in the organization, financing, and delivery of health care services.

The Council is composed of public members appointed by the Secretary. These members are: Robert A. Berenson, M.D.; F. Marion Bishop, Ph.D.; Linda Burnes Bolton, Dr. P.H.; John W. Danaher, M.D.; Helen Darling, M.A.; Nancy J. Kaufman, M.S.; William S. Kiser, M.D.; Robert M. Krughoff; Risa J. Lavizzo-Mourey, M.D.; W. David Leak, M.D.; Harold S. Luft, Ph.D.; Barbara J. McNeil, M.D.; Walter J. McNerney, M.H.A.; Edward B. Perrin, Ph.D.; Louis F. Rossiter, Ph.D.; Albert L. Siu, M.D.; and Ellen B. White, M.B.A.

There also are Federal ex officio members. These members are: Administrator, Substance Abuse and Mental Health Services Administration; Director, National Institutes of Health; Director, Centers for Disease Control and Prevention; Administrator, Health Care Financing Administration; Commissioner, Food and Drug Administration; Assistant Secretary of Defense (Health Affairs); and Chief Medical Director, Department of Veterans Affairs.

II. Agenda

On Tuesday, May 16, 1995, the open portion of the meeting will begin at 12:30 p.m. with the call to order by the Council Chairman. The Administrator, AHCPR, will update the status of current Agency issues and program initiatives. The meeting will adjourn at 5:30 p.m.

On Wednesday, May 17, 1995, the open portion of the Council meeting will resume at 8:30 a.m. with a discussion of the AHCPR grant application review process. The open meeting will adjourn at 10:15 a.m. The Council will begin the closed portion of the meeting to discuss the AHCPR grant portfolio from 10:15 a.m. to 12:00 p.m. The meeting will then adjourn at 12:00 p.m.

Agenda items are subject to change as priorities dictate.

Dated: April 19, 1995.

Clifton R. Gaus,

Administrator.

[FR Doc. 95–10121 Filed 4–24–95; 8:45 am]

BILLING CODE 4160–90–M

National Institutes of Health

National Cancer Institute: Opportunity for a Cooperative Research and Development Agreement (CRADA) for the Scientific and Commercial Development of Monoclonal Antibodies for the Therapy and/or Diagnosis of Cancer

AGENCY: National Institutes of Health, PHS, DHHS.

ACTION: Advertisement.

SUMMARY: The Laboratory of Tumor Immunology and Biology (LTIB), National Cancer Institute is seeking pharmaceutical or biotechnology collaborator(s) which can effectively pursue the scientific and commercial development of a panel of monoclonal antibodies generated against tumor associated antigens for use in the therapy and/or diagnosis of a range of human cancers. The primary focus of these collaborations will be the development and commercialization of a panel of monoclonal antibodies consisting of two major groups: (A) Monoclonal antibodies directed against the pancarcinoma antigen, TAG–72. TAG–72 is expressed on a range of human carcinomas including colorectal, gastric, pancreatic, ovarian, endometrial, breast, non-small cell lung, and prostate. Monoclonal antibody CC49 is the prototype monoclonal antibody of this group. Humanized and other genetically engineered variants of monoclonal antibody CC49 have already been developed. (B) Monoclonal antibodies directed against human carcinoembryonic antigen, which is expressed on the following carcinomas: colorectal, pancreatic, gastric, non-small cell lung, and breast carcinoma. The prototype for this group of monoclonal antibodies is COL–1. (C) Additionally, it may likely be a further goal of these collaborations to develop novel recombinant forms of these monoclonal antibodies.

It is anticipated that because of the magnitude, diversity, and expense of these proposed research projects the collaboration(s) may take the form of multiple CRADAs. The collaboration(s) will involve all aspects of diagnostic and/or therapeutic development from basic scientific inquiry to late stage clinical trials which selected sponsor(s) will be required to partially support. The selected sponsor(s) will collaborate in the development of one or more of the following diagnostic or therapeutic forms of these monoclonal antibodies: (1) Radiolabeled monoclonal antibodies (diagnostic (oncologic imaging) and/or therapeutics); (2) Drug and/or toxin conjugated monoclonal antibodies; (3) Pro-drug conjugated monoclonal antibodies; (4) Unconjugated monoclonal antibodies (including bifunctional forms).

Sponsors will be selected based upon their ability to collaborate with NCI for the development of any of these therapeutic or diagnostic forms in accordance with the corporate role and selection criteria outlined below. It is emphasized that selection of a collaborator will not be dependent upon an entity's ability to perform the largest portion of the research project. Rather, a collaborator will be selected based upon the scientific merit and intellectual contributions brought to each individual project(s). Potential collaborators are, therefore, urged to submit proposals which focus on particular area(s) of expertise in a well-organized and precise manner which clearly outlines a development and commercialization plan. Finally, it is also possible that logical extensions of these research protocols may be considered as potential collaborative projects. Accordingly, proposals must address the requested criteria and protocols, but in addition, may include any additional unique development projects relating to the core technology.

The term of the CRADA(s) is anticipated to be three (3) to five (5) years.

ADDRESSES: Inquiries and proposals regarding this opportunity should be addressed to either Michael Christini or Mark Noel (Tel #301–496–0477, Fax #301–402–2117), Office of Technology Development, National Cancer Institute, Building 31, Room 4A49, NIH, 9000 Rockville Pike, Bethesda, MD 20892.

DATES: Proposals must be received at the above address by 5 p.m. June 26, 1995.

SUPPLEMENTARY INFORMATION: Cooperative Research and Development Agreement or ''CRADA'' means the anticipated joint agreement to be entered into by NCI pursuant to the Federal Technology Transfer Act of 1986 and Executive Order 12591 of October 10, 1987 to collaborate on the specific research project described below. Under the present proposal, the Government is seeking collaborator(s), which in accordance with the requirements of the regulations governing the transfer of technology in which the Government has taken an active role in developing (37 CFR 404.8), can further develop this technology to a commercially available status to best meet the needs of the public.

This technology has been the focal point of much research and

development within the LTIB for many years. During that time, there has been continual advances in the field of antibody development within LTIB via extensive intramural research, corporate sponsored CRADA projects, and independent corporate development under licensing arrangements.

When the excellent tumor targeting characteristics of anti-TAG–72 monoclonal antibody B72.3 in the clinic were observed, the LTIB developed a series of second generation, higher affinity monoclonal antibodies for TAG–72. This ''CC'' series, of which monoclonal antibody CC49 is the prototype, has been extensively characterized both preclinically and clinically. Radiolabeled CC49 shows much better tumor targeting in the clinic than B72.3. CC49 reacts with the majority of the following carcinomas: Colorectal, gastric, pancreatic, non-small cell lung, ovarian, endometrial, breast and prostate.

The LTIB has also developed a series of anti-carcinoembryonic antigen monoclonal antibodies (COL series). The prototype (COL–1) reacts to the vast majority of gastrointestinal and pancreatic cancers, and also to 50% of breast cancers and 70% of non-small cell lung cancers. A Phase 1 trial has just been completed with radiolabeled COL–1.

The LTIB has shown successful tumor targeting in cancer patients with radiolabeled forms of both monoclonal antibodies which are the primary focus of these collaborations: CC49 and COL–1. Phase I therapy trials for both monoclonal antibodies have been completed. Additionally, radiolabeled forms of CC49 are currently in Phase II clinical trials for colorectal, breast, ovarian, and prostatic cancer as a murine monoclonal antibody.

As a corollary, the progression of the technology can be illustrated in two specific examples of ongoing research collaborations which will not be a part of the present CRADA:

(A) The LTIB, NCI initially developed a monoclonal antibody designated B72.3, which reacts to the pancacinoma antigen termed TAG–72. This breakthrough technology provided the basis for the first and still only monoclonal antibody approved by the FDA for any *in vivo* use in cancer. Under a separate licensing agreement, Cytogen Corporation conjugated B72.3 with ^{111} In and developed Onco Scint CR/OV® for oncologic imaging to be used in conjunction with CT scan. OncoScint CR/OV® has been approved for use in both colorectal cancer and ovarian cancer.

(B) Under a separate CRADA agreement, a Phase III multicenter trial is also in progress employing ^{125} I-labeled murine CC49 with an intraoperative hand held probe as a method of radioimmunoguided surgery.

Additional Background Information

- The LTIB has shown via immunohistochemistry that anti-TAG–72 and anti-carcinoembryonic antigen monoclonal antibodies complement each other extremely well in overcoming antigen heterogeneity. Serum assays for carcinoembryonic antigen and TAG–72 (CA72–4) are also complementary in that non-coordinate expression is observed.
- Previous collaborative studies on the use of the CC49 and COL–1 monoclonal antibodies as drug conjugates demonstrated anti-tumor effects in animal models.
- The LTIB has recently developed CDR grafted (humanized) forms of monoclonal antibody CC49, and other novel genetically engineered immunoglobulin forms for CC49 could be the subject of any CRADA. Similar constructs of anti-carcinoembryonic antigen monoclonal antibodies could also be the subject of any CRADA.
- Recent clinical trials have supported the preclinical observations that recombinant interferon will selectively upregulate both TAG–72 and carcinoembryonic antigen expression on the surface of tumor cells. This finding should enhance both diagnostic and therapeutic uses of these classes of monoclonal antibodies, and these studies could be included as CRADA activities.
- The NIH has exclusively licensed the rights for monoclonal antibody CC49 for use with the radioimmunoguided surgery intraoperative probe as part of a separate collaboration.
- A comprehensive list of publications relating to this technology, intellectual property and background licensing information, and general CRADA information will be provided upon initial contact with NCI.

Party Contributions

The role of the National Cancer Institute includes the following:

(1) Develop novel recombinant forms of monoclonal antibodies.

(2) Initial characterization of hybridoma cell lines producing monoclonal antibodies.

(3) Conduct preclinical testing (tumor targeting and therapy) of these monoclonal antibodies both *in vivo* and *in vitro* as unlabeled immunoglobulin forms and/or as antibody conjugates.

(4) Conduct preclinical studies on the use of biologic response modifiers to upregulate tumor targeting and therapy.

(5) Analyze pharmacokinetics and anti-immunoglobulin responses in some clinical trials.

The role of the successful corporate sponsor(s) will include:

(1) Develop high producer clones of the monoclonal antibodies and recombinant immunoglobulin producing cells lines and cultures supplied by the NCI and optimize production and purification procedures for experimental tumor targeting and therapy studies.

(2) Produce and purify clinical grade (GMP) monoclonal antibodies for clinical trials and submit Drug Master Files in support of the monoclonal antibody production.

(3) Conduct toxicity studies as required by the FDA.

(4) Develop methodologies for the conjugation of monoclonal antibodies with (A) Radionuclides, (B) Drugs and/or toxins, (C) Pro-drugs, (D) Bifunctional antibodies.

(5) Submit IND application in support of clinical trials.

(6) Conduct clinical trials using monoclonal antibody and immunoglobulin forms.

The role of both the National Cancer Institute and the successful corporate sponsor(s) will include:

(1) Optimize purification schemes for immunoglobulin forms, prior to and post conjugation.

(2) Collaborate on clinical trial design including protocols using biologic response modifiers (e.g., recombinant interferon).

(3) Collaborate on data analysis in support of clinical trials.

Selection Criteria

Proposals submitted for consideration should fully address each of the following qualifications:

(1) Experience in the GMP production, purification, quality control of monoclonal antibodies and regulatory requirements of monoclonal antibody clinical trials.

(2) Experience in the conjugation of monoclonal antibodies with one or more of the following: (A) Radionuclides, (B) Drugs and/or toxins, (C) Pro-drugs, (D) Bifunctional Antibodies *and* the analyses of these reagents.

(3) Ability to provide necessary reagents on a timely basis.

(4) Experience in conducting clinical trials.

(5) Willingness to cooperate with the National Cancer Institute in the collection and evaluation of data.

(6) Agreement to be bound by the DHHS rules involving the use of human and animal subject, and human tissue.

(7) Ability to obtain background license to relevant patent rights.

(8) Willingness to agree to Federal Statutory provisions for the equitable distribution of patent rights to any CRADA subject-matter inventions. Generally, the rights of ownership are retained by the organization which is the employer of the inventor, with (A) an irrevocable, non-exclusive, royalty-free research license to the Government (when a company employee is the sole inventor) or (B) an option for an exclusive or non-exclusive license to the company on terms that are appropriate (when the Government employee is the sole or joint inventor).

(9) Willingness to cost share in laboratory studies including the funding of personnel dedicated to completion of the CRADA research project.

(10) Submission of an initial response to the NIH Model CRADA boilerplate provisions.

Dated: April 13, 1995.

Dr. Thomas Mays,

Director, Office of Technology Development, National Cancer Institute, National Institutes of Health.

[FR Doc. 95–10110 Filed 4–24–95; 8:45 am]

BILLING CODE 4140–010–P

National Cancer Institute: Opportunity for a Clinical Trial Cooperative Research and Development Agreement (Clinical Trial ''CRADA'') for the Scientific and Commercial Development of the Signal Transduction Inhibitor, ''CAI'', as an Anticancer Agent

AGENCY: National Institutes of Health, PHS, DHHS.

ACTION: Notice.

SUMMARY: The Department of Health and Human Services (DHHS) seeks a pharmaceutical company which can effectively pursue the clinical development of the signal transduction inhibitor, carboxyamide-amino triazole (''CAI'', NSC 609974), for the treatment and/or prevention of cancer. The National Cancer Institute has data suggesting that CAI may have potential for the treatment and prevention of cancer. The selected sponsor will be awarded a CRADA for the co-development of this agent with the National Cancer Institute.

ADDRESSES: Questions about this opportunity may be addressed to Mark W. Noel, Office of Technology Development, NCI, Building 31/Room 4A51, 9000 Rockville Pike, Bethesda, Maryland 20892, (301) 496–0477, facsimile (301) 402–2117, from whom further information including a summary copy of the preclinical and clinical data may be obtained.

DATES: In view of the important priority of developing new agents for the treatment or prevention of cancer, interested parties should notify this office in writing no later than June 25, 1995. Respondents will then be provided an additional 60 days for the filing of formal proposals.

SUPPLEMENTARY INFORMATION: ''Cooperative Research and Development Agreement'' or ''CRADA'' means the anticipated joint agreement to be entered into by NCI pursuant to the Federal Technology Transfer Act of 1986 and Executive Order 12591 of October 10, 1987 to collaborate on the specific research project described below. The present opportunity will be for a Clinical Trial CRADA. The Clinical Trial CRADA is a modification of the standard NIH Model Agreement wherein additional language has been drafted to enable the Collaborator to access and utilitize clinical trial data.

The Government is seeking a pharmaceutical company which, in accordance with the requirements of the regulations governing the transfer of agents in which the Government has taken an active role in developing (37 CFR 404.8), can further develop CAI through Federal Food and Drug Administration approval and to a commercially available status to meet the needs of the public and with the best terms for the Government.

CAI is a novel chemically defined compound which has shown promising antitumor activity in several preclinical trials. The drug is under patent to Merck & Co., Inc. (U.S. Patent 4,590,201). The use of CAI in a method of treating peritoneal carcinomatosis of solid tumors is claimed in U.S. Patent 5,132,315 assigned to the Dept. of Health and Human Services. A method for the detection and quantitation of CAI levels in blood is claimed in U.S. Patent 5,405,782 which is also assigned to the Dept. of Health and Human Services. Its use in the treatment of cancer in patients with a surgically excised tumor with a high probability of metastasis and its use in treatment of cancers involving the transportation of individual cells to other tissue from a metastasizing tumor are claimed in U.S. Patent 5,045,543 (assigned to Merck & Co. Inc). The Clinical Trial CRADA will allow a pharmaceutical company to provide resources, in collaboration with the NCI, for the continuing preclinical and clinical development work for this agent and its eventual commercialization. Merck & Co.'s patent rights will be available for licensing on terms to be mutually agreed upon by Merck and the selected Collaborator. Similarly, the Government will make its relevant intellectual property rights available for licensing to the Collaborator.

Based on the promising data obtained from the ongoing Phase I clinical trials, there is a need to obtain greater quantities of CAI and to continue clinical development of this agent. The NCI is interested in establishing a Clinical Trial CRADA with a pharmaceutical company to assist in the continuing development of CAI. The government will provide all relevant available expertise and information to date and will jointly pursue new trials as required giving the pharmaceutical company exclusive rights to all preclinical and clinical data for regulatory approval and its New Drug Application (NDA). The successful pharmaceutical company will provide the necessary quantities of drug plus the necessary financial and organizational support to complete further development of CAI to establish clinical efficacy and possible commercial status.

The expected duration of the CRADA will be three (3) to five (5) years.

The role of the National Cancer Institute, includes the following:

1. The government has data for the bulk production of clinical grade CAI. The successful pharmaceutical company will be allowed access to this data.

2. The government will provide data concerning pharmaceutical manufacturing and controls, including dosage form development data for the finished product.

3. The government will allow the pharmaceutical company to review and cross-file the NCI's IND.

4. The government will make the NCI's IND proprietary under such circumstances and make the IND available (exclusively) to the pharmaceutical company.

5. The government will continue the clinical development of this compound under its clinical trials network in coordination with the pharmaceutical company.

6. Relevant Government intellectual property rights are available for licensing through the Office of Technology Transfer, National Institutes of Health. For further information contact Jack Spiegel, Office of Technology Transfer, National Institutes of Health, Box OTT, Bethesda, MD 20892; (301) 496–7735; facsimile (301) 402–0220.