UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
NATIONAL CENTER FOR ENVIRONMENTAL ASSESSMENT
WASHINGTON, DC 20460

APR - 7 2000

OFFICE OF
RESEARCH AND DEVELOPMENT

Mr. James F. Warchall
Sidley & Austin
Bank One Plaza
10 S. Dearborn Street
Chicago, Illinois 60603

Re: Freedom of Information Act
Request: HQ-RIN-01093-00

Dear Mr. Warchall:

This letter is in response to your Freedom of Information Act (FOIA) request of January 20, 2000, to the U.S. Environmental Protection Agency (EPA). Your request has been referred to various offices for response. I am responding for the National Center for Environmental Assessment (NCEA) within the Office of Research and Development (ORD) only. You may receive material from another office under separate cover.

NCEA's responses to each of the specific items requested in your letter are provided below. For your convenience, the responsive materials are grouped to correspond to the various items (a., b., etc.) of your request. Also enclosed are indices listing the materials provided by group.

a. *Any and all draft or final versions of the Toxicological Profile for Polychlorinated Biphenyls prepared by the Agency for Toxic Substances and Disease Registry ("ATSDR"), including without limitation the Draft for Public Comment dated December 1998.*

ATSDR has informed NCEA that they will be addressing this portion of your request in their response letter to you.

b. *The "Expert Panel" meeting held on September 27, 28, and 29, 1999, at ATSDR's offices in Atlanta, Georgia, to review the ATSDR Toxicological Profile for Polychlorinated Biphenyls (Draft for Public Comment) dated December 1998.*

Please see Group B for materials responsive to this portion of your request.

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c. *The selection of the "Expert Panel" which met on September 27, 28, and 29, 1999, at Atlanta, Georgia, to review the ATSDR Toxicological Profile for Polychlorinated Biphenyls (Draft for Public Comment) dated December 1998.*

NCEA was not involved in the selection process and does not have anything responsive.

d. *The decisions made by ATSDR in 1999 to (a) terminate its arrangement with Research Triangle Institute under Contract No. 205-93-0606 to revise the ATSDR Toxicological Profile for Polychlorinated Biphenyls and (b) retain Syracuse Research Corporation under Contract No. 205-1999-00024 for such purpose.*

NCEA has no responsive materials to this portion of your request.

e. *EPA's reasoning, analyses or calculations in determining the Cancer Slope Factor for PCBs or the Reference Doses for PCB Aroclors 1016 and 1254 which are set forth in the EPA's Integrated Risk Information System ("IRIS") database.*

The materials requested pertaining to the Cancer Slope Factor can be found in the enclosed copy of EPA's final document entitled, "PCBs: Cancer Dose-Response Assessment and Application to Environmental Mixtures" (EPA/600/P-96/001F, September 1996). In response to your inquiry concerning the Reference Doses for PCB Aroclors 1016 and 1254, also enclosed are the IRIS database printouts for both chemicals. We have also enclosed the IRIS printout for Polychlorinated Biphenyls.

f. *EPA's reasoning, analyses or calculations in determining a Cancer Slope Factor for 2,3,7,8-Tetrachlorodibenzo-p-dioxin from human epidemiological data.*

You have agreed to wait for the latest draft which will be made available on NCEA 's web site. At the time of your conversation with Michele Ranere, a member of my staff, you were informed the draft would be available on the NCEA Home Page in mid-March. We have experienced a few delays and the draft documents, which are expected to undergo independent scientific peer review in May, should be available for review and comment on the NCEA web site (www.epa.gov/ncea/dioxin.htm) in mid-May.

g. *EPA's reviews, analyses and critiques of scientific studies relating to the toxicity of PCBs that were conducted after September 1996.*

Please see Group G for materials responsive to this portion of your request.

h. *EPA's ongoing reassessment of the toxicity of PCBs which was announced on January 2, 1998 (63 Fed. Reg. 75) and December 10, 1998 (63 Fed. Reg. 68285), including the procedure, schedule and budget for that reassessment.*

NCEA has no responsive material to this portion of your request. Our procedure is

to contract out the writing of specific chapters of EPA's ongoing reassessment of the toxicity of PCBs (non-cancer) to technical experts, followed by internal synthesis by experts within NCEA. Two chapters are being written and we are preparing contracts for several additional chapters. At the present time, our schedule for the reassessment (non-cancer) specifies that the review process, beginning with internal peer review and followed by external peer review, will begin in March 2001. At this time, we do not have a formal budget for this process.

i. *The following published report: R.N. Kimbrough, M.L. Doemland, and M.E. LeVois, "Mortality in Male and Female Capacitor Workers Exposed to Polychlorinated Biphenyls," Journal of Occupational and Environmental Medicine, Vol. 41, No. 3 (March 1999).*

Please see Group I for materials responsive to this portion of your request.

j. *All data and methodological information which EPA is required to obtain pursuant to Public Law 105-277 or the amendments to OMB Circular A-110 made on October 8, 1999 (64 Fed. Reg. 54926), or which EPA has obtained prior to the date of this request, that was collected, generated or produced by the authors of the published reports listed in appendix 1, that support, contradict or otherwise relate to the findings or conclusions of such reports, including without limitation analytical reports, test results, calculations, laboratory or experiment notes, statistical analyses, data tables, cohort evaluations, all test and observational scores for each individual at each evaluation time point (coded by individual and tine point), lists and ratings for covariables, measurements of confounding factors, reference scores and standardization methods. (Note that five of these reports have been funded by EPA grant number CR808520010 and many of these reports have been relied upon, or cited by, EPA's Integrated Risk Information System ("IRIS") database in support of its derivation of Reference Doses for PCB Aroclors 1016 and 1254.)*

NCEA has no materials/data responsive to this portion of your request. We have conferred with the Agency's Grants Administration Division (GAD) concerning the funding of the grant number CR808520010. This is a very old grant and unfortunately, the only information available to NCEA from GAD is that CR808520010 was awarded to the University of Michigan (Gretta Sein) in September 1980 for the work product entitled, "Influence of Organic Toxins in Infant Development".

The data requested above are not in our possession. Public law 105-277 and the revisions of OMB Circular A-110 ("A-110"), which you have cited in your request, do not have retroactive effect (64 Fed. Reg. 54926).

For your information, EPA's Region VIII, in Denver, Colorado, has a web site on PCB's (http://www.epa.gov/natlibra/hqirc/inb.htm). This site helps explain how PCBs are still being used, the regulations to control their use, and new developments in the study of PCBs.

05/01/00 15:49 202 565 0079 Jim Cosillano → Region 2 004/017

Your request was placed in the Commercial category, and thus the Agency is allowed to charge you for searching, reviewing, and copying materials under the Freedom of Information Act. The charges total $350.00 (13 hours search and review @ $10.00 per half hour = $260.00; 600 pages @ $0.15 per page = $90.00). A Bill of Collection is enclosed for your use in remitting payment.

This completes NCEA's response to you. We appreciate your patience with the extra time we needed. If you have any questions concerning your request, please address any future correspondence to the Freedom of Information Office (1105), U.S. Environmental Protection Agency, Ariel Rios Building, 1200 Pennsylvania Avenue, N.W., Washington, DC 20460. Please cite the identification number (HQ-RIN-01093-00) assigned to your request of January 20, 2000.

Sincerely,

William H. Farland, Ph.D.
Director

Enclosures

804006

05/01/00 15:50 [1] 202 565 0079 Jim Cosillano →→ Region 2 005/017

Index of material responsive to Sidley & Austin FOIA request
(HQ-RIN-01093-00)

GROUP B

Request: The "Expert Panel" meeting held on September 27, 28, and 29, 1999, at ATSDR's offices in Atlanta, Georgia to review the ATSDR Toxicological Profile for Polychlorinated Biphenyls (Draft for Public Comment) dated December 1998.

1. Invitation letter from Dr. Christopher De Rosa (1 page)
2. Follow-up letter, dated August 10 (7 pages)
3. Follow-up letter, dated August 30 (4 pages)
4. Cover letter to ATSDR from Vanessa Vu (EPA) with EPA comments, dated April 21 (27 pages)
5. Annotated EPA comments on December Tox Profile (28 pages)
6. GE comments, dated April 26 (62 pages)
7. "Issues for PCB meeting" (13 pages)
8. Material received at the Expert Panel meeting Sept. 27-29, 1999 (agenda, participant list, logistical information (36 pages)
9. Excerpt from CMA/CCC comments distributed at meeting (3 pages)
10. Excerpt from Report on Carcinogens distributed at meeting (2 pages)
11. Abstract of Chou et al, article distributed at meeting (1 page)
12. Tilson, et al, article distributed at meeting (10 pages)
13. Background paper on children's uncertainty distributed at meeting (23 pages)
14. Thank-you letter after meeting (2 pages)
15. Summary report, dated December 10 (83 pages)
16. List of additional references (2 pages)

TOTAL PAGE COUNT FOR GROUP B - 304

804007

05/01/00 15:50 [TX] 202 565 0079 JIM COSILLANO →→ Region 2 006/017

Index of material responsive to Sidley & Austin FOIA request
(HQ-RIN-01093-00)

GROUP E

Request: EPA's reasoning, analyses or calculations in determining the Cancer Slope Factor for PCBs or the Reference Doses for PCB Aroclors 1016 and 1254 which are set forth in the EPA's Integrated Risk System ("IRIS") database.

1. Copy of the final document entitled, "PCBs: Cancer Dose-Response Assessment and Application to Environmental Mixtures" (EPA/600/P-96/001F, September 1996) (86 pages)

2. IRIS printout for Polychlorinated biphenyls (PCBs) CASRN 1336-36-3 CASRN 1336-36-3 (06/01/1997) (18 pages)

3. IRIS printout for Aroclor 1016
CASRN 12674-11-2 (16 pages)

4. IRIS printout for Aroclor 1254
CASRN 11097-69-1 (21 pages)

TOTAL PAGE COUNT FOR GROUP E - 134

804008

05/01/00 15:51 202 565 0079 JIM COSILIANO → Region 2 007/017

Index of material responsive to Sidley & Austin FOIA request (HQ-RIN-01093-00)

GROUP G

Request: EPA's reviews, analyses and critiques of scientific studies relating to the toxicity of PCBs that were conducted after September 1996.

1. "Public Health Implications" paper with ATSDR, December 1996 (26 pages)
2. Public Health Implications" paper with ATSDR, January 1999 (35 pages)
3. Cogliano (1998) article from Environmental Health Perspectives (7 pages)
4. Memo from David Bayliss on Loomis study, dated January 1998 (2 pages)
5. Presentation at public meetings in Pittsfield, MA (Oct 99) and Renssalaer, NY (Nov 99) (21 pages)
6. Presentation at American Fisheries Society meeting (Nov 99) (10 pages)

TOTAL PAGE COUNT FOR GROUP G - 101

804009

05/01/00 15:51 202 565 0079 Jim Cogliano →→ Region 2 008/017

Index of material responsive to Sidley & Austin FOIA request
(HQ-RIN-01093-00)

GROUP I

Request: The following published report: R.N. Kimbrough, M.L. Doemland, and M.E. LeVois, "Mortality in Male and Female Capacitor Workers Exposed to Polychlorinated Biphenyls," journal of Occupational and Environmental Medicine, Vol. 41, No. 3 (March 1999).

1. Attendance list for March 9 meeting with Dr. Kimbrough (1 page)
2. USA Today article, dated Match 9 (1 page)
3. New York Times article, dated March 10 (1 page)
4. IEHR press release, dated March 10 (4 pages)
5. Draft internal EPA discussion points, dated March 16 (3 pages)
6. Memorandum from M. Harnois (3 pages)
7. Letter to Dr. Thomas Mack (1 page)
8. Message to Dr. Mary Wolf (1 page)
9. Letter to Dr. Christopher Portier (1 page)
10. Letter to Dr. William Nicholson (1 page)
11. Letter to Dr. David Ozonoff (1 pages)
12. Letter from Dr. David Ozonoff (2 pages)
13. Letter from Dr. Mary Wolff (2 pages)
14. Letter from Dr. Thomas Mack (2 pages)
15. Letter from Dr. Kimbrough to Dr. Peter Boyer (8 pages)
16. Ontario Gazette enclosure from Dr. Kimbrough's letter (3 pages)
17. Letters to the Editor of JOEM (7 pages)
18. Presentation of Dr. Peter Grevatt (20 pages)

TOTAL PAGE COUNT FOR GROUP I - 61

804010

05/01/00 15:52 202 565 0079 Jim Costilano → Region 2 009/017

MEMORANDUM

TO: J. Cogliano, U.S. Environmental Protection Agency (EPA)
FROM: M. Hamois, Massachusetts Department of Environmental Protection (DEP) mah
CC: C. R. West, Director, Office of Research and Standards, DEP
C.M. Smith, Deputy Director, Office of Research and Standards, DEP
SUBJECT: Research report on PCBs by R. Kimbrough (JOEM 41:161, 1999)
DATE: March 23, 1999

Thank you for faxing a copy of this report, Mortality in Male and Female Capacitor Workers Exposed to Polychlorinated Biphenyls, to me before the SOT meeting. I have looked at it more carefully since returning from the meeting and find that it is not possible to relate the effects in humans to either the intensity or the duration of exposure. Nor is it possible to identify the type of PCBs to which exposure occurred. This, together with the shortness of the actual exposure period, results in an inadequate study. The negative results are not compelling evidence for lack of cancer or other effects in humans.

A subgroup that is masked in this study is the one containing hourly male workers exposed to Aroclor 1254 by dermal contact , incidental ingestion, and inhalation for at least 5 years and followed for at least 20 years. This group could have different cancer frequencies from those presented in the report, being definitely exposed to a known carcinogenic mixture for a prolonged interval and observed for an interval that could allow development of tumors.

The report deals mostly with deaths due to cancer effects, but we know that reproductive, nervous, and immunological effects can also occur. These are beyond the scope of the research report, but may be ignored by readers who assume that cancer is the only effect of PCBs.

SPECIFIC ISSUES

The confounding occurs at several points, some of which are noted below.

1. **Job categories are not clearly related to degree of exposure.**

There were job categories in which workers were actually exposed as a result of their activities: filling, impregnating, repairing, or moving PCB-filled capacitors were classified as high-exposure jobs. Here, exposure occurred through inhalation, dermal contact, and incidental ingestion. No estimates of doses per shift or otherwise are given; the workers doing this are mostly male hourly workers.

Operations in which no PCBs were used were called "low-exposure" jobs: winding, can, and cover manufacturing, assembling and shipping. Exposure here was only to ambient concentrations of PCBs. The same air concentration is assumed to prevail in the clean area where this type of work was done and the offices, since all operations were housed in one building.

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The authors state that 97% of the women (total of 3013) worked in low exposure jobs. Yet Table 3 shows 362 women with a high exposure job instead of the expected 90. This needs to be clarified.

Salaried persons were said to be involved in the manufacturing process, but there is no indication given that they actually filled the capacitors or handled PCBs. Yet they are assigned to the high exposure group in some cases, and their exposure lasts longer than the hourly workers (Table 3). This also needs clarification.

2. **Air concentrations vary considerably.**

The authors provide data on air concentrations measured in high and low exposure areas in 1975 and just before shut down in the spring of 1977 (see table).

Exposure	1975 results	1977 results
High	227-1500 ug/cu.m	170-576 ug/cu.m
Low	No data; estimate of 130 ug/cu.m based on proportionality (see text)	3-50 ug/cu.m

The capacitors were made over 31 years (1946-1977), yet the median duration of high exposure is <2 years for hourly workers. Some could have been exposed during the peak operational years, but others only in the phase out period. There is no distinction made within the high and low categories between people exposed at the peak of operation and people exposed during the phase out period.

The "low" exposure at the peak could be nearly as high as the "high" exposure during phase out if the air concentrations in the low exposure area were consistently proportional to those in the high exposure area. For example, 1500 ug/cu.m / 576 ug/cu.m x 50 ug/cu.m gives an upper bound proportional estimate of 130 ug/cu.m for the 1975 low dose. Inhalation exposures during the high operational period and phase out period need to be evaluated separately.

Exposure by inhalation is probably much lower than the dermal and incidental ingestion exposures of the workers. The hourly workers filling the transformers and retrofitting them would be more exposed than suggested by the air concentration data supplied by the authors.

3. **The PCB mixture used over this time varied significantly.**

The plant used PCB mixtures from the Monsanto Chemical Company (Aroclors). Exposure at the capacitor plant from 1946 through 1954 was to Aroclors 1254 and 1242; exposure from 1954 through 1971 was to only Aroclor 1242; exposure from 1971 to 1977 was to only Aroclor 1016. Aroclors 1016 and 1242 have a higher proportion of congeners with few chlorines, and are more volatile; Aroclor 1254 has more highly chlorinated (and thus heavier) congeners and is not particularly volatile.

Data from the animal tests sponsored by the General Electric Corporation showed that the mixtures of PCBs varied in potency for cancer effects. Aroclors 1016 and 1242 were

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less carcinogenic than Aroclors 1254 and 1260, indicating that exposure to the various PCB mixtures would not give a uniform dose of carcinogenic congeners.

Depending on when exposure occurred, the workers in the "high" exposure group could have been exposed to mixtures containing higher or lower concentrations of carcinogenic congeners. Exposure by inhalation ("low" exposure) could also vary, depending on which congeners were in the air.

Further, the lighter mixtures may cause other noncancer effects than those seen with Aroclors 1254 and 1260.

The reader needs an estimate of the doses received for each Aroclor mixture. People exposed to different mixtures should be considered separately in the analysis.

4. **Exposure to other chemicals occurs.**

It is not clear whether or not the people exposed to PCBs are exposed to other carcinogenic chemicals at the same time. Also, since the workers are said to have different jobs over their employment duration, there could be cumulative exposure to carcinogenic chemicals and this is not adequately described.

The reader would like to make comparisons of cancer incidence between worker subcohorts exposed to PCBs and those not exposed. In this report, this could unknowingly include comparison to workers exposed to other workplace carcinogens so would be misleading. The report would be more valuable to the reader if workers exposed to other workplace carcinogens were more clearly identified.

5 **The actual duration of exposure is not clearly defined and could be inadequate to allow detection of cancer effects.**

There is a mean employment duration of about 6 years but 1/3 worked for <1 year. In Table 3, the median period of actual exposure is given as 1.7 and 1.6 years, respectively, for hourly male and female workers. This is a relatively short period of exposure for occupational studies on cancer, and I agree with you that it may not be adequate to show a statistically significant difference.

6. **The incidence of deaths due to cancer is not related directly or indirectly to the dose of PCBs received.** In Table 4, the incidence is based on person-years of observation; in Tables 5 and 6, it is based on length of employment. Neither estimate relates exposure to PCBs and cancer.

7. **The report describes deaths due to cancer, not incidence of cancer.**

Some types of cancer (e.g., breast cancer) are treatable, so would not be representatively included in this report. The incidence of cancer in the cohort members who are still alive needs to be included in any evaluation of cancer potency in humans.

The data in this report are not adequate for relating exposure to PCBs and development of tumors.

804013

05/01/00 15:54 [1] 202 565 0079 Jim Cosillano →→ Region 2 012/017

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June 6, 1999

Dr. James Cogliano
USEPA
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Washington, DC 20460

Dear Dr. Cogliano

Recently an article by Kimbrough et al. appeared that has been widely touted as showing "no link" between PCB exposure and cancer mortality (Kimbrough R, Doemland M, Levois M, "Mortality in male and female capacitor workers exposed to polychlorinated biphenyls," *JOEM* 14:161-171, 1999). As a public health professional with a longstanding interest in the health effects of PCBs (I am currently a member of an expert committee convened by the Department of Public Health in Massachusetts to study the health risks of PCB exposure), I felt it might be useful if I provided to you some of my concerns over this misinterpretation of the Kimbrough et al. study, as it is the kind of data that are likely to be used as basis for future risk assessments.

The study in question has been competently designed and executed and does not itself make the extravagant claims contained in accompanying press releases. Having said that, I must add that it provides rather limited information on the issue. It is in fact a "plain vanilla" occupational mortality study with all the usual limitations of such designs, and with some additional problems as well.

First, it is a mortality study, not an incidence study, so it provides information only on the risk of dying (and being recorded as dying) from cancer, whereas the pertinent question is the risk of contracting cancer. Mortality is compounded from the risk of contracting the disease (the item of interest), the risk of dying from it once contracted (subject to a variety of variables such as care-seeking behavior, adequacy of medical care, etc.), and the risk that a death will be properly recorded as a cancer death from a specific site (correctly assigned). The same variables operate on the comparison group, of course, and unless it operated differently on them no bias would be involved. However, it is impossible to know if there is such a difference. In addition, the likely misclassification of outcome will tend to erase any existing differences.

This is just one example of potential confounding that was not taken into account in this study. Since the only confounders used were age and sex (the most important, of course), it is quite possible other factors might change the estimates if they were

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unequally distributed in the workforce compared to the general population. We know this occurs with the Health Worker Effect, which is sharply in evidence in this study and tends to mask any areal effect.

Another problem that diminishes the usefulness of this study is the strikingly young workforce, even after long follow up. In order to detect cancer risks the population must be at sufficient risk for contracting the disease. In this case this means old enough, and with sufficient latency since first exposure. It appears that most of the workers are just now entering the high risk cancer age groups. They should be followed for another decade or two. This problem is most obvious for looking at specific cancer sites, where the number of workers with sufficient latency is not enough to provide the kind of statistical power needed. Thus the analyses and interpretations tended to emphasize "all sites combined," a category which would require very high risks at certain sites to produce a significant finding.

As with all studies of this type, a particularly vexing problem is adequate exposure assessment. In this case, there is almost certainly a great deal of exposure misclassification, which is known to seriously bias positive effect estimates downwards. From the data given in the paper and other studies of this population, it is not at all clear that the majority of the workers studied had exposures much or at all higher than the general population. This would make any ability to look at trends almost impossible, and also make the comparison with the general population tenuous. The change in types of Arochlors used over time complicates the picture as well.

Despite these difficulties, I note that some cancer sites did show elevations (e.g., intestinal cancer, previously linked to PCB exposure). This takes on added significance in the face of the many factors and limitations which would tend to mask any associations.

In short, we have here another "data point." It should be judiciously interpreted and used with the caution appropriate to studies of this type. In particular, this means not giving undue weight to its failure to show associations previously revealed, since there are too many factors that would militate against being able to show them in this study.

I hope you will find these comments useful in your work.

Sincerely yours

David Ozonoff, MD, MPH
Professor and Chair, Department of Environmental Health
Boston University School of Public Health

804015

Division of Environmental and Occupational Medicine
Mount Sinai School of Medicine Box 1057
1 Gustave L. Levy Place
New York, New York 10029

September 1, 1999

To:	Jim Colleano	fax 202 565 0079	phone
From:	Mary S. Wolff	fax 212- 831-3046 or 996-0407 email: mary.wolff@mssm.edu	phone 212-241-6183

Jim, I annot find my review of the JOM Kimbrough article. As I recall, my critique addressed exposure issues (no intensity, nor kind, nor duration of exposure among the employees and therefore no dose-response effects could be seen). Also, as I recall I had some quesitnos about the control group.

Bill Nicholson is hard at work writing something up for you. As it turns out, that is really the best thing, because he has done mortality studies of that cohort and we chatted today and he has a number of really good points for you. He promised he would have something to you within the week. I gave him your phone/fax.

FYI his phone is 241 5822, but he is not in every day, and doesn't have phone-mail. So....good luck on this v. imp quesitno.

804016

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USC
SCHOOL OF
MEDICINE

James Cogliano, PhD
Chief, Quantitative Risk Methods Group
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US Environmental Protection Agency
401 M Street, SW (8623-D)
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Dear Jim:
This is written in response to your request to take a look at the recent Kimbrough et al paper on the PCB exposure cohort. After speaking with you I decided I should go back and look at the previous papers (i.e. Brown & Jones, Brown, Sinks et al, and Bertazzi et al) in order to get appropriate perspective.

As I indicated to you on the phone, I found the Kimbrough paper to be well designed, appropriately analyzed, and fairly interpreted. The follow-up was complete. The results are internally consistent, and show the expected social class effects. I am no expert in assessing the magnitude of exposure, but as far as I can see the magnitude of exposure implied by the various production tasks is similar to those previously studied. As in any environmental study, much less any occupational study, the individuals with the maximum exposure are probably few and unidentifiable. Nonetheless, the persons in this study probably have a higher average exposure than any population likely to come to our attention in terms of risk prediction.

When I looked at the previous studies, I was not very impressed with the positive findings, and not just because of the inconsistency. The Silk and Bertazzi papers in presenting the evidence for indications of risk for melanoma and lymphoma (actually mostly Hodgkin's disease) honestly described the compatibility with chance but did not assess the differences according to education, important in both of those outcomes. Unlike the Kimbrough study, neither investigator divided workers into salaried and hourly categories. The evidence for CNS tumors is statistically very flimsy, and that for liver from the Brown paper, ostensibly the most interesting because of the mouse data, actually represents an excess of biliary carcinomas and not liver at all. We know that the known determinants and risk factors are very different. The lung cancer excess in Bertazzi was not assessed with respect to smoking. What is described as gastrointestinal tract in the same paper are cancers of the stomach (2), pancreas (2), liver (1) and biliary (1).Again, these tumors have disparate epidemiology which, given the small numbers, greatly lessens the credibility of a common origin.

That really leaves cancers of the rectum, as a site that has appeared at least once and is worthy of suspicion a priori. The finding of a few extra rectal and "intestinal" (presumably colon, unlikely to be any small bowel) cancers here in low exposure hourly women is as strong as any previous

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05/01/00 15:57 ☎1 202 565 0079 Jim Cogliano →→ Region 2 ☑016/017

finding, that is to say not very strong at all. It is true that colorectal cancers are very complex etiologically, involving several heritable syndromes in interaction with several dietary (i.e chemical) constituents, and it is impossible to rule out some small causal role for PCB's.

I have not seen the reported excess of cases in the Yusho cohort, but it is my understanding that colorectal cancers were involved. However, the material contaminating the cooking oil contained not just PCB's but also PCDF's, and therefore might not be completely pertinent. On the other hand, superheating of PCB's is said to produce PCDF's, so maybe it is not completely irrelevant.

I guess my bottom line is that the summary statements ("lack of any significant elevations adds important information" and "lack of consistent findings----would suggest a lack of an association") in the paper are appropriate. I think that it is appropriate to downgrade the priority given to PCB's. However, based on the animal studies (and recognizing a. the possibly limited relevance to man and b. the absence of any confirmation of liver cancer in humans) and on this very small amount of information pointing to colorectal tumors, I don't think that the potential carcinogenicity of PCB's can be *completely* dismissed. I recognize the flimsiness of the evidence, and that a less conservative person could persuasively argue the other way.

I'm sure this has not been particularly useful for you, but it's the best I can do. If I can help in any other way, don't hesitate to ask.

Sincerely,

Thomas Mack, MD
Professor

804018

05/01/00 15:58 1 202 565 0079 Jim Cosliano → Region 2 017/017