be made. Informed consent, on the other hand, apprises potential research subjects of the possible risks and benefits associated with participating in the clinical investigation and, when executed, indicates their willingness to participate in the clinical investigation and their understanding of those risks and benefits. The Privacy Rule permits but does not require clinical investigators to combine an HIPAA authorization with informed consent documents, known as a compound authorization (see 45 CFR 164.508(b)(3)).

FDA and the HHS Secretary received requests for clarification of IRBs' responsibilities to review and approve stand-alone HIPAA authorizations under the Privacy Rule, Federal regulations governing human subject protection and IRBs (see 45 CFR part 46 and parts 50 and 56 (21 CFR parts 50 and 56)), and international guidelines (see, for example, International Conference on Harmonisation (ICH) Good Clinical Practice guidelines (E6)). The requests expressed concern that when the Privacy Rule went into effect, clinical investigations might be impeded because IRBs would be backlogged with requests to review thousands of stand-alone HIPAA authorizations. The requests further stated that some IRBs would halt enrollment in clinical investigations pending their review of these stand-alone HIPAA authorizations.

In response, the Office of Civil Rights, HHS, issued a letter, dated April 15, 2003, clarifying that IRBs are not required to review and approve stand-alone HIPAA authorizations under the Privacy Rule, HHS Protection of Human Subjects Regulations at 45 CFR part 46, ICH guidelines, or FDA regulations, so long as an IRB's written procedures, adopted under § 56.108(a), do not require such review and approval. The letter also announced FDA's intent to publish guidance on this subject, in accordance with its good guidance practice regulations.

FDA is issuing this guidance to address those cases in which IRBs have adopted written procedures that would require them to review and approve stand-alone HIPAA authorizations. Under § 56.108(a), IRBs must follow their written procedures. The guidance announces FDA's intention to exercise ongoing enforcement discretion with respect to the requirements of § 56.108(a) to the extent that an IRB's written procedures require the review and/or approval of stand-alone HIPAA authorizations. FDA is exercising this discretion in order to encourage IRBs to permit the continued enrollment of subjects in clinical investigations without IRBs' prior review and approval of stand-alone HIPAA authorizations. FDA believes that enrollment in well-designed and well-conducted clinical investigations should not be interrupted for the purpose of IRB review and approval of stand-alone HIPAA authorizations. Accordingly, FDA does not intend to take enforcement actions against IRBs that decide not to review stand-alone HIPAA authorizations even though the IRB's written procedures would otherwise require this review and/or approval. FDA's exercise of enforcement discretion in these limited circumstances is intended to allow important studies to proceed in the best interests of the public health.

This guidance is being issued consistent with FDA's good guidance practices regulation § 10.115 (21 CFR 10.115). This guidance document represents the agency's current thinking on IRBs' responsibilities under FDA regulations for reviewing and approving stand-alone HIPAA authorizations. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if it satisfies the requirements of the applicable statutes and regulations.

II. Comments

FDA is issuing this document as a final guidance that will be implemented upon posting on FDA's Web site. In accordance with § 10.115(g)(2) and (g)(3), FDA is implementing this guidance prior to seeking public comment because the agency has determined that this guidance is needed in conjunction with the HHS Office of Civil Rights guidance to help ensure that ongoing clinical trials are not halted while IRBs review HIPAA stand-alone authorizations, and therefore, prior public participation is not feasible or appropriate. However, FDA will review comments received after issuance of the guidance and revise the document when appropriate.

Interested persons may, at any time, submit written or electronic comments to the Division of Dockets Management (see **ADDRESSES**) regarding this guidance document. Two paper copies of mailed comments are to be submitted, except individuals may submit one copy. Comments should be identified with the docket number found in the brackets in the heading of this document. A copy of the document and received comments are available for public examination in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

III. Electronic Access

Persons with access to the Internet may obtain the document at either *http://www.fda.gov/oc/gcp/guidance.html* or *http://www.fda.gov/ohrms/dockets/default.htm*.

Dated: October 31, 2003.

Jeffrey Shuren,

Assistant Commissioner for Policy.

[FR Doc. 03–28044 Filed 11–6–03; 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, DHHS.

ACTION: Notice.

SUMMARY: The invention listed below is owned by an agency of the U.S. Government and is 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 application 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 application.

Eosinophil-Derived Neurotoxin, an Antimicrobial Protein With Ribonuclease Activity, Is an Immunostimulant

De Yang *et al.* (NCI).

U.S. Provisional Patent Application Nos. 60/466,797 and 60/466,796, filed 29 Apr 2003 (DHHS Reference Nos. E–175–2003/0–US–01 and E–191–2003/0–US–01).

Licensing Contact: Brenda Hefti; 301/435–4632; *heftib@mail.nih.gov.*

Eosinophil-derived neurotoxin (EDN) has in vitro anti-viral activity that is dependent on its ribonuclease activity. This invention discloses that EDN is a selective chemoattractant and activator of dendritic cells, resulting in dendritic

cell migration, maturation, and a production of a wide variety of cytokines. Based on these potent chemotactic and activating effects on dendritic cells, EDN might be useful as a clinical immunoadjuvant for the promotion of immune responses to specific antigens of tumors or pathogenic organisms.

Protein Kinase C Inhibitor, Related Composition, and Method of Use

Shaomeng Wang, Peter Blumberg (NCI), Nancy Lewin (NCI).
U.S. Provisional Patent Application No. 60/451,214 filed 28 Feb 2003 (DHHS Reference No. E–073–2003/0–US–01).
Licensing Contact: Brenda Hefti; 301/435–4632; *heftib@mail.nih.gov.*

Protein kinase C is a critical component in cellular signaling, involved in cellular growth, differentiation, and apoptosis. It has been identified as a promising therapeutic target for cancer, diabetic retinopathy, and Alzheimer's disease, among other indications.

This invention relates to lead compounds that can inhibit protein kinase C isoforms through disruption of their C1 domains. The inventors also found that these compounds possess isoform selectivity, an important feature for therapeutic specificity. Finally, although the disclosed compounds are previously known molecules, novel structures are described in the invention that have further improved specificity.

Applications for the HMGN1 Pathway

Michael Bustin (NCI).
U.S. Provisional Patent Application No. 60/455,728 filed 17 Mar 2003 (DHHS Reference No. E–208–2002/0–US–01).
Licensing Contact: Brenda Hefti; 301/435–4632; *heftib@mail.nih.gov.*

HMGN1 is a protein that binds to nucleosomes, changes chromatin structure and affects transcription, and the expression of this protein changes during differentiation. Mice lacking this protein have increased growth capacity of several skin components, including epidermis, epidermal appendages, and dermis. Conceivably, this change could be related to an alteration of stem cell differentiation or to cell cycling events. The current invention relates to interference with this pathway, which might lead to increased stem cell differentiation and increased hair cycling and growth in humans as well. This invention might be useful to increase hair growth, enhance wound healing for epidermal and dermal wounds, and enhance stem cell populations for tissue regeneration, gene targeting, or gene therapeutic indications.

Novel Stable Anti-CD22 Antibodies

Susanna Rybak, Juergen Krauss, Michaela Arndt (NCI).
U.S. Provisional Application No. 60/387,306 filed 06 Jun 2002 (DHHS Reference No. E–055–2002/0–US–01); PCT Patent Application PCT/US03/18201 filed 06 Jun 2003 (DHHS Reference No. E–055–2002/0–PCT–02).
Licensing Contact: Brenda Hefti; 301/435–4632; *heftib@mail.nih.gov.*

The current invention relates to engineered LL2 single chain antibodies possessing improved and/or unexpected properties. The first embodiment includes engineered single chain antibodies that have enhanced stability. Specific VH and VL residues were identified which might contribute to the instability, and these were substituted to create scFv variants with improved stability and biological half-life. In the second embodiment, an LL2 single chain Fv antibody was engineered with no linker between the VH and VL sequences. The antibody exhibited the surprising property of acting as a monomer (rather than a trimer or tetramer) and retained specific binding to CD22. This invention might be useful as a general method to produce therapeutic antibodies or immunoconjugates more easily, and for such antibodies or immunoconjugates to be more stable *in vivo.*

Dated: October 30, 2003.

Steven M. Ferguson,

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

[FR Doc. 03–28054 Filed 11–6–03; 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.

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Isolation of Hybridomas Producing Monoclonal Antibodies (MAbs) Inhibitory to Human CYP2J2

Dr. Darryl Zeldin (NIEHS), Dr. Harry Gelboin (NCI), *et al.*
DHHS Reference No. E–337–2003/0—Research Tool.
Licensing Contact: Marlene Shinn-Astor; 301/435–4426; *shinnm@mail.nih.gov.*

Cytochromes P450 catalyze the NADPH-dependent oxidation of arachidonic acid to various eicosanoids found in several species. The eicosanoids are biosynthesized in numerous tissues including pancreas, intestine, kidney, heart, and lung where they are involved in many different biological activities.

The NIH announces three specific monoclonal antibodies that strongly inhibit and/or immunoblot the human cytochrome P450 2J2 (CYP2J2). MAb 6–5–20–8 selectively inhibits CYP2J2-mediated arachidonic acid metabolism by more than 80% and also immunoblots the enzyme. MAb 6–2–16–1 also selectively inhibits arachidonic acid metabolism by more than 80%, but does not immunoblot the enzyme. MAb 5–3–2–2 is not inhibitory, but selectively immunoblots the enzyme. These antibodies can be used to identify and quantify inter-individual variation in physiological functions and to study pharmacological drug metabolism in various tissues.

This research is also described in: Sun *et al.*, *Circ. Res.* 90: 1020–1027, 2002; King *et al.*, *Mol. Pharmacol.* 61: 840–852, 2002; Yang *et al.*, *Mol. Pharmacol.* 60: 310–320, 2001; Zeldin, *J. Biol. Chem.* 276: 36059–36062, 2001; Node *et al.*, *J. Biol. Chem.* 276: 15983–15989, 2001; Node *et al., Science* 285: 1276–1279, 1999; Wu *et al., J. Biol. Chem.* 271: 3460–3468.

TNF-α Converting Enzyme Inhibitory Agents and Stimulatory Agents

Dr. Stewart Levine *et al.* (NHLBI).
U.S. Provisional Patent Application filed 24 Sep 2003 (DHHS Reference No. E–208–2003/0–US–01).
Licensing Contact: Marlene Shinn-Astor; 301/435–4426; *shinnm@mail.nih.gov.*