

# Chapter 3

## Pollution of the literature on occupational cancer

Richard Clapp

### 1. Introduction

In this chapter, we address the pollution of science and the creation of flawed literature on occupational causes of cancer. We present several examples, including international and national epidemiological studies, review articles and scientific presentations used in regulatory proceedings in the U.S. These are primarily from the author's personal experience, and many other examples may be found in books such as *Doubt is Their Product: How Industry's Assault on Science Threatens Your Health* (Michaels 2008) and *Deceit and Denial: The Deadly Politics of Industrial Pollution* (Markowitz and Rosner 2002). We conclude that these examples from the occupational cancer literature illustrate a contested territory that scientists and advocates must be aware of when evaluating new information about carcinogens.

### 2. The dioxin story

The forty-year history of occupational literature on dioxins and their ability to cause cancer is a dramatic example of the pollution of science by industry and its paid consultants. It illustrates the lengths to which the polluters will go in order to sow doubt about the causes of cancer in workers and thereby delay or undermine regulation of harmful exposures. The earliest publications that suggested that dioxin caused cancer in humans were published in Sweden in the 1970s (Hardell 1977; Hardell and Sandstrom 1979). These studies are widely cited as the first epidemiologic evidence that phenoxyacetic acid herbicides and their contaminants were associated with soft tissue sarcoma. Additional studies were published by Swedish authors (Eriksson *et al.* 1981; Hardell *et al.* 1981) that linked phenoxy herbicides to both lymphomas and sarcomas. At about the same time, workers at a BASF plant in Germany who had been exposed to dioxins in an accident in 1953 were found to have a higher mortality rate due to cancer twenty-seven years later (Thiess *et al.* 1982).

By the late 1970s, military veterans of the United States war in Vietnam also began to notice increased cancer rates associated with Agent Orange sprayed during the 1960s. The herbicide, a mixture of 2,4-D and 2,4,5-T, was contaminated with dioxin during production and contained substantial amounts of tetrachlorodibenzo-p-dioxin (TCDD). Agent Orange had been produced by Dow Chemical, Monsanto Corporation, Diamond Shamrock and Syntex Agribusiness, among others, and attorneys representing U.S. veterans filed a class action lawsuit against several of these companies in 1980. The outcome of the lawsuit was a settlement, in 1984, in which seven chemical companies

agreed to pay \$180 million to affected veterans and the veterans agreed not to pursue any future claims against the companies. The Federal Court Judge, Jack Weinstein, maintained that the settlement was fair, given the limited evidence at that time that Agent Orange caused cancer and other serious health effects.

In parallel with the veterans' lawsuit, government agencies in New Jersey and Massachusetts began research projects to determine the health impacts of Agent Orange on veterans who resided in their states. In Massachusetts, we had a state bonus system that gave cash bonuses to veterans who were in the military during the period of the Vietnam conflict and that distinguished between those who had served "in-country" in Vietnam and those who served elsewhere. Using this information, we produced a report that showed a nearly nine-fold increase in deaths due to soft tissue sarcoma in the "in-country" veterans. The analysis was done and the report written by two of us in the Massachusetts Department of Public Health, with financial support from another state agency, the Office of the Commissioner of Veterans Services. As we began to discuss the report within our agency, the Deputy Commissioner of Public Health initially argued that our analysis was "preliminary" and should not be released. He was eventually overruled and we proceeded to write a formal report summarizing our methods and results. On preparing to release the report publicly, we were told that we should not speak to the media and that all press communications should be handled by the Commissioner of Public Health. Employees of the other state agency that had provided funds were able to distribute the report, and a Vietnam veteran elected to the State House of Representatives also made sure the report was widely available.

The release of the Massachusetts report, which occurred after the Agent Orange lawsuit settlement, received wide media attention and spurred other states to conduct similar analyses of causes of death in veterans in their states. Two states which had bonus systems similar to the one in Massachusetts, West Virginia and Wisconsin, performed similar analyses and came up with similar results with regard to soft tissue sarcoma deaths in Vietnam veterans. The Massachusetts mortality study was eventually published in a scientific journal (Kogan and Clapp 1988) and added to the literature documenting adverse health impacts of military service in Vietnam.

By the late 1980s, considerable attention was being paid to dioxin and related chemicals and their potential mechanism of action in humans and experimental animals. A scientific conference was convened in Cold Spring Harbor, New York, with the major conclusion of the report of the proceedings being that a cellular receptor seemed to mediate all or most of the adverse effects of dioxin and dioxin-like compounds (Gallo *et al.* 1991). Since this means that a certain internal dose must occur before the effects begin to become manifest, the implication was that there is a safe "threshold" below which dioxin exposure would not pose a health risk. The U.S. regulatory agency most focused on dioxin was the Environmental Protection Agency (EPA), and the Administrator in the period 1989-1993, William Reilly, announced that the Agency would reassess its policies regarding dioxin with this new mechanistic information in mind. The compilation of the scientific basis for the reassessment began in 1991 and was supposed to be completed in eighteen months.

In the meantime, the U.S. Congress was considering a bill filed by two Vietnam veterans, Tom Daschle from South Dakota and John Kerry from Massachusetts. The hearings before the Senate Committee on Veterans Affairs included testimony by veterans, scientists and others concerned with the ongoing health effects of Agent Orange exposure. The legislation that eventually passed both houses of Congress was called "The Agent Orange Act of 1991." It mandated the Veterans Administration (VA) to compensate Vietnam veterans who had been diagnosed with soft tissue sarcoma, non-Hodgkin's lymphoma and chloracne because these were presumed to have been caused by exposure to Agent Orange and its contaminants in Vietnam. The bill also required the VA to support an ongoing review of the scientific literature by the National Academy of Sciences to determine whether other diseases were associated with Agent Orange exposure, leading to a need to compensate Vietnam veterans.

Shortly after the passage of the Agent Orange Act, researchers from the National Institute for Occupational Safety and Health (NIOSH) published an analysis of the causes of death in their dioxin workers registry (Fingerhut 1991). By this time, there were approximately fifteen studies in the scientific literature evaluating whether herbicides or dioxin were associated with particular cancers in humans. The NIOSH registry cohort was comprised of 5,172 male workers assembled from employees of twelve U.S. plants where they had been exposed to dioxin. Although the authors were very cautious in their conclusions, they reported significant excess cancer deaths from all cancers combined, and a nine-fold excess of soft tissue sarcoma in the sub-group of employees with more than one year of exposure and more than twenty years between first exposure and death. These authors also examined other cancers, such as non-Hodgkin's lymphoma, stomach cancer and multiple myeloma, finding excesses below the conventional levels of statistical significance. Nevertheless, this study was a watershed event in the assessment of the occupational cancer risks of dioxin exposure. An editorial accompanying the publication indicated that this article changed the balance of evidence, suggesting that when patients were diagnosed with soft tissue sarcoma, their physician should inquire about potential dioxin exposure (Bailar 1991).

Soon after the NIOSH dioxin workers registry study was published, Monsanto Company employees submitted an analysis of deaths in workers of one of its plants in Nitro, West Virginia (Collins *et al.* 1993). This plant had been included in the NIOSH study, and it was the location of a chemical manufacturing process accident in 1949 that exposed 754 workers to high levels of TCDD. The Monsanto Company authors noted that four of the confirmed cases of soft tissue sarcoma in the NIOSH study were from the Nitro, West Virginia plant. They went on to describe other exposures in the plant, especially 4-aminobiphenyl. This chemical had been associated with bladder cancer in previous studies, but not with soft tissue sarcoma. Nevertheless, Collins and co-authors produced a series of sub-group analyses which they claimed showed an increased risk of soft tissue sarcoma with exposure to 4-aminobiphenyl in the Nitro plant workers, but not with TCDD exposure. They stated: "these results suggest that STSs observed in the Fingerhut, et al study were not attributable to TCDD exposure alone ..." and furthermore that results from a recent follow-up of German BASF workers (Zober *et al.* 1990) should also take into account exposure to another bladder carcinogen. The

Monsanto authors therefore used their results to cast doubt on two other published studies showing increased cancer risks from TCDD exposure.

I had the opportunity to be on a panel with Dr. Collins at the International Society for Environmental Epidemiology meeting in Edmonton, Alberta in 1996. My presentation focused on the literature regarding Vietnam veterans and the diseases linked to Agent Orange exposure in the scientific literature at that point. Dr. Collins, who was by then working for Dow Chemical Company, said that his job was to raise doubt about epidemiological findings regarding occupational exposures. It appears that his 1993 publication of the West Virginia Monsanto workers was an example of him doing his job as he saw it.

### **3. 1994 EPA dioxin reassessment**

The first draft of the multiple-volume EPA dioxin reassessment was released for peer review in 1994. The first volume described what was then known about the mechanisms of dioxin toxicity, including immunotoxicity, developmental and reproductive toxicity, and carcinogenicity in experimental animals. The evidence assembled in this draft volume included studies published after 1989 and indicated that there was not likely to be a threshold. The second volume included an extensive review of human epidemiology and a draft dose-response model. The EPA authors relied on the NIOSH dioxin workers registry study, as well as animal studies, to characterize the dose-response relationship. The third volume was a risk characterization, which relied on the health assessment and exposure assessment in the other two volumes. All three volumes were then reviewed by a committee of the EPA Science Advisory Board, which then made recommendations back to the Agency for incorporation into the next draft of the reassessment.

I was a consultant member of the Science Advisory Board (SAB) Dioxin Reassessment Review Committee, and specifically the health panel that reviewed the human epidemiology and dose-response volume in early 1995. We met in a conference hotel over a two-day period and had both public and closed-door sessions. The public sessions included presentations by various Federal agency representatives, stakeholders and affected parties. One presentation was by Thomas Starr, PhD, chairing a panel for a consulting company called ENVIRON and commissioned by the American Forest & Paper Association. Dr. Starr, among other points critical of the EPA draft dioxin reassessment, asserted that Air Force Ranch Hand Vietnam veterans, who did aerial spraying of Agent Orange from in Vietnam, had exhibited no excess cancer. In particular, he asserted that none of the Air Force Ranch Hand veterans had been diagnosed with soft tissue sarcoma. I objected to this because I knew from conversations with Air Force researchers that this was not the case. At that time, there was already one case of STS in a Ranch Hand veteran, and more were found in later follow-up summaries.

The SAB review committee included members who clearly had conflicts of interest that were not revealed at the time of the meeting in 1995. For example, Dr. John Graham, who founded and directed the Harvard Center for Risk Analysis in Boston, received substantial funding from affected chemical companies such as Dow, Monsanto, BASF,

the Chemical Manufacturers Association, and several others at the time he participated in the SAB review. He organized separate lunch meetings in the hotel where the SAB review committee was meeting, presumably to discuss how to advance the agenda of the industry representatives in attendance. One of the other consultant participants in the 1995 SAB review committee was Dr. Dennis Paustenbach, at the time working for the ChemRisk Division of McLaren/Hart. His industry ties were also well-documented, and we will provide more examples of his pollution of the scientific literature later in this chapter.

The SAB Dioxin Reassessment Review Committee submitted its report and recommendations to the EPA Administrator in September 1995. The report commended the Agency for its comprehensive review of the scientific literature, but urged further refinement of the dose-response modeling. SAB reviewers declined to characterize the carcinogenicity but said that almost all of the members would “concur with the EPA’s judgment that 2,3,7,8-TCDD, under some conditions of exposure, is likely to increase human cancer incidence.” (Science Advisory Board 1995) Despite this, much of the subsequent commentary by John Graham and others emphasized the uncertainties remaining in the EPA reassessment, and the need for further research to fill in various gaps.

#### **4. Veterans and Agent Orange**

The first volume of the periodic reviews mandated by the Agent Orange Act of 1991 was published by the National Academy Press in 1994. The report was produced by the Committee to Review the Health Effects in Vietnam Veterans of Exposure to Herbicides, which was comprised of scientists who were generally familiar with the literature, but had not conducted Agent Orange research themselves. This first review concluded that there was sufficient evidence of an association between Agent Orange and other herbicides used in Vietnam and soft tissue sarcoma, non-Hodgkin’s lymphoma, Hodgkin’s Disease, chloracne and a condition called porphyria cutanea tarda (in genetically susceptible individuals). The review also listed respiratory cancers, prostate cancer and multiple myeloma as having limited/suggestive evidence of an association, and then a long list of other diseases or conditions for which the evidence was inadequate or insufficient to make a determination at that point (Institute of Medicine 1994:6).

The Veterans and Agent Orange (VAO) reviews continued to be updated every two years throughout the 1990s and up until 2012. Each update reviewed published studies of Vietnam veterans, including both U.S. and Australian veterans, as well as occupational studies of workers in Europe, North America, Asia and Oceania. The reviews also included environmental studies including the large series of studies of persons exposed to dioxin after a 1976 chemical plant explosion in Seveso, Italy. The first studies in this series were by Bertazzi, *et al.* and were published in the scientific literature beginning in 1989 (Bertazzi *et al.* 1989; Bertazzi *et al.* 1992). There were dozens of occupational studies cited in the 1994 Veterans and Agent Orange review, including the Collins *et al.* Monsanto workers study mentioned previously. The review included both production worker studies and agricultural worker studies.

The VAO authors noted that “Collins and his colleagues (1993) from Monsanto have recently hypothesized that heavy exposure to 4-aminobiphenyl alone or in combination with TCDD may explain the observed STS excess. A substantial body of evidence, however, points toward an association of STS with phenoxy herbicides and related compounds, whereas the possibility of a link to 4-aminobiphenyl has not been previously reported” (Institute of Medicine 1994:479). The authors of the first review put this study by Monsanto authors in the context of the large body of literature available at the time, concluding that there was sufficient evidence that herbicides used in Vietnam, and their contaminant TCDD, were associated with soft tissue sarcoma.

The authors of the 1994 Veterans and Agent Orange review also did a detailed analysis of the studies by Hardell and his Swedish colleagues, especially those reporting excess soft tissue sarcoma in herbicide-exposed workers. The reason for this was because “the strongest evidence for an association between STS and exposure to phenoxy herbicides ... although these studies have been criticized ...” What this is referring to are statements made by British epidemiologist Dr. Richard Doll who submitted a letter in 1985 to the Australian Judge who was holding an enquiry into the effects of Agent Orange on Australian veterans exposed during the Vietnam war. Doll’s letter said, among other things, “relating to 2,4-D and 2,4,5-T (the phenoxy herbicides in question), there is no reason to suppose that even TCDD (dioxin), which has been postulated to be a dangerous contaminant of the herbicides, is at the most, only weakly and inconsistently carcinogenic in animal experiments ... Your review of Hardell’s work, with the additional evidence obtained directly from him at interview, shows that many of his published statements were exaggerated or not supportable and that there were many opportunities for bias to have been introduced in the collection of his data. His conclusions cannot be sustained and, in my opinion, his work should no longer be cited as scientific evidence.”

After reviewing the work by Hardell and colleagues in Sweden, the VAO authors concluded in 1994 that “there is insufficient justification to discount the consistent pattern of elevated risks, and the clearly described and sound methods employed. These findings are supported by a significantly increased risk in the NIOSH study (SMR=9.2, CI 1.9-27.0) for the production workers most highly exposed to TCDD (Fingerhut *et al.* 1991), and a similar risk in the IARC cohort ...” (Institute of Medicine 1994:499). So, contrary to Doll’s claim that Hardell’s work should no longer be cited as scientific evidence, the VAO authors cited and included it as part of the evidence that there was a positive association between herbicides and their TCDD contaminant and soft tissue sarcoma. It was later revealed that Richard Doll was receiving substantial funds from Monsanto at the time that he wrote to the Australian Judge (Hardell *et al.* 2006).

## **5. 2000 EPA dioxin reassessment**

The next draft of the EPA dioxin reassessment was released for external review in 2000 and a large number of comments were incorporated before the Science Advisory Board convened another two-day meeting of the Dioxin Reassessment Review Subcommittee in November of that year. I participated in this Subcommittee, as did Drs. John

Graham, Dennis Paustenbach and several others who had been part of the SAB review five years earlier. At this meeting, more attention was paid to conflicts of interest and Subcommittee members were asked to declare any financial conflicts at the public session on the first day. None of the members indicated any financial conflicts, although Dr. Graham said that his wife was in a stock buyers' club and he was not sure whether any of her investments might be in companies that might be affected by the results of the review. An additional requirement at this meeting was that if any Subcommittee members worked at a company that had other employees that were involved in criticizing the EPA dioxin reassessment, then they should agree not to discuss the SAB review with them. Dr. Paustenbach agreed to this requirement, although he was a Vice President of Exponent, Inc. at the time of the November 2000 meeting.

The public session of the Subcommittee meeting was similar to the one held five years earlier, with comments by a range of groups. One speaker, Dr. Dimitrios Trichopoulos, the former Chair of Epidemiology at the Harvard School of Public Health, was speaking on behalf of an expert group assembled by Exponent, Inc. In his remarks, he was particularly critical of the EPA position on the probable human carcinogenicity of dioxin. He also criticized the International Agency for Research on Cancer (IARC) designation of TCDD as a Group I carcinogen. Dr. Trichopoulos claimed that the only way the IARC could have done this was by revising their classification system to include mechanistic information, something they had never done in previous carcinogen designations. A subsequent commenter, Dr. Ellen Silbergeld, pointed out that this was false and that the IARC had included mechanistic information in classifications of carcinogens prior to the dioxin designation in 1997. We will return to Dr. Trichopoulos and the Exponent, Inc. criticism later in this chapter.

After the November meeting, and as the Subcommittee was preparing its report for submission to the EPA Administrator, I reviewed a draft circulated by the EPA staff member in charge of this process. I noticed that there were references in a version of the draft report that we had never seen before and that were not discussed at the Subcommittee meetings. Furthermore, the references seemed out of place and did not refer to the text where they appeared. On inquiring about this, I was told that they were inserted by Dr. Paustenbach and that I should talk directly to him. I arranged a phone call at his office at Exponent, Inc. and when we began the call I found that he had included another staff member at his company on the phone call. He explained that this staff member, Senior Scientist Sean Hays, had provided the reference that he had then inserted in the Subcommittee draft report. As it turned out, this reference by another Exponent staff member was the wrong reference at the point it was inserted and was withdrawn by Dr. Paustenbach. A reference by Exponent, Inc. authors remained elsewhere in the SAB Subcommittee report, however, in a section critical of the EPA calculation of the cancer slope factor for dioxin.

This telephone exchange with Dr. Paustenbach and his Exponent colleague indicated that he had violated his agreement not to discuss the Subcommittee work with others in his company. I considered this an abuse of process and wrote a letter to the SAB Executive Committee to this effect. In my letter, I wrote, "the process leading to the final draft of the Dioxin Reassessment Review Subcommittee (DRRS) was not

transparent, and, in fact, was subverted by at least one member.” I also quoted another Subcommittee member who said “At times I felt that, instead of working in an open and collegial process, we had to maintain constant vigilance for members who were trying to see what could be slipped into the document without other members noticing.” To their credit, the EPA SAB Chair and staff at the time were very concerned about this problem and began a process of assuring more transparency in future Subcommittee deliberations. As it turned out, the SAB has not reconvened a Subcommittee to review further drafts of its dioxin reassessment and it still has not released a final statement about the carcinogenicity of TCDD.

The criticism of the EPA reassessment offered by Dr. Trichopoulos at the SAB Subcommittee meeting in November 2000 began to appear elsewhere. It was used by defendants in a lawsuit in Maine where the plaintiffs were alleging health effects caused by dioxin released from pulp and paper mill waste. The document critical of the literature linking dioxin to human cancers was co-authored by Drs. Philip Cole, Harris Pastides, Thomas Starr and Jack Mandel, along with Dr. Trichopoulos. This same group published their criticism in an article in the *Regulatory Toxicology and Pharmacology* journal in 2003 (Cole *et al.* 2003). Entitled “Dioxin and cancer: a critical review,” this article included some of the same comments that Dr. Trichopoulos had made about the IARC designation of dioxin as a Group I carcinogen, plus a criticism of several occupational epidemiology studies. Cole and co-authors criticized the NIOSH dioxin workers’ study, for example, saying that smoking information from some of the plants was missing or incomplete. They conclude that, “Hence, there is no basis for inferring that smoking was not a confounder in the Fingerhut study” (Cole *et al.* 2003:382).

In discussing an update of the Fingerhut, *et al.* study, Cole and co-authors emphasize that in six more years of follow-up, no additional deaths from soft tissue sarcoma occurred. What they fail to point out is that less than one death due to this rare cancer would have been expected in six additional years of following this cohort. These authors also criticize the EPA for its “failure to adjust adequately for known and possibly confounding exposures to other carcinogens such as asbestos, 4-aminobiphenyl, and smoking” (Cole *et al.* 2003:385). Here is the Collins, *et al.* argument being raised once again, although Cole and co-authors don’t explicitly refer to the 1993 Monsanto study. In their conclusion, the authors say that “the evidence indicates that TCDD is not carcinogenic to human beings at low levels and that it may not be carcinogenic to them even at high levels” (Cole *et al.* 2003:386). In their acknowledgments, they thank Sean Hays and note that “The project was sponsored by the Chlorine Chemistry Council.”

## **6. Cancer Epidemiology textbook**

The 2002 Textbook of Cancer Epidemiology, co-edited by Dimitrios Trichopoulos, summarizes some of the evidence of occupational causes in chapters on individual types of cancer. This often amounts to dismissing the workplace contribution to the overall burden, even in the chapter on bladder cancer, a cancer known to have many occupational causes. In the chapter on lymphomas, the authors misrepresent the results of a Centers for Disease Control study of Vietnam veterans presumed to be exposed

to Agent Orange by asserting that “the highest incidence of lymphomas was found in ground troops stationed in areas of lowest exposure and among sailors in navy ships off the coast of Vietnam” (Adami *et al.* 2002). This assertion is false, and the publication cited actually identifies the highest risk of non-Hodgkin’s lymphoma in Navy shore veterans and ground troops who served in an area of heavy exposure (I Corps). It is not clear why the authors of this textbook chapter, one of whom is Dr. Trichopoulos, made this error, but I first heard it from a consultant for Monsanto Company a few years earlier and it was subsequently repeated in the textbook chapter as if it were true.

## **7. The IBM mortality study and the battle to publish results**

A more recent example of contested information about workplace exposure and cancer developed over the past decade. The origins were in a lawsuit filed in a California County Court in which IBM employees were seeking compensation for illnesses they claimed were due to exposures at a San Jose manufacturing plant. As part of the background for the legal case, attorney Amanda Hawes discovered that IBM had a computerized file of deceased employees whose next of kin had received death benefits. She requested a copy of this file, and a work history file that would document where the deceased workers had worked and what their IBM job titles had been. Initially denying the request, IBM had to be compelled by the Court to provide the electronic data so that a colleague and I could analyze the pattern of deaths in this workforce. The information was eventually provided and was to be kept confidential with employee names encrypted so that no individual worker could be identified. In order to be in the death benefit database, the employee had to have worked at least five years for IBM and not been fired.

In 2003, we began our analysis of over 30,000 deaths that had occurred between 1969 and 2001. Although there had been a few published studies prior to 2003, this was the largest study of deaths in computer industry workers up to that point. With such a large database, we were able to calculate estimates of the risk of death of IBM workers compared to general populations of the U.S., California, and the four counties that comprised the Silicon Valley area. We used a standard occupational mortality statistical software package and carried out an analysis similar to the Vietnam veteran study I had co-authored fifteen years earlier. The results showed large excesses of deaths at IBM due to brain cancer, kidney cancer, non-Hodgkin’s lymphoma, melanoma of skin, leukemia and several other cancers. In females who had worked at the San Jose plant, there was a striking excess of breast cancer. In preparation for the trial, I was required to bring computer print-outs to a deposition and explain to IBM attorneys what my colleague and I had done and how we interpreted the results.

The IBM attorneys, after hearing my description of the calculations and findings, went to the Court and attempted to prevent the statistical results from being used in the trial. The Judge eventually ruled that the statistical analyses were not relevant to the issues in the lawsuit and might prejudice the jury, so I was not able to testify about the mortality study. I did testify about other studies in the literature that showed increased risk of non-Hodgkin’s lymphoma and breast cancer in workers exposed to some of the same chemicals as were used at the San Jose plant. The two plaintiffs whose case was

being presented to the jury in late 2003 and early 2004 had been diagnosed with these two cancers. Under the California law that allowed these two workers to sue IBM, they had to prove that the company had poisoned them, that the company medical staff knew they were poisoned at work, and that the company sent them back to the same environment without telling them that it had poisoned them. If all of that was proven, then the plaintiffs' attorneys also had to show that the cancers in these two workers were caused by the chemicals they worked with. Ultimately, the jury returned a not-guilty verdict.

At the end of the trial, the attorneys for the plaintiffs and IBM were discussing the outcome in the courtroom with members of the jury. This is standard practice in some Courts, and one of the plaintiffs' attorneys said he was disappointed that I had not been allowed to present the results of the mortality study to the jury, but at least I would be able to submit it to a journal for publication. In the following day or so, attorneys for IBM sent a letter to the plaintiffs' attorney saying that the information my colleague and I had analyzed was confidential and that I could not publish it. The IBM attorneys claimed confidentiality, even though the journal article was based on statistical summaries that had been presented at my deposition the previous year. These were in publicly available Court records and had not been stamped confidential at the time. By the time the trial ended, we had drafted a summary of our statistical results that was to be part of a special issue of *Clinics in Occupational and Environmental Medicine* on the electronics industry. This issue was intended to be edited by Dr. Joe LaDou and would include submissions from thirteen other authors (Bailar *et al.* 2007). After a series of exchanges with their lawyers and the editor of the special issue, the publisher, Elsevier, declined to accept my manuscript. The reason they offered was "it is an original research article and the *Clinics in Occupational and Environmental Medicine* publish only review articles." A review of issues for the previous two years revealed that there were six original research articles, so this could not have been the reason for declining my manuscript. The spokesperson for Elsevier said they had not been threatened or coerced by IBM.

In any event, Dr. LaDou and the thirteen authors who intended to publish in the special issue wrote a letter objecting to the exclusion of my manuscript and urging Elsevier to reconsider its decision. When the publisher declined to reconsider, the authors and guest editor boycotted the *Clinics* issue and this became an academic freedom issue. I had to hire my own attorney to get independent advice on whether to submit my manuscript to another journal. I also had to consult with attorneys for Boston University, where I was on the faculty at the time. My attorney advised me that since the statistical results were in the public domain and were not stamped confidential at my deposition, I could publish these findings. Attorneys for Boston University also said they would defend my right to publish if challenged by IBM.

At about this same time, a *Science* magazine journalist named Dan Ferber contacted me to write about the IBM mortality findings and the dispute over publishing them. He wrote an article that appeared in the May 14, 2004 issue of *Science* under the title "Beset by Lawsuits, IBM Blocks a Study That Uses Its Data" (Ferber 2004). In the article, Ferber summarized the main findings of the draft *Clinics* manuscript, which he had

obtained from some unnamed source, and quoted Dr. LaDou as saying the article was the most definitive cancer study to date on workers in the electronics industry. He also quoted one of the IBM attorneys, Robert Weber: “This is one of the clearest examples of what has been characterized as junk science.” Weber asserted that it was “a litigation-produced study in which lawyers supplied key data and gave direction on how the study was to be done.” Weber also stated in this Science article that IBM had commissioned a separate study, led by Elizabeth Delzell from the University of Alabama, who planned to publish it in a peer-reviewed journal.

Several years later, Dan Ferber told me that this was the most difficult article he ever wrote in his fifteen years as a freelance science journalist. He said that an attorney working on behalf of IBM had called him while he was writing the article, and that she had tried to get his editor to suppress the story. He said that his editor referred the article to the magazine’s lawyers and that every word was reviewed for potential liability. He also said that he was required to put in quotes from IBM spokespeople or from others suggested by IBM, something he had never been asked to do before. Ultimately, Ferber said that the Science editorial staff stood by his final draft and agreed to publish it.

The University of Alabama mortality study commissioned by IBM was published in 2005 (Beall *et al.* 2005). Its authors focused on mortality at three IBM manufacturing plants in San Jose, East Fishkill, New York and Burlington, Vermont. They used a different method of analysis and covered a different time period than my colleague and I had been able to analyze in the mortality file we received. One result of their analysis was lower than expected overall mortality, which is often seen in occupational studies and is called “the healthy worker effect.” They also found lower cancer mortality than expected, especially in male workers in these three plants; this latter finding was driven by very low lung cancer mortality in males. We had also found this in our study, which we attributed to low smoking rates in this group of workers because of the nature of their work. The IBM Medical Director said in a public statement that the University of Alabama study showed IBM workers had fewer cancers than expected, without referring to the healthy worker effect.

One finding that stood out in the University of Alabama study was an excess of central nervous system cancer at one of the facilities. The authors say that this was particularly associated with employment in process equipment maintenance, where there was a greater than two-fold excess that was statistically significant. At the end of the article, the authors say that “there was no conclusive evidence that any form of cancer was associated causally with employment,” and that “these positive results emerged in the context of thousands of comparisons and may be due to chance.” They do note that the association of central nervous system cancer with unknown work factors warrants further investigation.

One of the co-authors of the Beall *et al.* study was Robert Herrick, who directed a group at Harvard School of Public Health under a subcontract where they examined the work histories and potential occupational exposures in the three IBM manufacturing facilities. He told me that, as a stipulation in his subcontract agreement, he expected

to be able to publish the results of his group's work on the study. When they found the excess central nervous system cancer in process equipment maintenance workers, the IBM lawyers did not want it to be discussed in the published article. He said the IBM lawyers had a contentious meeting with the Harvard lawyers, and "the Harvard lawyers were more obnoxious" so they prevailed and were able to discuss the excess central nervous system cancer in the 2005 publication. In fact, a further study is underway and may be published in the next year or two. This is an unusual outcome of industry-sponsored studies, and it speaks to the importance of rights to publish results as part of any contract or subcontract by independent researchers. The more typical approach taken by affected industries is illustrated by the hexavalent chromium example.

## 8. Hexavalent chromium studies

There is an extensive literature on hexavalent chromium and lung cancer in exposed workers, going back many decades. Much of this is discussed by David Michaels in a chapter called "Chrome-Plated Mischief" in his book *Doubt Is Their Product*. Michaels begins the chapter by relating a story that "veteran employees at chromium-processing plants introduced new workers to the peculiarities of the job by inserting a dime in one nostril and withdrawing it from the other" (Michaels 2008:97). He then describes early studies by Thomas Mancuso (Mancuso and Hueper 1951; Mancuso 1975; Mancuso 1997) of workers exposed to hexavalent chromium in a U.S. chromate production plant in Paineville, Ohio. In response to these studies, which showed workers to be at increased risk of death from lung cancer, OSHA announced plans to update its workplace hexavalent chromium standard in 1976, but this was derailed for twenty years by the Reagan and Bush Administrations. Then, in 1993, the Oil, Chemical, and Atomic Workers International Union teamed up with an advocacy group called Public Citizen to petition OSHA for an emergency temporary standard of 0.5 micrograms of hexavalent chromium per cubic meter of workplace air. This was denied, but OSHA in 1996 began the process of updating its out-of-date chromium standard by the normal rule-making process.

The Chrome Coalition, an industry association, began its efforts to counter OSHA in 1996. According to Michaels, the plan was as follows: "Reanalyze old studies, and commission new ones that would yield better results. Quickly get some studies into peer-reviewed journals, and make points to influence OSHA's deliberations" (Michaels 2008:101). Another part of the strategy included a project to "Develop an anti-Mancuso manuscript." The result of this strategy was that OSHA was forced to review and respond to a series of manipulated and deceitful analyses of occupational studies, and ten years later promulgated a new workplace hexavalent chromium standard of 5 micrograms per cubic meter of workplace air. This was an improvement over the previous standard of 52 micrograms per cubic meter, but arguably would still allow the half million U.S. workers exposed to hexavalent chromium to be at excessive risk of cancer.

My own involvement in the hexavalent chromium issue came when I was asked in 2011 to be an epidemiology expert for the U.S. Environmental Protection Agency in an enforcement action against Elementis Chromium. The basis for the enforcement

action was the Toxic Substances Control Act (TSCA) requirement that “Any person who manufactures, processes, or distributes in commerce a chemical substance or mixture and who obtains information which reasonably supports the conclusion that such substance or mixture presents a substantial risk of injury to health or the environment shall immediately inform the Administrator of such information ...” As it happened, Elementis Chromium was one of the companies that had participated in a four-plant study, two in the U.S. and two in Germany, and had information about lung cancer risks in workers with low-level exposure to hexavalent chromium. They were one of the companies that were part of the strategy described by Michaels in his “Chrome-Plated Mischief” chapter; the plan was to introduce new studies that would complicate the OSHA standard-setting process.

Briefly, the question before the Court in the Elementis enforcement case was whether the company knew that a new method of manufacturing chrome-based chemical substances, which was purported to be safer, still resulted in increased risks of lung cancer in the workers. If the company knew this, and failed to notify EPA, they were in violation of the Toxic Substances Control Act and would be fined. The company, through its expert witnesses, claimed that there was nothing in the four-plant study results that EPA did not already know, and therefore they were under no obligation to report their findings. One of the company’s experts, Herman Gibb, had already published a study that showed lung cancer risk at low hexavalent chromium exposure levels in an older plant (Gibb 2000). The point of the four-plant study, however, was to evaluate risk in workers using the newer method of manufacturing and processing chrome.

As Michaels pointed out, the authors of the industry-sponsored four-plant study had previously published some of their results, but only after splitting the study into two sub-groups. The lung cancer risk in the U.S. plants, owned by Elementis, was presented in one article (Luippold *et al.* 2005), with the authors stating: “Mortality among chromium chemical workers generally was lower than expected ... Lung cancer mortality was 16% lower than expected, with only three lung cancer deaths (3.59 expected).” The lung cancer risk in the German workers was presented in another article (Birk *et al.* 2006), with its authors noting that, although “lung cancers appeared to be increased (SMR=1.48, 95% CI=0.93-2.25)” there was no clear dose-response. They concluded that there was “a possible threshold effect of occupational hexavalent chromium exposure” (Birk *et al.* 2006:426). So, the effect of splitting the four plants into two groups was to create an ambiguous picture of the risk of lung cancer in workers in the plants using the new chromium processing method. Moreover, the authors of the second study even suggested a threshold, below which there was no risk of lung cancer from hexavalent chromium exposure. This challenges the long-held assumption that there is no safe level of exposure for most carcinogens, including hexavalent chromium.

EPA scientists were able to analyze the trend in lung cancer risk with increasing exposure using data from the entire four-plant study as part of the evidence presented to the Court in the TSCA enforcement action. Using all the data in the Modern Four Plant Report, a steady increase in risk of death due to lung cancer was found with increasing cumulative exposure to hexavalent chromium. As the data extended and filled in gaps that remained after the Gibb study, the EPA conclusion was that this provided “additional information

about substantial risk due to low exposures to hexavalent chromium.” I agreed with this in my testimony before the Court, as did another epidemiologist who testified on behalf of the EPA on the same day.

The administrative decision of Judge Susan Biro was issued in 2013. She found that Elementis had failed to disclose information about substantial risk of injury to human health as a result of exposure to hexavalent chromium, as required under the TSCA. The fine for this was \$2.5 million, but Elementis appealed against this decision and managed to avoid the fine.

Another well-documented example of pollution of the scientific literature also involves hexavalent chromium exposure, although through ingestion of contaminated water and not occupational exposures. This example concerns a series of analyses and re-analyses of cancer mortality in five Chinese villages with hexavalent chromium-contaminated water (Zhang and Li 1987; Zhang and Li 1997). The source of hexavalent chromium was a ferrochromium factory that included a smelter. The first study showed excess overall cancer mortality in the five villages combined, while the second found no association with cancer mortality and hexavalent chromium in the three villages nearest to the source of contamination. The two articles were published in the *Journal of Occupational and Environmental Medicine*, and it later came to light during litigation proceedings that the Chinese authors had received undisclosed payments and intellectual input from U.S. consulting company McLaren/Hart-ChemRisk and the aforementioned Dennis Paustenbach. When this became known publicly, the editor of the journal took the unusual step of retracting the 1997 Shang and Li article in 2006 (Brandt-Rauf 2006).

Two years later, a group from the California Environmental Protection Agency and the Department of Conservation re-visited the data in the Chinese villages with contaminated water and used actual concentrations of hexavalent chromium instead of distance from the factory as the exposure metric (Beaumont *et al.* 2008). In this article, the authors reported substantial increases in stomach cancer mortality in the exposed population compared to the whole province. They also reported somewhat increased lung cancer mortality in the exposed population, although they found this less impressive than the relationship for stomach cancer. They concluded that: “our reanalysis of the Chinese data shows a substantial association between stomach cancer mortality and exposure to Cr6-contaminated drinking water in the 1970-1978 observation period, compared with nearby uncontaminated regions and with Liaoning Province” (Beaumont *et al.* 2008:21).

## 9. Conclusion

These examples are by no means exhaustive, and they are primarily from my personal experience in conducting and reviewing occupational cancer studies over the past three decades. Others have documented similar examples of pollution of the literature and deliberate attempts to distort the scientific record by specific industries or their consultants. The examples I have cited are perhaps unusual in that these attempts have sometimes been exposed, and in one case retracted, or have failed to achieve

their intended results. Nevertheless, they illustrate the problem of “manufacture of doubt” that permeates the literature and makes its way into the regulatory process. The occupational causes of cancer have been and will continue to be contested territory. It is clear that advocates for workers’ health must continue to be vigilant and bring conflicts of interest and outright scientific misconduct in occupational cancer studies to the light of day.

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