Scientific Research and Corporate Influence: Smoking, Mental Illness, and the Tobacco Industry

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Abstract. Mentally ill individuals have always smoked at high rates and continue to do so, despite public health efforts to encourage smoking cessation. In the last half century, the tobacco industry became interested in this connection, and conducted and supported psychiatric and basic science research on the mental health implications of smoking, long before most mental health professionals outside the industry investigated this issue. Initially, representatives of tobacco industry research organizations supported genetics and psychosomatic research to try to disprove findings that smoking causes lung cancer. Tobacco industry research leaders engaged with investigators because of shared priorities and interests in the brain effects of nicotine. By the 1980s, collaborative funding programs and individual company research and development teams engaged in intramural and extramural basic science studies on the neuropharmacology of nicotine. When mental health researchers outside the industry became interested in the issue of the mentally ill and smoking in the mid-1990s, they increasingly explained it in terms of a disease of nicotine addiction. Both the idea that smoking/nicotine does something positive for the mentally ill and the conclusion that it is the result of nicotine dependence have the potential to support corporate agendas (tobacco or pharmaceutical). ***Keywords:*** nicotine, schizophrenia, psychiatry, mental health, corporate–academic interactions.

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THERE is a common quip among psychiatrists that eleven out of ten schizophrenics smoke. Mental health professionals over time have engaged with the mentally ill on issues relating to smoking spaces and privileges.[1] Despite the nationwide decrease in smoking over the last several decades, mentally ill individuals have continued to smoke at high rates.[2] Policy analyst and tobacco control expert Kenneth Warner pointed out that the mentally ill, including individuals with serious illnesses such as schizophrenia, constitute a significant portion of what he has called "hard core smokers."[3] This population seems to smoke despite widespread education about its health consequences.[4] We could probably expect, given all that historians have recently told us about the inner workings of the tobacco industry, that cigarette companies would be aware of the special connection that the mentally ill seem to have to their cigarettes.[5] Indeed, the tobacco industry made particular efforts to support mentally ill and homeless individuals in their smoking habit.[6]

But the cigarette companies did more than just sell their products to vulnerable consumers. As part of their effort to innovate in the wake of increasing criticism of cigarettes beginning in the 1950s, the tobacco industry conducted internal research and supported external investigations to not only deflect accusations about cigarettes but also to explore the effects of smoking on particular populations. In the process, tobacco companies became closely involved with selected academic researchers and helped shape research questions (and

1. See, for example, Karl M. Bowman, "A Constructive Criticism of Certain Hospital Procedures," *Am. J. Psychiatry*, 1938, *94*, 1141–52; Ralph Slovenko, "The Psychiatric Patient, Liberty, and the Law," *Am. J. Psychiatry*, 1964, *121*, 534–48.

2. John R. Hughes et al., "Prevalence of Smoking among Psychiatric Outpatients," *Am. J. Psychiatry*, 1986, *143*, 993–97; Bridget F. Grant et al., "Nicotine Dependence and Psychiatric Disorders in the United States: Results from the National Epidemiologic Survey on Alcohol and Related Conditions," *Arch. Gen. Psychiatry*, 2004, *61*, 1107–15.

3. Kenneth E. Warner and David M. Burns, "Hardening and the Hard-Core Smoker: Concepts, Evidence, and Implications," *Nicotine Tob. Res.*, 2003, *5*, 37–48.

4. Karl Fagerstrom and Henri-Jean Aubin, "Management of Smoking Cessation in Patients with Psychiatric Disorders," *Curr. Med. Res. Opin.*, 2009, *25*, 511–18.

5. See, in particular, Allan M. Brandt, *The Cigarette Century: The Rise, Fall, and Deadly Persistence of the Product that Defined America* (New York: Basic Books, 2007). See also Richard Kluger, *Ashes to Ashes: America's Hundred-Year Cigarette War, the Public Health, and the Unabashed Triumph of Philip Morris* (New York: Alfred A. Knopf, 1996).

6. Dorie Apollonio and Ruth E. Malone, "Marketing to the Marginalized: Tobacco Industry Targeting of the Homeless and Mentally Ill," *Tob. Control*, 2005, *14*, 409–15.

answers) about the relationship between smoking and mental illness. For example, as several investigators have pointed out, the tobacco industry has supported and encouraged the idea that schizophrenics smoke to self-medicate.[7] While a number of scholars have analyzed the levels at which corporate sponsorship of research affects results with regard to pharmaceutical agents, the bias of research findings in tobacco-sponsored investigations is sometimes less direct. Researchers over time who have accepted tobacco funding usually did not endorse wholesale use of cigarettes. Rather, the tobacco industry sponsorship of research in the area of smoking and mental illness helped support corporate–academic interactions and infrastructures, and as well as product-based solutions to problems.

This paper explores the evolution of tobacco industry interest in smoking and mental illness and the multiple levels on which the influence of industry affected questions and answers about mentally ill smokers.[8] Industry scientists first became aware of the connection between mental illness and smoking in the 1950s and 1960s in the context of exploring alternative explanations for the rise of lung cancer. Tobacco leaders cultivated relationships with sympathetic psychiatrists who shared priorities with the industry. By the 1970s and 1980s, intramural and extramural tobacco-funded researchers were looking at the neurochemistry of nicotine and speculating about the role of the nicotinic brain receptor in the mechanism of schizophrenia. During these decades, few mental health researchers without ties to the industry were exploring the relationship between smoking and mental illness. But with the growing awareness of the physical harms of cigarettes, as well as revelations about the role of the tobacco industry in influencing science that came to light in the 1990s, mental health professionals became increasingly focused on smoking as a disease of nicotine

7. Judith J. Prochaska, Sharon M. Hall, and Lisa A. Bero, "Tobacco Use among Individuals with Schizophrenia: What Role Has the Tobacco Industry Played?," *Schizophr. Bull.*, 2008, *34*, 555–67. For revelations about the misbehavior of the tobacco industry, see Stanton A. Glantz et al., *The Cigarette Papers* (Berkeley: University of California Press, 1996).

8. This project makes use of the Legacy Tobacco Documents Library (hereafter LTDL), an online repository of the internal tobacco industry documents obtained through lawsuits involving the industry. The web site for the archive is http://legacy.library.ucsf.edu/ (accessed 9 March 2011). For the promises and pitfalls of this resource, see Ruth E. Malone and Edith D. Balback, "Tobacco Industry Documents: Treasure Trove or Quagmire?," *Tob. Control*, 2000, *9*, 334–38.

dependence. Those who had accepted research funding from tobacco began to appear suspect, as were the questions they proposed. Yet as the tobacco industry as a whole has continued to innovate, companies and investigators with ties to formative tobacco-sponsored research have positioned themselves to take advantage of new treatment markets.[9] Scholars have pointed out that researchers with tobacco funding often reach different conclusions about the role of smoking and nicotine than those not sponsored by industry. In addition, the tobacco industry exploration of the interactions between mentally ill individuals and their cigarettes also affected research questions.[10] As a result of tobacco industry involvement, as well as the backlash against the industry, it is almost impossible to get a good answer to the question of why the mentally ill smoke.

EARLY INDUSTRY INTEREST IN SMOKING AND MENTAL ILLNESS

When several prominent epidemiologists and pathologists in the 1950s announced that smoking caused cancer, the tobacco companies responded by creating research organizations to disprove (or at least dispute) these findings. Though, as many scholars have pointed out, the tobacco industry research organizations largely functioned as public relations tools of the industry, they also provided important grants to external researchers.[11] The tobacco industry used multiple mechanisms to support internal and external research in many areas of science and clinical medicine. In the United States, the companies collaborated to form the Tobacco Industry Research Committee (TIRC, later called the Council for Tobacco Research, abbreviated here to CTR). The Tobacco Research Council (TRC)

9. For the importance of innovation to successful business, see Louis Galambos, "Recasting the Organizational Synthesis: Structure and Process in the Twentieth and Twenty-First Centuries," *Bus. Hist. Rev.*, 2005, *79*, 1–38.

10. Christina Turner and George J. Spilich, "Research into Smoking or Nicotine and Human Cognitive Performance: Does the Source of Funding Make a Difference?," *Addiction*, 1997, *92*, 1423–26; Lisa A. Bero, "Tobacco Industry Manipulation of Research," *Public Health Rep.*, 2005, *120*, 200–8.

11. See Brandt, *The Cigarette Century*; Karen S. Miller, *The Voice of Business: Hill & Knowlton and Postwar Public Relations* (Chapel Hill: University of North Carolina Press, 1999); David T. Courtwright, "'Carry on Smoking': Public Relations and Advertising Strategies of American and British Tobacco Companies since 1950," *Bus. Hist.*, 2005, *47*, 421–32.

in Great Britain (originally called the Tobacco Manufacturers Standing Committee, abbreviated here to TMSC) organized research efforts in Europe and Canada. In addition, tobacco companies conducted their own internal research and provided grants to well-respected researchers at major universities such as Harvard and Johns Hopkins, while the industry's lobbying organization (the Tobacco Institute) also offered funds.[12] Researchers sometimes received large grants from one tobacco organization while consulting for another. Many internal and external researchers shared files, and information passed freely around the industry (though some individual company research and development projects appear to have been more secretive).[13] While the executives and public relations elements within the industry directed company priorities, the research organizations in the tobacco industry were generally run by investigators who were able to engage with external academics on the level of science. These interactions proved to be key for industry influence in psychiatric and mental health research.

In their early years, the tobacco research organizations attempted to deflect blame from cigarettes by supporting physicians and scientists who advocated for a constitutional explanation for major physical ailments.[14] These researchers focused on one of two major hypotheses for vulnerability to disease: heredity or psychosomatic ailments. In their pursuit of hereditary causes of disease, tobacco leaders were able to engage researchers in the evolving field of human genetics. These groups' interests dovetailed nicely—tobacco

12. The CTR and the TRC were disbanded in 1997 as part of the Master Settlement Agreement (in which the tobacco companies gave billions to the states in exchange for immunity from further lawsuits), but Schick and Glantz have pointed out that the tobacco companies continued to provide (and hide) research support after that time. See Suzaynn F. Schick and Stanton A. Glantz, "Old Ways, New Means: Tobacco Industry Funding of Academic and Private Sector Scientists since the Master Settlement Agreement," *Tob. Control*, 2007, *16*, 157–64.

13. See, for example, Memo from R. J. Reynolds researcher Carr Smith regarding his conversation with CTR scientist Donald Ford about Alzheimer's research, 14 May 1987, Bates 506553111, LTDL, available at http://legacy.library.ucsf.edu/tid/ovy28c00 (accessed 19 March 2011). Research personnel at Philip Morris evidently tried to find out about the internal research program at R. J. Reynolds. See, for example, Memo from T. S. Osdene, Philip Morris, 5 March 1984, Bates 2083045604/5605, LTDL, available at: http://legacy.library.ucsf.edu/tid/yfb62c00 (accessed 19 March 2011).

14. See, for example, "Research Directly Supported by T.M.S.C., 1956–1961," 1961, Bates 105410191/105410212, LTDL, available at: http://legacy.library.ucsf.edu/tid/ybb20a99 (accessed 19 March 2011).

leaders wanted to exonerate smoking, while genetics researchers were trying to gain credibility (and funding) as they wrested hereditarian medicine from the shadow of the eugenics movement.[15] The two groups were both enthusiastic about twin research. By studying which diseases occurred more often in both twins of a pair than would be expected in the general incidence of the diseases, it seemed possible to separate genetic effects from those of the environment. From the 1950s through the 1970s, the TIRC and the TRC supported the creation and maintenance of a number of twin registries that tracked what investigators proclaimed were likely genetic diseases, including cancer and mental illness. The tobacco industry support for twin studies, in places as diverse as Finland, Sweden, Virginia, and California, had an important impact on the field of genetics in general.[16]

In the course of funding investigations in heredity, tobacco industry researchers frequently came across a model disease to support their argument that public health researchers had formed too hasty a conclusion regarding environmental causes of disease: schizophrenia. In this time period, psychiatrists were increasingly divided on the issue of whether mental illness was due to family influence (environment) or biological factors (including genetics). Biologically oriented psychiatrists and psychoanalysts argued fiercely about illnesses such as schizophrenia—was it a brain disease or was it due to faulty

15. On the history of eugenics and genetics, see especially Daniel J. Kevles, *In the Name of Eugenics: Genetics and the Uses of Human Heredity* (Berkeley: University of California Press, 1985); Mark H. Haller, *Eugenics: Hereditarian Attitudes in American Thought* (New Brunswick, New Jersey: Rutgers University Press, 1963). On the continuities between genetics and eugenics, see especially, Alexandra Minna Stern, *Eugenic Nation: Faults and Frontiers of Better Breeding in Modern America* (Berkeley: University of California Press, 2005).

16. See "Twin Registries in the Study of Chronic Disease," *Acta Med. Scand.*, Report of an International Symposium in San Juan, Puerto Rico, 1–4 December 1969, Bates 50739765/9806, LTDL, available at: http://legacy.library.ucsf.edu/tid/arb36d00 (accessed 21 March 2011). See also, CTR Grant Progress Report, 1 January to 30 June 1981, Bates 50107084/7092, LTDL, available at: http://legacy.library.ucsf.edu/tid/lwc69c00 (accessed 21 March 2011); Peter N. Lee, "Fourth International Congress on Twin Studies," 29 June 1983, Bates 100277305/100277323, LTDL, available at: http://legacy.library.ucsf.edu/tid/eth62a99 (accessed 21 March 2011). On twin studies and genetics, see Dorret Boomsma, Andreas Busjahn, and Leena Peltonen, "Classical Twin Studies and Beyond," *Nat. Rev. Genet.*, 2002, *3*, 872–82. A number of the twin studies named in this article were supported by the tobacco industry. For more information on the industry's support of genetics research, see Kenneth R. Gundle, Molly J. Dingel, and Barbara A. Koenig, "'To Prove This Is the Industry's Best Hope': Big Tobacco's Support of Research on the Genetics of Nicotine Addiction," *Addiction*, 2010, *105*, 974–83.

parenting?[17] Genetics researchers supported by the tobacco industry proposed that not only was schizophrenia genetic, but also that scientific discovery in this area provided an example of what they hoped to see regarding elimination of environmental blame for illness. As one report explained in 1974, "Because of early theoretical emphasis on parental influence, this common mental illness was generally thought to be environmentally caused. However, recent studies of twins and adopted children born to schizophrenic mothers but raised in foster families free of the disease have made it clear that genetic factors play a major role in causation, although environmental factors may play a role in precipitating the illness."[18] Through their support for genetics research, tobacco industry representatives learned that it was entirely possible to dispute claims about environmental causes of disease. But they also began to speculate about a biological connection between smoking and mental illness, as they noticed that schizophrenics appeared to smoke in high numbers.[19]

At the same time that tobacco industry researchers weighed in on the hereditary nature of disease (including mental illness), they also took advantage of another discussion within mental health circles regarding the relationship between mind and body: psychosomatic ideas about disease. By the 1950s, the widespread acceptance of psychosomatic medicine led many to believe that personality was the best predictor of chronic illness.[20] Peptic ulcers and heart disease were

17. On the conflict between biological and psychoanalytic psychiatry, see Edward Shorter, *A History of Psychiatry: From the Era of the Asylum to the Age of Prozac* (New York: John Wiley & Sons, 1997), 239–87. For a contemporary effort to reconcile the two, see David Rosenthal and Seymour S. Kety, eds., *The Transmission of Schizophrenia: Proceedings of the Second Research Conference of the Foundations' Fund for Research in Psychiatry, Dorado, Puerto Rico, 26 June to 1 July 1967* (Oxford: Pergamon Press, 1968). For the best overview of the history of American psychiatry, see Gerald N. Grob, *The Mad among Us: A History of the Care of America's Mentally Ill* (Cambridge, Massachusetts: Harvard University Press, 1994).

18. "Genetic Studies on Smoking," 1974, Bates ZN8325/8337, LTDL, available at: http://legacy.library.ucsf.edu/tid/ylw2aa00 (accessed 21 March 2011).

19. See, for example, Tobacco Manufacturers Standing Committee, "Outline of a Comprehensive Research Programme for T.M.S.C., 12 February 1959, Bates 105406844/105406851, LTDL available at: http://legacy.library.ucsf.edu/tid/arc54a99 (accessed 21 March 2011); "Genetic and Environmental Basis of Tobacco-Related Behavior," 18 November 1974, Bates 1003289374/1003289422, LTDL, available at: http://legacy.library.ucsf.edu/tid/vrs56b00 (accessed 21 March 2011).

20. Edward Shorter, *From Paralysis to Fatigue: A History of Psychosomatic Illness in the Modern Era* (New York: Free Press, 1992); John C. Burnham, *Accident Prone: A History of Technology, Psychology, and Misfits of the Machine Age* (Chicago: University of Chicago Press, 2009).

paradigmatic cases of the body playing out unconscious conflicts.[21] In 1957, the British TMSC issued an internal report suggesting that there might be a connection among personality types, smoking, and lung cancer. As they explained, "It would, of course, be particularly interesting to discover whether smoking is, or is not, associated with the personality types (if any) which are associated with cancer, in general, and lung-cancer in particular."[22] The tobacco industry researchers looked for an alternative explanation to the strong association between smoking and cancer, and contemporary psychosomatic ideas about disease causation seemed to support this.

One of the most visible elements of the tobacco industry's support for emotional factors related to disease was in their sponsorship of British psychologist Hans Eysenck and his work on personality.[23] Eysenck was a colorful—and controversial figure—who was notorious both for his views on the heredity of intelligence and his unabashed support for the tobacco industry.[24] Eysenck conducted a number of tobacco industry-funded projects looking at personality characteristics of smokers, and emphasized that some people were driven to smoke because of stress. He further argued that genetic makeup was a greater predictor of cancer than exposure to smoke. Eysenck's personality assessment tools were used by a number of researchers within the tobacco industry as part of their ongoing investigation between personality structure, disease, and smoking.[25]

21. See, for example, O. Spurgeon English and Stuart M. Finch, *Introduction to Psychiatry* (New York: W.W. Norton & Company, 1954).

22. Tobacco Manufacturers Standing Committee, "Opportunities for Further Research on Cancer in the Psychosomatic Field," 6 February 1957, quote from p. 5, Bates 950178332/8354, LTDL, available at: http://legacy.library.ucsf.edu/tid/npf54f00 (accessed 21 March 2011).

23. Glantz has pointed out that Eysenck's work (along with other researchers) was supported as a "special project"—it was funded at the recommendation of industry attorneys rather than through peer review (Glantz et al., *Cigarette Papers,* 288–338). Eysenck himself barely noted tobacco industry funding in his autobiography and implied that his convictions regarding smoking were his own. Hans Eysenck, *Rebel with a Cause: The Autobiography of Hans Eysenck* (New Brunswick, New Jersey: Transaction Publishers, 1997).

24. H. B. Gibson, *Hans Eysenck: The Man and His Work* (London: Peter Owen, 1981); Sohan Modgil and Celia Modgil, eds., *Hans Eysenck: Consensus and Controversy* (Philadelphia: Falmer Press, 1986).

25. Eysenck Personality Inventory, CTR, 1963, Bates HK0093004/3009, LTDL, available at: http://legacy.library.ucsf.edu/tid/pfd3aa00 (accessed 21 March 2011). Both R. J. Reynolds and Philip Morris researchers used this inventory. See "Manual for the Eysenck Personality Inventory," R. J. Reynolds, undated, Bates 502829100/9126, LTDL, available at: http://legacy.library.ucsf.edu/tid/hya78d00 (accessed 21 March 2011); Letter from Jeffrey Durgee to Gregory Novack, 16 October 1980, Bates 501232038/2041, LTDL,

As a result of their sponsorship of work in genetics and personality—as well as their aggressive tracking of medical research through published literature—tobacco industry leaders increasingly commented on the fact that mentally ill patients smoked at high rates. Further, tobacco investigators were intrigued by the observations by several psychiatrists that schizophrenics appeared to have a low incidence of lung cancer (an observation that some continue to debate in published epidemiological literature).[26] Eysenck discussed this finding in his 1980 book, *The Causes and Effects of Smoking*: "There does, however, seem to be no doubt that there is a (negative) relationship between cancer and schizophrenia, and probably psychosis as a whole. This again suggests that genetic factors play a part in determining who shall be at risk to cancer."[27] If mentally ill patients—who smoked at high rates—were not as likely to develop cancer, there had to be more to cancer than smoking.

Not only were industry leaders anxious to find alternative mechanisms for cancer, they also tried to promote the idea that smoking might have widespread benefits for stress reduction. By the 1960s and 1970s, the tobacco companies were exploring psychological factors associated with smoking, especially in circumstances of heightened emotional stress. In 1969, the Consumer Psychology program at Philip Morris (PM) planned a smoking survey study in Virginia psychiatric hospitals. Their hypothesis was that, "Certain people who experience high levels of tension and anxiety, and people subject to more distressing inner emotions are more likely

available at: http://legacy.library.ucsf.edu/tid/pbv49d00 (accessed 21 March 2011); P. G. Martin to W. L. Dunn, 1 November 1976, Bates 1003285984/5985, LTDL available at: http://legacy.library.ucsf.edu/tid/dju97e00 (accessed 21 March 2011).

26. For tobacco industry tracking of these observations, see, for example, David Rice, Letter to the Editor, *Br. J. Psychiatry*, January 1979, 5 Bates 01729733, LTDL, available at: http://legacy.library.ucsf.edu/tid/rog23a00 (accessed 21 March 2011). For a more recent report of the conflicting information on this topic, see, for example, V. S. Catts et al., "Cancer Incidence in Patients with Schizophrenia and Their First-Degree Relatives—a Meta-Analysis," *Acta Psychiatr. Scand.*, 2008, *117*, 323–36.

27. H. J. Eysenck, *The Causes and Effects of Smoking* (Beverly Hills, California: Sage, 1980), 86. See also, C. B. Bahnson and M. B. Bahnson, "Cancer as an Alternative to Psychosis: A Theoretical Model of Somatic and Psychologic Regression," in *Psychosomatic Aspects of Neoplastic Disease*, ed. D. M. Kissen and L. L. LeShan (1964), Bates 70104587/4597, LTDL, available at: http://legacy.library.ucsf.edu/tid/ojb56d00 (accessed 21 March 2011).

than others to find cigarette smoking gratifying."[28] In 1977, a work group within the British-based TRC decided to investigate the effects of smoking on emotion, especially in patients in mental hospitals.[29] There was something about smoking and its relationship to emotional factors that needed further investigation, and the tobacco industry funded that work through a number of external grant programs and internal research groups. Along the way, some researchers speculated that many individuals were essentially using cigarettes as drug delivery systems—most likely for the nicotine. Further, they wondered whether mentally ill individuals might be medicating themselves through their smoking behaviors.[30]

SHARED PRIORITIES

Representatives from the tobacco industry easily engaged with genetics and psychosomatic researchers in the 1960s and 1970s, and also developed close relationships with a number of prominent psychiatrists and mental health researchers from the 1970s through the 1990s, because of shared priorities. Psychiatrist and genetics researcher Seymour Kety was a cheerful participant in several industry-supported research conferences, apparently because of his love of smoking. And it was Kety's work on schizophrenia in adopted children that inspired tobacco researchers regarding the genetic basis of diseases formerly assumed to be caused by the environment.[31] Columbia University psychologist Stanley Schachter enthusiastically collaborated with researchers at PM regarding the psychology of smoking. Schachter's PM contacts noted that the psychologist was engaged with tobacco on both an intellectual and a

28. See Project 1600 Consumer Psychology, Outline for Annual Report, 10 June 1969, Bates 1000852085/2089, LTDL, available at: http://legacy.library.ucsf.edu/tid/fvg12a00 (accessed 21 March 2011).

29. Minutes of the 15th Meeting of the Human Smoking Subcommittee of the TRC, 15 February 1977, Bates 100135447/100135452, LTDL, available at: http://legacy.library.ucsf.edu/tid/zih22a99 (accessed 21 March 2011).

30. See, for example, grant application from Samuel Siris to the CTR, "Smoking and Symptom Relief in Schizophrenic Patients," 29 July 1993, Bates 50623913–50623989, LTDL, available at: http://legacy.library.ucsf.edu/tid/bwo72b00 (accessed 21 March 2011).

31. See Seymour Kety, "Summarization of the Conference on Motivation in Cigarette Smoking," 1972, Bates 96748058/8075, LTDL, available at: http://legacy.library.ucsf.edu/tid/tbx44c00 (accessed 21 March 2011); Seymour S. Kety et al., "Mental Illness in the Biological and Adoptive Families of Adopted Schizophrenics," *Am. J. Psychiatry*, 1971, *128*, 302–6.

personal level (as evidenced by his two-pack-a-day smoking habit).[32] Bernice Sachs, an influential figure in psychosomatic medicine and president of the American Medical Women's Association in the 1960s, testified before the U.S. Senate on behalf of the tobacco industry in 1965 because she felt that the 1964 Surgeon General's report on smoking ignored the extensive medical literature on psychosomatic causes of disease.[33] Alfred Freedman, who was a president of the American Psychiatric Association in the 1970s, developed a project with the tobacco industry in the early 1980s because of his strong feelings about personal freedoms and the dangers of government intrusion into private habits.[34]

Research psychiatrists may have been particularly eager to take advantage of what seemed to be the unlimited pocketbook of the tobacco industry, especially during the 1970s and 1980s, when biologically oriented psychiatrists were struggling against their psychoanalytic colleagues for control of the profession. The industry was able to organize symposia in tropical locations and fly in internationally known researchers on topics of interest to the industry. For example, in 1972 PM senior scientist William Dunn worked with the CTR to organize a conference at St. Martin that brought together industry researchers with major academic figures. The conferees—including Hans Selye (the "father" of stress research), Carl Seltzer from the Harvard School of Public Health, and Seymour Kety (often considered the "father" of biological psychiatry)—enjoyed the lavish setting and discussed the physical and psychological mechanisms of smoking.[35] Many of the attendees

32. Memo from H. Wakeham to W. L. Dunn, 22 September 1972, Bates 1003290434, LTDL, available at: http://legacy.library.ucsf.edu/tid/wsv97e00 (accessed 21 March 2011).

33. See statement of Bernice C. Sachs, M.D., Seattle, Washington, 1965, Bates 680008539/8756, LTDL, available at: http://legacy.library.ucsf.edu/tid/pdl43f00 (accessed 21 March 2011).

34. Letter from William Shinn to Arthur Stevens, 10 November 1978, Bates 01335541/5542, LTDL, available at: http://legacy.library.ucsf.edu/tid/ozp99d00 (accessed 21 March 2011); Memo by Timothy Finnegan, 2 February 1982, Bates 03747267/7271, LTDL, available at: http://legacy.library.ucsf.edu/tid/zpp99d00 (accessed 21 March 2011).

35. William L. Dunn, Jr., *Smoking Behavior: Motives and Incentives* (Washington, D.C.: V.H. Winston & Sons, 1973). For Selye's role in stress research, see David S. Goldstein and Irwin J. Kopin, "Evolution of Concepts of Stress," *Stress*, 2007, *10*, 109–20. For more on Seltzer's work with the tobacco industry, see Glantz et al., *Cigarette Papers*, 293–96. For biographical information on Kety, see R. N. Butler, "Seymour Kety: In Memory of the Father of Neuroscience and Biological Psychiatry," *Geriatrics*, 2000, *55*, 3–4.

of the conference later continued to do fruitful work on smoking or nicotine—often supported by the industry.

Biological research was expensive, and the tobacco industry's help was often gratefully acknowledged by researchers struggling to pursue their scientific work. Renowned psychiatric researcher and academic leader Samuel Guze from Washington University in St. Louis (in his position as Vice Chancellor for medical affairs) wrote appreciative letters to several tobacco funding groups in the 1970s and 1980s thanking tobacco for the "vote of confidence" in supporting research. Guze emphasized that, with the decline in federal funding, medical researchers depended on private contributions, including those provided by the tobacco industry.[36] Of course, the tobacco industry in turn cited its apparent approval by research universities. Horace Kornegay, the head of the industry's lobbying group, the Tobacco Institute, used Guze's statements to shore up the reputation of tobacco. As Kornegay explained, "Our task is formidable. Our view of it has been expressed perfectly by Samuel B. Guze, M.D., Vice Chancellor for medical affairs at Washington University, where a tobacco industry grant supports very basic research. In thanking our industry for its participation, he said: 'Success cannot be guaranteed, even if the effort is made; but failure is assured if the effort is not made.'"[37]

At the same time that they funded basic science research, industry leaders also tried to build relationships with high-quality researchers to buttress their credibility. Sometimes those relationships evolved to the point that investigators went to work for the industry itself. For example, Donald Ford—a neuroscientist from the Downstate campus of the State University of New York who was an early president of the International Society of Psychoneuroendocrinology (hereafter ISPE)—went to work for the CTR in 1976.[38] Ford remained active in the ISPE and continued to go to their meetings after he joined the tobacco industry research

36. See, for example, Guze to Horace Kornegay, 30 November 1973, Bates LG0052709/LG0052711, LTDL, available at: http://legacy.library.ucsf.edu/tid/yml37a00 (accessed 21 March 2011).

37. Tobacco Institute Newsletter, 23 December 1975, Bates TI03781123/TI03781131, LTDL, available at: http://legacy.library.ucsf.edu/tid/ryh19a00 (accessed 21 March 2011).

38. See press release by CTR, 1976, Bates TI46753184/TI46753185, LTDL, available at: http://legacy.library.ucsf.edu/tid/fvb73b00 (accessed 21 March 2011).

team. When Ford was being recruited for his position with the CTR, some of his former collaborators wrote letters of recommendation on his behalf.[39] Not surprisingly, these individuals were subsequently given grants through the CTR.[40] Ford was an outspoken critic of psychoanalytic psychiatry, and helped develop biological psychiatry research with CTR grant funds.[41]

While tobacco leaders cultivated professional relationships inside and outside the industry, they also remained vigilant about new applications for their products—including some in mental health. Much of this research, which consisted more of internally funded inquiry rather than external grants, took off from the observation that nicotine had significant effects in the brain. Although tobacco industry researchers clearly knew that nicotine was addictive, they were also interested in how nicotine's effects might be used.[42] Some took note of external reports that nicotine had physiological properties that might promote stress reduction.[43] Internal researchers speculated that—in light of the popularity of anti-anxiety medications such as Miltown and Valium—cigarettes might be a cheap and easy competitor in the growing pharmaceutical marketplace.[44]

39. See, for example, letter from Abel Lajtha to William Gardner, 10 September 1976, Bates 70042452/70042453, LTDL, available at: http://legacy.library.ucsf.edu/tid/kds62b00 (accessed 21 March 2011).

40. Lajtha was well funded by the CTR in the 1980s and 1990s. See, for example, Grant Proposals, Bates 50137278/7279 and Bates 40036662/6662, LTDL, available at: http://legacy.library.ucsf.edu/tid/gfn99c00 (accessed 21 March 2011).

41. See, for example, memo from Ford to W. U. Gardner, 3 June 1981, Bates HK1167002/7006, LTDL, available at: http://legacy.library.ucsf.edu/tid/ytf20a00 (accessed 21 March 2011).

42. On the issue of the companies' knowledge about nicotine addiction, see Glantz et al., *Cigarette Papers*, 58–107. See also, Philip J. Hilts, *Smoke Screen: The Truth behind the Tobacco Industry Cover-Up* (New York: Addison-Wesley Publishing Co., 1996); Michael Orey, *Assuming the Risk: The Mavericks, the Lawyers, and the Whistle-Blowers Who Beat Big Tobacco* (Boston: Little, Brown and Company, 1999). On the history of changing ideas about nicotine addiction, see Allan M. Brandt, "From Nicotine to Nicotrol: Addiction, Cigarettes, and American Culture," in *Altering American Consciousness: The History of Alcohol and Drug Use in the United States, 1800–2000*, ed. Sarah W. Tracy and Caroline Jean Acker (Amherst: University of Massachusetts Press, 2004), 383–402.

43. See, "The Effects of Nicotine and Smoking on the Central Nervous System," *Ann. N.Y. Acad. Sci.*, 1967, *142*, 1–333, Bates 2025050241/0579, LTDL, available at: http://legacy.library.ucsf.edu/tid/tnb81f00 (accessed 21 March 2011).

44. Philip Morris proposed a "tranquilizer cigarette" among its marketing ideas in the 1980s. "Philip Morris Cigarettes: Ideas for New Products," 1988, Bates 2041501054/1070, LTDL, available at: http://legacy.library.ucsf.edu/tid/knb78a00 (accessed 21 March 2011). The companies also supported research in nicotine analogs as substitutes for tranquilizers. See, for example, Leo Abood to T. S. Osdene, Philip Morris, 16 March 1983,

INDUSTRY INTEREST IN THE PHARMACOLOGY OF NICOTINE

Tobacco companies have long recognized that their products have pharmacological applications. Indeed, in 1972 an internal industry research planning memo explicitly stated, "In a sense, the tobacco industry may be thought of as being a specialized, highly ritualized and stylized segment of the pharmaceutical industry."[45] Even as their executives and attorneys sought to manufacture a false controversy about the role of smoking in lung cancer and heart disease, industry researchers were looking to develop new products, particularly pharmaceutical agents. By the 1980s and 1990s, the tobacco industry was proceeding in this area both through internal research and development and through targeted partnerships within academia. One of the internal scientists at R. J. Reynolds explained at a 1986 conference on sponsored research in nicotine that, "The development of new products is vital to the future of the company, and we believe that success depends on developing a much better understanding of the pharmacology of nicotine."[46] This advice appears to have been heeded. The tobacco industry branched out from studying smoking behaviors to more specific basic science research that could have clinical implications. Among the applications were agents that might affect brain function, including treatments for individuals with mental illness.

By the 1980s and 1990s, tobacco industry researchers were employing collaborative investigations, a form of research that had become increasingly important in clinical medicine and basic science.[47] But tobacco researchers did not just use these collaborations

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Bates 1000127513/7514, LTDL, available at: http://legacy.library.ucsf.edu/tid/wvc08e00 (accessed 21 March 2011). On the history of tranquilizers, see Andrea Tone, *The Age of Anxiety: A History of America's Turbulent Affair with Tranquilizers* (New York: Basic Books, 2008); David Herzberg, *Happy Pills in America: From Miltown to Prozac* (Baltimore: Johns Hopkins University Press, 2009).

45. Claude E. Teague, Jr., "Research Planning Memorandum on the Nature of Tobacco Research and the Crucial Role of Nicotine Therein," 14 April 1972, Bates 500915683/500915691EXHIBIT12, LTDL, available at: http://legacy.library.ucsf.edu/tid/kfp76b00 (accessed 21 March 2011).

46. Memo from J. H. Robinson to Dr. A. W. Hayes, Nicotine Conference, 3 November 1986, Bates 512051685/1688, LTDL, available at: http://legacy.library.ucsf.edu/tid/rqf43d00 (accessed 21 March 2011).

47. On the history of collaborative arrangements in clinical research, see Harry M. Marks, *The Progress of Experiment: Science and Therapeutic Reform in the United States, 1900–1990* (New York: Cambridge University Press, 1997).

to increase the scientific power of their work—they used them to continue relationships between their companies and the academic scientific world. For example, members of the CTR made site visits and engaged in extensive personal contacts with grant recipients.[48] Researchers within the industry also worked to develop ties in science and academia. R. J. Reynolds researchers investigating nicotine pharmacology had adjunct positions at Bowman Gray and Duke Universities.[49] The CTR had an extensive research collaboration program with the Nathan Kline Research Institute in New York and funded a number of tobacco and nicotine researchers there.[50] Grantees also visited their industry sponsors. R. J. Reynolds, for example, held regular internal conferences to allow grantees to learn about the company's research programs and foster collaborative relationships.[51] PM invited its grantees to company headquarters to give talks on the state of their research.[52] Through the industry's funding programs, potential grantees who had good relationships with internal researchers were given assistance on revising their grants to ensure acceptance. Scientists inside and outside the industry believed in collaborative work, and generally

48. See, for example, memo regarding Ford's site visit with Dr. R. Lukas, Barrow Institute, Phoenix, AZ, 2 March 1988, Bates 50178287/8288, LTDL, available at: http://legacy.library.ucsf.edu/tid/iss69c00 (accessed 21 March 2011).

49. See, for example, "Draft Report for the R. J. Reynolds Biobehavioral Research and Development Division," 19 November 1986, Bates 506215637/5662, LTDL, available at: http://legacy.library.ucsf.edu/tid/ead84d00 (accessed 21 March 2011). The tobacco industry also funded a nicotine research program at Duke University, staffed by individuals who had extensive research grant support by the industry. Press Release, Nicotine Research at Duke University Medical Center, 23 August 1996, Bates 2070157462/7466, LTDL, available at: http://legacy.library.ucsf.edu/tid/gqy08d00 (accessed 21 March 2011).

50. For example, Abel Lajtha and Henry Sershen received grants in the 1980s and 1990s from the CTR, see: "1985 Report of the Council for Tobacco Research," Bates 80410134/0351, LTDL, available at: http://legacy.library.ucsf.edu/tid/fmw41e00 (accessed 21 March 2011); "Council for Tobacco Research Grant Funding and Payment History," 1996, Bates CTRGRANT.SHEETS000001/1395, LTDL, available at: http://legacy.library.ucsf.edu/tid/jbx30a00 (accessed 21 March 2011). D. Robert Brebbia received a grant in the 1980s from R. J. Reynolds: Letter from G. Robert DiMarco to Brebbia, 22 April 1987, Bates 510843587/3589, LTDL, available at: http://legacy.library.ucsf.edu/tid/hmr53d00 (accessed 21 March 2011) and Bernard Wagner had an ongoing relationship with R. J. Reynolds (see p. 19).

51. See, for example, Biobehavioral Conference on Sponsored Nicotine Research, 25–26 September 1986, Bowman Gray Technical Center, R. J. Reynolds, Bates 506218812, LTDL, available at: http://legacy.library.ucsf.edu/tid/dqc84d00 (accessed 21 March 2011).

52. See, for example, Abel Lajtha talk at Philip Morris, 1997, Bates 2078498233, LTDL, available at: http://legacy.library.ucsf.edu/tid/jnp87d00 (accessed 21 March 2011).

saw no problem with the connection of their research funding to tobacco.

Within tobacco industry-funded research networks, investigators used basic science techniques—including animal models and sophisticated cell culture methodology—to develop an understanding of the mechanisms for nicotine in the brain. As a result, at the same time that the CEOs of the American tobacco companies were publicly claiming that nicotine was only a flavor enhancer, industry scientists were developing an extensive psychopharmacology of nicotine.[53] R. J. Reynolds, for example, developed an internal research program around nicotine receptor action—investigators looked at nicotine and drugs similar to nicotine to see what they could to. One of their researchers came to R. J. Reynolds from the Bowman Gray Medical Center to develop a program in nicotine pharmacology in 1982. In 1986, the R. J. Reynolds research and development program began to explore the pharmacology at brain nicotine receptors.[54] By the late 1980s, they were beginning to use that information to develop pharmaceutical agents based on nicotine or nicotine analogs.[55] These researchers suggested a variety of different applications for drugs that might act at the nicotine receptors—including possible drugs for schizophrenia.

The research on the biology and neurochemistry of nicotine conducted and supported by the tobacco industry was not fringe but rather integrated into the fields of brain receptors and neuroscience in general. Not only did the industry continue to fund expensive biological psychiatry research, industry scientists also built relationships with academics through their regular attendance at national meetings of major neuroscience organizations such as the American College of Neuropsychopharmacology (hereafter ACNP).[56]

53. David Kessler, *A Question of Intent: A Great American Battle with a Deadly Industry* (New York: PublicAffairs, 2001). See also Kluger, *Ashes to Ashes*, 746–47.

54. See Biochemical/Biobehavioral R&D, "1986 Fourth Quarter Project Status Report," 31 December 1986, Bates 506216960/7014, LTDL, available at: http://legacy.library.ucsf.edu/tid/ivc84d00 (accessed 21 March 2011).

55. P. M. Lippiello to G. R. DiMarco, Memo regarding R. J. Reynolds Tobacco Company/Hoechst-Roussel Collaboration, 25 October 1990, Bates 508480463/0466, LTDL, available at: http://legacy.library.ucsf.edu/tid/dyq92d00 (accessed 21 March 2011).

56. For example, in 1989, Johns Hopkins scientist Edythe London corresponded with the CTR regarding her grant and her request to have the CTR sponsor her symposium to be held at the next meeting of the ACNP. Letter from London to Harmon McAllister, 12 February 1989, Bates 60011883/1883, LTDL, available at: http://legacy.library.ucsf.edu/

Industry scientists partnered with academics to produce influential publications. For example, the Biobehavioral Research Division within R. J. Reynolds Tobacco Company prepared several articles on the mechanism of nicotine in the brain that were published in a 1992 issue of the journal *Psychopharmacology*.[57] They identified neurochemical effects of nicotine—including the release of acetylcholine, the release of dopamine, and the possible release of serotonin and interaction with GABA. Members of the R. J. Reynolds Tobacco Company staff frequently worked with university-based researchers to publish articles in peer-reviewed journals and books.[58] One volume of research collaboration—which was published in 2000 by the American Psychiatric Press—contained work by researchers with varying degrees of ties to the tobacco industry.[59]

SMOKING AND NICOTINE RESEARCH IN A POST-TOBACCO LITIGATION ERA

Although the tobacco industry—and its sponsored investigators—had engaged in extensive research about smoking (including its relationship with mental illness) for decades, other psychiatrists and mental health researchers came to the topic of smoking and nicotine research somewhat later. While psychiatrists noted that their patients tended to smoke, it was not a major issue for research inquiry.[60] This changed in the 1990s, however. The disease category of nicotine dependence had been included in the 1994 revision of the *Diagnostic and Statistical Manual*, and psychiatric researchers began to more energetically diagnose and propose treatment for the

tid/knl30a00 (accessed 21 March 2011). See also, Robert M. Bilder, Tabitha Thomas, and Abel Lajtha, "Nicotine Effects on Cognition: Meta-Analysis and Implications for Neuroimaging," Abstract of a paper presented at the ACNP Annual Meeting, December 1999, Bates 2073808322, LTDL, available at: http://legacy.library.ucsf.edu/tid/nmu85c00 (accessed 21 March 2011).

57. *Psychopharmacology*, 1992, *4*, entire issue, especially pages 393–526.

58. See, for example, R. J. Reynolds memo regarding co-publishing an article with Ezio Giacobini, 21 May 1993, Bates 510662850/2851, LTDL, available at: http://legacy.library.ucsf.edu/tid/qcy53d00 (accessed 21 March 2011).

59. Melissa Piasecki and Paul A. Newhouse, eds., *Nicotine in Psychiatry: Psychopathology and Emerging Therapeutics* (Washington, D.C.: American Psychiatric Press, 2000).

60. In 1993, Columbia psychiatrist Alexander Glassman acknowledged his colleagues' lack of interest in this area and called for further research. Alexander H. Glassman, "Cigarette Smoking: Implications for Psychiatric Illness," *Am. J. Psychiatry*, 1993, *150*, 546–53.

disorder.[61] The disease category of nicotine dependence became the primary way in which mental health professionals addressed the issue of smoking among the mentally ill. At the same time that tobacco control activists became aggressive in public health campaigns against smoking and revelations about the tobacco industry came to light, psychiatrists began to insist on the importance of treating nicotine dependence in their patients.[62]

Not only did psychiatrists begin to emphasize the disease aspect of smoking, the relationships between academia and the tobacco industry became more troubled. As lawyers and scholars increasingly uncovered what appeared to be malfeasance on the part of the tobacco industry, the issues of what to do regarding industry funding for research became more difficult. For example, in 1994, a small group of researchers founded the Society for Research on Nicotine and Tobacco (SRNT) because they were frustrated by their marginal status within other research organizations. While the leaders of the organization were not tied to the tobacco companies, some of their members were researchers either in the industry or supported by the industry. This created conflict within the organization. In 1996, the SRNT decided to only allow members employed by companies when their employers agreed to abide by a statement that their company supported exchange of ideas about tobacco as well as public health endeavors to help people quit smoking. In 2001, the society faced significant controversy over the issue of tobacco industry funding, and finally issued a statement strongly discouraging its members from accepting tobacco funds.[63]

61. A disease category of nicotine dependence appeared in the revised third edition of the *DSM* in 1987, but it was characterized as something common to a huge portion of American society that did not affect social and occupational functioning. In *DSM-IV,* it became included with substance dependence in general. See American Psychiatric Association, *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed. (Washington, D.C.: American Psychiatric Association, 1994), and American Psychiatric Association, *Diagnostic and Statistical Manual of Mental Disorders*, 3rd rev. ed. (Washington, D.C.: American Psychiatric Press, 1987).

62. The American Psychiatric Association issued a position statement in 1994 that explicitly mentioned the need to counter the marketing of the tobacco companies. American Psychiatric Association, "Position Statement on Nicotine Dependence," *Am. J. Psychiatry,* 1995, *152*, 481–82.

63. See http://www.srnt.org/about/history/briefhistory.cfm (accessed 15 February 2011).

The result of both the tobacco industry encouragement of research and the mental health professionals recent reaction to the industry is that the question of the relationship between mental illness and smoking has become highly contested. Public health advocates and many psychiatrists are increasingly arguing that individuals with serious mental illness need acceptance of, and treatment for, their disease of nicotine dependence. Hypotheses about whether mentally ill individuals might have an attachment to their cigarettes outside their addiction or might be self-medicating are approached only with extreme caution, and are treated as suspect by some who argue that any position that acknowledges the benefits of smoking is (intentionally or unintentionally) replicating tobacco industry propaganda.[64]

IMPLICATIONS OF INDUSTRY INFLUENCE

In some ways, the efforts of the tobacco industry to support basic and applied science research for the good of their companies resemble the interactions of other industries—including the pharmaceutical industry—with academic researchers. Investigators who accepted industry funding did so with the understanding that each side was getting something from the deal. As several historians have pointed out, there is a long history of fruitful collaborations between the pharmaceutical industry and academic researchers, and such work has led to new drug discoveries as well as troublesome questions about standards for medical treatment.[65] Some have argued, though, that tobacco industry funding is different because, while pharmaceutical companies are presumably making products to help people, cigarette companies are marketing deadly products.[66]

64. For some suggestion that patients with schizophrenia might have a stronger attachment to their cigarettes, see Bonnie Spring, Regina Pingitore, and Dennis E. McChargue, "Reward Value of Cigarette Smoking for Comparably Heavy Smoking Schizohprenic, Depressed, and Nonpatient Smokers," *Am. J. Psychiatry*, 2003, *160*, 316–22. For concerns about tobacco company propaganda, see Prochaska, Hall, and Bero, "Tobacco Use among Individuals with Schizophrenia."

65. On the history of pharmaceutical industry and academic collaborations, see John P. Swann, *Academic Scientists and the Pharmaceutical Industry: Cooperative Research in Twentieth-Century America* (Baltimore: Johns Hopkins University Press, 1988); Jeremy A. Greene, *Prescribing by Numbers: Drugs and the Definition of Disease* (Baltimore: Johns Hopkins University Press, 2007).

66. See, for example, Brandt, *Cigarette Century*.

One way of conceptualizing the issues of corporate influence on research is to understand the ways in which it creates conflicts of interest. Some debates about conflict of interest in scientific research focus on the issue of transparency—theoretically, it should be possible to evaluate the research that has been paid for by industry as long as readers know about the source of funding. Yet as Doucet and Sismondo recently pointed out, sponsorship bias of research extends to all levels of inquiry, from framing of questions to designing research trials to reporting results.[67] The tobacco industry case is illustrative because so much internal company detail is now accessible to the public, and it is clear that tobacco companies helped to shape behavioral and biochemical research on the issue of smoking and mental illness.

Of course, the tobacco industry case is also subject to hyperbole. After revelations about the tobacco companies and their work in burying evidence—sensationalized in Hollywood productions such as *The Insider* (1999)—it would be easy to dramatically highlight the actions of the tobacco industry with regard to mental illness and smoking. Yet most of the research conducted and supported by the tobacco industry was not illegal or even particularly immoral (at least by the standards of the time). Further, investigators appreciated the networks of collegiality they experienced working with the industry. For example, Bernard Wagner, who was a pathologist with the Nathan Kline Institute for Psychiatric Research when he began to consult for R. J. Reynolds, helped to advise the tobacco company on fruitful research endeavors while holding positions in both academia and the federal government. In 1987, he suggested that the tobacco company pursue explorations into the role of nicotine in the central nervous system structure and function, a suggestion that they followed with enthusiasm.[68] In 1997 when he retired, Wagner expressed gratitude for his friendships in the industry: "I have thoroughly enjoyed my tenure at R. J. Reynolds Tobacco Company and being a part of the amazing world of tobacco research. The current situation is too complicated for me to

67. M. Doucet and S. Sismondo, "Evaluating Solutions to Sponsorship Bias," *J. Med. Ethics,* 2008, *34*, 627–30.

68. R. J. Reynolds internal memo from Carr Smith to Sam Simmons, "March 24 Conversation with Bernard Wagner," 2 April 1987, Bates 506553126, LTDL, available at: http://legacy.library.ucsf.edu/tid/qqx54d00 (accessed 21 March 2011).

understand and no doubt, the tobacco industry will never be the same. However, I am convinced that humans will continue to smoke for personal pleasure and comfort." (Wagner endorsed the company, though he did put in a plug for a safer cigarette in development.)[69]

Wagner saw no conflict between his feelings about the industry and his work in government and academia. While the substantial funds he collected as a tobacco consultant probably did not hurt, he emphasized the relationships with his contacts in tobacco. Another investigator, though, had some pangs about the implications of his collaboration with the tobacco industry. This University of Rochester professor had been involved with PM (as well as the CTR) for many years. He wrote a letter in 1991 expressing some reservations that his work—as important as it seemed to be from the point of view of nicotine receptors in the brain—might have unintentionally helped the tobacco company.[70] (Though this remorse seems heartfelt, it did not stop the researcher from continuing to draw major funds from the tobacco industry, right until the moment of his death—a heart attack suffered while he was traveling to New York to consult for PM.)[71]

The inside story on the connections between the tobacco industry and psychiatric researchers illuminates the trade-offs in academic–industry relationships. The tobacco industry was an eager partner for researchers who wanted to ask questions about the possible benefits of nicotine and/or smoking. Not only was money for research an obvious inducement to researchers to work with the industry, but also the tobacco companies helped to publicize the work of their grantees. At the same time that researchers were speculating about the potential therapeutic effects of nicotine, articles appeared in a variety of media venues (nudged by tobacco industry contacts) about the biochemical

69. Letter from Wagner to R. Suber, R. J. Reynolds, 8 July 1997, Bates 51777304/7306, LTDL, available at: http://legacy.library.ucsf.edu/tid/yok01d00 (accessed 21 March 2011).

70. Letter from Leo Abood to Thomas Osdene, Philip Morris, Inc., 1 March 1991, Bates 2021587942/7943, LTDL, available at: http://legacy.library.ucsf.edu/tid/vth58e00 (accessed 21 March 2011).

71. Memo from James Glenn to the Board of Directors of the CTR, 21 January 1998, Bates 70011923/1923, LTDL, available at: http://legacy.library.ucsf.edu/tid/fjt46d00 (accessed 21 March 2011).

benefits of nicotine.[72] The knowledge generated about nicotine—aided by significant tobacco funding—has been used to develop new pharmaceutical agents for Alzheimer's, Parkinson's, depression, schizophrenia, and Tourette's syndrome.[73] And the tobacco industry's century of expertise with public relations has been a boon to academic researchers looking for a boost to their research careers. Although not all researchers who currently advocate for therapeutic effects of nicotine-analogs in the brains of the mentally ill are or have been sponsored by the tobacco industry, many of the neuroscience hypotheses about nicotine have historical ties to the tobacco industry.

It is, of course, impossible to know what the issue of smoking and mental illness would have looked like without the involvement of the tobacco industry in funding inquiry into this area. Would other funding sources and/or other priorities have shifted things a different direction? (We could perhaps engage in debates about whether there is such a thing as bias-free research at all.)[74] Whether or not tobacco companies (or other industries) are successful in sponsoring research that serves their own interests, industry-funded research is generally biased in at least one direction—it supports a market-based medical and research practice in which companies (often in collaboration with academics) design products to solve problems (that were sometimes constructed by the companies or researchers who offered the solutions).[75]

72. See, for example, memo from David Kelson to Peggy Carter, R. J. Reynolds, 21 April 1994, Bates 512028560, LTDL, available at: http://legacy.library.ucsf.edu/tid/xsg43d00 (accessed 21 March 2011); "Scientific Research Highlights Evidence in Smoking's Favor," 1994, Bates 512685257/5264, LTDL, available at: http://legacy.library.ucsf.edu/tid/yyg33d00 (accessed 21 March 2011).

73. The company Targacept, an offshoot of R. J. Reynolds, is developing novel pharmaceutical agents at the nicotinic acetylcholine receptors with the promise of aiding in a variety of mental and cognitive disorders. See: http://www.targacept.com/wt/page/history (accessed 15 February 2011).

74. For the most eloquent statement about the human factors involved in research (including bias), see Stephen Jay Gould, *The Mismeasure of Man*, rev. ed. (New York: W.W. Norton & Company, 1996).

75. For an exploration of the ways in which public health policy is influenced by different agendas, including corporate interests, see Charles E. Rosenberg, "Anticipated Consequences: Historians, History, and Health Policy," in *History & Health Policy in the United States: Putting the Past Back In*, ed. Rosemary A. Stevens, Charles E. Rosenberg, and Lawton R. Burns (New Brunswick, New Jersey: Rutgers University Press, 2006), 13–31.

Most of the researchers sponsored by the tobacco industry were not necessarily invested in helping companies with their bottom line. Instead, those who expressed their opinions about the motives of the tobacco industry supported either the companies' rights to market their products or were happy about tobacco's obvious interest in the mechanisms of nicotine. What the tobacco industry most influenced in mental health research was the inquiry into the connection between smoking and mental illness. But the revelations about the industry efforts in this area have not necessarily led to noncorporate interventions on this issue. The idea that the mentally ill smoke because of the disease of nicotine addiction is also potentially problematic. As critics have pointed out, medicalizing human behavior serves the interest of mental health professionals as well as pharmaceutical companies.[76] Indeed, some of the same academics who now express concern about the health effects of smoking in the mentally ill are also involved with pharmaceutical companies who are researching and marketing smoking cessation aides.[77]

In the history of the interactions between smoking and mental illness, the tobacco companies had a great deal to gain from understanding the issues. But not only have tobacco companies sponsored research, they have also tried to gain support for the broader idea of corporate freedom over public health efforts (including regulation). Although smoking itself is now becoming increasingly regulated, medical practice and research on the issue of mental illness remain tied to market forces. While community mental health centers and psychosocial interventions for individuals with serious mental illness remain woefully underfunded, companies accumulate profits through marketing pharmaceutical interventions—now including treatments for nicotine dependence.

We need to understand more about the tobacco industry's work on the connections between smoking and mental illness—whatever else we can say about their work, they certainly devoted considerable resources to the problem. At the same time, we need to continue to understand the interactions among business, medicine, and

76. See especially, Allan V. Horwitz, *Creating Mental Illness* (Chicago: University of Chicago Press, 2002).

77. See especially the disclosure statement at the end of the review, Douglas Ziedonis et al., "Tobacco Use and Cessation in Psychiatric Disorders: National Institute of Mental Health Report," *Nicotine Tob. Res.* 2008, *10*, 1691–715, 1715.

research. One contribution of a historical approach toward this problem is that it can help unravel the complex interactions among professionals, industry, and academic structures. While the current crises around conflicts of interest highlight what appear to be new incursions into medicine and science by companies interested in their own bottom line, the history of corporate interactions is much longer and deeper. What we know—and what we argue about—regarding mentally ill individuals who smoke has everything to do with the history of who asked the questions and why they thought the questions were important.

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