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Industry-Funded Research and Conflict of Interest: An Analysis of Research Sponsored by the Tobacco Industry through the Center for Indoor Air Research

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Abstract

The Center for Indoor Air Research (CIAR) was created by three United States tobacco companies in 1988. Its stated mission is to fund high-quality, objective research related to indoor air, including studies of environmental tobacco smoke (ETS). CIAR states publicly that it is independent of the industry, and that the research it funds is unbiased. The purpose of our study was to examine the content, quality and use of research funded by CIAR, to determine whether CIAR is fulfilling its mission. We found that two-thirds of CIAR's projects were awarded following peer-review by an independent group of scientists, while one-third underwent a special review process and were awarded directly by tobacco industry executives. CIAR's "special-reviewed" projects were more likely than its "peer-reviewed" projects to be related to ETS; to be awarded to non-academic investigators; to be awarded to investigators who publish in non-peer-reviewed and symposia publications; and to support the tobacco industry position that ETS has not been proven harmful to health. In addition, investigators who received funding for "special-reviewed" projects were more likely to have testified on the industry's behalf at federal hearings related to ETS. At least two of CIAR's "special-reviewed" projects appear to have significant design flaws that would tend to bias their results toward the tobacco industry position. Our findings suggest that the tobacco industry is funding "special-reviewed" projects through CIAR to develop scientific data that it can use in legal and legislative settings. The industry may be funding "peer-reviewed" projects through CIAR to enhance its credibility, to provide good publicity, and to distract attention away from ETS as an indoor air pollutant.

Introduction

During the 1980s, scientific evidence began to suggest that passive smoking, as well as active smoking, was harmful to health. Three studies were published in 1981 suggesting that nonsmokers exposed to environmental tobacco smoke (ETS) had an increased risk of lung cancer (Garfinkel 1981; Hirayama 1981; Trichopoulos et al. 1981). In 1986, two scientific consensus reports on the harmful effects of exposure to ETS were published independently by the U.S. Surgeon General and the National Academy of Sciences (National Academy of Sciences 1986; U.S. Department of Health and Human Services 1986). And in 1992, the U.S. Environmental Protection Agency classified ETS as a Group A (known human) carcinogen (U.S. Environmental Protection Agency 1992). These reports have led to increasing restrictions on smoking indoors in order to minimize exposure of nonsmokers to ETS.

In contrast, a study published in 1992 in a peer-reviewed journal concluded that "... acceptable air quality can be maintained [indoors] with moderate amounts of smoking (Turner et al. 1992)." This study was funded by the Center for Indoor Air Research (CIAR), which was created by U.S. tobacco companies in 1988. CIAR's stated mission is to fund high-quality, objective research related to indoor air, including studies of environmental tobacco smoke (Center for Indoor Air Research 1989). Tobacco companies provide the bulk of funding for CIAR, and tobacco company executives sit on CIAR's Board of Directors. Both CIAR and the tobacco industry state that CIAR is an independent organization. In particular, they emphasize that CIAR's projects are funded in a "scientifically rigorous and objective manner" based on peer review by a group of independent scientists known as the

Science Advisory Board (Center for Indoor Air Research 1994:3). CIAR states that this peer-review process "ensures that only high quality research ... is recommended for funding (Center for Indoor Air Research 1994:3)."

Whenever an industry funds research that is directly related to its product, there is concern that conflict of interest may influence the research in some way (Bond 1991; Hillman et al. 1991; Blank 1992; Rothman 1993; Chren 1994; Witt and Gostin 1994). In particular, there is concern that the sponsor may apply overt or covert pressure on the investigator to produce results that will be favorable (Hillman et al. 1991). For example, the sponsor could recommend that the investigator employ a study design that would be more likely to favor its product. Or the sponsor could encourage a researcher to emphasize certain conclusions in the final publication of the data. Even without any sort of external pressure, investigators may feel consciously or subconsciously compelled to publish findings that are pleasing, or at least not damaging, to their sponsors (Hillman et al. 1991). In particular, investigators may fear that future funding will be denied if they publish unfavorable data (Hillman et al. 1991).

Several studies on the effects of industry sponsorship indicate that these concerns over conflict of interest may be justified. One study showed that research funded by the chemical industry was more likely than government-funded research to conclude that occupational exposure to chemical agents was not harmful (Swaen and Meijers 1988). Another study found that research sponsored by the pharmaceutical industry was more likely than research funded through other sources to favor the new drug under evaluation (Davidson 1986). Similarly, a third study showed that research

sponsored by drug companies almost always concluded that the sponsor's drug was equivalent or superior to comparison drugs, even when the data did not completely support this conclusion (Rochon et al. 1994). These studies provide strong evidence that industry funding may influence the type of research conducted and the conclusions drawn from the data.

History has also shown that, when scientific findings are particularly damaging, industry may attempt to conceal, manipulate or deny the findings. The asbestos industry, for example, funded external contract research on the health effects of asbestos from the 1930s to the 1950s (Lilienfeld 1991). According to internal memos, these studies suggested that exposure to asbestos could cause asbestosis and lung cancer. However, the study results were suppressed, and the industry continued to deny that asbestos was hazardous to health (Lilienfeld 1991). Similarly, the lead industry has denied or downplayed evidence suggesting that lead in paint is a common cause of disease in children (Rabin 1989).

The tobacco industry has a history of funding scientific research that it claims is independent but is actually designed to fulfill the industry's needs (Bero et al. submitted). In 1954, U.S. tobacco companies created the Tobacco Industry Research Committee, which was later renamed the Council for Tobacco Research-U.S.A., Inc. (CTR). The industry stated publicly that CTR's purpose was to fund independent scientific research on the health effects of smoking and that, to ensure the objectivity of the research, projects would be selected based on peer review by an independent Science Advisory Board (SAB) (Council for Tobacco Research 1992). However, internal tobacco industry documents have revealed the existence of

a "special projects" division within CTR (Cipollone v. Liggett Group 1988; Freedman and Cohen 1993; Bero et al. submitted). Special projects were funded based on the recommendations of tobacco industry lawyers, rather than the SAB, and were not peer reviewed prior to funding. The primary purpose of special projects, according to tobacco industry lawyers, was to develop scientific data that could be used to defend tobacco companies against litigation (Sarokin 1988; Bero et al. submitted). In addition, the special projects allowed the industry to cultivate relationships with scientists who could later be called upon to testify on the industry's behalf (Bero et al. submitted).

CTR's special projects were often specifically designed to distract attention away from tobacco as a cause of disease (Bero et al. submitted). For example, studies were funded to show that poor nutrition, occupation, or genetic predisposition could cause the diseases attributed to smoking. In addition, the study designs of the special projects were sometimes altered so they would be more likely to produce results that would support the tobacco industry position (Bero et al. submitted). Although the tobacco industry began funding special projects through CTR in 1966, their existence was not disclosed until 1988, during the trial of Rose Cipollone vs. Liggett et. al in New Jersey (Cipollone v. Liggett Group 1988).

Given general evidence suggesting that industry sponsorship can impact the results or conclusions of sponsored research, as well as specific evidence of previous efforts by the tobacco industry to control the direction of research it funds, we hypothesized that research funded by the Center for Indoor Air Research might be affected by conflict of interest. The tobacco industry argues that exposure to ETS is

too low to cause any real damage, and that epidemiologic studies on passive smoking are flawed and do not prove that ETS is harmful (Tobacco Institute 1986). The industry has an obvious interest in producing scientific data to support these arguments, since policy makers and juries would be more likely to accept the industry's claims if there were hard data to support them. In fact, a confidential report prepared by the Roper Organization for the Tobacco Institute in 1978 noted that the industry's best strategy for countering public concern over passive smoking was to fund scientific research. The report stated: "The strategic and long run antidote to the passive smoking issue is, as we see it, developing and widely publicizing clear-cut, credible, medical evidence that passive smoking is not harmful to the non-smoker's health (Roper Organization 1978:A-7)."

We therefore hypothesized that, although CIAR claims to be objective and independent, the tobacco industry might be funding research through CIAR to support its position that passive smoking has not been proven harmful to health. The purpose of our study was to analyze the content, quality and use of research funded by CIAR, in order to determine whether CIAR is funding truly independent research or whether it is funding research that appears to be motivated by tobacco industry interests.

CIAR's Peer-Reviewed and Special-Reviewed Projects

The Center for Indoor Air Research (CIAR) was formed in 1988 by three U.S. tobacco companies: Philip Morris U.S.A., R.J. Reynolds Tobacco Company and Lorillard Corporation (Center for Indoor Air Research 1989). Svenska Tobaks A.B., a Swedish

domestic tobacco company, was added to the list of sponsoring members in 1994 (Center for Indoor Air Research 1994). These four tobacco companies are referred to as CIAR's "charter" members. Other companies may participate in CIAR as "regular" or "associate" members. The primary difference between these types of memberships is that charter members provide the bulk of funding for CIAR, and that charter and regular members are represented on the Board of Directors, while associate members are not (Center for Indoor Air Research 1994). CIAR currently has two "regular" members: Hoechst Celanese and Mead Paper; its "associate" members include several paper and packaging companies.

CIAR's mission, as stated in its 1989-90 Research Agenda, is: "To create a focal point organization of the highest scientific caliber to sponsor and foster quality, objective research in indoor air issues including environmental tobacco smoke, and to effectively communicate research findings to the broad scientific community (Center for Indoor Air Research 1989:1)." This mission statement was modified in 1992 and no longer includes a specific reference to environmental tobacco smoke (Center for Indoor Air Research 1992a). According to CIAR, this mission is accomplished primarily by funding original scientific and technical research related to indoor air.

The peer-review process used to fund CIAR's research projects is described in its *Request for Applications* (Center for Indoor Air Research 1994). First, the research agenda is established by the Science Advisory Board (SAB), an independent group of scientists with expertise in indoor air issues. Once the agenda has been established, CIAR issues a *Request for Applications* to the scientific community at large. All applications are reviewed first by a group of peers, who are selected from a

pool of scientists that have volunteered to evaluate CIAR's applications. The SAB then reviews the applications along with the peer evaluations and makes recommendations regarding which projects should receive funding. The SAB's recommendations are subject to final approval by the Board of Directors. CIAR's peer review process is similar to the grant approval process used by many foundations.

Although CIAR's publications state that its projects are funded through the peer review process described above, we have found that some projects are funded through a special review process. CIAR publishes a brochure that lists the projects it has funded to date (Center for Indoor Air Research 1992b). The projects are classified as "research," "applied" or "other," but the differences between these categories are not explained. Through interviews with CIAR staff members, we were informed that "research" projects are traditional scientific investigations that are funded through the peer review process described above and in CIAR's publications; "applied" and "other" projects are more goal-oriented studies that are funded directly by the Board of Directors, without undergoing peer review (Marquardt, oral communication, 1993). None of CIAR's publications mention that some of its projects are funded through a special review process.

Because CIAR's "applied" and "other" projects undergo a special review process, and because we hypothesized that they might be similar to CTR's special projects, we will refer to them collectively as "special-reviewed" projects throughout this paper. CIAR's "research" projects will be referred to as "peer-reviewed" projects. CIAR awarded $11,135,961 for "peer-reviewed" projects and $4,262,168 for "special-

reviewed" projects from 1989 to 1993, based on information in CIAR's tax forms, which we obtained from the Internal Revenue Service. (These figures do not include awards made in 1990 because these tax forms were not available.)

This paper will present our analysis of the content, quality and use of research sponsored by CIAR. The content of CIAR-funded research was assessed by examining the types of projects and the affiliations of principal investigators funded by CIAR. The quality of CIAR-funded research was assessed by examining articles published by CIAR-funded principal investigators. Specifically, we determined whether the articles had been peer-reviewed; whether they had been published in symposia proceedings; and what source(s) of funding were acknowledged. The use of CIAR-funded research was assessed by analyzing testimony presented by CIAR-funded researchers at federal hearings related to environmental tobacco smoke. In all cases, we compared our findings for CIAR's peer-reviewed projects versus special-reviewed projects. We will also present two case studies of special-reviewed projects, which suggest that conflict of interest may have influenced the study design of the projects. Finally, we will discuss the implications of our findings with respect to tobacco industry-funded research in particular, and industry-funded research in general.

Content of Research Funded by CIAR

The first phase of our study involved a content analysis of CIAR's peer-reviewed projects and special-reviewed projects. We were particularly interested in determining what percentage of CIAR-funded research is related to environmental

tobacco smoke (ETS). As noted above, research related to ETS has a high potential for being influenced by conflict of interest, since the tobacco industry could use the results in legal and legislative settings.

We obtained information from CIAR regarding projects funded from January, 1988 to October, 1993 (Center for Indoor Air Research 1992b; Center for Indoor Air Research, written communication, 1993). The information included the title of each project, the name and affiliation of each principal investigator, the date the project was originally funded, and a one paragraph description of the purpose of the project.

Based on the one paragraph description, we classified the topic of each project as either related to ETS or not related to ETS. A project was considered ETS-related if it studied an aspect of tobacco, tobacco smoke or a tobacco-specific substance such as nicotine. Studies of general indoor air quality that did not specifically mention tobacco were considered non-ETS studies.

We then sub-classified the topics of the projects into the categories of health effects, exposure measurements, or other. A 'health effects' study evaluated the effects of exposure to a substance; the effects could be either acute or chronic, and they could be measured in cells, animals or humans. For example, a study that measured lung development in rats exposed to ETS was considered a 'health effects' study, as was a study of allergic reactions to ETS in asthmatics. An 'exposure' study measured the amount of exposure to a substance, either directly or indirectly, but did not evaluate the effects of that exposure. For example, studies of substance uptake in the body were considered exposure studies, as were measurements of exposure markers such as cotinine (a nicotine metabolite) in urine. In addition, studies that

measured the levels of various substances, such as the amount of nicotine in indoor air, were considered exposure studies. Studies that did not evaluate either health effects or exposure were classified in the 'other' category. One project, for example, studied whether tobacco smoke is perceived primarily through sight or smell.

Our findings on the types of projects funded by CIAR are summarized in Table 1. CIAR funded 40 peer-reviewed and 19 special-reviewed projects from 1988 to 1993. Thirty percent (12/40) of the peer-reviewed projects studied issues related to ETS, compared to 63% (12/19) of the special-reviewed projects (ChiSq=5.869, df=1, P=.0154). In addition, most special-reviewed projects studied exposure to ETS, while peer-reviewed projects were evenly divided between health effects studies and exposure studies.

We also examined the affiliations of CIAR-funded principal investigators, in order to determine whether CIAR was funding primarily academics. Based on the information provided by CIAR, we coded the affiliation of each principal investigator (PI) as either academic, corporate or other. PIs were classified as 'academic' if their stated affiliation was a university or college. They were classified as 'corporate' if their stated affiliation was a private sector business, consulting firm or contracting agency. All other affiliations were classified as 'other.' None of the PIs had more than one affiliation listed.

Our findings regarding the affiliations of CIAR-funded principal investigators (PIs) are summarized in Table 2. CIAR funded 52 PIs from 1988 to 1993. Thirty-four PIs received funding for one or more peer-reviewed projects, while 18 PIs received

funding for one or more special-reviewed projects.[1] There was a significant difference between the affiliations of PIs on peer-reviewed and special-reviewed projects (ChiSq=12.262, df=2, P=.0022). Ninety-four percent (32/34) of PIs on peer-reviewed projects had academic affiliations, compared to 56% (10/18) of PIs on special-reviewed projects. Thirty-nine percent (7/18) of PIs on special-reviewed projects were affiliated with private sector companies. We also observed that three of the PIs on special-reviewed projects are currently members of CIAR's Science Advisory Board (two had academic affiliations and one was affiliated with the private sector).

Our content analysis of projects funded by CIAR shows that there are several significant differences between CIAR's peer-reviewed projects and its special-reviewed projects. First, special-reviewed projects are more likely than peer-reviewed projects to study issues related to ETS. This finding raises concern about conflict of interest, since these projects are awarded based on the recommendations of tobacco industry executives and do not undergo peer review prior to funding. This concern is heightened by the fact that CIAR does not generally disclose that its special-reviewed projects are funded through a non-traditional process.

Our second finding was that special-reviewed projects tend to measure exposure to ETS, rather than study its health effects. One of the tobacco industry's main arguments regarding passive smoking is that people are not generally exposed to high enough levels of ETS to cause any serious damage (Tobacco Institute 1986). Since CIAR's special-reviewed projects tend to study exposure, it is possible that the

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[1]Two principal investigators (PIs) received funding for both peer-reviewed and special-reviewed projects. They were classified as PIs on special-reviewed projects in our analyses. However, our results would not have changed if we had classified them as PIs on peer-reviewed projects or if we had placed them in a separate category.

tobacco industry is using them to develop evidence to support its claims that public exposure to ETS is generally low. In addition, from a legal standpoint, a study showing direct health effects caused by ETS would be much more damaging to the industry than a study measuring exposure to ETS; thus, it is "safer" for the industry to sponsor exposure research.

Our third finding was that almost 40% of CIAR's special-reviewed projects are awarded to private sector consultants and contractors, while virtually all of its peer-reviewed projects are awarded to academic investigators. It is possible that academic investigators may be wary of accepting funding, particularly from the tobacco industry, for research that has not been peer reviewed. Alternatively, tobacco industry executives may prefer to collaborate with private sector investigators. There is some evidence suggesting that the tobacco industry sometimes develops special relationships with private sector companies, in which it provides virtually all of the funding for an organization in exchange for consulting services (Levin 1993).

Finally, it is interesting to note that 16% (3/19) of CIAR's special-reviewed projects were awarded to principal investigators who are currently members of CIAR's Science Advisory Board. This sort of financial relationship between the supposedly independent SAB and the tobacco industry could raise concern about the independence of the SAB. It also suggests that the industry may reward some members of the SAB by providing funding for their projects.

Quality of Research Funded by CIAR

The next phase of our study involved an evaluation of the quality of research being funded through CIAR's peer-reviewed and special-reviewed projects. We could not directly evaluate the quality of the projects themselves, because we did not have access to the proposals submitted to CIAR. As a surrogate, we evaluated the quality of *publications* associated with CIAR-funded research. We first conducted a historical analysis of the body of work associated with CIAR-funded researchers by analyzing any articles they had published from 1989 to 1993. We then analyzed the quality of articles that had specifically resulted from CIAR-funded projects. Quality assessments were based on whether the article had been peer reviewed; whether the article had been published as a symposium; and what source(s) of funding were acknowledged. Mutually exclusive categories were used in all cases.

Peer-review status of journal in which publication appeared: peer-reviewed, non-peer-reviewed. Peer-reviewed publications have been associated with higher quality (Rochon 1994; Barnes and Bero, unpublished data) and a more balanced presentation of information (Bero et al. 1992) than non-peer-reviewed publications. In addition, the tobacco industry often cites data from non-peer-reviewed publications to support its position that ETS has not been proven harmful to health (Bero and Glantz 1993).

To test the hypothesis that PIs on special-reviewed projects would be more likely than PIs on peer-reviewed projects to publish in non-peer-reviewed journals, we determined the peer-review status of the parent journal for each article evaluated. A journal was considered peer-reviewed if it stated that it was peer-reviewed, if it

published a list of peer reviewers, or if it required that a manuscript be submitted for review prior to publication. In all other cases, the journal was considered non-peer-reviewed.

Type of article: symposium / conference proceeding, original research, review, other. Several studies have suggested that some types of articles are associated with higher quality or a more balanced presentation of information than others. For example, original research articles published in symposia proceedings have been associated with lower quality than original research articles published in peer-reviewed journals (Rochon 1994; Barnes and Bero, unpublished data). In addition, review articles in general have been associated with biases based on the affiliation of the reviewer (Chalmers et al. 1990). Also, symposia articles on ETS, regardless of whether they are original research articles or reviews, are more likely than original research articles from peer-reviewed journals to support the tobacco industry position on the health effects of ETS (Bero et al. 1994), and the tobacco industry often cites symposia articles and letters to the editor as if they had been peer reviewed (Bero and Glantz 1993).

To test the hypothesis that PIs on special-reviewed projects would publish a smaller proportion of original research articles compared to PIs on peer-reviewed projects, we classified each article examined as either a symposium, an original research article, a review or other type of article. Classifications were based on how the article was described in the table of contents of the journal in which it appeared. For example, if the table of contents stated that all of the articles in the issue were

being published as part of a symposium or conference proceeding, the article was coded as a symposium. If the table of contents listed an article in the letters-to-the-editor section, it was classified in the 'other' category. All articles published in symposia were classified as symposium articles, regardless of whether they were original research articles or reviews, because of previous studies suggesting that symposia publications in general may be associated with biases (Bero et al. 1994).

Source(s) of funding acknowledged: government, tobacco industry, other / multiple, none. Source of funding has been associated with the quality and outcome of research (Davidson 1986; Swaen and Meijers 1988; Lexchin 1993; Rochon et al. 1994; Cho and Bero, submitted). Therefore, we wanted to determine whether CIAR-funded researchers had previously published research sponsored by the tobacco industry. We categorized the source(s) of funding acknowledged for each article examined. Government sources included any international, federal, state, or local government agency, such as the National Institutes of Health. Tobacco industry sources of funding included any tobacco company, the Tobacco Institute, CIAR or CTR. Sources of funding classified as 'other/multiple' included non-profit health organizations, such as the American Cancer Society; private-sector corporations, such as Ford Motor Company; universities and academic institutions; etc. Publications with more than one type of funding acknowledged were coded as 'tobacco industry' if the tobacco industry was one of the sources acknowledged; otherwise, publications with multiple types of funding were coded as 'other/multiple.' If no source of funding was acknowledged, it was classified as 'none.'

Attitude of publication toward tobacco industry position on the health effects of tobacco: pro-industry, con-industry, neutral. There is some evidence suggesting that the tobacco industry awarded CTR special projects to investigators with histories of publishing pro-industry articles (Freedman and Cohen 1993). To test the hypothesis that PIs on CIAR special-reviewed projects were more likely than PIs on CIAR peer-reviewed projects to publish pro-industry articles, we categorized each article as pro, con, or neutral to the tobacco industry position on the health effects of exposure to tobacco smoke (either active or passive). An article was considered 'pro-industry' if it concluded there is no evidence that tobacco smoke is associated with adverse health effects; that the evidence is inconclusive; that confounding variables are responsible for health effects attributed to tobacco smoke; that studies on tobacco smoke are statistically flawed; or that the level of exposure to tobacco smoke is not high enough to cause health problems. An article was also considered 'pro-industry' if it discussed exposure to tobacco smoke without mentioning the documented hazards of exposure at any point. For example, an article that concluded smoking could be tolerated indoors, without making any statements about the potential risks of exposure, was considered 'pro-industry.' An article was considered 'neutral' if it did not discuss tobacco or tobacco smoke. An article was considered 'con-industry' if it concluded that either active or passive exposure to tobacco smoke is associated with adverse health effects. These categories have been used previously (Bero and Glantz 1993; Bero et al. 1994) and are based on the written statements of the tobacco industry (Tobacco Institute 1986).

Quality of articles published by CIAR-funded researchers, 1989-1993

We first conducted a historical analysis of the body of work associated with CIAR-funded principal investigators from 1989 to 1993. We searched two on-line databases of the medical and scientific literature, MEDLINE and Current Contents, as well as a database of symposia studies on ETS that had been developed for a previous study (Bero et al. 1994). Searches were conducted using the last name and first initial of each principal investigator. Articles were included if they appeared to have been written or co-authored by the CIAR-funded researcher, based on an examination of the full name and affiliation of the author of the article and the general topic area of research. Publications such as editorials and letters-to-the-editor were included in our analysis. MEDLINE searches retrieved articles published from January, 1989 to August, 1993; Current Contents searches retrieved articles published from May, 1989 to October, 1993.

We identified 617 articles published by CIAR-funded PIs. Fifty-four (8.6%) of these could not be located in libraries within the University of California system or Stanford University. For the remaining 563 articles, we compared the quality of articles published by PIs on peer-reviewed projects to the quality of articles published by PIs on special-reviewed projects, using the criteria described above.[2]

Our findings regarding the publication histories of CIAR-funded principal investigators are summarized in Table 3. PIs on peer-reviewed projects published an

[2]Articles published by the two principal investigators (PIs) who received funding for both peer-reviewed and special-reviewed projects were classified as articles by PIs on special-reviewed projects. However, our results would not have changed if we had classified them as articles by PIs on peer-reviewed projects.

average of 14 (95% CI:10,19) articles, compared to 6 (95% CI:1,10) articles for PIs on special-reviewed projects (Mann-Whitney U tied P-value=.0003). Sixty-seven percent (12/18) of PIs on special-reviewed projects had published fewer than 5 articles during the four-year period examined, compared to 12% (4/34) of PIs on peer-reviewed projects.

PIs on peer-reviewed projects were more likely than PIs on special-reviewed projects to publish in peer-reviewed journals (ChiSq=26.072, df=1, p<.0001). Virtually all (97%, 458/472) of the articles by PIs on peer-reviewed projects were published in peer-reviewed journals, compared to 84% (85/101) of articles by PIs on special-reviewed projects.

PIs on peer-reviewed and special-reviewed projects also published different types of articles (ChiSq=8.986, df=3, p=.0295). PIs on peer-reviewed projects were more likely to publish original research articles and less likely to publish symposia articles, compared to PIs on special-reviewed projects.

We also observed a marginally significant difference between the sources of funding acknowledged by PIs on peer-reviewed versus special-reviewed projects (ChiSq=7.606, df=3, p=.0549). PIs on peer-reviewed projects were more likely than PIs on special-reviewed projects to acknowledge government support as the sole source of funding. No source of funding was disclosed for 30% (30/101) of articles by PIs on special-reviewed projects, compared to 19% (90/472) of articles by PIs on peer-reviewed projects. There was no difference between the two groups, however, in the percent of articles that acknowledged the tobacco industry as a source of funding.

Finally, we found that there was a significant difference in the conclusions of

articles published by PIs on peer-reviewed versus special-reviewed projects, as measured by their likelihood to support the tobacco industry position that exposure to tobacco smoke has not been proven harmful to health (ChiSq=11.619, df=2, p=.003). Articles by PIs on special-reviewed projects were more than three times as likely as articles by PIs on peer-reviewed projects to support the tobacco industry position (10% vs. 3%, respectively). Virtually all (94%, 444/472) of the articles by PIs on peer-reviewed projects were neutral, compared to 86% (87/101) of the articles by PIs on special-reviewed projects.

Our findings show that PIs on special-reviewed projects tend to publish fewer articles, on average, than PIs on peer-reviewed projects. This finding may be partially explained by our content analysis, which showed that roughly 40% of PIs on special-reviewed projects are affiliated with corporate institutions, since it is likely that private sector investigators are under less pressure to publish than academic investigators.

However, our data also suggest that PIs on special-reviewed projects tend to publish lower quality articles than PIs on peer-reviewed projects. PIs on special-reviewed projects were more likely to publish symposia articles and non-peer-reviewed articles, which tend to be of lower quality than original research articles published in peer-reviewed journals (Rochon 1994; Barnes and Bero, unpublished data). In addition, PIs on special-reviewed projects were more likely than PIs on peer-reviewed projects to publish articles supporting the tobacco industry position that exposure to ETS has not been proven harmful to health. Taken together, these findings suggest that the publications of PIs on special-reviewed projects may be

biased in favor of the tobacco industry position.

Quality of Articles Resulting from CIAR-Funded Projects

The second part of our quality analysis involved an examination of the sub-group of articles that specifically resulted from CIAR-funded projects. We obtained a list from CIAR of 63 project-related articles. An additional 8 articles that acknowledged CIAR as a source of funding were identified during our historical analysis of articles published by CIAR-funded researchers, giving us a total of 71 possible articles for inclusion. Fifteen (21%) of these were excluded because they could not be located at any of the University of California libraries or at Stanford University. Many of the excluded articles appear to have been published in symposia, and two-thirds (10/15) had been authored by PIs on special-reviewed projects. Thus, if these articles had been included, it is likely that they would have increased any differences observed between articles published by PIs on peer-reviewed and special-reviewed projects.

We analyzed the 56 available articles based on the same criteria used above: whether the article was published in a peer-reviewed publication; whether it was a symposia article, original research article, review, or other type of publication; and the source(s) of funding acknowledged. These categories were defined as above, with one exception: since CIAR should have been listed as a source of funding on all articles, we classified an article as having mixed funding if both CIAR and another non-tobacco source of funding were acknowledged.

Our findings regarding CIAR's project-related publications are summarized in Table 4. Forty-three of the articles resulted from peer-reviewed projects, while 13

resulted from special-reviewed projects. There was no statistical difference between articles resulting from peer-reviewed vs. special-reviewed projects in terms of their peer-review status (Fisher's exact p>.9999). In addition, there was no statistical difference between the two groups in terms of the proportion of symposia, original research, review and other types of articles published (ChiSq=2.131, df=3, p=.5457), although we did observe that special-reviewed projects were almost twice as likely as peer-reviewed projects to be published in symposia (23% vs. 12%, respectively).

There was a statistically significant difference between the sources of funding acknowledged for articles resulting from peer-reviewed vs. special-reviewed projects (ChiSq=19.574, df=3, p=.0002). Sixty-nine percent (9/13) of the articles related to special-reviewed projects acknowledged the tobacco industry as the sole source of funding, compared to 16% (7/43) of the articles related to peer-reviewed projects. In addition, no source of funding was acknowledged for 15% (2/13) of articles resulting from special-reviewed projects, compared to 2% (1/43) of articles resulting from peer-reviewed projects.

We also observed a significant difference between the attitudes of the articles toward the tobacco industry position on the health effects of ETS (ChiSq=12.481, df=2, p=.0019). Articles resulting from special-reviewed projects were more likely than articles resulting from peer-reviewed projects to be pro-industry (31% vs. 2%, respectively). The vast majority of articles resulting from peer-reviewed projects were neutral to the tobacco industry position (93%, 40/43), compared to 54% (7/13) of articles resulting from special-reviewed projects.

Our data show that articles associated with CIAR's special-reviewed projects

tend to acknowledge the tobacco industry as the sole source of funding, and that they are more likely than articles associated with peer-reviewed projects to support the tobacco industry position that exposure to ETS has not been proven harmful to health. This finding supports evidence from previous studies suggesting that industry funding is associated with pro-industry outcomes (Davidson 1986; Swaen and Meijers 1988; Lexchin 1993; Rochon, Gurwitz et al. 1994). In addition, it supports the conclusion that research funded through CIAR's special-reviewed projects may be biased in favor of the tobacco industry.

Use of CIAR-Funded Research

The final phase of our study involved an analysis of the use of research funded by CIAR. We hypothesized that, although CIAR-funded research has led to publications both pro and con to the tobacco industry position, the industry would selectively cite the studies that supported its claims. In addition, we hypothesized that principal investigators on special-reviewed projects would be more likely to testify on the industry's behalf than principal investigators on peer-reviewed projects. We therefore analyzed testimony presented by CIAR-funded researchers at federal hearings related to environmental tobacco smoke to determine how CIAR-funded research was being used.

To identify relevant Congressional hearings, we searched the Congressional Information Services (CIS) Index from 1970 to 1994 using the key words "smoking" and "tobacco." We identified 9 Congressional hearings that have been held on issues related to ETS (cited in Table 5). These included three hearings regarding proposals

to restrict or ban smoking in federal buildings; two regarding proposals to restrict smoking in public places nationwide; two regarding proposals to ban smoking on airline flights; one on the health effects of exposure to ETS; and one involving a critical review of the U.S. Environmental Protection Agency's (EPA) risk assessment of ETS. In addition, we examined testimony presented before the Occupational Safety and Health Administration (OSHA) regarding its proposed Indoor Air Quality Standard, which recommends restricting smoking in workplaces nationwide, as well as technical comments submitted to the EPA in response to its draft risk assessment of ETS. (These technical comments had been obtained for a previous study (Bero and Glantz 1993).

We examined the table of contents for each hearing to determine whether any CIAR-funded researchers had submitted a written statement. We analyzed the written statement, rather than the transcript of the oral testimony, because we believed it would be less likely to contain errors or omissions. In addition, some people submit written statements without testifying orally, and we wanted to include as many pieces of testimony as possible. Each piece of testimony was categorized based on: whether it was related to CIAR-funded research; whether tobacco industry sponsorship was disclosed; and whether the testimony supported the tobacco industry position on ETS.

Was testimony related to CIAR-funded research? We read each piece of testimony to determine whether it discussed the results of CIAR-funded research or some other topic related to ETS.

Disclosure of tobacco industry relationship: disclosed, not disclosed, not applicable. There has been an increasing demand for researchers to publicly disclose any potential conflicts of interest, particularly financial conflicts (Relman 1984; Southgate 1987; International Committee of Medical Journal Editors 1988; Lundberg and Flanagin 1989; Relman 1990; Parish et al. 1991; Koshland 1992), although some investigators do not support this trend (Bond 1991; Rothman 1993). We were therefore interested in determining whether or not CIAR-funded researchers had disclosed their relationship with the tobacco industry in their written statements. We classified researchers as having disclosed their tobacco industry relationship if they acknowledged that they had received funding from CIAR or the tobacco industry, or if they acknowledged that they were testifying on behalf of the tobacco industry. If they stated that they were independent experts, we classified them as having not disclosed their tobacco industry affiliations. Disclosure was considered 'not applicable' for researchers that submitted testimony prior to the date they began receiving funding from CIAR.

Attitude of testimony toward tobacco industry position: pro, con, neutral. Defined as above for analysis of publications.

We found that 28% (5/18) of PIs on special-reviewed projects had presented written testimony in response to hearings related to ETS, compared to 3% (1/34) of PIs on peer-reviewed projects (Fisher's Exact P=.0154). One of the special-reviewed project

PIs testified on five separate occasions, while all other PIs testified once.

Four of the five PIs on special-reviewed projects who testified disclosed their relationship with the tobacco industry in their written testimony, while one did not; the one PI on a peer-reviewed project who testified did not disclose his tobacco industry affiliations. Both of the researchers who failed to disclose that they had received tobacco industry funding stated that they were independent experts, and both had submitted statements to the EPA regarding its risk assessment of ETS. Two of the PIs on special-reviewed projects testified regarding their CIAR-funded research, and both acknowledged CIAR as their funding source.

All of the testimony we examined supported the tobacco industry position on the health effects of ETS. The PI who had testified five times consistently argued that smoking could be accommodated indoors. Of the other PIs on special-reviewed projects who testified, two argued that there is insufficient evidence to conclude that ETS causes disease; one argued that ETS is not a major cause of sick building syndrome and poor indoor air quality; and one argued that workplace exposure to ETS is very low (implying that the exposure is too low to cause disease). The PI on the peer-reviewed project argued that there is a lack of biological plausibility for concluding that ETS is harmful, and that confounding variables could explain the statistical association between ETS exposure and disease. None of the testimony we examined acknowledged that ETS is harmful to health.

Our findings support our hypothesis that PIs on special-reviewed projects are more likely than PIs on peer-reviewed projects to testify on the industry's behalf. In addition, both of the CIAR-funded projects that were presented as testimony

supported the tobacco industry's position that ETS has not been proven harmful to health. Our findings suggest that the tobacco industry may be using CIAR's special-reviewed projects to produce data which it can use in legislative and legal settings. In addition, the tobacco industry may be using CIAR to develop relationships with researchers who might be willing to testify on its behalf.

Two Examples of Flawed Methodology in Special-Reviewed Projects

Two special-reviewed projects funded by CIAR deserve additional discussion. One, conducted by Healthy Buildings International, has been investigated by a Congressional subcommittee for falsification of data. The other, conducted by Oak Ridge National Laboratory, has admitted that most of the data collection and analysis for its project were conducted by the tobacco industry, rather than Oak Ridge. In both cases, the study designs appear to be biased in ways that would tend to favor the tobacco industry position.

Healthy Buildings International

Healthy Buildings International (HBI -- formerly known as ACVA Atlantic, Inc.) is a company that specializes in conducting indoor air quality studies and in diagnosing the causes of sick building syndrome. The president of HBI, Gray Robertson, has received funding for two special-reviewed projects from CIAR. The first, titled "Role of foliage plants in indoor pollution control," was conducted in conjunction with researchers at the National Aeronautics and Space Administration (NASA). The study involved an analysis of the ability of house plants to absorb various pollutants,

including substances in tobacco smoke, from their environments (Center for Indoor Air Research 1992b). According to CIAR's 1989 tax forms, HBI received $18,000 to conduct this study. CIAR's brochures state that this project was completed (Center for Indoor Air Research 1992b) but, to our knowledge, the data have never been published.

HBI conducted a second special-reviewed project for CIAR, and the findings of this study have been questioned by the House of Representatives' Subcommittee on Health and the Environment. The title of the project was "Indoor air quality in general office areas," and the purpose was to measure levels of environmental tobacco smoke in typical office environments. According to CIAR's 1989 tax forms, HBI received $118,415 to conduct the study, which was published in a peer-reviewed journal in 1992 (Turner et al. 1992). HBI conducted the study by simply adding an ETS analysis on to its standard group of tests when it was hired to survey indoor air quality in office buildings. A total of 585 buildings were surveyed in this manner. Although the buildings were not randomly selected, HBI stated that they appeared to be representative of typical offices. According the published results, the data suggested that ETS levels in rooms used for "light smoking" were similar to ETS levels in no-smoking rooms. The article concluded that "with good ventilation, acceptable air quality can be maintained with moderate amounts of smoking (Turner et al. 1992:19)."

The Subcommittee on Health and the Environment has recently gathered evidence suggesting that more than 25% of the data used in the HBI study may have been falsified or fabricated (Subcommittee on Health and the Environment 1994).

For example, employees of HBI who conducted the study stated that they had been instructed to put their measuring devices in lobbies and other open areas, in order to keep ETS readings as low as possible. In addition, HBI employees stated that their data collection sheets were routinely altered, so that levels of ETS reported were lower than those actually measured. Congress requested an independent analysis of HBI's data, which concluded that "the data is so marred by unsubstantiated data entries, discrepancies, and misclassifications that it raises serious questions of scientific fraud (Subcommittee on Health and the Environment 1994:6)." Gray Robertson, the president of HBI, has denied the Congressional findings (Subcommittee on Health and the Environment 1994; Fry 1995).

According to data submitted to the Subcommittee by the Tobacco Institute, representatives of HBI have testified on at least 129 occasions before federal, state or local government agencies on issues related to ETS (Subcommittee on Health and the Environment 1994). In our analysis of federal hearings on ETS, we found that the HBI's president, Gray Robertson, had testified in 5 of the 11 hearings we examined. Robertson's standard statement was that adequate air quality could be maintained with moderate amounts of smoking.

Oak Ridge National Laboratory

Oak Ridge National Laboratory is a research facility located in eastern Tennessee that conducts both basic and applied studies. The facility itself is owned by the U.S. Department of Energy, but research is conducted on a contractual basis with many different entities. CIAR has funded several special-reviewed projects at Oak Ridge.

According to CIAR's tax forms, these include: $102,516 to Roger A. Jenkins in 1989 for a special-reviewed project titled "Comparison of a personal and area monitor for the measurement of ambient nicotine;" $71,832 in 1991 to Marvin A. Kastenbaum and K.O. Bowman for a special-reviewed project titled "Efficient laboratory experiments for testing the mutagenicity of components of indoor ambient air;" and $103,400 in 1989 to Michael Guerin for a monograph on the chemistry of environmental tobacco smoke (Guerin et al. 1992). (Guerin is a member of CIAR's Science Advisory Board.)

Most recently, Oak Ridge received $797,892 in 1993 to conduct a special-reviewed project titled "Determination of human exposure to environmental tobacco smoke." The purpose of this study was to measure exposure to environmental tobacco smoke in the workplace, and to compare the levels of workplace and non-workplace exposure. The results of this study have not yet been published. However, preliminary findings were presented by Jenkins before OSHA regarding its proposed Indoor Air Quality Standard (Jenkins 1995). Jenkins stated orally that he was not appearing as an advocate for or against OSHA's proposed standard, but "as a scientist that's been conducting a study and gathering some information I think is going to be useful to OSHA (Jenkins 1995:9690)."

Jenkins testified that the Oak Ridge study involved 100 non-smoking individuals in each of 16 cities, which were distributed geographically around the US. The researchers attempted to recruit non-smokers exposed to ETS at work but not at home; non-smokers exposed to ETS at home but not at work; non-smokers exposed to ETS both at home and at work; and non-smokers without exposure to ETS

either at home or at work. Subjects were given two personal air sampling devices – one to wear at work and the other to wear at all other times. Air samples were collected over a single 24-hour period.

According to Jenkins, three organizations participated in the study design and collection of data: Bellomy Research, R.J. Reynolds Tobacco Company (RJR), and Oak Ridge. Bellomy, a marketing research firm based in Winston Salem, North Carolina, recruited the subjects for the study. Jenkins noted during his oral testimony that Bellomy often conducts marketing research for RJR. RJR conducted all of the laboratory analyses to determine the levels of exposure to ETS in the various groups. Oak Ridge was responsible for approving the overall study design and for analyzing and interpreting the data.

The study design described by Jenkins contains several potential sources of bias. Specifically, it is highly unusual for a firm with a strong interest in the outcome of a study to be allowed to select the study subjects and to conduct the laboratory analyses, particularly when other firms could have been hired. During his testimony, Jenkins stressed that several steps had been taken to ensure that RJR did not tamper with the data in any way. However, it is unlikely that peer reviewers would have approved a study design with such a high potential for bias.

Jenkins also noted that the demographics of the study group were slightly skewed. For example, the subjects were more likely than normal to be women, to have high socioeconomic status, to have high education levels, to be white, and to work in white collar occupations. It is likely that all of these factors would tend to lower the amount of ETS exposure measured in the study.

According to Jenkins, the preliminary results from the study suggested that exposure to ETS is much higher away from the workplace than it is within the workplace. This conclusion supports the tobacco industry position that workplace exposure to ETS is not high enough to warrant regulation of smoking in the workplace.

Discussion

Our findings suggest that CIAR is funding two types of projects. Peer-reviewed projects are funded based on the recommendations of independent scientists. They are awarded primarily to academic investigators with distinguished publication records, and they study a wide range of issues related to indoor air. Special-reviewed projects, on the other hand, are awarded based on the recommendations of tobacco industry executives. They are more likely than peer-reviewed projects to be related to ETS; to be awarded to private sector consultants; to be awarded to principal investigators who publish non-peer-reviewed and symposia articles; and to support the tobacco industry position that ETS has not been proven harmful to health.

Our findings also suggest that the tobacco industry may be funding peer-reviewed and special-reviewed projects for different purposes. The tobacco industry may be funding special-reviewed projects in order to develop scientific data that it can use in legislative and legal settings. For example, data from two of CIAR's special-reviewed projects have been presented before OSHA to support the tobacco industry position that smoking should not be regulated in the workplace. In addition, PIs on special-reviewed projects are more likely than PIs on peer-reviewed projects to testify

on the industry's behalf on issues related to ETS. The motivation behind CIAR's peer-reviewed projects is less clear. It is possible that the industry is using them to deflect attention away from ETS as an indoor air pollutant, since most of them are not related to ETS. In addition, it is possible that peer-reviewed projects are being funded to gain good publicity and credibility for the industry.

Influencing Policy

Our analysis of federal hearings on ETS suggests that the tobacco industry is using CIAR to develop scientific data that it can use to influence policy related to ETS. For example, three researchers who received funding for special-reviewed projects testified before OSHA regarding its proposed Indoor Air Quality Standards, which recommend that smoking be restricted in workplaces nationwide. Two of these researchers specifically discussed the results of their CIAR-funded research. All three presented testimony that supported the tobacco industry position that smoking should not be regulated.

Several of CIAR's special-reviewed projects were related to measuring levels of ETS on aircraft. Although none of these researchers testified at hearings related to the federal smoking ban on aircraft, the Tobacco Institute presented preliminary results from one of the CIAR studies. The data supported the tobacco industry position that people are general exposed to very little ETS while flying.

The lack of peer review associated with CIAR's special-reviewed projects appears to have resulted in compromised data in at least two instances, which may minimize the impact these studies have on policy decisions. For example, the

Subcommittee report on Healthy Buildings International strongly suggests that HBI engaged in activities that were specifically designed to produce results that would be favorable to the tobacco industry. It is not clear from the Subcommittee report whether HBI acted independently or with the approval of its tobacco industry sponsors. However, it is likely that testimony and research results presented by HBI will be examined with a particularly critical eye by policy makers in the future.

The Oak Ridge study demonstrates how the lack of peer review associated with CIAR's special-reviewed projects led to a study design with a high potential for bias. Subjects were selected for the study by a marketing research firm rather than a scientific research firm, and laboratory tests were conducted by RJR chemists. Given these sorts of compromises in study design, policy makers may be unwilling to accept the conclusions of the study, which support the tobacco industry position that workplace smoking should not be regulated.

Deflecting Attention Away From ETS

Our study leaves open the question of why the tobacco industry is funding peer-reviewed projects through CIAR. One possibility is that peer-reviewed projects are being used to deflect attention away from ETS as an indoor air pollutant, since more than two-thirds of CIAR's peer-reviewed projects study substances unrelated to tobacco. This hypothesis is supported by a document that was obtained as part of the Congressional inquiry into Healthy Buildings International. The document, which was circulated within HBI in late 1991 or 1992, stated that "the key objective of the HBI concept is to broaden the debate on indoor air quality to deflect the ETS

challenge (Subcommittee on Health and the Environment 1994:5)." In particular, HBI was to promote the belief that ETS is "a minor contributor" to indoor air problems.

The tobacco industry may also be attempting to draw attention away from ETS by funding projects it believes will support its position that ETS is not a health hazard, and by cutting funding off when data suggest that ETS is harmful. For example, CIAR did not renew funding for a peer-reviewed project which suggested that chickens exposed to ETS had an increased risk of heart disease, whereas funding was renewed for a peer-reviewed project that suggested lung development in rats was not affected by ETS exposure (Stolberg 1994).

The tobacco industry's power to deflect attention away from ETS is dramatically increased by the fact that, to our knowledge, there is no other nationally-based organization currently funding research on ETS.

Good Publicity

The tobacco industry may also be funding peer-reviewed projects through CIAR to provide it with good publicity and enhanced credibility. As our findings showed, the vast majority of CIAR's peer-reviewed projects are being awarded to academic investigators with distinguished publication records. The tobacco industry often cites its funding of independent research to enhance its public image. For example, a publication produced by the Tobacco Institute titled *Three decades of initiatives by a responsible cigarette industry,* states:

Industry support of independent research exceeds $162 million through

> 1988 and has resulted in publication of more than 3,000 scientific papers. ... Pursuing its effort to advance scientific knowledge, tobacco industry support led to establishment of the Center for Indoor Air Research (CIAR) to award funds to independent investigators in the field of air quality in enclosed spaces.

In addition, the industry often uses the fact that it funds research to argue that 'more research is needed.' For example, a 1978 tobacco industry memo stated that, "It is extremely important that the industry continue to spend their dollars on research to show that we don't agree that the case against smoking is closed (Bloch 1994:297)."

It is also possible that the tobacco industry may be using CIAR's peer-reviewed projects to enhance CIAR's credibility, so that the results of its special-reviewed projects will be more likely to be accepted. The industry has little to lose by funding peer-reviewed projects through CIAR, since most of them are not related to ETS.

Implications Regarding Industry Funding in General

Whenever an industry funds scientific research that will have a direct impact on its business, the potential for conflict of interest is created. This conflict arises because the researcher has a responsibility to conduct methodologically sound, unbiased research and to disseminate the findings, regardless of how those findings might affect the industry. The industry, on the other hand, has a responsibility to maximize its profits, and its money is best spent on research that produces favorable data.

As many authors have pointed out, there are a variety of ways in which

industry sponsorship can overtly or covertly influence the conduct and publication of research (Hillman et al. 1991; Blank 1992; Chren 1994; Witt and Gostin 1994). Industry may be more likely to fund research studies that it believes will produce desirable data. In addition, investigators may consciously or unconsciously design their research studies or present their findings in a way that is likely to be favorable to their sponsors. Investigators who rely heavily on industry funding may be particularly susceptible to pressures from industry (Hillman et al. 1991).

Several commentators have suggested that guidelines should be imposed to minimize the potential for conflict of interest in industry-funded research (Hillman et al. 1991; Blank 1992; Chren 1994; Witt and Gostin 1994). Chren (1994) has proposed that industry-funded research should be awarded through an independent third party, in order to minimize contact between industry and investigators. In addition, Chren suggested that all industry-funded research should be awarded through contracts, rather than grants, which should specifically state that investigators will retain complete scientific freedom regarding study design, data analysis, and publication of findings.

CIAR fulfills the criteria proposed by Chren. It is a non-profit corporation that acts as an intermediary between investigators and the tobacco industry. In addition, all of CIAR's projects are funded through contracts, rather than grants, and these contracts explicitly state that the investigators retain control over the data and are free to publish their findings. However, our analysis of CIAR-funded research suggests that this arrangement does not necessarily minimize conflict of interest. In particular, our study shows that CIAR's Board of Directors developed a system for

circumventing its own peer review process.

It is perhaps not so surprising that research funded by the tobacco industry, or any other industry, would tend to support the industry's position. Any industry or company clearly has a strong incentive to fund only those studies that will be valuable to the company. What is disturbing about tobacco industry sponsorship of research through CIAR is its claim of objectivity. The tobacco industry has gone to great lengths to attempt to show that research funded through CIAR is objective and unbiased: it has established a Science Advisory Board composed of independent scientists; it has developed a sophisticated peer-review system for funding CIAR's peer-reviewed projects; and it has spent a great deal of money funding research that is unrelated to tobacco. And yet, CIAR has managed to develop a system for circumventing this carefully constructed peer review process for the studies that are most likely to be subject to conflict of interest, and it has not disclosed this fact in any of its informational brochures. If we had not specifically asked CIAR about its peer review process, we would not have known that special-reviewed projects are not awarded through the traditional mechanism.

Our study does suggest at least one technique for minimizing the conflict of interest that arises when industry funds research related to its products: truly independent peer review. CIAR's peer-reviewed projects appear to be high-quality studies that have not been unduly influenced by conflict of interest. They study a wide range of issues related to indoor air, including ETS, and they are published upon completion in peer-reviewed journals. It is unlikely that many of CIAR's special-reviewed projects would have been funded if they had been subjected to independent

peer review. The Oak Ridge project, for example, would probably not have been funded due to the high potential for bias in its study design. Although a flawed study design certainly does not disprove a study's conclusions, policy makers would be much more likely to believe the results of the Oak Ridge study if it did not contain so many sources of potential bias.

Our study also raises important questions about the issue of disclosure. Journal editors and policy makers have increasingly called for researchers to disclose any potential conflicts of interest, particularly financial ones (Relman 1984; Southgate 1987; International Committee of Medical Journal Editors 1988; Lundberg and Flanagin 1989; Relman 1990; Parish et al. 1991; Koshland 1992). We found that most CIAR-funded researchers disclosed CIAR as a source of funding in their publications and during their testimony on tobacco-related issues. However, as others have noted, disclosure has its limitations (Rodwin 1989). CIAR-funded investigators tended to simply state that their research had been funded by the Center for Indoor Air Research. However, most people have never heard of CIAR and do not know that it is financed by the tobacco industry. Even in CIAR's *Request for Applications*, the fact that CIAR is tobacco industry-supported is only mentioned in the Appendix, on page 14 of a 27-page pamphlet (Center for Indoor Air Research 1994).

An excellent example of full disclosure is provided by the Health Effects Institute (HEI). Publications that acknowledge HEI as a source of funding typically state that HEI is "an organization jointly funded by the U.S. Environmental Protection Agency and automotive manufacturers." An appropriate way for

researchers to disclose funding from CIAR would be to state that CIAR is "an organization created and financed by tobacco companies." In addition, special-reviewed projects should further state: "This project was conducted at the request of tobacco industry executives. The methodology has not been peer reviewed." When the true nature of the funding process is disclosed in this manner, the full potential for conflict of interest is made apparent.

Many commentators have argued that researchers should not accept funding of any sort from the tobacco industry (White, undated; Anonymous 1985; Wolinsky 1985; Bloch 1994). In addition, Dr. James S. Todd, executive vice-president of the American Medical Association, recently wrote to the deans of all medical schools in the U.S., urging them not to accept support from the tobacco industry (Houston, written communication, 1995). The argument against taking tobacco industry money is that researchers will provide the industry with undeserved respectability; will be less likely to oppose the industry in other matters; and may be more likely to conduct biased research as a result. The argument in favor of accepting industry funding is that it is often one of the few, and sometimes the only, source of funding available. We believe that the tobacco industry's credibility is enhanced through its association with independent investigators. The scientists who sit on CIAR's Science Advisory Board, as well as those who accept funding through its peer-reviewed projects, all provide the tobacco industry with the opportunity to claim that it is funding objective research. However, the true purpose of CIAR is made clear by the industry's use of its special-reviewed projects to lobby against regulation of smoking in public places. All researchers associated with CIAR, even those who do not study

tobacco-related issues, are contributing to the tobacco industry's agenda.

Conclusion

Although the tobacco industry claims that CIAR is an independent organization that funds unbiased research, it appears to be funding special-reviewed projects through CIAR in order to develop scientific data to support its position that passive smoking is not a serious public health hazard. The industry is using this data to lobby against regulation of smoking in public. The purpose of CIAR's peer-reviewed projects is less clear. The tobacco industry may be using them to deflect attention away from ETS as an indoor air pollutant, to gain good publicity and to enhance its credibility.

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TABLE 1 Topics of Projects Funded by CIAR, 1988 to 1993

		Number of Peer-reviewed Projects (n=40)	Number of Special-reviewed Projects (n=19)
Topic:	ETS health effects	6	2
	ETS exposure	6	8
	Other ETS	0	2
	Total ETS	12 (30%)	12 (63%)
	Non-ETS health effects	14	0
	Non-ETS exposure	13	6
	Other Non-ETS	1	1
	Total Non-ETS	28 (70%)	7 (37%)

Comparison of total ETS vs. total non-ETS for peer-reviewed vs. special-reviewed projects: ChiSq=5.869, df=1, P=.0154

TABLE 2 Affiliations of CIAR-Funded Principal Investigators (PIs) Who Received Funding for Peer-Reviewed vs. Special-Reviewed Projects*

		Percent of PIs who received funding for peer-reviewed projects (n=34)	Percent of PIs who received funding for special-reviewed projects** (n=18)
Affiliation of PI:	Academic	94%	56%
	Corporate	3%	39%
	Other	3%	6%

ChiSq=12.262, df=2, p=.0022

* Two PIs received funding for both peer-reviewed and special-reviewed projects. They were coded as PIs on special-reviewed projects throughout our analyses.

** Three of the PIs who received funding for special-reviewed projects are currently members of CIAR's Science Advisory Board.

TABLE 3: Articles Published by CIAR-Funded Principal Investigators (PIs) on Peer-Reviewed Projects vs. Special-Reviewed Projects, 1989-1993

		Percent of articles by PIs on peer-reviewed projects (n=472)	Percent of articles by PIs on special-reviewed projects (n=101)	Statistical analyses
Peer-status:	peer	97%	84%	
	non-peer	3%	16%	
				ChiSq=26.072 df=1 P<.0001
Type of article:	symposia	11%	21%	
	original	79%	67%	
	review	6%	6%	
	other	4%	6%	
				ChiSq=8.986 df=3 P=.0295
Funding:	government	39%	28%	
	tobacco	10%	11%	
	other/mixed	32%	32%	
	none stated	19%	30%	
				ChiSq=7.606 df=3 P=.0549
Attitude:	pro-industry	3%	10%	
	con-industry	3%	4%	
	neutral	94%	86%	
				ChiSq=11.619 df=2 P=.0030

TABLE 4: Articles Resulting Directly from CIAR-Funded Research

		Percent of articles related to peer-reviewed projects (n=43)	Percent of articles related to special-reviewed projects (n=13)	Statistical analyses
Peer-status:	peer	86%	85%	
	non-peer	14%	15%	
				Fisher's Exact P > .9999 df=1
Type of article:	symposia	12%	23%	
	original	79%	78%	
	review	2%	0%	
	other	7%	0%	
				ChiSq=2.131 df=3 P=.5457
Funding:	government	2%	0%	
	tobacco	16%	69%	
	other/mixed	79%	15%	
	none stated	2%	15%	
				ChiSq=19.574 df=3 P=.0002
Attitude:	pro-industry	2%	31%	
	con-industry	5%	15%	
	neutral	93%	54%	
				ChiSq=12.481 df=2 P=.0019

TABLE 5: Congressional Hearings Related to Environmental Tobacco Smoke*

Title of Hearing	Date
Environmental Tobacco Smoke (Part 2): Hearings before the Subcommittee on Health and the Environment of the Committee on Energy and Commerce, House of Representatives, 103rd Congress, regarding legislation to restrict smoking in public places nationwide.	February 3 and March 17, 1994
Environmental Tobacco Smoke: Hearing before the Subcommittee on Health and the Environment of the Committee on Energy and Commerce, House of Representatives, 103rd Congress, regarding legislation to restrict smoking in public places nationwide.	July 21, 1993
Review of the U.S. Environmental Protection Agency's Tobacco and Smoke Study: Hearing before the Subcommittee on Specialty Crops and Natural Resources of the Committee on Agriculture, House of Representatives, 103rd Congress, regarding criticisms of the EPA's conclusions in its Risk Assessment of Environmental Tobacco Smoke	July 21, 1993
To Prohibit Smoking in Federal Buildings: Hearings before the Subcommittee on Public Buildings and Grounds of the Committee on Public Works and Transportation, House of Representatives, 103rd Congress, regarding legislation to prohibit smoking in federal buildings.	March 11 and April 22, 1993
To Ban Smoking on Airline Aircraft: Hearing before the Subcommittee on Aviation of the Committee on Public Works and Transportation, House of Representatives, 101st Congress, regarding legislation to ban smoking on aircraft.	June 22, 1989
To Ban Smoking on Airline Aircraft: Hearing before the Subcommittee on Aviation of the Committee on Public Works and Transportation, House of Representatives, 100th Congress, regarding legislation to ban smoking on aircraft.	October 7, 1987
Designation of Smoking Areas in Federal Buildings: Hearings before the Subcommittee on Health and the Environment of the Committee on Energy and Commerce, House of Representatives, 99th Congress, regarding legislation to restrict smoking to designated areas in federal buildings.	June 12 and 27, 1986
Non-Smokers Rights Act of 1985: Hearings before the Subcommittee on Civil Service, Post Office, and General Services of the Committee on Governmental Affairs, Senate, 99th Congress, regarding legislation to restrict smoking to designated areas in federal buildings.	September 30, October 1 and 2, 1985
Effect of Smoking on Nonsmokers: Hearing before the Subcommittee on Tobacco of the Committee on Agriculture, House of Representatives, 95th Congress, regarding the health effects of exposure to environmental tobacco smoke.	September 7, 1978

*We also examined written statements submitted to the Occupational Safety and Health Administration regarding its proposed Indoor Air Quality Standards, and technical comments submitted to the Environmental Protection Agency in response to its draft risk assessment of environmental tobacco smoke.

References

Anonymous. 1985. Taking Money from the Devil [editorial]. *British Medical Journal* 291(6511):1743-1744.

Barnes, D. E. and L. A. Bero. Quality of Research Articles on Environmental Tobacco Smoke Published in Symposia and Peer-Reviewed Journals [unpublished data].

Bero, L. A., A. Galbraith, and D. Rennie. 1992. The Publication of Sponsored Symposiums in Medical Journals. *New Eng J Med* 327:1135-1140.

Bero, L. A. and S. A. Glantz. 1993. Tobacco Industry Response to a Risk Assessment of Environmental Tobacco Smoke. *Tobacco Control* 2(2):103-113.

Bero, L. A., A. Galbraith, and D. Rennie. 1994. Sponsored Symposia on Environmental Tobacco Smoke. *JAMA* 271(8):612-617.

Bero, L., D. E. Barnes, P. Hanauer, J. Slade, and S. A. Glantz. The Brown and Williamson Documents: Lawyer Control of the Tobacco Industry's External Research Program [submitted].

Blank, I. H. 1992. Industry-Funded Dermatologic Research Within Academia in the United States: Fiscal and Ethical Considerations [editorial]. *Journal of Investigative*

Dermatology 98(3):265-268.

Bloch, M. 1994. Tobacco Industry Funding of Biomedical Research [editorial]. *Tobacco Control* 3(297-298).

Bond, G. G. 1991. Ethical Issues Relating to the Conduct and Interpretation of Epidemiologic Research in Private Industry. *Journal of Clinical Epidemiology* 44(Suppl 1):29S-34S.

Center for Indoor Air Research. 1989. 1989-90 Research Agenda: Request for Applications. Linthicum, MD: Center for Indoor Air Research.

Center for Indoor Air Research. 1992a. 1992-93 Research Agenda: Request for Applications. Linthicum, MD: Center for Indoor Air Research.

Center for Indoor Air Research. 1992b. Supported Studies. Linthicum, MD: Center for Indoor Air Research.

Center for Indoor Air Research. 1993. List of Supported Studies [written communication].

Center for Indoor Air Research. 1994. 1994 Research Agenda: Request for Applications. Linthicum, MD: Center for Indoor Air Research.

Chalmers, T. C., C. S. Frank, and D. Reitman. 1990. Minimizing the Three Stages of Publication Bias. *Journal of the American Medical Association* 263(10):1392-1395.

Cho, M and L. A. Bero. [abstract submitted].

Chren, M. 1994. Independent Investigators and For-Profit Companies: Guidelines for Biomedical Scientists Considering Funding by Industry. *Archives of Dermatology* 130:432-437.

Cipollone v. Liggett Group, et al. 1988. Transcript of Proceedings of Antonio Cipollone, Individually and as an Executor of the Estate of Rose D. Cipollone, Plaintiff v. Liggett Group, Inc., a Delaware Corporation; Phillip Morris, Inc. a Virginia Corporation; and Loew's Theatres, Inc., a New York Corporation, Defendants. Civil Action no. 83-2864(SA):TPLR 3.431 - 3.468.

Council for Tobacco Research. 1992. *Report of the Council for Tobacco Research - USA, Inc.* New York: Council for Tobacco Research.

Davidson, R. 1986. Source of Funding and Outcome of Clinical Trials. *Journal of General Internal Medicine* 1:155-158.

Freedman, A. M. and L. P. Cohen. 1993. Smoke and Mirrors: How Cigarette Makers

Keep Health Question 'Open' Year After Year. *Wall Street Journal*, February 11, p. A1.

Fry, J. 1995. HBI President Denies Charges, Decries Report. *Indoor Air Review*, p. 1.

Garfinkel, L. 1981. Time Trends in Lung Cancer Mortality Among Nonsmokers and a Note on Passive Smoking. *Journal of the National Cancer Institute* 66(6):1061-1066.

Guerin, M. R., R. A. Jenkins, and B. A. Tomkins. 1992. *The Chemistry of Environmental Tobacco Smoke: Composition and Measurement*. Ann Arbor, MI: Lewis Publishers, Inc.

Hillman, A. L., J. M. Eisenberg, Mark V. Pauly, B. S. Bloom, H. Glick, B. Kinosian, and J. S. Schwartz. 1991. Avoiding Bias in the Conduct and Reporting of Cost-Effectiveness Research Sponsored by Pharmaceutical Companies. *New England Journal of Medicine* 324(19):1362-1365.

Hirayama, T. 1981. Non-Smoking Wives of Heavy Smokers Have a Higher Risk of Lung Cancer: A Study from Japan. *British Medical Journal* 282(6259):183-185.

Houston, T. Oral communication regarding letter sent from American Medical Association to Deans of all U.S. medical schools. March 17, 1995.

International Committee of Medical Journal Editors. 1988. Uniform Requirements for Manuscripts Submitted to Biomedical Journals. *Annals of Internal Medicine* 108:258-265.

Jenkins, R. A. 1995. *Transcript of Oral Testimony Presented before the Occupational Safety and Health Administration Regarding the Proposed Standard for Indoor Air Quality*. Washington, DC: Bayley Reporting, Inc.

Koshland, D. E. J. 1992. Conflict of Interest Policy. *Science* 257:595.

Levin, M. 1993. Who's Behind the Building Doctor. *The Nation*. August 9/16:168-171.

Lexchin, J. 1993. Interactions Between Physicians and the Pharmaceutical Industry: What Does the Literature Say? *Canadian Medical Association Journal* 149(10):1401-1407.

Lilienfeld, D. E. 1991. The Silence: The Asbestos Industry and Early Occupational Cancer Research--A Case Study. *American Journal of Public Health* 81(6):791-800.

Lundberg, G. D. and A. Flanagin. 1989. New Requirements for Authors: Signed Statements of Authorship Responsibility and Financial Disclosure. *Journal of the American Medical Association* 262(14):2003-2004.

Marquardt, C. Oral communication regarding review process for CIAR-funded research. October 13, 1993.

National Academy of Sciences. 1986. *Environmental Tobacco Smoke: Measuring Exposures and Assessing Health Effects*. Washington, DC: National Academy Press.

Parish, L. C., J. A. Witkowski, and L. E. Miilikan. 1991. Conflict of Interest and Scientific Publications. *International Journal of Dermatology* 30(4):250-251.

Rabin, R. 1989. Warnings Unheeded: A History of Child Lead Poisoning. *American Journal of Public Health* 79(12):1668-1674.

Relman, A. S. 1984. Dealing with Conflicts of Interest. *New England Journal of Medicine* 310(18):1182-1183.

Relman, A. S. 1990. New "Information for Authors" -- and Readers. *New England Journal of Medicine* 323:56.

Rochon, P. 1994. Evaluating the Quality of Articles Published in Journal Supplements Compared with the Quality of Those Published in the Parent Journal. *JAMA* 272(2):108-113.

Rochon, P., J. Gurwitz, R. W. Simms, P. R. Fortin, D. T. Felson, K. L. Minaker, and T.

C. Chalmers. 1994. A Study of Manufacturer-Supported Trials of Nonsteroidal Anti-Inflammatory Drugs in the Treatment of Arthritis. *Archives of Internal Medicine* 154:157-163.

Rodwin, M. A. 1989. Physicians' Conflicts of Interest: The Limitations of Disclosure. *The New England Journal of Medicine* 321(20):1405-1408.

Roper Organization. 1978. *A Study of Public Attitudes Towards Cigarette Smoking and the Tobacco Industry in 1978*. The Roper Organization, Inc.

Rothman, K. J. 1993. Conflict of Interest: The New McCarthyism in Science. *Journal of the American Medical Association* 269(21):2782-2784.

Sarokin, H. L. 1988. *Cipollone v. Liggett Group et al., opinion by Judge H. Lee Sarokin.*

Southgate, M. T. 1987. Conflict of Interest and the Peer Review Process. *Journal of the American Medical Association* 258(10):1375.

Stolberg, S. 1994. Researchers Try to Separate Smoking Fact from Fiction. *Los Angeles Times*, May 28, 1994, p. A1.

Subcommittee on Health and the Environment, Committee on Energy and Commerce, U.S. House of Representatives. 1994. *Environmental Tobacco Smoke Investigation: Staff Report Prepared by the Majority Staff, Subcommittee on Health*

and the Environment, December 20, 1994.

Swaen, G. and J. Meijers. 1988. Influence of Design Characteristics on the Outcome of Retrospective Cohort Studies. *British Journal of Industrial Medicine* 45:624-629.

Tobacco Institute. 1986. *Tobacco Smoke and the Non-Smoker: Scientific Integrity at the Crossroads*. Washington, DC: The Tobacco Institute.

Tobacco Institute. circa 1988. *Three Decades of Initiatives by a Responsible Cigarette Industry*. Washington, DC: The Tobacco Institute.

Trichopoulos, D., A. Kalandidi, L. Sparros, and B. MacMahon. 1981. Lung Cancer and Passive Smoking. *International Journal of Cancer* 27(1):1-4.

Turner, S., L. Cyr, and A. J. Gross. 1992. The Measurement of Environmental Tobacco Smoke in 585 Office Environments. *Environment International* 18(1):19-28.

U.S. Department of Health and Human Services. 1986. *The Health Consequences of Involuntary Smoking: A Report of the Surgeon General*. Rockville, MD: U.S. Public Health Service.

U.S. Environmental Protection Agency. 1992. *Respiratory Health Effects of Passive Smoking: Lung Cancer and Other Disorders*. Washington, DC: U.S. Environmental

Protection Agency.

White, L. C. *Ethical Considerations of Accepting Financial Support from the Tobacco Industry*. New York: American Council on Science and Health.

Witt, M. D. and L. O. Gostin. 1994. Conflict of Interest Dilemmas in Biomedical Research. *Journal of the American Medical Association* 271(7):547-551.

Wolinsky, H. 1985. When Researchers Accept Funding from the Tobacco Industry, Do Ethics Go Up in Smoke? *New York State Journal of Medicine*:451-455.