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April 28, 2008

*BY HAND DELIVERY*

Office of the Assistant Attorney General
Antitrust Division
Department of Justice
Main Justice Building
Room 3109
950 Pennsylvania Ave., N.W.
Washington, DC 20530

Re: Request for Business Review Letter

Dear Mr. Barnett:

Pursuant to 28 CFR § 50.6, the CEO Roundtable on Cancer ("CRC"), which is working in partnership with the National Cancer Institute ("NCI"), hereby requests a business review letter from the Department of Justice concerning the proposed action described below.

NCI is the federal government's principal agency for cancer research and training. The CRC is a non-profit organization with the principal goal of making continual progress toward the elimination of cancer as a personal disease and public health problem. NCI and CRC independently have concluded that the negotiation of clinical trial agreements between trial sponsors and research institutions is one of the most significant contributors to delay in the startup of cancer clinical trials. Both NCI and CRC have an interest in streamlining the clinical trial negotiation process, thereby expediting the performance of clinical trials and thus the availability of important medical treatments for diseases such as cancer. Towards that goal, NCI and CRC recently identified the standardization of key clinical trial agreement clauses as a top priority. Based on this common interest, NCI and CRC decided to work together to develop and circulate options for standardized agreement clauses to be used on a voluntary basis by trial sponsors and research institutions as the foundation for the negotiation of clinical trial agreements. The project plan is described in more detail in Section II of this letter.

NCI and CRC believe that this effort will result in reduced transaction costs and greater efficiency in negotiating agreements, without any adverse competitive effects. As described in more detail below, the project will not address price or price-related clauses. It will be made clear that the use of the standardized clauses is entirely voluntary – parties to a clinical trial agreement are free to adopt, modify, or choose not to use any, or all, of the standardized clauses. Moreover, the

project will be implemented in a way so as to not cause or increase the possibility of sharing competitively sensitive information.

## I. Background

### *A. Rationale for the Project*

Clinical trials are a critical component in developing new treatments for cancer and other diseases. Before a new pharmaceutical product or medical device can be marketed legally in the United States and many foreign countries, it must be proven, to the satisfaction of the U.S. Food and Drug Administration ("FDA") or other local regulatory agency, to be safe and effective when used in humans. The data necessary for establishing safety and effectiveness are collected through clinical trials – basically human research projects – that are performed at public and private hospitals, clinics and universities throughout the world.

Clinical trials are customarily performed pursuant to contracts, known as clinical trial agreements, that typically involve three parties: (1) the pharmaceutical or device company, known as the "sponsor," (2) the hospital, clinic or university where the research is performed, known as the "research institution," and (3) the physician who is in charge of the trial, known as the "principal investigator." A variety of complex issues arise in connection with clinical trials, including confidentiality, coordination with other research sites, exposure to liability for patient injury, allocation of ownership of any resulting inventions, and Medicare and other third-party payer reimbursement, all of which are typically the subject of clinical trial agreements.1

Representatives of research institutions and sponsors who engage in the negotiation of clinical trial agreements have concluded that these negotiations are a significant barrier to the initiation of clinical trials. One study published in the Journal of Clinical Oncology investigated the various administrative barriers that impact the opening of clinical trials and concluded that "it is immediately apparent that the process taking the longest time . . . is the contract and grants process."2 The study found that it takes a median of 172 days to open a clinical trial, irrespective of the phase of the study; contracts and grant review alone take a median of 78.5 days (ranging anywhere from 7 to 461 days), compared to 47 days for review and approval by an Institutional Review Board.3 The authors concluded that "enhancing the efficiency of opening clinical trials would make the process faster and enhance overall patient treatment options without compromising research integrity or patient safety."4 A separate study concluded that notwithstanding the delay caused by the negotiation of terms of clinical trial agreements, the participants rarely or never end negotiations without an agreement, meaning "the end result is a good agreement that took an undue

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1 See sample "Clinical Trial Agreement" (Attachment A).

2 See David M. Dilts and Alan B. Sandler, *Invisible Barriers to Clinical Trials: The Impact of Structural, Infrastructural, and Procedural Barriers to Opening Oncology Clinical Trials*, 24 J. CLINICAL ONCOLOGY 4545, 4551 (Oct. 1, 2006) (Attachment B).

3 See Attachment B at 4548 (Table B), 4549.

4 See Attachment B at 4551.

amount of time to reach – and, on some unfortunate occasions, so much time that the opportunity to enroll patients in the study had passed."5

The goal of the proposed NCI/CRC standardization project described in this letter is to increase the efficiency of the clinical research negotiation process so that the delays in beginning crucial clinical research can be reduced substantially.

***B. Standardization Project Leaders***

The project to standardize clinical trial agreement clauses will be jointly led by the NCI Coordinating Center for Clinical Trials and the Clinical Operations Team of the CEO Roundtable Life Sciences Consortium, under the auspices of the NCI Clinical Trials Advisory Committee ("CTAC") Public/Private Partnership Subcommittee. NCI has also hired the Science and Technology Policy Institute as an independent organization to manage this project in coordination with outside legal counsel.

*1. CEO Roundtable on Cancer's Life Sciences Consortium*

The CRC is a multi-industry effort to facilitate cross-company and cross-sector collaboration to help expedite oncology drug discovery and development. Its membership includes executives from major American companies as well as representatives from the federal government and non-profit organizations. It is a 501(c)(3) non-profit organization that is supported in full by annual contributions from its membership. The goal of the organization is to make continual progress toward the elimination of cancer as a personal disease and public health problem.6

The CEO Roundtable on Cancer's Life Sciences Consortium ("LSC") is a CRC task force comprised of individuals with expertise and interest in the life sciences, particularly as it applies to finding a cure for cancer. Members include, among others, executives from biotechnology and pharmaceutical companies. In early 2007, the Clinical Operations Team of the LSC chose standardization of key clinical trial agreement clauses as one of its top priorities.

*2. National Cancer Institute*

The National Cancer Institute ("NCI"), established under the National Cancer Act of 1937, is the federal government's principal agency for cancer research and training. It is a component of the National Institutes of Health ("NIH") and one of eight agencies that compose the Public Health Service in the Department of Health and Human Services.

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5 See Nikki J. Zapol, *Negotiating Industry-Sponsored Clinical Trial Agreements, A View from the Trenches*, 949(1) ANNALS NEW YORK ACADEMY OF SCIENCES 349-351 (2001) (describing the aspects of the clinical trial negotiation process which make it difficult to execute clinical trial agreements in a timely manner) (Attachment C).

6 See "CEO Roundtable on Cancer," at http://www.ceoroundtableoncancer.org//index.php?option=com_frontpage&Itemid=56.

The National Cancer Advisory Board ("NCAB") is an advisory committee to the NCI and governed by the provisions of the Federal Advisory Committee Act ("FACA").7 In January 2004, the NCAB created the Clinical Trials Working Group ("CTWG") to advise the NCAB on the development, conduct, infrastructure, and support necessary for the optimal coordination and future progress of the entire range of intramural and extramural clinical research trials supported by NCI.

The CTWG was comprised of experts from academic research institutions, the pharmaceutical industry, cancer patient advocacy groups, NCI, NIH, other federal agencies (such as the Food and Drug Administration and the Centers for Medicare & Medicaid Services), and leaders from major grant and cooperative-agreement programs supported by the NCI, including the Cooperative Groups, specialized programs of research excellence ("SPOREs"), the Cancer Community Oncology Program ("CCOP"), and NCI-designated Cancer Centers.8

In June 2005, CTWG issued a report that included as one of its initiatives the development of commonly accepted clauses for the clinical trial agreements negotiated between industry and research institutions.9 CTWG developed this initiative because it concluded that the lack of standardized agreement language is one of the important contributors to the delays often encountered in the startup of clinical trials.

The NCI's Coordinating Center for Clinical Trials ("CCCT") is the organization charged with implementing the initiatives set forth in CTWG's June 2005 report, including the project to standardize clinical trial agreement clauses. CCCT implements these initiatives in conjunction with NCI's operating divisions, centers, and offices. Its responsibilities include the management, coordination, administration, and/or support of a variety of projects.10

*3. Clinical Trials Advisory Committee's Public/Private Partnership Subcommittee*

The Clinical Trials Advisory Committee ("CTAC") is a FACA committee created as a result of the June 2005 CTWG report. It provides advice to the NCI Director, Deputy Directors, and Division Directors on the NCI-supported national clinical trials enterprise. Its goal is to build a strong scientific infrastructure by bringing together a broadly developed and engaged coalition of stakeholders involved in clinical trials.11 One of the CTAC's Public/Private Partnership ("PPP") ad hoc Subcommittee functions is to provide advice on the joint project of NCI and CRC to develop standardized clinical trial agreement clauses.

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7 See "National Cancer Advisory Board – Charter Summary," at http://deainfo.nci.nih.gov/Advisory/ncabchr.htm; see also Federal Advisory Committee Act, 5 U.S.C. Appendix 2.

8 See "Overview – Clinical Trials Working Group," at http://ccct.nci.nih.gov/about_us.

9 See "Report of the Clinical Trials Working Group of the National Cancer Advisory Board – Restructuring the National Cancer Clinical Trials Enterprise," National Cancer Institute (June 2005), at 40-41 (Attachment D).

10 See "About Us – CCCT," at http://ccct.nci.nih.gov/about_us.

11 See "Clinical Trials Advisory Committee," at http://deainfo.nci.nih.gov/advisory/ctac/ctacfo.htm.

*4. Science and Technology Policy Institute*

The Science and Technology Policy Institute ("STPI") is a federally-funded research and development center ("FFRDC") that assists the federal government in formulating science and technology policy. It provides objective analytic support to inform policymakers at the Office of Science and Technology Policy and other Executive branch agencies, offices, and councils involved in the national science and technology enterprise. It comprises a broad array of capabilities spanning information technology, space and physical sciences, social/behavior sciences and education, life sciences and the environment, homeland security, and economic competitiveness. As a FFRDC, STPI can only work for the federal government and hence cannot be involved in advising sponsors or research institutions regarding the negotiation of specific clinical trial agreements.

NCI hired STPI as an independent organization to lead the effort to standardize clinical trial agreement clauses. Specifically, Dr. Judith A. Hautala has been given responsibility for managing and coordinating this project. Since joining STPI in 2005, Dr. Hautala has been involved with various strategic planning processes for NCI and NIH, including the CTWG. Before joining STPI, Dr. Hautala was Vice President, Research and Development, American Red Cross Biomedical Services and Director of the Jerome H. Holland Laboratory for the Biomedical Sciences. Other individuals associated with STPI or hired by STPI will advise and assist Dr. Hautala with this project as necessary.12

***C. Other Project Participants***

Each participating organization listed below has identified members of its business and legal staff who will participate in this project in a consulting capacity (hereinafter "Stakeholder Consultants").

*1. NCI-Designated Cancer Centers*

The NCI has identified the following sixteen NCI-Designated Cancer Centers ("Cancer Centers") to participate in this project:

- Abramson Cancer Center
- Arizona Cancer Center

12 Two of the individuals currently on staff for this project include Oren Grad, M.D./Ph.D. and D. Dale Shoemaker, Ph.D. Dr. Grad is a consultant with STPI. He has been active in the fields of medical technology assessment and health and science policy analysis for more than 20 years. He previously served as a principal in one of the leading pharmacoeconomics and health care outcomes research practices in the United States. Dr. Shoemaker spent over 30 years at NCI, primarily with the Cancer Therapy Evaluation Program, Division of Cancer Treatment and Diagnosis, serving as the Head of the Drug Regulatory Affairs Section, Investigational Drug Branch, for two years, and then Chief of the Regulatory Affairs Branch. He retired from NCI in March 2007.

- City of Hope National Medical Center
- Dana Farber/Harvard Cancer Center
- Fox Chase Cancer Center
- Moffitt Cancer Center
- Mayo Clinic Cancer Center
- MD Anderson Cancer Center
- Ohio State University
- Roswell Park Cancer Institute
- Sidney Kimmel Cancer Center
- UCSF Cancer Center
- UNC Lineberger Cancer Center
- University of Colorado Cancer Center
- University of Chicago Cancer Research Center
- University of Pittsburg Cancer Center

*2. NCI Clinical Trial Cooperative Groups*

Cooperative Groups are comprised of a large network of researchers, physicians, and health care professionals at public and private institutions across the country working toward the common goal of designing and conducting large-scale cancer clinical trials in a multi-institutional setting. 13

The PPT Subcommittee of the CTAC has also identified five Cooperative Groups to participate in this project, including:

- Cancer and Acute Leukemia Group B
- Children's Oncology Group
- Eastern Cooperative Oncology Group
- Gynecologic Oncology Group
- Southwest Oncology Group

*3. Life Sciences Consortium Companies*

The LSC includes the following eleven companies ("LSC Companies") which support cancer clinical trials at research institutions, including the above Cancer Centers and Cooperative Groups and which will participate in this project:

- AstraZeneca
- Eli Lilly
- GlaxoSmithKline
- Johnson & Johnson
- Novartis
- OSI Pharmaceuticals
- Pfizer

13 See "Clinical Trials Cooperative Group Program," at http://ctep.cancer.gov/resources/coop2.html.

- Quintiles
- Sanofi-Aventis
- Schering-Plough
- Wyeth

*4. Non-LSC Companies*

The NCI and the PPP Subcommittee of the CTAC may also identify at least five smaller companies that support cancer clinical trials but are not part of the LSC to participate in this project. These Non-LSC Companies have not yet been determined.

## II. Proposed Conduct

As discussed above, the lack of standardized language in clinical trial agreements contributes substantially to delay in the startup of clinical trials. Nearly each time a new trial is initiated, the research institution and trial sponsor must negotiate a new agreement, even though most of the issues addressed are common across trials and sponsors.14 This creates large inefficiencies in the system, both in terms of time requirements, manpower needs, direct costs, and opportunity costs. Moreover, many participants with experience in the negotiation process believe that ultimately a large portion of final clinical trial agreements contain clauses that are relatively similar.

NCI and CRC believe that developing standardized clauses for certain key issues that typically arise in clinical trial agreement negotiations could significantly help reduce the time and effort for initiating a clinical trial. These clauses could be used as a common starting point for agreement negotiations, thereby "jump starting" such efforts. The use of the standardized clauses would be entirely voluntary, and there would be no agreement among participants that they would use only the standardized clauses.

At the current stage of the project, the main participants – Cancer Centers, LSC Companies, and Cooperative Groups – have shared their template clinical trial agreements with NCI. These participants have also shared with NCI final negotiated agreements that have been redacted to exclude all pricing terms and any information that could identify the parties to the agreement. To date, NCI has received a total of 64 clinical trial agreements from the participants – 38 are model or template agreements and 26 are redacted copies of final agreements as negotiated.

NCI has forwarded these clinical trial agreements to Dr. Hautala and STPI for analysis. STPI, in conjunction with outside legal counsel, are in the process of analyzing these clinical trial agreements to identify the differences in key terms and options for standardization and/or harmonization. None of the individuals at NCI or STPI who have access to the template or actual agreements are currently involved in negotiating clinical trial agreements themselves. Dr. Hautala and others at STPI are also in the process of reviewing and analyzing studies and articles published by other organizations on the topic of standardization of clinical trial agreements.

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14 See Attachment C at 350-51.

The future stages of the project are as follows:

*1. Identify and reach consensus on which specific clinical trial agreement clauses most frequently delay or complicate negotiations between sponsors and research institutions.*

The STPI, led by Dr. Judith Hautala will work with the Stakeholder Consultants and the CCCT staff to reach a consensus on the specific clauses to be addressed during this project. The clauses most likely to be addressed include the following:

- Intellectual Property and Licensing
- Publishing Rights
- Confidentiality
- Ownership of Data
- Risk and Indemnification
- Rights to Bio-specimens

Outside legal counsel will review the list to ensure that none of these proposed agreement clauses include price or price-related terms. The final list of target clauses will be reviewed and ratified by the PPP Subcommittee of the CTAC.

Although these clauses may be the subject of lengthy negotiation, they are not the most important clauses from a competitive standpoint. From the perspective of the sponsor, the three most important factors considered when determining whether to choose a particular research institution are as follows: (1) price, (2) ability to accrue patients, and (3) access to quality investigators. These factors will not be the subject of this standardization project.

*2. Recommend potential clinical trial agreement clauses for inclusion in the standardization project.*

STPI, with the assistance of outside legal counsel, will generate a list of the key differences in the clinical trial agreement clauses identified for standardization. They will also generate a list of options for standardization for each of these clauses.

STPI and outside legal counsel will then consult with the Stakeholder Consultants and the CCCT staff to refine these lists of key differences and options for standardized language. The goal will be to develop a group of potential standardized clauses to send to the LSC Clinical Operations Team and the PPP Subcommittee of the CTAC for review.

For some of the issues under consideration, for example those which are addressed in clauses that are relatively similar across a wide range of agreements, the participants may be able to agree to suggested standardized language. For other issues where there are more diverse approaches, the participants may not be able to reach a consensus on proposed standardized language. In these cases, the project may result in two or more alternative options for standardized clauses, or perhaps it will not be possible to propose any suggested provisions. In all cases, of course, to the extent standardized language is proposed, it will be only a starting point for

negotiations between the contracting parties, and the use of any provision will be left to the individual determination of each party acting independently.

*3. Develop an approach to achieve buy-in and consensus on the standardization/ harmonization options by key stakeholders.*

The NCI and the LSC Clinical Operations Team will work together to develop a structured approach for achieving consensus on the group of standardized agreement clauses. While the exact method of consensus-building is still undetermined, it is likely to include one of the following methods:

- *Consensus Conference or Roundtable:* Stakeholder representatives from a broader range of industry sponsors and research institutions, as well as those organizations participating in the earlier stage of the project, will attend a conference at which they will consider all potential standardized clauses developed by STPI and reviewed by the LSC Clinical Operations Team and the PPP Subcommittee.

- *Series of focus groups:* A series of smaller focus groups, involving the same range of stakeholder representatives, will meet to consider a subset of the standardized clauses. This may or may not be followed with a Consensus Conference or Roundtable attended by all stakeholder representatives involved in the focus groups.

Legal counsel will provide guidance to all participants with respect to consensus-building conferences, roundtables, or focus groups to ensure that communications among participants are limited to the subject of standardized clauses and that no competitively-sensitive information is exchanged.

*4. Disseminate and promote use of the standardized agreement clauses.*

NCI and the LSC will then work with industry, including biotechnology and pharmaceutical companies, to promote the adoption of the standardized agreement clauses by clinical trial sponsors. They will also work with academic medical centers and other research institutions to encourage them to adopt the standardized clauses. It will be made clear, however, to both sponsors and research institutions that use of these standardized clauses are not mandatory, and that they are to be used simply as a starting point for further independent negotiations by the parties.

Dissemination and promotion of the voluntary standardized agreement clauses likely will be an ongoing process involving various conferences and roundtables with the wider community of stakeholders and others.

## III. Legal Analysis

The proposed project to develop and disseminate standardized clinical trial agreement clauses does not violate Section 1 of the Sherman Act or any other antitrust law.

This project is likely to have several procompetitive benefits. The availability of standardized clinical trial agreement clauses will greatly enhance the efficiency and reduce the transactions costs involved in negotiating clinical trial agreements, which has been a significant source of delay in implementing clinical trials. The proposed standardized clauses will give parties, at their option, the ability to get a head-start in the negotiations. The availability of standardized clauses may be particularly helpful to smaller pharmaceutical companies and research institutions who lack in-house resources or expertise in clinical trial agreement negotiations.

There is little or no likelihood that the proposed project would restrain competition or facilitate collusion among the parties. The standardized agreement clauses will not address price or price-related issues. Also, the standardized agreement clauses are not key competitive factors in negotiating clinical trial agreements. The proposed methods of developing and disseminating the standardized agreement clauses will protect against any potential anticompetitive coordination among participants. Specifically, the sample agreement clauses that are being analyzed will be collected by NCI's CCCT and STPI, neither of which is involved in clinical trial negotiations, and will be redacted to ensure that they do not contain price or price-related terms or information that could identify the parties. None of the participants, including the LSC Companies, the Cooperative Groups, nor the Cancer Centers, will have access to competitively sensitive information during the course of developing the proposed or final standardized agreement clauses that are disseminated. Counsel will provide guidance for meetings of sponsors and research institutions to develop and discuss the proposed clauses to ensure that competitively-sensitive information is not exchanged. The standardized agreement clauses will be disseminated for use on a voluntary basis, allowing research institutions and trial sponsors to adopt, amend or disregard the standardized clauses in developing their clinical trial agreements.

In submitting this advisory opinion request, we are aware of two requests for Business Review Letters submitted to the Department of Justice ("DOJ") relating to efforts to develop standardized contract terms in other industries. In 2006, the DOJ approved a proposal of the American Trucking Association ("ATA") which expanded upon the ATA's model contract program previously approved by the DOJ in November of 2002.15 The stated purpose of the ATA model agreements was to increase efficiency in contract negotiations and reduce transaction costs for the negotiating parties, which included both motor carriers and freight transportation brokers. The ATA agreements were made available for use on a voluntary basis – there was no obligation of parties to use model agreements in whole or in part. The DOJ found that the proposal was unlikely to reduce competition.

Also in 2006, the DOJ approved the proposal of the American Peanut Shellers Association ("APSA") regarding its amendment to the Association's rules in order to standardize terms for "offers, sales, and purchases of peanuts to help contracting parties avoid misunderstandings, make more definite the terms of contracts of purchase and sale, avoid the necessity of drafting in each

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15 Dep't of Justice, Antitrust Div., Business Review Letter to American Trucking Association (Aug. 10, 2006), *available at* http://www.usdoj.gov/atr/public/busreview/217742.htm.

instance a lengthy and cumbersome document, and otherwise increase transaction efficiency."16 The DOJ concluded that the proposed revisions to the rules and standardized terms would not reduce competition because both are used as base standards from which the parties are free to negotiate their own contract terms that may diverge from the standardized terms.

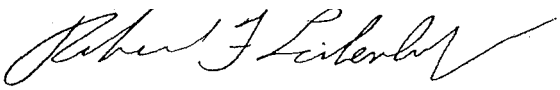
The proposed standardized agreement clauses for clinical trial agreements are analogous to those proposed and approved by the DOJ in previous Business Review Letters. The standardized clauses will increase the efficiency in negotiations for clinical trial agreements between principal investigators, trial sponsors, and research institutions. The availability of standardized clauses will reduce transaction costs, expedite the clinical trials startup process, and alleviate the need for parties to negotiate individual clauses of each agreement. Furthermore, the voluntary nature of the standardized agreement clauses (which will not include price or price-related terms) ensures that parties are free to negotiate all clauses of clinical trial agreements, thereby opting out of the standardized agreement clauses.

## IV. Conclusion

NCI and the CRC believe the lack of standardized language in clinical trial agreements leads to the renegotiation of agreement clauses for each new trial that is initiated, even though most of the issues addressed are common across trials and sponsors, which leads to significant delays in trial startup. This duplication of efforts creates large inefficiencies in the system, both in terms of time requirements, manpower needs, direct costs, and opportunity costs. Developing standardized agreement clauses will alleviate this burden on all parties to a clinical trial agreement, significantly reduce the time and effort expended on this aspect of trial startup, and hopefully shorten the time needed to get life-saving therapies to patients in need. And as described in this letter, this effort can be undertaken so that it will not result in any anticompetitive effects.

Of course, we would be glad to respond to any questions or requests for further information regarding this request.

Sincerely,



Robert F. Leibenluft

Enclosures: Attachments

cc: Martin Murphy, M.D., CEO Roundtable on Cancer
Sheila Prindiville, M.D., M.P.H., National Cancer Institute
John Niederhuber, M.D., National Cancer Institute
Joshua H. Soven, Chief, Litigation I Section, Department of Justice

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16 Dep't of Justice, Antitrust Div., Business Review Letter to American Peanut Shellers Association (Feb. 2, 2006), *available at* http://www.usdoj.gov/atr/public/busreview/214772.htm.