use with valve prostheses. One possible embodiment of the invention includes a self-expandable stent with an elastic tubular latticework having radial and longitudinal direction. The stent geometry and mechanical parameters provide more anatomically-correct placement and the flexible scaffolding of the valve (using an interconnected four-sided polygons and longitudinal rods comprising a self-expanding stent with a plurality of struts connecting a plurality of rods) allow for secure implantation with adaptable apposition of the prosthesis in the aorta.

Applications: Cardiac Surgery; Cardiology; Surgery; Stent implantation.

Inventors: Keith Horvath, Dumitru Mazilu, Ming Li (NHLBI).

Publications:

1. M Li, D Mazilu, KA Horvath. Robotic system for transapical aortic valve replacement with MRI guidance. Med Image Comput Comput Assist Interv Int Conf Med Image Comput Comput Assist Interv. 2008;11(Pt 2):476–484.

2. KA Horvath, M Li, D Mazilu, MA Guttman, ER McVeigh. Real-time magnetic resonance imaging guidance for cardiovascular procedures. Semin Thorac Cardiovasc Surg. 2007 Winter;19(4):330–335. Review.

Patent Status: U.S. Provisional Application No. 61/172,568 filed 24 Apr 2009 (HHS Reference No. E–337–2008/0–US–01).

Licensing Status: Available for licensing.

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

Collaborative Research Opportunity: The National Heart, Lung, and Blood Institute, Cardiothoracic Surgery Research Program, is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize this technology. Please contact Peg Koelbe at 301–594–4095 or *koelblep@nhlbi.nih.gov* for more information.

Method of Diagnosing Multidrug Resistant Tuberculosis

Description of Technology: The invention can be used to develop tests that are much more rapid than conventional tests for determining drug resistance. It relates to the discovery that a putative gene of *Mycobacterium tuberculosis* (MTb) with no previously identified function is responsible for the ability of the bacteria to activate a class of second line thioamide drugs used for MTb infections. The gene, termed ''etaA,'' codes for the synthesis of a monooxygenase, the enzyme responsible for the oxidative activation of the drugs. Mutation in the etaA gene leads to the expression of mutated, inactivated enzyme, thus resulting in thioamide drug-resistant bacteria. The significance of this discovery is that now, resistance to the class of thioamide drugs in clinical isolates can be identified in a relatively short time, eliminating the need to perform lengthy culturing procedures.

The invention claims test methods for determining resistance to thioamide drugs by detecting gene mutation. These include (a) amplifying the etaA gene or a portion of it containing the mutation, with a set of primers which provide amplified product, and sequencing the amplified product to compare the sequence with a known sequence of the wild-type etaA; a difference in sequence patterns indicates mutation; (b) subjecting the amplified gene product to digestion by restriction enzymes and comparing the cleaved DNA gel pattern to the one obtained from digestion of the wild-type etaA gene; a difference indicates mutation in etaA; and (c) detecting the mutations by probe hybridization techniques, where the amplified product hybridizes to a nucleic acid of known sequence under stringent conditions, and the hybridized product is detected. In addition to the above, the invention proposes other detection methods such as commonly used for SNPs. Other methods claimed in the invention are immunoassay (*i.e.,* ELISA) for the etaA gene product or mutated versions of it, or immunoassay and chemical analysis of the drug metabolites, whereby the absence of the metabolites indicates gene mutation and impaired activating ability.

Applications: Infectious diseases, diagnostics (bacterial); Infectious diseases, therapeutics (anti-bacterial).

Advantages: Novel methods for diagnosing multidrug resistant tuberculosis that are much more rapid than conventional tests.

Inventors: Clifton E. Barry III (NIAID), Andrea E. DeBarber (NIAID), Khisimuzi Mdluli (NIAID), *et al.*

Publication: AE DeBarber *et al.* Ethionamide activation and sensitivity in multidrug-resistant Mycobacterium tuberculosis. Proc Natl Acad Sci U S A. 2000 Aug 15;97(17):9677–9682.

Patent Status:

- U.S. Patent No. 6,905,822 issued 14 Jun 2005 (HHS Reference No. E–093–2000/0–US–02).
- U.S. Patent Application No. 11/058,484 filed 14 Feb 2005 and allowed 17 Feb 2009 (HHS Reference No. E–093–2000/0–US–03).

Licensing Status: Available for licensing.

Licensing Contact: RC Tang, JD, LLM; 301–435–5031; *tangrc@mail.nih.gov*

A Novel Chimeric Protein for Prevention and Treatment of HIV Infection

Description of Technology: This invention relates to bifunctional fusion proteins effective in HIV neutralization. Specifically, the invention is a genetically engineered chimeric protein composed of a soluble extracellular region of human CD4 (sCD4) attached via a flexible polypeptide linker to a single-chain construct of a human monoclonal antibody directed against a CD4-induced, highly conserved gp120 determinant involved in co-receptor interaction and virus entry. Mechanistically, the binding of the sCD4 moiety to the HIV gp120 Env glycoprotein induces a conformational change that enables the antibody moiety to bind, thereby blocking Env function and virus entry. This novel design provides the protein with unique characteristics that enable its extremely strong binding to gp120, thus rendering it a potential effective antiviral agent against HIV. Recent studies indicate that this novel bispecific protein displays extremely broad neutralizing activity against genetically diverse primary HIV–1 isolates, with breadth much greater than previously described (Dey *et al.* J. Virology 2003). The potency is generally at least 10-fold greater than the best described HIV–1 neutralizing monoclonal antibodies, and the protein is highly active against many HIV–1 isolates that are refractory to neutralization by these antibodies. Importantly, the protein is composed of almost entirely human sequences.

The chimeric protein of this invention has considerable potential for prevention of HIV–1 infection, both as a topical microbicide and as a systemic agent to protect during and after acute exposure (*e.g.* vertical transmission, post exposure prophylaxis). It also has potential utility for treatment of chronic infection, including gene therapy strategies involving hematopoietic stem cells and/or viral vectors. Such proteins, nucleic acid molecules encoding them, and their production and use in

preventing or treating viral infections are claimed in the patents issued for this invention.

Applications:

• Prophylactic and/or therapeutic treatment for HIV infection.

• Topical microbicide treatment to protect against HIV infection.

• Imaging of HIV infected cells in tissues.

Advantages:

• High neutralization efficiency due to unique bifunctional binding characteristics.

• Potentially minimally immunogenic or toxic (human sequences and possibly low treatment doses).

• Broad neutralizing activity.

• Mechanism of action less susceptible to resistance.

Development Status:

• Reproducible production and scale-up of chimeric protein has been demonstrated.

• Potent and broad neutralization of genetically diverse HIV–1 clinical isolates was demonstrated.

Market: The race to develop effective antiviral strategies against HIV infection is ongoing. The problems exhibited by conventional drugs (*i.e.* toxicity and resistance) have triggered the pursuit of alternative approaches to HIV/AIDS prevention and treatment. One of the new approaches is the development of neutralizing antibodies against the HIV envelope proteins. This approach has not yet yielded any commercially viable treatment. It is believed that the approach presented in the subject invention will circumvent many of the shortcomings of the existing drugs and other pursued approaches. If this approach is successful the commercial rewards will be huge because of the global magnitude of HIV epidemics.

Inventor: Edward A. Berger (NIAID).

Publication: B Dey, CS Del Castillo, EA Berger. Neutralization of human immunodeficiency virus type 1 by sCD4–17b, a single-chain chimeric protein, based on sequential interaction of gp120 with CD4 and coreceptor. J Virol. 2003 March;77(5):2859–2865.

Patent Status:

HHS Reference No. E–039–1999/0—

• U.S. Patent No. 7,115,262, issued 03 October 2006.

• U.S. Application No. 11/535,957, filed 27 September 2006, published 18 October 2007 as 20070243208.

• Australian Patent No. 765218, issued 30 July 2003.

• Applications pending in Canada, France, Germany, Great Britain, Italy, Japan, Spain.

Licensing Status: Available for licensing.

Licensing Contacts: Uri Reichman, Ph.D, MBA; 301–435–4616; *ur7a@nih.gov*; RC Tang, JD, LLM; 301–435–5031; tangrc@mail.nih.gov.

Collaborative Research Opportunity: The NIAID Office of Technology Development is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize ''A Novel Chimeric Protein for Prevention and Treatment of HIV Infection.'' Please contact Rick Williams at 301–402–0960 for more information.

Dated: June 1, 2009.

Richard U. Rodriguez,

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

[FR Doc. E9–13284 Filed 6–5–09; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2009–D–0217]

Guidance for Industry on Medication Guides—Adding a Toll-Free Number for Reporting Adverse Events; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a guidance for industry entitled ''Medication Guides—Adding a Toll-Free Number for Reporting Adverse Events.'' Beginning July 1, 2009, manufacturers of prescription drug products approved under the Federal Food, Drug, and Cosmetic Act (the act) that are required to have a Medication Guide must add a verbatim statement to their Medication Guides containing FDA's toll-free number for reporting side effects. These manufacturers are also required to report to FDA that they have complied with this requirement. This guidance explains what statement to add to Medication Guides, where to add it, and how to notify the agency that such a statement has been added.

DATES: Submit written or electronic comments on agency guidances at any time.

ADDRESSES: Submit written requests for single copies of this draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 2201, Silver Spring, MD 20993–0002. Send one self-addressed adhesive label to assist that office in processing your requests. Submit written comments on the draft guidance to the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to *http://www.regulations.gov*. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the guidance document.

FOR FURTHER INFORMATION CONTACT: Nancy Clark, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Silver Spring, MD 20993, 301–796–5400, *Nancy.Clark@fda.hhs.gov*.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a guidance for industry entitled ''Medication Guides—Adding a Toll-Free Number for Reporting Adverse Events.'' On September 27, 2007, the President signed into law the Food and Drug Administration Amendments Act (FDAAA) (Public Law 110–85). Among other things, FDAAA reauthorized the Best Pharmaceuticals for Children Act (BPCA) (Public Law 107–109). When enacted in 2001, the BPCA directed FDA to issue a final rule requiring the labeling of each human drug product for which an application is approved under section 505 of the act (21 U.S.C. 355) to include: (1) A toll-free number maintained by FDA for the purpose of receiving reports of adverse events regarding drugs and (2) a statement that the number is to be used for reporting purposes only, not to receive medical advice. The BPCA stated that the final rule must reach the broadest consumer audience and minimize the cost to the pharmacy profession. As required, FDA issued a proposed rule entitled ''Toll-Free Number for Reporting Adverse Events on Labeling for Human Drug Products'' (69 FR 21778, April 22, 2004), which would require, among other things, that a side effects statement be included in FDA-approved Medication Guides for drug products approved under section 505 of the act.

FDA received 22 comments on this proposed rule and was in the process of analyzing the comments and conducting research on consumer comprehension of the side effects statement when FDAAA was enacted. Section 502(f) of FDAAA stated that ''the proposed rule * * * entitled 'Toll-Free Number for Reporting Adverse Events on Labeling for Human Drug Products' * * * shall take effect on January 1, 2008,'' unless FDA issues a final rule before that date. FDA did not issue a final rule by January 1, 2008, so