B. *Concerning the mechanisms of the formation of furan in food, FDA has identified the following data needs*:

1. Data and information on possible mechanisms of furan formation.

2. Data and information on variables that enhance or mitigate furan formation in foods.

3. Data on the stability or dissipation of furan in foods.

4. Data about the effect of post-production practices, such as consumer heating of canned foods, on furan levels in foods.

C. *Concerning the toxicology of furan, FDA has identified the following data needs*:

1. Data and information on mechanism(s) of furan toxicity, mutagenicity, and carcinogenesis.

2. Data and information on the reproductive and developmental toxicology of furan.

3. Data and information on the metabolism of furan in vivo, including characterization of any reactive furan metabolites in addition to *cis*-2-butene-1,4-dial, and data on the role of such metabolites in producing furan's adverse effects, including carcinogenesis.

4. Data and information on the diversity of furan pharmacokinetics in humans or the alteration of furan metabolism as a result of dietary, medical, or environmental interactions.

5. Data and information on whether sub-cytotoxic furan doses produce any adverse effect, such as a change in enzyme activities or ATP levels.

6. In the NTP furan study, Cytotoxic and carcinogenic effects were seen at all doses, and a no adverse effect level (NOAEL) was not identified. A preliminary report by Goldsworthy et al. showed an NOAEL dose of 2.0 mg/kg bw in female mice, but data from this study are not yet available (Ref. 12). FDA would like to acquire data on the effects of furan doses lower than those used in the NTP study in order to accomplish the following objectives: (a) Establish a dose-response curve for the various toxicological endpoints, (b) Determine whether furan toxicity, including carcinogenesis, is a threshold-dependent event; and (c) determine whether the carcinogenic activity of furan is secondary to its hepatotoxic effects.

7. Additional data on the mutagenicity of furan in the TA100 strain in the Ames test, given the two existing contradictory reports.

8. Additional data and information on the behavior of furan in other in vivo assays for mutagenicity or toxicity.

III. References

The following references are on display in the Division of Dockets Management (see **ADDRESSES**) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. FDA, ''Determination of Furan in Foods,'' 2004, *http://www.cfsan.fda.gov/~lrd/pestadd.html#furan*.

2. Maga, J. A., *CRC Critical Reviews in Food Science and Nutrition*, ''Furans in foods,'' pp. 355–400, 1979.

3. NRC (National Research Council), *Spacecraft Maximum Allowable Concentrations for Selected Airborne Contaminants*, vol. 4., appendix B14, ''Furan,'' pp. 307–329, National Academy Press, Washington, DC, 1994.

4. Persson, T. and E. von Sydow, ''Aroma of canned beef: Gas chromatographic and mass spectrometric analysis of the volatiles,'' *Journal of Food Science*, 38: 377–385, 1973.

5. Stoffelsma, J., G. Sipma, D. K. Kettenes, and J. Pypker, ''Volatile components of roasted coffee,'' *Journal of Agricultural Food Chemistry*, 16(6): 1000–1004, 1968.

6. IARC, *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*, Volume 63: ''Dry Cleaning, Some Chlorinated Solvents and Other Industrial Chemicals,'' pp. 394–407, Lyon, France, 1995.

7. NTP, ''Toxicology and carcinogenesis studies of furan (CAS No. 110–00–9) in F344/N rats and B6C3F_1 mice (gavage studies),'' NTP Technical Report No. 402., U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, Research Triangle Park, NC, 1993.

8. Goldsworthy, T. L., R. Goodwin, R. M. Burnett, P. King, H. El-Sourady, G. Moser, J. Foley, and R. R. Maronpot, ''Dose Response Relationships Between Furan Induced Cytotoxicity and Liver Cancer,'' Society of Toxicologic Pathology Annual Conference, Orlando, FL, 2001.

9. Fransson-Steen, R., T. L. Goldsworthy, G. L. Kedderis, and R. R. Maronpot, ''Furan-induced liver cell proliferation and apoptosis in female B6C3F1 mice,'' *Toxicology*, 118(2–3): 195–204, 1997.

10. Mugford, C. A., M. A. Carfagna, and G. L. Kedderis, ''Furan-mediated uncoupling of hepatic oxidative phosphorylation in Fischer-344 rats—an early event in cell death,'' *Toxicology Applied Pharmacology*, 144(1):1–11, 1997.

11. Burka, L. T., K. D. Washburn, and R. D. Irwin, ''Disposition of [^{14}C]furan in the male F344 rat,'' *Journal of Toxicology and Environonmental Health*, 34(2): 245–257, 1991.

12. Chen L.-J., S. S. Hecht , and L. A. Peterson, ''Identification of *cis*-2-butene-1,4-dial as a microsomal metabolite of furan,'' *Chemical Research in Toxicology* 8(7): 903–906, 1995.

13. Byrns, M. C., D. P. Predecki, and L. A. Peterson, ''Characterization of nucleoside adducts of *cis*-2-butene-1,4-dial, a reactive metabolite of furan,'' *Chemical Research in Toxicology* 15(3):373–9, 2002.

14. Parmar, D. and L. T. Burka. ''Studies on the interaction of furan with hepatic cytochrome P-450,'' *Journal of Biochemical Toxicology*, 8: 1–9, 1993.

15. Lee, H., S. S. Bian, and Y. L. Chen, ''Genotoxicity of 1,3-dithiane and 1,4-dithiane in the CHO/SCE assay and the *Salmonella*/microsomal test,'' *Mutation Research*, 321(4): 213–218, 1994.

16. Peterson, L. A., K. C. Naruko, and D. P. Predercki, ''A reactive metabolite of furan, *cis*-2-butene-1,4-dial, is mutagenic in the Ames assay,'' *Chemical Research in Toxicology*, 13(7): 531–534, 2000.

17. Foureman, P., J. M. Mason, R. Valencia, and S. Zimmering, ''Chemical mutagenesis testing in Drosophila, IX. Results of 50 coded compounds tested for the National Toxicology Program,'' *Environmental and Molecular Mutagenesis*, 23(1): 51–63,1994

18. Mugford, C.A. and G. L. Kedderis, ''Furan-mediated DNA double strand breaks in isolated rat hepatocytes,'' *Fundamental Applied Toxicology*, 30(1, Part 2):128, 1996.

19. Wilson, D. M., T. L. Goldsworthy, J. A. Popp, and B. E. Butterworth, ''Evaluation of genotoxicity, pathological lesions, and cell proliferation in livers of rats and mice treated with furan,'' *Environmental and Molecular Mutagenesis*, 19(3): 209–222, 1992.

20. National Toxicology Program (NTP), Report on Carcinogens, 10th ed., U.S. Department of Health and Human Services, Public Health Service, 2002.

21. Kedderis G. L. and S. A. Ploch, ''The Biochemical Toxicology of Furan,'' CIIT Activities 19(12), 1999.

Dated: May 4, 2004.

Jeffrey Shuren,

Assistant Commissioner for Policy.

[FR Doc. 04–10588 Filed 5–7–04; 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 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.

Rapid Integration Site Mapping

Shawn Burgess (NHGRI).
U.S. Provisional Application filed 20 Apr 2004 (DHHS Reference No. E–027–2004/0–US–01).
Licensing Contact: Michael Ambrose; 301/594–6565; *ambrosem@mail.nih.gov.*

This invention describes a novel method for mapping retroviral integration sites within genomic DNA. The invention provides for rapid integration profiling with reduced labor and time required and reduces the inherent biases resulting from other techniques.

The technology uses pre-selected frequent cutting restriction enzymes and proprietary linkers to produce smaller amplicons that, in practice, reduce the bias effects of other more commonly used mapping techniques that often include linear amplification as a first step. Further, the technology does not require the use of measurable phenotypic characteristics to analysis or distinguish integration events. Thus, knowledge of potential cellular changes is not required. This invention can be used to provide rapid, cost-effective screening of cells treated with retroviruses for gene therapy. The ability to identify potentially harmful integrations and eliminating them from therapeutic use is essential for safer gene therapy applications.

Additional information may be found in X. Wu *et al.*, ''Transcription Start Regions in the Human Genome are Favored Targets for MLV Integration'', *Science* Jun 13 2003 300:1749–1751.

Novel Method of Fat Suppression in Steady State Free Precession (SSFP) Based Magnetic Resonance Imaging (MRI)

John Derbyshire, Daniel Herzka, Elliot McVeigh (NHLBI).
U.S. Provisional Application filed 08 Mar 2004 (DHHS Reference No. E–237–2003/0–US–01).
Licensing Contact: Michael Shmilovich; 301/435–5019; *shmilovm@mail.nih.gov.*

Available for licensing is a technique for improving magnetic resonance imaging (MRI) that employs steady state free precession (SSFP). One such technique, fast imaging with steady-state free precession (FISP), is a well established and is a fast MR imaging method commonly used to evaluate cardiovascular anatomy and function. FISP provides high signal to noise ratio (SNR) images with excellent contrast between blood and the myocardium. However, these images are often contaminated with high signal from fatty tissue resulting in image artifacts. Conventional methods of fat signal suppression in FISP are often inefficient and result in a loss of temporal resolution. The present pulse sequence provides intrinsic chemical selectivity and significant attenuation of fat-based signals (by a factor of four compared to conventional FISP imaging) while maintaining the preferred high SNR for water-based tissues provided by standard FISP. In addition, the pulse sequence design is such that the high temporal resolution of FISP is not compromised. Thus, this technology offers a valuable improvement to standard cardiac MRI methods.

γPGA Conjugates for Eliciting Immune Responses Directed Against *Bacillus Anthracis* and Other Bacilli

Rachel Schneerson (NICHD), Stephen Leppla (NIAID), John Robbins (NICHD), Joseph Shiloach (NIDDK), Joanna Kubler-Kielb (NICHD), Darrell Liu (NIDCR), Fathy Majadly (NICHD).
U.S. Provisional Application No. 60/476,598 filed 05 Jun 2003 (DHHS Reference No. E–343–2002/0–US–01).
Licensing Contact: Peter Soukas; 301/435–4646; *soukasp@mail.nih.gov.*

This invention claims immunogenic conjugates of a poly-γ-glutamic acid (γPGA) of *B. anthracis,* or of another bacillus that expresses a γPGA that elicit a serum antibody response against *B. anthracis,* in mammalian hosts to which the conjugates are administered. The invention also relates methods which are useful for eliciting an immunogenic response in mammals, particularly humans, including responses which provide protection against, or reduce the severity of, infections caused by *B. anthracis.* The vaccines claimed in this application are intended for active immunization for prevention of *B. anthracis* infection, and for preparation of immune antibodies. The vaccines of this invention are designed to confer specific immunity against infection with *B. anthracis,* and to induce antibodies specific to *B. anthracis* γPGA. The *B. anthracis* vaccine is composed of non-toxic bacterial components, suitable for infants, children of all ages, and adults.

This vaccine is further described in Schneerson R. *et al.*, ''Poly(gamma-D-glutamic acid) protein conjugates induce IgG antibodies in mice to the capsule of *Bacillus anthracis*: a potential addition to the anthrax vaccine,'' *Proc. Natl. Acad. Sci.* U. S. A. 2003 Jul 22;100(15):8945–50.

Contrast Agent Enhancement of Chemical Exchange Dependent Saturation Transfer (CEDST) MRI

Robert S. Balaban, Kathleen Ward, Anthony H. Aletras (NHLBI).
U.S. Patent Application No. 09/959,138 filed 17 Oct 2001 (DHHS Reference No. E–240–1998/0–US–04).
Licensing Contact: Michael Shmilovich; 301/435–5019; *shmilovm@mail.nih.gov.*

Available for licensing is an MRI image improving system wherein at least one contrast agent is administered to a subject in amounts effective to perform chemical exchange dependent saturation transfer (CEDST) MRI analysis.

Examples of contrast agents suitable for administration as exogenous contrast agents include at least one functional group bearing a proton capable of chemical exchange. Examples of these functional groups include, without limitation, amides, amines, and carboxyl, hydroxyl, and sulfhydryl groups.

The contrast agent can be administered as a solid, as a dispersion or solution, such as an aqueous composition, as a mixture of two or more agents, etc. The contrast agent may also be in the form of a polymer.

One feature of the present invention involved identifying contrast agents, which contain the functional groups having the appropriate proton exchange and chemical shift properties at physiological pH and temperature to function effectively for performing CEDST MRI analyses in vivo. A number of different contrast agents can be used to practice the present method for performing CEDST MRI analyses in vivo can be selected from the group consisting of: Sugars, including oligosaccharides and polysaccharides, such as dextran; amino acids, such as 5-hydroxy-tryptophan (which also includes an indole -NH) and including oligomers of amino acids and proteins; nitrogen-containing heterocycles generally; indoles, purines and pyrimidines; nucleosides; imidazole and derivatives thereof, such as 2-imidazolidone and 2-imidazoldinethione; imino acids, including azetidines, such as azetidine-2-carboxylic acid, pyrolidines, such as 4-trans-hydroxy-proline, and piperidines, such as pipecolinic acid; barbituric acid and analogs thereof, such as 2-thio-barbituric acid and 5,5-diethylbarbituric acid; miscellaneous materials, such as guanidine, hydantoin, parabanic acid, and biologically active salts thereof; and mixtures of these contrast agents.

Working embodiments of the invention used the all of above materials at a variety of concentration levels for in-vitro experiments and, using a 500 mM solution of barbituric acid, in an in-vivo rabbit model.

The method of the present invention is useful for enhancing the contrast of MRI images, including images produced in vivo, using CEDST.

A second feature of the present invention involved identifying contrast agents which contained the functional groups which could be used, either alone or in combination, to function effectively at performing pH measurement using CEDST in vivo.

Working embodiments of this feature of the invention used either dihydrouracil or a combination solution of 5-Hydroxytryptophan and 2-Imidazolidinethione as the contrast agent, which was provided as an aqueous composition having about 62.5 mM of each chemical in the solution. Other chemicals with more than one chemical exchange site or mixtures of other contrast agents may also be used to practice the second feature of the present invention. A standard pH curve is prepared by performing in vitro CEDST MRI analyses of the contrast agent, which is then used to evaluate the in vivo pH measurement results.

A third feature of the present invention involved identifying contrast agents which contained the functional groups which could be used to function effectively at performing temperature measurement using CEDST in vivo.

Working embodiments of this feature of the invention used barbituric acid as the contrast agent, which was provided as an aqueous composition having about 62.5 mM of chemical in the solution. Other chemicals may be used to practice the third feature of the present invention. A standardized temperature curve is prepared performing in vitro CEDST MRI analyses of the contrast agent, which is then used to evaluate the in vivo temperature results.

A fourth feature of the present invention involved identifying contrast agents which contained the function groups which could be used to function effectively at measuring a metabolite of interest using CEDST in vivo.

Working embodiments of this feature of the invention used dihydrouracil as the contrast agent, which was provided as an aqueous composition having about 62.5 mM with phosphate as the metabolite of interest. Other chemicals may be used to practice the third feature of the present invention. A standardized metabolite curve is prepared performing in vitro CEDST MRI analyses of the contrast agent, which is then used to evaluate the in vivo metabolite results.

Dated: May 3, 2004.

Steven M. Ferguson,

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

[FR Doc. 04–10495 Filed 5–7–04; 8:45 am]

BILLING CODE 4140–01–P

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 Initial Review Group, Subcommittee H—Clinical Groups.

Date: July 6–7, 2004.

Time: 4 p.m. to 5 p.m.

Agenda: To review and evaluate grant applications.

Place: Hilton Houston Plaza, 6633 Travis Street, Houston, TX 77030.

Contact Person: Deborah R. Jaffe, PhD., Scientific Review Administrator, Resources and Training Review Branch, National Cancer Institute, Division of Extramural Activities, 6116 Executive Blvd., Rm 8135, Bethesda, MD 20892, (301) 496–7721, *jaffed@mail.nih.gov.*

(Catalogue of Federal Domestic Assistance Program Nos. 93.392, Cancer Construction; 93.393, Cancer Cause and Prevention Research; 93.394, Cancer Detection and Diagnosis Research; 93.395, Cancer Treatment Research; 93.396, Cancer Biology Research; 93.397, Cancer Centers Support; 93.398, Cancer Research Manpower; 93.399, Cancer Control, National Institutes of Health, HHS)

Dated: April 30, 2004.

LaVerne Y. Stringfield,

Director, Office of Federal Advisory Committee Policy.

[FR Doc. 04–10493 Filed 5–7–04; 8:45 am]

BILLING CODE 4140–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institute of Mental Health; 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 contract proposals and the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the contract proposals, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: National Institute of Mental Health Special Emphasis Panel, Molecular Libraries Repository RFP.

Date: May 17, 2004.

Time: 8 a.m. to 5 p.m.

Agenda: To review and evaluate contract proposals.

Place: Four Points by Sheraton Bethesda, 8400 Wisconsin Avenue, Bethesda, MD 20814.

Contact Person: Lois M. Winsky, PhD, Scientific Review Administrator, Division of Extramural Activities, National Institute of Mental Health, NIH, Neuroscience Center, 6001 Executive Blvd., Room 7184, MSC 9641, Bethesda, MD 20892–9641, (301) 443–5288 *twinsky@mail.nih.gov.*

This notice is being published less than 15 days prior to the meeting due to the timing limitations imposed by the review and funding cycle.

(Catalogue of Federal Domestic Assistance Program Nos. 93242, Mental Health Research Grants; 93.281, Scientist Development Award, Scientist Development Award for Clinicians, and Research Scientist Award; 93.282, Mental Health National Research Service Awards for Research Training, National Institutes of Health, HHS)

Dated: April 30, 2004.

LaVerne Y. Stringfield,

Director, Office of Federal Advisory Committee Policy.

[FR Doc. 04–10492 Filed 5–7–04; 8:45 am]

BILLING CODE 4140–01–M