and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, or Office of Communication, Training and Manufacturers Assistance (HFM–40), 1401 Rockville Pike, Rockville, MD 20852–1448, or by calling 1–800–835–4709 or 301–827–1800. Submit written comments on the guidance to the Dockets Management Branch (HFA–305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1–23, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT:

Shiew-Mei Huang, Center for Drug Evaluation and Research (HFD–850), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–594–5671; or

Martin D. Green, Center for Biologics Evaluation and Research (HFM–579), 1401 Rockville Pike, Rockville, MD 20852–1448, 301–827–5344.

SUPPLEMENTARY INFORMATION: FDA is announcing the availability of a guidance entitled ''Pharmacokinetics in Patients with Impaired Renal Function—Study Design, Data Analysis, and Impact on Dosing and Labeling.''

The pharmacokinetics (PK) and pharmacodynamics (PD) of drugs primarily eliminated through the kidneys may be altered by impaired renal function to the extent that the dosage regimen needs to be changed from that used in patients with normal renal function. Although the most obvious type of change arising from renal impairment is a decrease in renal excretion (or possibly renal metabolism) of a drug or its metabolites, renal impairment also has been associated with other changes, such as changes in hepatic metabolism, plasma protein binding, and drug distribution. These changes may be particularly prominent in patients with severely impaired renal function and have been observed even when the renal route is not the primary route of elimination of a drug. Thus, for most drugs that are likely to be administered to patients with renal impairment, PK characterization may need to be assessed in subjects with such impairment to provide appropriate dosing recommendations.

The guidance provides specific information on when studies of PK in patients with impaired renal function should be performed and when they may be unnecessary. It also addresses the design and conduct of PK studies in patients with impaired renal function, the design and conduct of PK studies in end stage renal disease patients treated with dialysis, the analysis and reporting of the results of such studies, and representation of these results in approved product labeling.

In the **Federal Register** of June 16, 1997 (62 FR 32617), FDA announced the availability of a draft version of this guidance, entitled ''Pharmacokinetics and Pharmacodynamics in Patients with Impaired Rental Function: Study Design, Data Analysis, and Impact on Dosing and Labeling.'' The June 16, 1997, document gave interested persons an opportunity to submit comments through August 15, 1997. All comments received through the end of September have been carefully reviewed and incorporated, where appropriate, in this revised guidance.

This guidance is being issued as a Level 1 guidance consistent with FDA's good guidance practices (62 FR 8961, February 27, 1997). It represents the agency's current thinking on conducting PK studies on patients with impaired renal function. 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 such approach satisfies the requirement of the applicable statute, regulations, or both.

Interested persons may, at any time, submit written comments on the guidance to the Dockets Management Branch (address above). Comments should be identified with the docket number found in brackets in the heading of this document. A copy of the guidance is available for public examination in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

Dated: May 8, 1998.

William K. Hubbard,

Associate Commissioner for Policy Coordination.

[FR Doc. 98–12898 Filed 5–14–98; 8:45 am]

BILLING CODE 4160–01–F

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.

Molecular Computing Elements: Gates and Flip-Flops

TD Schneider, PN Hengen (NCI)
DHHS Reference No. E–170–97/0 filed Feb. 20, 1998
Licensing Contact: John Fahner-Vihtelic, 301/496–7735 ext. 270

The present invention is a method and apparatus for molecular computing which provides for molecular logic devices analogous to those of electronic computers, such as flip-flops, AND gates, etc. Coupling of the gates allows for molecular computing. The method allows data storage, the transformation of binary information and signal readout. Possible applications include encoding ''read only'' memory for microscopic identifiers, digital control of gene expression, and quantification of analytes. The computing elements also provide means for complex regulation of gene expression.

Lipooligosaccharide-Based Vaccine for the Prevention of Moraxella (Branhamella) Catarrhalis Infections In Humans

X–X Gu, JB Robbins (NIDCD)
Serial No. 60/071,483 filed Jan 13, 1998
Licensing Contact: Robert Benson, 301/496–7056 ext. 267

This invention is a vaccine for the prevention of disease caused by M. catarrhalis, which is the third most common causative agent of otitis media (middle ear infection) and sinusitis in children. The emergence of antibiotic resistant bacteria has caused concern that treatment of otitis media will become more problematic. This invention offers a new approach to managing otitis media. The vaccine is composed of lipooligosaccharide (LOS), isolated from the surface of strains of M. catarrhalis and detoxified by removing esterified fatty acids to produce detoxified LOS (dLOS), which is then conjugated to an immunogenic protein carrier such as tetanus toxiod. The conjugates have been shown to be nontoxic by the limulus amebocyte

assay. Antisera raised in rabbits immunized with the conjugate is bacteriocidal *in vitro* against homologous and many heterologous strains of *M. catarrhalis.*

Conjugate Vaccine for Nontypeable Haemophilus Influenzae

X–X Gu, C–M Tsao, DJ Lim, JB Robbins (NIDCD)
Serial No. 08/842,409 filed April 23, 1997
Licensing Contact: Robert Benson, 301/496–7056 ext. 267

This invention is a vaccine for the prevention of disease caused by nontypeable H. influenzae (NTHi), which causes 25%–40% of otitis media cases (middle ear infections) in children. The emergence of antibiotic resistant bacteria has caused concern that treatment of otitis media will become more problematic. This invention offers a new approach to managing otitis media. The vaccine is composed of lipooligosaccharide, isolated from the surface of strains of NTHi and treated with hydrazine to remove esterified fatty acids, covalently conjugated to an immunogenic carrier, such as tetanus toxoid. The conjugates have been shown to be nontoxic by the limulus amebocyte assay, rabbit pyrogen test and in an mouse lethal toxicity test. Antisera raised in rabbits immunized with the conjugate is bacteriocidal in vitro against homologous and many heterologous strains of NTHi. A blind controlled trial in chinchillas, an animal model for otitis media, showed that the vaccines are protective against challenge by NTHi.

Calorimeter and Method for Simultaneous Measurement of Thermal Conductivity and Specific Heat of Fluids

NL Gershfeld, CP Mudd, AJ Jin, K Fukada (NIAMS)
Serial No. 08/994,230 filed December 19, 1997
Licensing Contact: John Fahner-Vihtelic, 301/496–7735 ext. 270

The present invention is a novel calorimeter and calorimetry apparatus and method for the ultrasensitive simultaneous measurement of heat capacity and thermal conductivity of fluids. The unique simultaneous measurement of the two parameters avoids sources of error in other methods. The calorimeter shows excellent accuracy of 1 part in 10,000 and run-to-run variability of 1 part in 100,000, as well as excellent long-term reproducibility. The invention is well suited for the study of biomaterials, such as lipids and proteins and other colloidal systems, which are not easily analyzed using conventional commercial instruments.

A Multi-Slice PET Scanner Constructed From Side-Looking Phoswich Scintillators Coupled to Miniature Position-Sensitive Photomultiplier Tubes: Application in Small Animal Imaging

MV Green (CC)
DHHS Reference No. E–288–97/0 filed Nov 12, 1997
Licensing Contact: John Fahner-Vihtelic, 301/496–7735 ext. 270

The present application describes a new positron emission tomography (PET) scanner. The design of this scanner allows reduction of the detector ring size relative to conventional scanners (thereby reducing cost) while increasing resolution, resolution uniformity and sensitivity. This combination of features makes the invention particularly well-suited for small animal imaging in biomedical research, e.g. evaluating changes in organ function due to genetic manipulations.

Chimeric Vaccine Against Tick-Borne Encephalitis Virus

A Pletenev, R Men, RM Chanock, C–J Lai (NIAID)
Serial No. 60/061, 441 filed Oct 08, 1997
Licensing Contact: Carol Salata, 301/496–7735 ext. 232

The present invention relates to a chimeric virus vaccine against tick-borne encephalitis virus (TBEV). The preM and E structural genes of the tick-borne encephalitis Langat virus and the non-structural genes of the mosquito-borne dengue virus form a live, attenuated chimeric virus vaccine against tick-borne encephalitis virus. The live chimeric vaccine was administered intraperitoneally and exhibited complete attenuation in mice while at the same time providing protection against subsequent challenge with the virulent parental Langat virus which is virulent for mice.

Methods and Apparatuses for Processing Synthesized Models of Complex Medical Structures

RM Summers (CC)
Serial No. 60/056, 452 filed Aug 19, 1997
Licensing Contact: John Fahner-Vihtelic, 301/496–7735 ext. 270

The present invention provides a new algorithm for generating computer models of complex anatomical structures from data such as CT. This algorithm minimizes the problem of ''leakage'' found in existing algorithms, which leads to incorrect assignment of voxels as belonging to the feature of interest. This improvement greatly speeds computation time, and anatomical features modeled with this algorithm may be displayed in real time, allowing ''virtual endoscopy.'' The method has been demonstrated in clinical ''virtual bronchoscopy.'' A method for computer-assisted detection of lesions within body cavities is also disclosed.

Simultaneous Multicolor Visualization of Chromogenic Dyes Using Brightfield Microscopy and Spectral Imaging

T Ried, M MacVille (NHGRI)
Serial No. 60/055,439 filed Aug 8, 1997
Licensing Contact: John Fahner-Vihtelic, 301/496–7735 ext. 270

The present application describes a method and apparatus for spectral imaging. This invention enables one to distinguish permanent chromogenic dyes attached to DNA probes and hybridized to interphase cells from cytological preparations. This technology has application in areas such as analysis of Pap smears or cells from fine needle aspirations. Color identification is based on the measurement of the entire absorption spectrum of chromogenic dyes by means of spectral imaging, which allows for the unambiguous identification of otherwise not discernable dyes. This approach also allows for multi-parameter analysis of immunocytochemical markers and RNA in situ hybridization. The diagnosis, staging, and prognosis of human cancers could be greatly improved by complementing morphology with genetic markers for tumor progression using this method.

Methods For Treating Parasitic Infection Using Thiopeptides

MJ Rogers, TF McCutchan, GA McConkey, A Fairfield (NIAID) DHHS Reference No. E–202–97/0; PCT/US97/11939 filed July 7, 1997.
Licensing Contact: Carol Salata, 301/496–7735 ext. 232

This invention provides a method for treating a parasitic infection (when the parasite has a plastid-like organelle) with a thiopeptide. The parasitic infection may be caused by parasites of the Apicomplexa phylum, the Microspora phylum or the Ascetospora phylum. The thiopeptide used to treat the parasitic infection can be any member of the class of compounds characterized as sulfur-rich peptide antibiotics with multiple thiazole rings which inhibit protein synthesis in the plastid-like organelle of the parasites.

The disclosed thiopeptides can be, but are not limited to, thiostrepin, micrococcin P. nosiheptide, siomycin, sporangiomycin, althiomycin, the thiocillins and/or thiopeptin, as well as sulfur-rich peptide antibiotic containing multiple thiazole rings, produced by streptomycetes or other peptide antibiotic-producing organisms.

Image Registration Using Closest Corresponding Voxels With an Iterative Registration Process

J Ostuni (LDRR)
Serial No. 08/847,733 filed Apr 28, 1997 (claiming priority date of Apr 29, 1996)
Licensing Contract: John Fahner-Vihtelic, 301/496-7735 ext. 270

The present invention provides a novel method of 3D medical image registration, that is, the alignment of two or more related 3D images. This method overcomes problems seen in conventional registration techniques arising from mismatching of voxel intensities. This is of particular importance when registering images derived from different techniques, such as MRI and CT. The invention allows the registration of images despite the lack of direct relationship between intensity levels in the different techniques, varying patient placement, and occlusion and noise in the image.

System for Synergistic Combination of Multiple Automatic Induction Methods and Automatic Re-Representation of Data

L Hunter (NLM)
DH Reference No. E–118–96/0; PCT/US97/08951 filed May 23 1996
Licensing Contact: John Fahner-Vihtelic, 301/496-–7735 ext. 270

The present application describes a unique prototype of an advanced framework which relates to the field of multidimensional data mining, machine learning, and analysis that has been named COEV (for COEVolutional). COEV synergistically combines different methods of statistical analysis, neural networks, decision trees and genetic algorithms for the resolution of data queries. COEV automatically determines the optimal methods and data representations to apply at each step of inquiry and, as a result, can provide outcomes that are significantly more accurate than can be achieved by use of any one methodology alone. The invention uses an evolutionary learning technology to improve predictive outcomes with continued use. COEV is designed to advance the accuracy, flexibility, speed and ease of use of advanced data analysis technologies.

Characteristics of problems that are appropriate for the application of the COEV method are: (1) Appropriate for machine learning, in that there is a well-defined set of input variables and a clear prediction target; (2) difficult for traditional methods, and where a modest improvement in accuracy over existing machine learning methods (e.g., neural networks) would be significant; (3) there is a large amount of training data, ideally thousands of cases.

Possible application areas of interest include the analysis of high-throughput screening data for pharmaceutical discovery, detecting patterns of fraud in insurance claims, or automating screening of medical images.

This invention requires further R&D and testing to make it a practical system for widespread use.

Dated: May 7, 1998.

Jack Spiegel,

Director, Division of Technology Development and Transfer, Office of Technology Transfer.

[FR Doc. 98–13011 Filed 5–14–98; 8:45 am]

BILLING CODE 4140–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institute on Aging; Closed Meetings

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 meetings:

Name of SEP: National Institute on Aging Special Emphasis Panel Stress, Aging and Wound Healing.
Date of Meeting: May 27, 1998.
Time of Meeting: 12:00 p.m. to adjournment.
Place of Meeting: Holiday Inn on the Lane, Columbus, Ohio.
Purpose/Agenda: To review a program project application.
Contact Person: Dr. Mary Nekola, Scientific Review Administrator, Gateway Building, Room 2C212, National Institutes of Health, Bethesda, Maryland 20892–9205, (301) 496–9666.

Name of SEP: National Institute on Aging Special Emphasis Panel QTL, Analysis of Age-Related Phenotypes.
Date of Meeting: May 29, 1998.
Time of Meeting: 11:00 a.m. to adjournment.
Place of Meeting: Chicago O'Hare Marriott, Chicago, Illinois.
Purpose/Agenda: To review a program project application.
Contact Person: Dr. James Harwood, Scientific Review Administrator, Gateway Building, Room 2C212, National Institutes of Health, Bethesda, Maryland 20892–9205, (301) 496–9666.

Name of Committee: National Institute on Aging, Initial Review Group Biology, Aging Review Committee.
Dates of Meeting: June 1–2, 1998.
Times of Meeting: June 1–7:30 p.m. to recess, June 2–8:00 a.m. to adjournment.
Place of Meeting: Chevy Chase Holiday Inn, 5520 Wisconsin Avenue, Chevy chase, Maryland 20815.
Purpose/Agenda: To review a program project application.
Contact Person: Dr. James Harwood, Scientific Review Administrator, Gateway Building, Room 2C212, National Institutes of Health, Bethesda, Maryland 20892–9205, (301) 496–9666.

Name of Committee: National Institute on Aging Initial Review Group, Clinical Aging Review Committee.
Date of Meeting: June 2, 1998.
Time of Meeting: 8:00 a.m. to adjournment.
Place of Meeting: Holiday Inn Bethesda, 8120 Wisconsin Avenue, Bethesda, Maryland 20815.
Purpose/Agenda: to perform the various grant applications.
Contact Person: Dr. William Kachadorian, Scientific Review Administrator, Gateway Building, Room 2C212, National Institutes of Health Bethesda, Maryland 20892–9205, (301) 496–9666.

Name of Committee: National Institute on Aging Initial Review Group, Neurosciences of Aging Review Committee.
Date of Meeting: June 8–10, 1998.
Times of Meeting: June 8–7:00 p.m. to recess, June 9–8:00 a.m. to recess, June 10–8:00 a.m. to adjournment.
Place of Meeting: Chevy Chase Holiday Inn, 5520 Wisconsin Avenue, Chevy Chase, Maryland 20815.
Purpose/Agenda: To review grant applications.
Contact Person: Dr. Louise Hsu, Scientific Review Administrator, Gateway Building, Room 2C212, National Institutes of Health, Bethesda, Maryland 20892–9205, (301) 496–9666.

Name of SEP: National Institute on Aging Special Emphasis Panel Alzheimers Disease Patient Registry.
Date of Meeting: June 10, 1998.
Time of Meeting: 4:00 p.m. to adjournment.
Place of Meeting: Chevy Chase Holiday Inn, 5520 Wisconsin Avenue, Chevy Chase, Maryland 20815.
Purpose/Agenda: To review research project.
Contact Person: Dr. Louise Hsu, Scientific Review Administrator, Gateway Building, Room 2C212, National Institutes of Health, Bethesda, Maryland 20892–9205, (301) 496–9666.

Name of SEP: National Institute on Aging Special emphasis Panel Group A.
Date of Meeting: June 10, 1998.
Time of Meeting: 8:00 a.m. to 12:00 noon.
Place of Meeting: Chevy Chase Holiday Inn, 5520 Wisconsin Avenue, Chevy Chase, Maryland 20815.
Purpose/Agenda: To pilot study review a grant application mostly concerning molecular biology, Alzheimer's disease, biochemistry and neurology of aging.
Contact Person: Dr. Arthur Schaerdel, Scientific Review Administrator, Gateway