of the limitations of sterility testing, FDA has determined that alternative methods are available that may more reliably confirm the integrity of the container and closure system in the final form throughout the entire dating period.

The draft guidance was prepared jointly by the following Centers: Center for Biologics Evaluation and Research (CBER), Center for Drug Evaluation and Research (CDER), Center for Veterinary Medicine (CVM), and Center for Devices and Radiological Health (CDRH). At the request of CBER's Stability and Formulation Committee, representatives from the Centers met on May 19, 1994, to discuss sterility testing as a component of the stability protocol. The ability of containers/packaging to maintain sterility should be proven for all sterile products.

As with other guidance documents, FDA does not intend this document to be all-inclusive and cautions that not all information may be applicable to all situations. The document is intended to provide information and does not set forth requirements. Alternative approaches may be warranted in specific situations, and certain aspects may not be applicable to all situations. If a manufacturer believes that the procedure described in the draft guidance is inapplicable to a particular method and other procedures are appropriate for FDA's consideration, the manufacturer may wish to discuss the matter further with the agency to prevent expenditure of money and effort on activities that later may be determined to be unacceptable by FDA. FDA will continue to review alternative methods on a case-by-case basis.

The draft guidance represents the agency's current thinking on container and closure integrity testing during stability monitoring for sterile products. 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 requirements of the applicable statute, regulations, or both. The draft guidance document is being distributed for comment purposes only and is not intended for implementation at this time.

II. Request for Comments

Interested persons may, at any time, submit written comments to the Dockets Management Branch (address above) regarding this draft guidance document. Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments and requests for copies are to be identified with the docket number found in the brackets in the heading of this document. A copy of the draft guidance and received comments are available for public examination in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

III. Electronic Access

In order to receive the ''Guidance for Industry: Container and Closure Integrity Testing *in Lieu* of Sterility Testing as a Component of the Stability Protocol for Sterile Products'' via your fax machine, call the FAX Information System at 1–888–CBER–FAX or 301–827–3844.

Persons with access to the Internet may obtain the draft guidance document by using the World Wide Web (WWW). For WWW access, connect to CBER at ''http://www.fda.gov/cber/guidelines.htm''. Received comments will be considered in determining whether further revision of the draft guidance document is warranted.

Dated: January 21, 1998.

William K. Hubbard,

Associate Commissioner for Policy Coordination.

[FR Doc. 98–2021 Filed 1–27–98; 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, HHS.

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.

Novel Attenuated Strains Mycobacterium Tuberculosis

CE Barry, Y. Yuan (NIAID).

Serial No.: 60/025,199 filed 10 July 97.

Licensing Contact: Carol Salata, 301/496–7735 ext 232.

This invention provides for novel attenuated strains of *Mycobacterium tuberculosis* and *M. bovis.* Attenuation is achieved by down-regulating the expression of the α-crystallin heat shock protein gene (''acr gene''). This gene is essential for virulence of the organism. Since this strain is isogenic with virulent *M. tuberculosis* but for this deletion, the full complement of antigens remains present and the organism is viable in vitro. The invention provides for vaccines and methods of vaccinating mammals for protection against *Mycobacterium sp.* that cause tuberculosis.

Method of Promoting Tumor Necrosis Using MIG

G Tosato (FDA), J Farber (NIAID), C Sgardari (FDA).

Serial No.: 08/850,914 filed 2 May 97.

Licensing Contact: Jaconda Wagner, 301/496–7735 ext 284.

Monokine induced by IFN–γ (Mig), which is structurally related to interferon-inducible protein 10 (IP–10), has been shown to exhibit antitumor activity. Mig is a member of the α chemokine family. Members of this chemokine family, PF4, PBP, CTAP–III βTG, NAP–2, IL–8 GROα, GROβ, GROγ, and IP–10, have been shown to act as an angiogenic or angiostatic factor. This invention relates to the use of Mig to promote the death of tumor tissue. It also relates to a method of inhibiting angiogenesis at a tumor site using Mig.

This research has been published in Blood 1997 Apr 15;89(8):2635–43 and J Leukoc Biol 1997 Mar;61(3):246–57.

A related case is also available for licensing: Serial No. 08/455,079 filed 31 May 95 entitled ''Interferon-Inducible 10 (IP–10) is a Potent Inhibitor of Angiogenesis''; inventors are G Tosato, AL Angiolillo, and C Sgardari.

Formation of Human Bone In Vivo

PG Robey (NIDR), P Bianco (Universita dell Aquilla), Sa Kuznetsov (NIDR), PH Krebsback (NIDR), DW Rowe (University of Connecticut.

Serial No.: 08/798, 715 filed 12 Feb. 97.

Licensing Contact: Jaconda Wagner, 301/496–7735 ext 284.

This invention provides a model for studying human bone metabolism *in*

vivo. The model system can be used to screen compounds which inhibit or stimulate bone formation. A protocol using marrow stromal fibroblasts is also presented. Use of the protocol results in the formation of self-maintained human bone which supports hematopoiesis. The marrow stromal fibroblasts combined with the described delivery vehicles can be implanted into humans to augment bone implants or to repair bone defects.

This research has been published in J Bone Miner Res 1997 Sep;12(9):1335–47 and Transplantation 1997 Apr 27;63(8):1059–69.

Synthesis and Purification of Hepatitis C Virus Like Particles In Vitro

TJ Liang and TF Baumert (NIDDK).
Serial No.: 60/030,238 filed 8 Nov 96; PCT/US97/05096 filed 25 Mar. 97.
Licensing Contact: Carol Salata, 301/496–7735 ext 232.

Hepatitis C virus (HCV) is a major causative agent of posttransfusion and community-acquired hepatitis world-wide. Analysis of the structural features of HCV has been hampered by the inability to propagate the virus efficiently in cultural cells and the lack of a convenient animal model. This invention discloses the production and purification of HCV-like particles in eukaryotic cells. Infection of insect cells with a recombinant baculovirus containing the cDNA for the HCV structural proteins resulted in the formation of HCV-like particles in cytoplasmic cisternae of the insect cells. Sucrose gradient purification HCV-like particles exhibited similar biophysical properties as putative HCV virions. HCV-like particles, purified in large quantities, may be useful in HCV vaccine development or in diagnostic kits.

An Enzyme-Linked Immunosorbent Assay (ELISA) to Detect Antibodies to a Nonstructural Protein of Hepatitis A Virus (HAV)

RH Purcell, T Schultheiss, D Stewart, S Emerson (NIAID).
Serial No.: 60/013, 333 filed 13 Mar. 96; PCT/US97/03428 filed 13 Mar. 97.
Licensing Contact: George Keller, 301/496–7735 ext 246.

The current invention embodies an assay which can differentiate between an individual who has been vaccinated against Hepatitis A Virus (HAV), and one who has actually been infected with the virus. HAV infection results in the production of antibodies against both structural and nonstructural proteins of the virus. Inactivated HAV vaccines, which are commonly used for immunization against HAV, cause the production of antibodies against the structural proteins. Assays currently in use for determining exposure to HAV measure only antibodies to structural proteins, and therefore are incapable of differentiating between individuals who have been infected with HAV and those who have merely been immunized with the inactivated virus.

The assay embodied in the current invention is capable of detecting antibodies to the 3C proteinase, which is a nonstructural protein of HAV. This assay, which utilizes an ELISA for the detection of such antibodies, should represent a significant improvement over assays which are currently available.

Restriction Display (RD–PCR) of Differentially Expressed mRNAs

JN Weinstein, J. Buolamwini (NCI).
Serial No.: 60/011, 379 filed 09 Feb 96; PCT/US97/02009 filed 7 Feb. 97.
Licensing Contact: J. Peter Kim, 301/496–7056 ext 264.

This invention provides a kit and methods for detecting gene expression in cells by reverse transcribing mRNA molecules into cDNA, and selectively amplifying a subset of the cDNA by a polymerase chain reaction (PCR) to present a two-dimensional display of the fragments or for cloning into a vector using restriction enzyme recognition sites added during the PCR. In one aspect of this invention, only cDNA corresponding to the 3′ end of the mRNA is amplified and displayed or cloned. In another aspect of the invention, cDNA corresponding to the entire mRNA molecule is amplified for display or cloning. The method and kit may be useful in characterizing cells based on their mRNA content, representing expressed genes, and discovering therapeutics that alter cellular gene expression by characterizing cells of different types under a variety of physiological conditions. In addition to drug discovery, this approach may be used whenever expression of mRNA is to be assessed, for example, in studies of malignant transformation, carcinogenesis, immune activation, and developmental biology.

Selective Elimination of T-Cells that Recognize Specific Preselected Targets

A Rosenberg (FDA).
Serial No.: 60/002, 964 filed 30 Aug. 95; PCT filed 30 /Aug. 96.
Licensing Contact: Jaconda Wagner, 301/496–7735 ext 284

The invention relates to methods and compositions for the elimination of T cells that recognize specific preselected targets which can be used to threat autoimmune diseases and graft rejection.

The invention provides a method for selectively inhibiting or killing T cells that recognize a specific preselected target molecule and also for modified killer cells that bear a signal transduction molecule to which is attached the preselected target molecule. Recognition of the preselected molecule by a T cell activates the killer cell which then kills or inhibits the T cell. Where the preselected molecule is an extracellular domain of an MHC from a xenograft or an allograft, treatment of the graft recipient with the modified killer T cells delays or inhibits graft rejection. Similarly, where the preselected molecule is an MHC that binds the antigenic determinant of the autoimmune disease, treatment of the organism with the modified T cells mitigates the autoimmune response directed against the antigenic determinant.

This research was published in Transpl Immunol 1993; 1(2):93–9.

Dated: January 16, 1998.

Barbara M. McGarey,

Deputy Director, Office of Technology Transfer.

[FR Doc. 98–1967 Filed 1–27–98; 8:45 am]

BILLING CODE 4140–01–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institute of General Medical Sciences; Closed Meeting

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 United States Code Appendix 2), notice is hereby given of the following National Institute of General Medical Sciences Initial Review Group (IRG) meeting:

Name of IRG: Minority Biomedical Research Support.
Date: March 10–12, 1998.
Time: March 10—8 p.m.–11 p.m.; March 11—8:30 a.m–6 p.m.; March 12—8:30 a.m.–adjournment.
Place: Holiday Inn—Bethesda, 8120 Wisconsin Avenue, Bethesda, Maryland 20814.
Contact Person: Dr. Michael A. Sesma, Scientific Review Administrators, NIGMS, Natcher Building—Room 1AS–19, Bethesda, Maryland 20892, Telephone: 301–594–2048.
Purpose/Agenda: To evaluate and review research training grant applications.

The meeting will be closed in accordance with the provisions set forth in secs. 552b(c)(4) and 552b(c)(6), Title 5 U.S.C. The