Dated: July 12, 1999.

**Margaret M. Dotzel,**

*Acting Associate Commissioner for Policy Coordination.*

[FR Doc. 99–18234 Filed 7–16–99; 8:45 am]

**BILLING CODE 4160–01–F**

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

**[Docket No. 99N–1833]**

### SoloPak Laboratories, Inc.; Withdrawal of Approval of 1 New Drug Application and 38 Abbreviated New Drug Applications; Correction

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Notice; correction.

**SUMMARY:** The Food and Drug Administration (FDA) is correcting a notice that appeared in the **Federal Register** of June 21, 1999 (64 FR 33097). The document announced the withdrawal of approval of 1 new drug application (NDA) and 38 abbreviated new drug applications (ANDA's) held by SoloPak Laboratories, Inc. The document omitted language explaining that the sponsor voluntarily removed the products from the market because of discrepancies concerning the data submitted to support continued approval of the applications. This document corrects that omission.

**EFFECTIVE DATE: JULY 19, 1999.**

**FOR FURTHER INFORMATION CONTACT:** Olivia A. Pritzlaff, Center for Drug Evaluation and Research (HFD–7), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–594–2041.

In FR Doc. 99–15581, appearing on page 33097 in the **Federal Register** of Monday, June 21, 1999, the following correction is made: Onpage 33098, immediately preceding the table, add the following two paragraphs to read as follows:

Recently, FDA became aware of discrepancies concerning the data submitted to support continued approval of the following ANDA's held by SoloPak:

ANDA 88–457; Heparin Lock Flush Solution USP, 10 units/milliliter (mL); and

ANDA 88–519; Phenytoin Sodium Injection USP, 50 milligrams (mg)/mL.

After careful review of inspectional findings, the agency determined that there was sufficient justification to initiate proceedings to withdraw approval of the two products listed above. SoloPak was notified in writing of the determinations and, in accordance with § 314.150(d) (21 CFR 314.150(d)), was offered an opportunity to permit FDA to withdraw the applications. Subsequently, in letters dated December 15, 1998, and March 31, 1999, SoloPak requested withdrawal under § 314.150(d) of the applications listed in the following table, thereby waiving its opportunity for a hearing.

Dated: July 8, 1999.

**Janet Woodcock,**

*Director, Center for Drug Evaluation and Research.*

[FR Doc. 99–18235 Filed 7–16–99; 8:45 am]

**BILLING CODE 4160–01–F**

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

### Statement of Organization, Functions, and Delegations of Authority; Correction

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Notice; correction.

**SUMMARY:** The Food and Drug Administration (FDA) is correcting a notice that appeared in the **Federal Register** of July 6, 1999 (64 FR 36361). The document announced that FDA is being restructured to create a more streamlined and efficient Office of the Commissioner that will provide leadership without compromising programmatic effectiveness. The restructuring document, which became effective on June 20, 1999, was published with an inadvertent error. This document corrects that error.

**FOR FURTHER INFORMATION CONTACT:** LaJuana D. Caldwell, Office of Policy (HF–27), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–7010.

In FR Doc. 99–17019, appearing on page 36361 in the **Federal Register** of Tuesday, July 6, 1999, the following correction is made:

1. On page 36362, in the first column, in the fourth paragraph, beginning in the twelfth line ''Center for Devices and Radiological Health'' is corrected to read ''Center for Drug Evaluation and Research.''

Dated: July 12, 1999.

**Margaret M. Dotzel,**

*Acting Associate Commissioner for Policy Coordination.*

[FR Doc. 99–18236 Filed 7–16–99; 8:45 am]

**BILLING CODE 4160–01–F**

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### National Institutes of Health

### Availability of New E-mail Service for Government-Owned Inventions Available for Licensing and Cooperative Research Opportunities

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

**ACTION:** Notice.

**SUMMARY:** The Office of Technology Transfer (OTT), National Institutes of Health desires to announce the availability of a new e-mail service concerning government-owned inventions available for licensing and cooperative research opportunities.

OTT has initiated a Techbrief e-mail list service to inform companies, institutions and anyone interested in biomedical technology transfer about NIH and FDA technologies available for licensing, as well as Cooperative Research and Development (CRADA) opportunities with PHS scientists.

**ADDRESSES:** Persons may subscribe to the list at no charge upon request to: Dr. George Keller, Technology Licensing Specialist, Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, MD 20852 (telephone: (301) 496–7735, extension 246; fax: (301) 402–0220, e-mail: gk40j@nih.gov). Please include: company affiliation, title, address, phone and fax numbers, and e-mail address. A convenient form is available at the OTT web site: http://www.nih.gov/od/ott/.

Dated: July 12, 1999.

**Jack Spiegel, PhD.,**

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

[FR Doc. 99–18373 Filed 7–16–99; 8:45 am]

**BILLING CODE 4140–01–M**

## 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 agencies 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.

**Quantitative Assessment of Changes in Tissue Status in Disease, Development, Aging, or Degeneration Using Diffusion Tensor Magnetic Resonance Imaging**

Peter J. Basser (NICHD), Sinisa Pajevic (CIT)

DHHS Reference No. E–192–99/0 filed 21 May 1999

Licensing Contact: John Fahner-Vihtelic; 301/496–7735, ext. 270; e-mail: jf36z@nih.gov

This invention significantly enhances the quality and utility of diffusion tensor magnetic resonance imaging (DT–MRI) data. The patent application for the invention describes quantitative statistical methodology to extract novel clinical and biological information from DT–MRI data. These parametric and non-parametric statistical methods help distinguish changes in tissue state from background noise inherent in all MRI measurements. The invention also includes hypothesis tests to determine the statistical significance of changes observed in MRI ''stains'' (e.g., the Trace of the diffusion tensor, Trace (D), and the mean apparent diffusion coefficient, ADC), which are widely used in the diagnosis of stroke. Further, this invention describes how to detect systematic artifacts in each pixel of a diffusion weighted image (e.g., artifacts caused by patient motion). Indeed, this new statistical methodology for analyzing and interpreting diffusion tensor MIR data should improve the efficacy of drug screening studies, as well as streamline multi-site and longitudinal studies designed to assess the safety and efficacy of drugs undergoing clinical evaluation.

**Magnetic Resonance Tracking of Magnetically Labeled Cells**

J. Bulte, I. Duncan, and J. Frank (CC)

DHHS Reference No. E–013–99/0 filed 21 May 1999

Licensing Contact: Leopold J. Luberecki, Jr., J.D.; 301/496–7735, ext. 223; e-mail: LL87A@NIH.GOV

Demyelination is a common pathological finding in human neurological diseases and frequently persists as a result of failure of endogenous repair. It has recently been demonstrated that transplanted oligodendrocytes and their precursor cells can remyelinate axons. The survival, acute dispersion, and migratory pattern of these cell lines is crucial for the extent and limit of remyelination. Presently, the assessment of survival and migratory pattern is unpredictable and requires invasive, irreversible procedures. This invention describes a real time in vivo imaging of neural cells using nuclear magnetic resonance (NMR) imaging. The technique involves an ex vivo delivery of the contrasting agent into the target cells, which are then either injected or transplanted into the subject. These target cells can then be non-invasively monitored for their translocation. This technique has been successfully applied to the imaging of spinal cord samples and has potential for monitoring the treatment of neurodegenerative diseases and for monitoring the successful delivery and location of genetically modified cells for treatment of Parkinson's Disease. It may also have possible applications in the monitoring of cellular differentiation.

**Oligodeoxynucleotide and Its Use To Induce an Immune Response**

Dennis Klinman (FDA), Daniela Verthelyi (FDA), Kenji Ishii (NINDS)

Serial No. 60/128,898 filed 12 Apr 1999

Licensing Contact: Peter Soukas; 301/496–7056, ext. 268; e-mail: ps193c@nih.gov

This invention comprises oligodeoxynucleotides (ODNs) having at least 10 nucleotides with an unmethylated central CpG motif that are immunostimulatory in humans. The inventors have shown that the various ODNs of this invention (having different CpG notifs and backbones) induce immune responses from human non-B and B cells. The motif that stimulates non-B cells induces production and release of multiple T cell cytokines and chemokines; specifically, the Th1 cytokine IFN–γ, which facilitates the development of a cytotoxic T cell response. In contrast, the motif that stimulates B cells induces production and release of various cytokines, including, but not limited to IL–6, which supports a Th2 antibody response. The inventors have generated in vitro and ex vivo data showing the ODNs of this invention have utility in precisely regulating the type and magnitude of the immune response in human cells. The present invention has multiple therapeutic uses, including but not limited to cancer, vaccine adjuvants, treating autoimmune disorders and immune system deficiencies, as well as an anti-infective agent and in combination with any antisense therapy.

**Methods of Treating Colitis Using STAT–4 Antisense Oligonucleotide**

Warren Strober, Ivan Fuss, Markus Neurath, Atsushi Kitani (NIAID)

Serial No. 60/125,877 filed 24 Mar 1999

Licensing Contact: Richard U. Rodriguez; 301/496–7056, ext. 287; e-mail: rr154z@nih.gov

This invention described in this patent application relates to compositions and methods which can be used to treat diseases such as Crohn's disease, a form of inflammatory bowel disease. This disease has been linked to the interferon gamma (IFNγ) response induced by interleukin 12 (IL–12) production. Recent work has shown that IFNγ production is also a product of the activation of the signal transduction molecule Signal Transducer and Activator of Transcription-4 (STAT–4). Therefore, regulation of IFNγ production rather than IL–12 production may be a more effective means of treatment.

The methods and compositions described in this patent application are antisense oligonucleotides derived from STAT–4 which inhibit the STAT–4 pathway. The antisense compositions have been studied in animal models, IL–10 knockout mice and mice having TNBS colitis. In these studies local administration of the antisense oligonucleotides rapidly reversed intestinal inflammation.

**Ac-HEHA and Related Compounds, Methods of Synthesis and Methods of Use**

Martin W. Brechbiel, Kim Deal (NCI)

Serial No. 60/125,764 filed 23 Mar 1999 Licensing Contact: Girish C. Barua; 301/496–7056 ext. 263; e-mail: gb18t@nih.gov

The invention is directed to a chelation complex comprising $^{225}$Actinium ($^{225}$Ac) and 1,4,7,10,13,16-hexaazacyclohexadecane-N,N′, N″,N‴,N⁗,N⁗′-hexaacetic acid (HEHA) as well as bi-functional complexes consisting of $^{225}$Ac, HEHA and targeting agents in various combinations. Radioisotopes are chosen, in part, by the type of disease to be treated, and two important functions are tissue penetration of the emitted particles and

the toxicity of the treatment agents. $^{225}$Ac, an alpha-emitter, offers high cytotoxicity with a short tissue range, and HEHA chelates $^{225}$Ac in such a manner as to provide increased in vivo stability to enable its use as a radiotherapeutic agent. Additionally, $^{225}$Ac's radioactive decay chain ends in a non-radiocative material. A targeting agent can be conjugated to $^{225}$Ac–HEHA in order to selectively affect a defined population of cells through a receptor, a substrate, an antigenic determinant or any other binding site on the target cell population. Therefore, the invention yields improvements over existing related technologies for the radiotherapeutic treatment of disease states such as cancer. The disclosed complexes could also be used in radioimaging, decontamination and detoxification protocols.

**Low Level Exposure to Extract of Neurotoxin for Protection From Brain Injury**

WB Jonas (OD) and FC Tortella (U.S. Army) Serial No. 09/271,009 filed 17 Mar 1999 Licensing Specialist: Leopold J. Luberecki, Jr., J.D.; 301/496–7735 ext. 223; e–mail: LL87A@NIH.GOV

Approximately 438,000 persons will suffer a stroke per year; approximately 200,000 deaths can be attributed to stroke, thereby ranking stroke as the third leading cause of death in the United States. Strokes may affect anyone, but strokes strike approximately two-thirds of those individuals over 65 years of age. Reducing brain damage due to strokes or ischemic events would save many lives and significantly reduce the associated long-term health care costs associated of a stroke victim. This technology embodies an injectable preparation of the plant-derived neurotoxin and combinations with low doses of the amino acid glutamate, and has been shown to have the ability to reduce the damage in an animal stroke model by 50%. In addition to the neuroprotective qualities when given post trauma, a formulation, in preliminary tests, indicates that the neurotoxin may have preventive neuroprotective qualities when given prior to the trauma. This would be very beneficial for individuals at high risk.

**A Novel Chimeric Protein for Prevention and Treatment of HIV Infection**

Edward A. Berger (NIAID), Christie M. Del Castillo Serial No. 60/124,681 filed 16 Mar 99 Licensing Contact: Carol Salata; 301/496–7735 ext. 232; e-mail: cs253n@nih.gov

This invention relates to bispecific fusion proteins effective in viral neutralization. Such proteins have two different binding domains, an inducing-binding domain and an induced-binding domain, functionally linked by a peptide linker. More specifically, the invention is a genetically engineered chimeric protein containing a region of CD4 attached via a flexible polypeptide linker to a human single chain MAb directed against CD4-induced, highly conserved HIV gp120 determinants involved in binding to coreceptor. The molecule is expected to have the properties of a potent, broadly cross-reactive neutralizing antibody against HIV. This novel agent will have considerable potential in the prevention of infection during or immediately following HIV exposure (e.g. vertical transmission; post-exposure prophylaxis) and possibly in the treatment of chronic infection. Such proteins, nucleic acid molecules encoding them, and their production and use in preventing or treating viral infections are claimed.

**UPA, a Universal Protein Array System for Quantitative Detection of Protein-Protein, Protein-DNA, Protein-RNA and Protein-Ligand Interactions**

Dr. Hui Ge (NICHD), Serial No. 60/123,586 filed 08 Mar 1999, Licensing Contact: Marlene Shinn; 301/496–7057 ext. 285; e-mail: ms482m@nih.gov

The Universal Protein Array (UPA) system is a newly developed research tool for the analysis and screening of potential drug targets. This technology uses the three dimensional structure of active proteins (without denaturation and renaturation) to determine specific protein-protein, protein-DNA, protein-RNA, protein-ligand or protein-chemical interactions. Unlike most conventional DNA chips or DNA microarrays currently on the market, the UPA system requires no sophisticated equipment and is in fact more sensitive than existing methods. The UPA system is able to analyze thousands of protein samples in a single experiment, thereby making it a highly efficient way to screen proteins for potential drug targets. Also, because it can be used multiple times for different targets, it is economically affordable for most laboratories or hospitals.

In addition to being useful as a screening tool, the UPA system can also be used to study gene regulation pathways such as transcription, RNA processing, replication, translation, and signal transduction, to name a few. The technology found in the UPA system could also potentially be commercialized in a kit form and be applied to the diagnosis of disease states in patients in the clinical setting.

**Methods for Mitochondrial Gene Therapy**

Steven J. Zullo (NIMH), Jerome M. Eisenstadt, Wayne A. Fenton, DHHS Reference No. E–121–99/0 filed 08 Mar 1999, Licensing Contact: Dennis Penn; 301/496–7056 ext. 211; e-mail: dp144q@nih.gov

Although the role of the mitochondrion in providing energy for the cell by the process of oxidative phosphorylation has been known for a long time, the role of the mitochondrial genome and the consequences of defects in the mitochondrial genome are just being understood. These mutations or defects in the mitochondrial genome are responsible for many diseases, conditions, or syndromes.

This invention is directed to methods for functionally complementing at least one defect, mutation, or deletion in the mitochondrial genome which comprises: (1) Selecting a mitochondrial gene; (2) determining the nucleic acid sequence of the gene; (3) optionally, where the nucleic acid sequence encodes a protein and at least one of the codons encoding the protein has a different meaning in the mitochondrial genetic code and the universal genetic code, mutating the nucleic acid sequence to reflect the difference between the mitochondrial and universal genetic codes so that, in the mutated sequence, a polypeptide that is expressed as the result of nuclear transcription of the nucleic acid sequence, and cytoplasmic translation of the messenger RNA, has the same amino acid sequence as the polypeptide originally expressed in the mitochondrion; (4) optionally, attaching the coding sequence of a functional mitochondrial protein targeting sequence to the nucleic acid sequence for nuclear expression; (5) operatively linking the protein targeting sequence, if present, and the nucleic acid sequence to at least one control element that provides constitutive expression to generate a nucleic acid construct; and (6) inserting the nucleic acid construct into the nuclear genome of a eukaryotic cell for expression of the nucleic acid segment in the cell to provide functional complementation of at least one defect, mutation, or deletion in the mitochondrial genome. The method can also be used for the total replacement of mitochondrial genome function, including the use of transgenic techniques.

**Monoclonal Antibodies Specific and Inhibitory to Human Cytochrome P450 2C8, 2C9, 2C18 And 2C19—New Avenues for Drug Discovery**

Harry V. Gelboin, Frank J. Gonzalez, Kristopher W. Krausz, (NCI),

DHHS Reference No. E–077–99/0 filed 12 Feb 99

Licensing Contract: Dennis Penn; 301/496–7056 ext. 211; e-mail: dp144q@nih.gov

The cytochrome P450 family of enzymes has primary responsibility for the metabolism of xenobiotic drugs and non-drug carcinogens and environmental chemicals, as well as some endobiotics. This laboratory has isolated monoclonal antibodies (MAbs) that are specific to and inhibit the ten major human cytochrome P450s (CYPs) that are responsible for the metabolism of most drugs. The MAb based analytic system identifies the P450s responsible for metabolism of a drug and is thus an entirely new system for Drug Discovery. Drug-drug toxicity can be due to drug partners competing for an individual P450 and be a cause of drug toxicity. Certain drugs given to genetically polymorphic individuals that are defective in a specific P450 can cause serious toxicity to the defective individual. In one case 6–10% of the world population are missing an important P450 (2D6).

The 2C family of cytochrome P450s metabolizes a very large and extensive number of drugs which include tolbutamide, S-Warfarin, mephenytoin, diazepam and taxol. The invention reports the production of inhibitory MAbs to the P450 2C family. The invention describes MAb 5–1–5 and 281–1–1 that specifically inhibit CYP 2C8. MAb 292–2–3 that specifically inhibit CYP 2C9 and MAb 592–2–5 that specifically inhibit both CYP 2C9 and 2C18. MAb 5–7–5 specifically inhibits CYP 2C9, 2C18, and 2C19. In addition MAb 1–68–11 previously reported specifically inhibits all four members of the 2C family, 2C8, 2C9, 2C18, and 2C19. The MAbs may be used as diagnostic probes identifying the single or several P450s responsible for a drugs metabolism and also yield important information on inter-individual differences. The MAb system identifies and characterizes the P450 based metabolism of drugs currently in use and drugs in the screening and development stages of Drug Discovery.

Dated: July 13, 1999.

**Jack Spiegel, Ph.D.**

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

[FR Doc. 99–18374 Filed 7–16–99; 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.

**ACTION:** Notice.

**SUMMARY:** The invention listed below is owned by an agency of the US Government and is available for licensing in the US 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 a copy of the U.S. patent application listed below may be obtained by contacting Susan S. Rucker, J.D., at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852–3804; telephone: 301/496–7056 ext. 245; fax: 301/402–0220; e-mail:sr156v@nih.gov. A signed Confidential Disclosure Agreement will be required to receive a copy of the patent application.

**Immunoadhesins and Methods of Production Thereof**

KG Csaky, E Anglade, DM Sullivan (all of NEI), WJ Larochelle (NCI)

Serial No. 08/814,567 filed 10 Mar 97

This patent application relates to the field of immunoadhesins. Immunoadhesins, also known as immunoligands, Ig- or Fc- fusion proteins or chimeras are chimeric molecules comprised of a non-immunoglobulin binding region (e.g., cell surface receptor, ligand, cell adhesion molecule) and an antibody constant domain. Such molecules can be used to identify receptors or ligands, in structure-function studies or as therapeutic agents.

In particular, the application describes a method for producing immunoadhesins which utilizes a replication-deficient adenoviral expression system. This system addresses some of the defects of other immunoadhesion production systems utilizing transfection of plasmid DNA in either a transient or stable system by providing efficient, high level gene expression, appropriate assembly/post-translation modification and ease of purification. Particular immunoadhesins which have been produced using this system are incorporate IL–10, IL–2, IL–13, IL2ra, IL–1ra, mutant IL–4, ICAM, TGF–1β1, or TGF-$\beta1^{223,225}$ as the non-immunoglobulin portion.

This research has been published, in part, in Anglade, et al. ''Interleukin-10 immunoadhesin production by a replication-defective adenovirus'' J. Immunol. Methods 202(1): 41–8 (March 10, 1997).

Dated: July 13, 1999.

**Jack Spiegel, Ph.D.,**

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

[FR Doc. 99–18375 Filed 7–16–99; 8:45 am]

**BILLING CODE 4140–01–M**

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### National Institutes of Health

### National Cancer Institute; Notice of Closed Meeting

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of the following meeting.

The meeting will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., as amended. The grant applications and the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the grant applications, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

*Name of Committee:* National Cancer Institute Review Group; Subcommittee A—Cancer Centers.

*Date:* August 5–6, 1999.

*Time:* 7:00 PM to 1:00 PM.

*Agenda:* to review and evaluate grant applications.

*Place:* Embassy Suites, Chevy Chase Pavilion, 4300 Military Rd., Wisconsin at Western Ave., Washington, DC 20015.

*Contact:* David E. Maslow, PHD, Scientific Review Administrator, Grants Review Branch, Division of Extramural Activities, National Cancer Institute, National Institutes of Health, 6130 Executive Boulevard—EPN