Scientific Integrity: implications of tobacco industry involvement in the conduct of research

Mi-Kyung Hong, MPH
University of Washington
Lisa Bero, PhD
Stanton Glantz, PhD
University of California, San Francisco

The tobacco industry and the scientific community: internal documents
- Tobacco industry has had long-standing relations with the scientific community
- Release of internal memos in 1998
- Attorneys General of 46 states sign the master settlement agreement with the nation’s seven major tobacco industry organizations
- Industry strategy to recruit scientists to promote a public relations agenda regarding health effects and secondhand smoke

Scientific Integrity: Is Public Health Compromised by Tobacco Industry Affiliations?
- Failure to disclose the tobacco industry’s role in research and inadequate disclosure of industry financial ties
- Two case studies
  - The “Japanese Spousal Study”
  - James Enstrom and the American Cancer Society’s Cancer Prevention Study (CPS I)

Methods
- Legacy Tobacco Documents Library, University of California, San Francisco (www.legacy.library.ucsf.edu)
- Documents provided by U.S. tobacco companies as required by the 1998 Master Settlement Agreement – 27+ million documents
- Search terms:
  - Hirayama Study
  - Japanese Spousal Study
  - ETS
  - Meta-analysis
  - Enstrom, Kabat, CIAR
  - CPS I, CPS II
  - Womble Carlyle
  - Shook, Hardy and Bacon

The Hirayama Study
- 1981, Takeshi Hirayama publishes a cohort study examining the effect of passive smoking among non-smoking wives of smokers in Japan (BMJ)
- Wives of heavy smokers had an up to 2-fold risk of developing lung cancer compared to wives of non-smokers
- Hirayama study: most frequently cited study in regulatory proceedings on the U.S EPA risk assessment of passive smoking
- The political influence of Hirayama’s study motivates the industry to disprove Hirayama’s conclusions

The tobacco industry’s response: the “Japanese Spousal Study”
- Japanese Principal Investigators: Honorary Principal Investigators
- Tobacco industry scientist Chris Proctor directs study but his contribution is never disclosed
- CIAR-Center for Indoor Air Research: Tobacco-sponsored research foundation funds project
- Ghost Authorship
CIAR: Center for Indoor Air Research

- foundation funded by the tobacco industry to support studies related to indoor air research, created in 1988
- mission was to fund high-quality objective research related to indoor air; maintained that they were an independent organization
- CIAR operated as a cover organization to promote tobacco industry agendas for scientific inquiry

Publishing the Japanese Spousal Study

- Two grant proposals
- Industry modifies the original proposal submitted by Japanese investigators
- Industry instates project management of the study to their lawyers, Covington and Burling
Typical Research Protocol and Authorship

Principal Investigators
Jun Kagawa
Eiji Yano

Project Research Staff
Assistants

Tobacco Industry Authorship

Philip Morris
Other Tobacco Industry Companies

Covington and Burling (Industry Law Firm)
Chris Prorctor
Chief Scientist
British American Tobacco

P.N. Lee
(Industry Consultant)

Jun Kagawa
Eiji Yano
(Honorary Investigators)

Contributor Criteria for Authorship:

- conception and design
- acquisition of data
- analysis and interpretation of data
- drafting of the manuscript
- critical revision of the manuscript for important intellectual content
- statistical expertise
- obtaining funding
- administrative, technical, or material support
- supervision


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Conclusion

- Tobacco industry goal: credible peer-reviewed publication
- Authorship standards disregarded in the process
- Calls into question the quality of the research

James Enstrom and the American Cancer Society's Cancer Prevention Study (CPS I)

- Effectiveness of conflict of interest disclosure policies and a competing interests statement: a comparison using the industry documents
- Requirements for financial disclosure by the journal does not provide a full picture of tobacco industry involvement with study authors

Introduction

- American Cancer Society cohort data circa 1959 (CPS-I data set)
- Concluded secondhand smoke does not increase the risk of lung cancer or heart disease

Thesis

- Enstrom and Kabat study sponsored in part by the tobacco industry's Center for Indoor Air Research (CIAR)
- Earlier studies show tobacco industry does not disclose their full involvement in industry funded research
- Internal memos document financial ties between the tobacco industry and authors of the study
- Enstrom and Kabat disclosure did not adequately describe the tobacco industry's role in their study

American Cancer Society (ACS) and California Tobacco Related Disease Research Program (TRDRP)

- Disclosure acknowledged ACS developed the CPS-I dataset; but, head epidemiologist at ACS advised against the use of the CPS-I data set
- Study initially supported by TRDRP; funds terminated in 1994
- Disclosure suggests TRDRP's political climate was responsible for funding termination, and tobacco industry funds were accepted only after TRDRP resources became unavailable

Enstrom: Early interactions with the tobacco industry

- 1975: first record of Enstrom approaching the tobacco industry for funding
- Enstrom requests the Council for Tobacco Research (CTR) to fund a study of cancer among Mormons living in the United States
- No record if proposal was ever funded
Enstrom: pro-tobacco or anti-tobacco?

- Enstrom asserts "Environmental pollution including environmental tobacco smoke" may play a causal role in lung cancer risk

Developing a relationship with the tobacco industry

- 1990: Tobacco industry initiates contact with Enstrom to critique research on secondhand tobacco smoke
- Enstrom is asked by the industry to comment on work by Luis Varela, which concluded that secondhand smoke exposure was not associated with disease
- Enstrom declined to comment
- Enstrom uses Varela critique as an opportunity to request funding from Philip Morris to support his work

Developing a relationship with the tobacco industry: CIAR

Regarding your inquiry about research funds, Philip Morris does not usually fund research projects. However, Philip Morris does support two independent research foundations: the Center of Tobacco Research and the Center of Indoor Air Research. If you like, I can provide you with the appropriate addresses so that you can apply to these organizations directly. If you have any further questions or if you would like to share your research ideas with me, please call.
Strengthening the relationship with the tobacco industry

- 1997: Enstrom submits a proposal entitled “Relationship of low levels of active smoking to mortality” for funding to Phillip Morris Scientific Research Review Committee (SRRC)

- Enstrom states “level of trust must be developed...commitment [needed] on your part to compete against the epidemiologic data and opinions that already exist regarding the health effects of ETS” [2075873003]

Minimizing University Oversight

Proposed: Research and education relating to the relationship of smoking to estate values and other societal issues. The money could be used for the research.

Committee: Phillip Morris Research Committee

The amount of money asked for seems rather high when considering the work proposed. The outcome, most probably, will not add much new scientific information. The applicant seems to have good connections/resources which might make this gift relatively low overhead.

As the study relies on an exterior completion, 1997: As proposed, the study does not meet the requirements of the budget. The proposal states that the study will be complete within the stated timeframe. The timeframe should be extended to allow for the completion of the study.

The halting of the study will reduce the validity of the results. The proposal states that it is necessary to have the study completed within the stated timeframe. The timeframe should be extended to allow for the completion of the study.

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Research on Passive Smoking

- Enstrom submits pre-proposals to the tobacco industry’s Center for Indoor Air Research (CIAR) to fund research related to secondhand smoke
- Proposes to analyze California CPS I cohort
- “Analysis will examine spousal smoking and death from lung cancer, coronary heart disease, and all causes”

CIAR votes to fund CPS I analysis

- CIAR board discussions re: Enstrom and Kabat; “the possibility of their collaboration”  [May, 1997]
- The CIAR board votes to fund passive smoking proposal  [November 1997]
- The proposal for the CPS I analysis was funded for $525,000 from June 1, 1998 through May 31, 2001  [November 1997]

‘Flawed Science’—but good scientists

The proposal fails to distinguish between “ETS exposure” and “living with a spouse who smokes,” makes light of the substantial true-follow-up exposure in the cohort, falsely assuages genuine adjustment can be made for the co-correlates of the initial cohort, underplays the impact of spousal cessation on the analyses, and is unaccordant with positions established by the anti-smoking community.

The list of consulting authors (Enstrom, Kabat, Gerliket) is impressive and should add credibility to interpretation of results.

Summary

- BMJ’s policy: disclosure of relevant financial ties within the last 5 years
- Is Enstrom’s disclosure accurate, given his long steady history of funding from the tobacco industry?
- Should journals stop publishing tobacco industry funded research?
- Enstrom study raises question of accepting tobacco industry money for academic research

References

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