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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
REGION 2
290 BROADWAY
NEW YORK, NY 10007-1866

US Environmental Protection Agency
Hudson River PCBs Reassessment Remedial Investigation/Feasibility Study
Community Interaction Program

Steering Committee Meeting
October 26, 1999
Saratoga Springs, NY

On October 26, 1999, a Steering Committee meeting was held at The Inn at Saratoga in Saratoga Springs, NY. The agenda for the meeting is Attachment 1. Sign-in sheets are found in Attachment 2. The use of brackets - [ ] - indicates clarifications made by the writer in cases where unclarified text would be unclear to those not at the meeting. Copies of the audio tapes recorded at the meeting are available on request.

Attending were the following:

- Ann Rychlenski, United States Environmental Protection Agency (EPA) Community Relations Coordinator for the Hudson River PCBs Superfund Site and Steering Committee Chairperson;
- Doug Tomchuk, EPA Project Manager;
- Alison Hess, EPA Project Manager;
- Bruce Bentley, New York State Department of Environmental Conservation (NYSDEC) Public Affairs;
- Bill Ports, NYSDEC Project Manager for Hudson River remedial project;
- Judith Dean, Citizen Liaison Group Chairperson;
- Katie DeGroot, Citizen Liaison Group Cochairperson;
- John Santacrose, Environmental Liaison Group Chairperson;
- Marion Trieste, Environmental Liaison Group Cochairperson;
- Carl Deppe, Environmental Liaison Group Cochairperson;
- Tom Bordon, Agricultural Liaison Group Chairperson; and
- Dave Adams, representing Darryl Decker, Government Liaison Group Chairperson.

Ann Rychlenski opened the meeting asking for report-outs for each liaison group.

Environmental Liaison Group: No meetings have been held. John Santacrose raised a question about "River Voices," noting it has not come out recently, and that to his knowledge people have not been asked to contribute.

Ms. Rychlenski stated there was some discussion by her management to discontinue accepting contributions from members of the liaison groups and convert "River Voices" into an EPA publication. Ms. Trieste strongly objected, stating that the "River Voices" was a way to get the process occurring "in this room out beyond this room," and felt contributions should be solicited as they have been in the past. Ms. Dean commented that "with your administration's attitude and the brouhaha over the last publication," she didn't "know that it has

much to say anymore." Ms. Trieste indicated that as many vehicles for public input as possible are needed, and the issue of not being able to put anything into the paper needs to be addressed.

Citizen Liaison Group: Judy Dean asked about money for an additional TAG grant. Ms. Rychlenski clarified that additional monies are sometimes available for the existing TAG grant (the same recipients) but that there is only one TAG grant permitted by law for a site. Ms. Dean stated she thought the possibility of an additional grant had been discussed at a previous meeting, "considering the absurdity of this one."

Ms. Dean's second item was to request an independent peer review of both models. Mr. Tomchuk stated that EPA is having an independent peer review of its model, but [comparing two models] is not the way peer review is conducted. He said, "no, we are not giving you what you are asking for precisely; we are following our guidance as to how to do a peer review, and we will have an independent peer review." A comparison review is not peer review.

Mr. Adams said academics he had asked said they had not been constrained as to what information they could look at in the process of the peer review, they were free to look at any information they feel is appropriate. He said to tell a peer reviewer when he has two papers both dealing with the same subject - that have differences but both have merit - that he shouldn't look at the second one "is contrary to everything I know about how the peer review process is done in the scientific community."

Mr. Tomchuk agreed wholeheartedly about not limiting peer reviewers as to what they look at; EPA's responsiveness summary includes all responses to GE's comments. EPA is addressing whether they will be receiving [GE's] entire modeling report; EPA has stated that the agency is looking at whether to view GE's model as a comment to their report, and will be responding to that. EPA is allowing the peer reviewers to look at anything they want to look at; there is a difference in looking at something in the review of one document vs. reviewing both documents, and [to Mr. Adams] "I don't think you asked them that question."

Mr. Adams said if one is "given a scientific paper to review on a particular subject, the normal process in reviewing that is to compare it to its peers, to other papers that are applicable and deal with the same subject matter." He complained that EPA issues limited charge documents that direct [the peer reviewers] in..." the path you want them to follow." He suggested that the peer reviewers be given no charge document.

Mr. Tomchuk stated a specific charge is necessary for a peer review to limit the effort from the universe of any question to the fundamental questions on the document at hand; he stated EPA has not limited the peer reviewers to "get the answer you want."

Marian Olsen, EPA's human health risk assessor for Superfund, clarified that, based on her experience from working in a research laboratory, single papers were submitted that would be reviewed individually to determine whether they should be published; reviewers were not asked to review the paper submitted vs. other papers. This is peer review within the academic community.

Dr. David Carpenter of SUNY Albany's School of Public Health, Environment and Health Toxicology affirmed; he stated peer review is a review of one document. Reviewers may use any information from anywhere they want, but peer review is a critique of strengths and weaknesses of one document. In response to Mr. Adams' continued pressing for no charge to be given to the reviewers, Ms. Olsen pointed out that EPA guidance requires a charge to be developed to direct the peer reviewers on specific questions the agency has identified as requiring reviewers' scientific interpretation. Mr. Adams commented that although this is agency policy, he is hearing that this policy is not satisfactory.

Ms. DeGroot questioned Dr. Carpenter's presence. Ms. Rychlenski explained that in response to letters she had sent to all chairpeople and to liaison group members at large requesting agenda items, Scenic Hudson requested that Dr. Carpenter be on the agenda. Ms. DeGroot requested that in the future she have "prior warning as to what the agenda is going to be." She stated she resented having a presentation done without being able to prepare questions in advance or have a rebuttal. She stated it is "unforgivable not to give us warning." Ms. DeGroot stated she felt she was continually presented with one position when "we know there are two sides and two viable very different answers to some of the questions." She objected to having two of what she termed as biased presentations without an opportunity to be prepared to ask questions and to have someone here to debate them. Ms. Rychlenski acknowledged the conflicting opinions, and pointed out that at any given time, Ms. DeGroot could also ask for a speaker. Ms. Rychlenski stated the request [for prior notification of the agenda] would be considered and that Ms. DeGroot's opinions would be put on the record.

Ms. Trieste suggested a process for bringing in speakers be developed, acknowledging Ms. DeGroot's position that not being able to discuss information in a presentation due to lack of preparation was a legitimate point. She stated this is not a one-sided opportunity being presented by EPA; "we are all being given an opportunity. It's just that we be better prepared." Mr. Adams supported the request to inform liaison groups of the agenda in advance.

Agricultural Liaison Group: Mr. Borden stated he felt GE's model had to be peer reviewed in some fashion in relation to this process.

Ms. Dean interjected the importance of getting an economic study into the process. "These are international waters with international businesses; there are too many people affected by this that not only live on the river [but are dependent upon it] for their businesses." She stated "we cannot ignore it anymore; we have got to figure out a way to work it in." EPA is here because it is their job, not as the rest of the people who are living there; "we're the ones this is all about."

Mr. Adams inquired as to a proposed meeting between EPA and the Agency for Toxic Substances and Disease Registry (ATSDR). Ms. Olsen stated the meeting occurred in September, 1999, to discuss comments submitted by EPA and other organizations on ATSDR's draft toxicological profile [per Ms. Olsen for the purpose of these minutes: *Profile for Polychlorinated Biphenyls Update*, 12/98; sent out for public comment through April 16, 1999]. ATSDR will review the comments and will then revise the document. Dr. Carpenter, who is on the review committee, stated the committee recommended extensive revisions to the organization of the draft profile, not the substance, which will push release of the revised document into mid- to late spring. Ms. Olsen and Ms. Rychlenski committed to providing updates as they are available.

EPA: Mr. Tomchuk first announced the National Academy of Sciences' (NAS) Research Council meeting being held in Albany, New York, on from 1:00 PM to 9:30 at the Desmond Hotel, November 8, 1999. This is part of a panel formed to evaluate remediation of PCB-contaminated sediments. There are open microphone sessions available and Mr. Tomchuk urged interested parties to register. There have been two prior meetings as part of this study. A report is expected in autumn of 2000.

The next peer review kick-off meeting will be in the second week of January, 2000. Details will be provided as they become available. This meeting will not have a public comment session as do the actual peer review panel discussions.

EPA is updating the Hudson River website. Suggestions to Mr. Tomchuk or Ms. Hess are welcome. The address is: www.epa.gov/hudson.

EPA will be doing a debris and velocity survey of the river bottom to be able to fully evaluate the alternatives in the feasibility study (FS) during the first and second week of November. Some of the capping and dredging alternatives depend upon what and how much debris is on the bottom that might have to be cleared; this information will contribute to the economic comparison of some of the alternatives. Mr. Tomchuk emphasized that this is part of the FS process. In response to a question, Mr. Tomchuk indicated the activity would be occurring at approximately seven locations including the Thompson Island Pool.

Ms. Hess pointed out that the human health and ecological risk assessments were released in August, 1999, followed by a 30-day public comment period. Responsiveness summaries will be published in March, 1999. Two risk assessment addenda, the Mid-Hudson Human Health Risk Assessment and pert of the ecological risk assessment looking at future risk in the lower Hudson River, are not on the published schedule for the reassessment but both will be released sometime this fall. Public comment will be taken and responsiveness summaries will be issued on both these reports.

All risk assessments will go out for peer review. A kick-off in March will be followed by the actual peer review sessions in May. EPA will solicit input from the public on the charge questions the peer reviewers are asked to answer. The same grade system - Acceptable As Is, Acceptable with Minor Revisions, Acceptable with Major Revisions, Unacceptable - will be used as in prior peer reviews.

Ms. Hess announced a conference in Pittsfield, MA, Saturday, October 30, 1999, at the Crowne Plaza Hotel on the health risks associated with PCB exposure. A representative from EPA headquarters will be present to discuss toxicology of PCBs, as will Dr. Renata Kimbrough, author of the recent mortality study on GE plant sites. There is a $45 attendance fee.

Mr. Tomchuk added that EPA is also soliciting input for charge questions on the baseline modeling peer review scheduled for January, 2000. A written solicitation will be forthcoming; deadline for input will probably be before the holidays. A compilation of comments will be done and the charge questions will be developed using that compilation.

NYSDEC: NYSDEC is working on the proposed plans (PRAPS) for the Hudson Falls plant site and in the process of issuing a Record of Decision (ROD) for the Ft. Edward plant site. The responsiveness summary for that ROD is being completed.

Dr. Carpenter followed the report-outs and discussion with his presentation summarizing how he sees the health effects of PCBs. He began by describing the structure of PCBs, biphenyl rings with up to ten chlorines. Because chlorines can appear in various positions on the rings, up to 209 PCB chemical compounds are possible. Biological effects of the compounds vary depending upon how many chlorines there are and where they are on the rings. Positioning of the chlorines on the rings appears to determine whether they are associated with cancer or non-cancer effects. PCBs, although banned in the United States, are still manufactured in Russia and Korea, and widely used in developing countries. The worldwide problem still exists, therefore.

Dr. Carpenter went on to describe the different characteristics of more and less heavily chlorinated biphenyls, discussed health and ecological effects believed to be attributable to PCBs, and referred to some of the studies

recently performed. The slides used in the presentation can be found as Attachment 3. These minutes contain highlights of the entire discussion; the complete dialogues are available on the tapes.

Ms. DeGroot took issue with Dr. Carpenter on the Jacobson study, which she understands not to be considered a good study. Dr. Carpenter said that is not correct; any study can be criticized. He emphasized that the issue does not rise or fall on any single study, but rather on the aggregate body of information. Ms. DeGroot contended the subjects could have received other toxic substances through the umbilical cord, and other substances such as alcohol and tobacco were not controlled.

Ms. DeGroot insisted there still is no evidence that PCBs cause cancer in humans. Dr. Carpenter said, "That is not true." He agreed "there is not absolutely definitive, conclusive evidence," but emphasized that what is important is the consistency across all the studies; the majority of the studies showed statistically significant elevation of some kind of cancer. The aggregate of human studies in consideration with the animal studies "makes a coherent picture."

Dr. Carpenter said he is not contending that PCBs are the most dangerous hazard to public health; he contends that smoking is. He stated he is focused on effects on intelligence and behavior in children because he believes them to be irreversible, and that has "enormous societal implications."

Ms. Trieste expressed concern over the constant debate occurring in these forums about the health risk associated with PCBs. There is an EPA-established, ATSDR-confirmed national policy that PCBs are probably human carcinogens and are considered a human health risk. She stressed that this is law, not her opinion, and that what the guidance is based on. It is not an issue for cleanup of the Hudson River. She asked Dr. Carpenter if he had an idea of what is in the Hudson in terms of toxicity. He said chlorination of PCBs in sediments changes due to bacterial action, so what was originally there is not what is there now. PCBs with fewer chlorines are more water-soluble and will resuspend and flow away and/or be volatilized. This bacterial action in the absence of oxygen does not destroy PCBs, it changes them chemically. It is also difficult to compare health risks of people exposed to PCBs in the Hudson and elsewhere, because the types of PCBs they were exposed to were different.

Mr. Ron Sloan of NSYDEC clarified that Aroclor 1242 was not the only aroclor in the Hudson, there was a mixture of other aroclors also. Aroclor 1254 was the one principally found in the fish.

Mr. Adams asked how the PCBs in the fish compare to the PCBs workers were exposed to in the Hudson Falls and Ft. Edward plants. He understands the PCBs in the fish to be primarily associated with Aroclor 1242, which would have been the aroclor in the air in those plants.

Mr. Tomchuk disagreed; he said what you will see in the fish because of a preferential bioaccumulation from an Aroclor 1242-like mixture is a PCB mixture with four, five, and six chlorines, resembling Aroclor 1254. What you see in volatilization from 1242 are the monos, dis, and tris that will volatilize more quickly; therefore, exposure in the plant sites will probably be on the lighter end due to volatilization compared to exposure from fish. This is reflected in EPA's cancer slope factor. EPA uses different cancer slope factors in its assessments for each route of exposure because of this differential in volatility rates and bioaccumulation. Dr. Carpenter added that inhalation exposure would be the lower chlorinated congeners of 1242, not 1242 itself.

Brian Mayes from GE asked for a clarification for the audience of Dr. Carpenter's comparison to PCBs to radiation. "Radiation is a clear human toxin; PCBs are not." Dr. Carpenter agreed, but said his point was only

to illustrate that exposure caused increases in various types of cancer. Mr. Mayes contended that the weight of evidence "30-some-odd" epidemiological studies that exist does not support PCBs as human carcinogens. Dr. Carpenter: "I do not agree with that at all, and I guarantee the ATSDR panel does not agree with that at all. That is not the consensus of the scientific community."

Ms. Olsen clarified that when the agency did the reassessment of PCBs in 1996, it came out with a weight of evidence for PCBs to be classified as a probable human carcinogen, based on the epidemiological studies, so the agency has gone through that. This reassessment was also peer reviewed by a panel of independent peer reviewers. The agency says PCBs are a *probable* human carcinogen based on the evidence presented at that time and reviewed by those scientists.

Ms. DeGroot contended that a lot of people disagreed with how the agency came up with that assessment, and what they really mean. In response to Ms. DeGroot's comment "...and the government never makes mistakes," Ms. Olsen reemphasized that an external panel of 25 scientists; the assessment went through that entire process and also went before congress.

Leigh Foster referred to Dr. Carpenter's position that different populations have different exposures and therefore have different risks. He asked Dr. Carpenter if there is any information on complications caused by additional risk factors, different lifestyle impacts of people exposed to PCBs, and cumulative effects. Dr. Carpenter said there is very little information; it is the direction "our own" research is moving right now. "There is the possibility that each of our different unique genetic make-ups make us more vulnerable to diseases; it is quite clear that breast cancer runs in families. That is one variable and in our new study we are going to be looking at breast cancer, prostate cancer, thyroid disease, asthma, and male infertility as a function of the body burden of PCBs and the body burden of lead, with the idea that both lead and PCBs do a lot of the same things in a lot of people's organ systems. When you are exposed to both, do you get just an additive effect, or do you get a synergistic effect, or do you get an antagonistic effect?" Dr. Carpenter said the study would also consider 24 different genetic polymorphisms, some for the immune system and some for the liver enzymes that degrade PCBs.

Mr. Adams stated that he understood that the ATSDR draft document said the weight of evidence does not support "a causal association for PCBs and human cancer at this time." He questioned whether this comment would be in the final document. There was some discussion as to what toxicological profile actually contained this statement, the 96/97 version or the 1999 version; if it was in the 1999 draft, Dr. Carpenter said he did not feel it would be in the final. Mr. Adams said the fact that ATSDR made the statement indicates that the "entire scientific community does not necessarily agree with your conclusions."

He will search for someone who can adequately present "the other side of the story" and will then request presentation time. Dr. Carpenter clarified that he did not mean to imply that everyone agreed with him.

Mr. Olsen stated that EPA provided comments to ATSDR on the statements in the draft regarding cancer assessment to clarify the agency's [EPA's] position and some problems on what was quoted from the agency documents. She stated that at this time that document is still a draft; ATSDR has comments; and Ms. Olsen feels the public may see some changes in the final document.

Ms. Trieste again asked how many debates are we going to have on the cancer-causing or non cancer-causing effects of PCBs. Mr. Adams said there needed to be another one, and will request that. Ms. Trieste asked, "if we don't come to an agreement, does it matter?" Ms. Rychlenski pointed out that we are not talking about consensus in the group. "That's not what this is about; it is about getting information out."

Jay Silkworth from GE acknowledged that we do not have the answers to this very complex issue; he feels what is becoming apparent is that we can make decisions based on consistency and weight the evidence. Dr. Carpenter pointed that out that consistency is important. Mr. Silkworth said the consistency he sees is that it is very difficult to detect any effects of PCBs. If we see statistical effects, there are barely statistically significant and disappear over time, so we lack statistical consistency throughout the studies. After four days at a conference on neuro-toxicity, the consistency he sees is that we really can't be sure; "the data is not good enough to make a clear decision but it doesn't look like anything is there consistently."

Specifically regarding synergism, two chemicals acting worse together than they would independently, Mr. Silkworth feels that the cohorts being evaluated are a perfect example of synergy; they have the most likely possibility of synergy - between methylmercury, lead, PCBs, and any other compound including ethanol, alcohol, mother's IQ, etc. - and we consistently cannot see any dramatic effect. To him, if there is synergy it is extremely low; therefore the chemicals independently have a "much, much, much" lower effect, again, that we can't see. He is not personally worried about PCBs' causing any of these effects. Finally, Mr. Silkworth contended that in speaking with investigators of large groups in Europe, he was told they could not follow one particular child through the study and detect consistently a change in their IQ or their performance.

Mr. Tomchuk said the Rensselaer County Environmental Management Council has organized a meeting in Hoosic, New York, toward the end of November to talk about PCB health effects. Speakers have been invited, including EPA and GE. It is not firm yet whether EPA has staff available to attend.

Tony Maresco asked Dr. Carpenter if he knew of any other studies with regard to [polymorphisms] and any other type of cancer related to PCBs. Dr. Carpenter did not know of any other study that looked at polymorphisms, cancer, and PCBs. A number have looked at cigarette smoking and polymorphisms.

Robert Foster, Citizens Committee for the Environment: question regarding estrogenic PCBs and anti-estrogenic PCBs, and whether in the presence of both, the estrogenic compound has an impact on the cellular level, and then the anti-estrogenic compound also has an impact on the cellular level, or is there a balancing in the mixture before hand so there is no impact. Dr. Carpenter said he did not think there is a balancing mechanism. The estrogenic actions are mediated by a totally different process than the anti-estrogenic compounds. Each congener seems to have a different potency in its actions. Currently we look at total PCBs because of that. He said "our hypothesis is if we know the concentrations of each of those 209 congeners, and add all the metabolites of all those congeners, and if we know the actions of each of them, then we will be able to predict what disease I would be particularly vulnerable for on the basis of my particular profile."

Ms. Dean asked, "If you don't eat the fish who have accumulated PCBs, you don't have a health risk, do you?" Dr. Carpenter stated the major risk is eating fish, but said her statement was too strong with regard to people who live along the river and have other pathways of exposure. Animal studies exist that show animals can absorb and inhale PCBs, producing changes in their thyroid glands. We don't have a controlled population because none of us are unexposed [to PCBs]. We are seeing health hazards from the higher exposed people; that does not mean there are no biological effects that are problems to [those] much less exposed. If you don't eat the fish, the health risk is lower.

Mark Behan challenged Dr. Carpenter on a statement he said the professor had made at a meeting with the Hudson River Environmental Society several years ago that there was no evidence that PCBs "have contributed to human cancer in any study that I know of." Dr. Carpenter said he had no idea why he would have made a statement like that; he recalled saying "there was no conclusive evidence," and he agrees with that statement: [the evidence] is not conclusive, but evidence that strongly indicates that PCBs do cause cancer exists in really

convincing studies, particularly as relate to breast cancer. Human studies are consistent with animal studies. Dr. Carpenter stated that the statement quoted, correctly or not, was clearly not his position now.

Question from GE: Why was the Hunter study from the Harvard School of Public Health not shown?

Dr. Carpenter: The Hunter study looked at PCB levels in a number of women with breast cancer and a number of control women. The PCBs they measured were entirely the anti-estrogenic PCBs. They didn't measure estrogenic PCBs. From Dr. Mayes' study in rats, the incidence of breast cancer was less than in the case of the controls.

GE speaker said his analysis of that study showed that the incidence of total cancers - all cancers combined - in that study, in every treated group, was less, and in some cases statistically significantly less, than the control group. He said if you look at all cancers, to make a weight of evidence argument for all kinds of cancer in the rat study (not looking at individual types such as thyroid, liver, etc.), incidence is less. Liver cancer was elevated.

Dr. Carpenter: If polymorphisms are important, you wouldn't expect a relationship between total serum PCBs and breast cancer. There are a lot of studies on breast cancer; about half show statistically significant relationships and the other half do not. There are reasons for both negative studies and positive studies that are fallacious, though it is more difficult to get a positive study than a negative study. In [the Hunter] study, they didn't pick the right PCBs, and one would predict if estrogen is the main risk factor, that if you have elevated anti-estrogenic PCBs, it would protect against breast cancer. So in his mind that study, Dr. Carpenter said, was flawed. He said, "I don't think there is a direct relationship between PCBs and breast cancer, but I do think there is a vulnerable subpopulation to which there is a strong relationship. If you look at the general population without taking those into account, you are going to get misconceptions. This may apply to other cancers as well."

Additional discussion ensued on statistical significance.

John Santacrose asked if it is the role of the project team to come up with a new classification for PCBs, or if the team is working on the existing classification. He observed if EPA is working from the existing classification, this discussion is a waste of time. Where can people go to have the classification changed?

Marian Olsen stated that the classification is handled at the national level within EPA. The Office of Research and Development has a process for submitting chemicals for reassessment. A reassessment [for cancer risks of PCBs] just occurred in 1996. Within the region, this classification is being used. The region would not change that classification; it would have to be done at the national level. If anyone wants to do so, PCBs can be submitted to the Integrated Risk Information System (IRIS) database folks in the ORD for reassessment. Currently they are reassessing non-cancer risks.

Rich Schiafo of Scenic Hudson provided an update on the TAG grant. Scenic Hudson has had a TAG grant from 1995 to 1998 that has been renewed. Mr. Schiafo read the comments of Dr. Nisbet, the TAG advisor, on EPA's human health risk assessment (Attachment 4), summarized as follows:

- The document was found to be a "thorough, clear, and reasonable assessment of the baseline risk posed to the general population by the presence of PCBs in the sediments of the Hudson River for the present and foreseeable future."

- The exposure assessment used existing data on PCB contamination appropriately, incorporates results from an up-to-date and acceptable contaminant fate and transport model, and "analyzes data on the current population and their activities in a thorough and reasonable way."
- Dr. Nisbet commended EPA for its thorough review of available data on angling habits and application of these data to the Hudson River population.

Dr. Nisbet urged EPA to complete its update on the cancer and non-cancer toxicological profiles of PCBs. With that exception, Dr. Nisbet stated he found the "information on toxicity of PCBs was appropriately incorporated into the risk assessments, and that the estimates of risk in the human health risk assessment are reasonable and scientifically defensible." Further, he approved use of the Monte Carlo analysis.

Mr. Deppe requested that GE present its comments on the human health risk assessment at the next meeting. Ms. Rychlenski asked for the request in writing.

Mr. Schiafo then brought to the attention of the committee two letters to the editor (Attachment 5) that appeared in the September 1999 issue of the *Journal of Occupational and Environmental Medicine* regarding the study conducted by Dr. Renata Kimbrough.

Two other speakers referenced the response to those letters contained in the same issue, also part of Attachment 5.

John Santacrose quoted a letter from George Hodgson to *The Albany Times Union* containing a paragraph on the "dysfunctionality" of the community involvement program for the RRI/FS and the "agency's lack of public response." Mr. Santacrose objected, and stated he does not think the Community Interaction Program is dysfunctional, and proposed a meeting on December 2 to entertain any opinions and comments about the community involvement process, and volunteered to moderate. Mr. Santacrose said he went back to the original Community Relations Plan containing the objectives for the Community Interaction Program. He suggested that people use this as a tool to determine whether or not the program has met the objectives stated.

Ms. Rychlenski agreed, stating that the upcoming year is crucial, and will be a very active year for the public. She referred to new members who have joined, particularly the Appalachian Mountain Club, the Sierra Club, Citizens' Campaign for the Environment, and the New York State Conservation Council, and cited the interest of Congresswoman Sue Kelly, Congresswoman Nita Lowey, Congressman Maurice Hinchey, and Congressman Michael McNulty in having representatives participate.

There being no further question or comment, Ms. Rychlenski adjourned the meeting.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
REGION 2
290 BROADWAY
NEW YORK, NY 10007-1866

ATTACHMENT 1

HUDSON RIVER PCBs REASSESSMENT

COMMUNITY INTERACTION PROGRAM

Steering Committee Meeting
Tuesday, October 26, 1999
7:30 p.m.
Saratoga Springs, NY

AGENDA

Welcome & Introduction	Ann Rychlenski, USEPA Chair, Steering Committee
Report Out by Committee Members	Liaison Group Chairs, EPA, NYSDEC
Presentation: Health Effects of PCBs	Dr. David Carpenter, School of Public Health, Environment & Health Toxicology
Report on Dr. Ian Nesbit's Findings on EPA's Human Health Risk Assessment (TAG Advisor)	Rich Schiafo, Scenic Hudson
Community Relations Issues	John Santacrose, Chair Environmental Liaison Group

Questions & Answers

10.10177

ATTACHMENT 2
1-2

US ENVIRONMENTAL PROTECTION AGENCY
HUDSON RIVER PCBs RRI/FS
COMMUNITY INTERACTION PROGRAM
STEERING COMMITTEE MEETING
Saratoga Springs, NY
October 26, 1999

NAME	ADDRESS	AFFILIATION/TELEPHONE
George Halgson	50 W. High St. Ballston Spa, NY 12020	Saratoga Co. EMC
Bob Gibson	320 Great Oaks Park Albany NY 12203	GE
Judy Schmotzer	Schuylle	Chair - Citizens Group.
Robert Foster	170 Washington Ave Albany, N.Y. 12210	Citizens Campaign for the Environment
Tony Maresco	3A Duryea Pl. Nyack, N.Y. 10960	Citizen Liaison
Lois L Fosh	200 Henry Johnson Blvd Albany, NY 12210	AWEJ

US ENVIRONMENTAL PROTECTION AGENCY
HUDSON RIVER PCBs RRI/FS
COMMUNITY INTERACTION PROGRAM
STEERING COMMITTEE MEETING
Saratoga Springs, NY
October 26, 1999

NAME	ADDRESS	AFFILIATION/TELEPHONE
William Parks	NJ	NYS DEC
John Santacrose	251 New Scotland Rd. Albany, NY 12205	Chair - Envir Liaison Group.
Jim Hayes	2545 Coundt, Rt 3 Olive Bridge NY	Sierra Club 914 657 2013
Carl DEPPE	28 THOMAS HUDSON FALLS NY 12839	CO-CHAIR ENV. LIAISON GROUP
Scott Emslie	17 Corliss Ave Poughkeepsie, NY 12601	NYS Conservation Council
Katie DeBrock	18 DeBrock Rd FE.	co chair Citizens Coord Group
Marion Triest	463 RT 32 Schuylerville NY	Triest Assoc.
David Adams	216 Stage Rd. Charlton NY	SCEMC 518-399-1690
Jan Gebhardt	13 Locust St. Glens Falls, NY 12801	GE
Mark Behan	13 Locust St. Glens Falls. NY 1280	GE

ATTACHMENT 2
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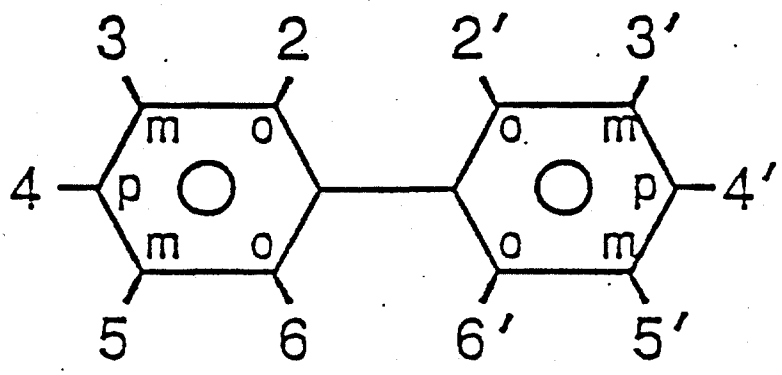
US ENVIRONMENTAL PROTECTION AGENCY
HUDSON RIVER PCBs RRI/FS
COMMUNITY INTERACTION PROGRAM
STEERING COMMITTEE MEETING
Saratoga Springs, NY
October 26, 1999

NAME	ADDRESS	AFFILIATION/TELEPHONE
Joe Gardner	68 Carson Rd Delmar, NY 12054	Mohawk Hudson Chapter Appalachian Mt Club (518) 439-1674
Jay Silkworth	PO Box 5 Schenectady NY 12301	GE
Chris Walbrecht	560 Delaware Ave Buffalo, NY 14202	Citizens Campaign for the Environment
Rich Schiafo	9 Vassar St Poughkeepsie, NY 12601	Scenic Hudson
Brian Mayes	185 Pictureway Rd Selkirk, NY	GE
Tom Burden	2041 Valley Falls Rd Schaghticoke, NY	Ag Liaison Comm.
Jim Reagan	32 Dublin Dr Ballston Spa, N.Y. 12020	NYSDEC
Bruce Bentley	50 Wolf Rd Albany NY	NYSDEC

ATTACHMENT 3
1 – 8

Polychlorinated Biphenyl



HISTORY OF PCBs

2.4 billion pounds produced–half in the US

Used as hydraulic fluid, in transformers, paints, inks, insulating fluids, etc.

New production banned in US in 1977

Many PCB-containing transformers still in operation in the US

PCBs still manufactured in Russia & North Korea

PCBs are mixtures of up to 209 different chemical compounds

CHARACTERISTICS OF PCBs

Very stable and persistent in animals and in the environment

Tend to bioaccumulate in the food chain, especially in fat

Lower chlorinated PCBs are more volatile and water soluble

Major source of human exposure is from food, especially fish

The polar regions of the earth are highly contaminated via atmospheric transport

HEALTH EFFECTS OF PCBs

Cancer

Immune suppression

Reduced IQ

Reduced attention span

Altered thyroid function

Altered sex hormone function

GE STUDY OF PCB CARCINOGENICITY IN RATS

All Aroclor mixtures cause liver cancer, especially in females.

Higher chlorinated Aroclor mixtures cause thyroid cancer.

Mayes et al., 1998.

OCCUPATIONAL EXPOSURE TO PCBs AND PBBs AND CANCER

Brown et al. (1987) 2,567 capacitor workers. Statistically significant elevation of cancers of the liver, gall bladder and biliary tract.

Bertazzi et al. (1987) 2,100 capacitor workers. Statistically significant elevation of cancers of the gastrointestinal tract. Elevated leukemia and lung cancer, but not statistically significant.

Sinks et al (1992) 3,588 capacitor workers. Statistically significant elevation of skin cancers (melanoma). Non-significant elevation in brain cancer.

Loomis et al. (1997) 20,068 dead utility workers and estimated cumulative PCB exposure. Statistically significant 4.8-fold excess in malignant melanoma.

Hogue et al. (1998) 3,899 farmers exposed to PBBs. Statistically significant, dose dependent increase in digestive system cancer and lymphoma.

Kimbrough et al. (1999) 7,075 capacitor workers (at least 90 days). No significant elevations of cancer.

PCBS AND NON-HODGKIN'S LYMPHOMA

PCB Concentration (ng/ml)	Odds Ratio
3.8	1.0
5.5	1.3 (0.5-3.3)
6.7	2.7 (0.9-7.8)
10.3	4.1 (1.4-11.9)

Rothman et al., 1997.

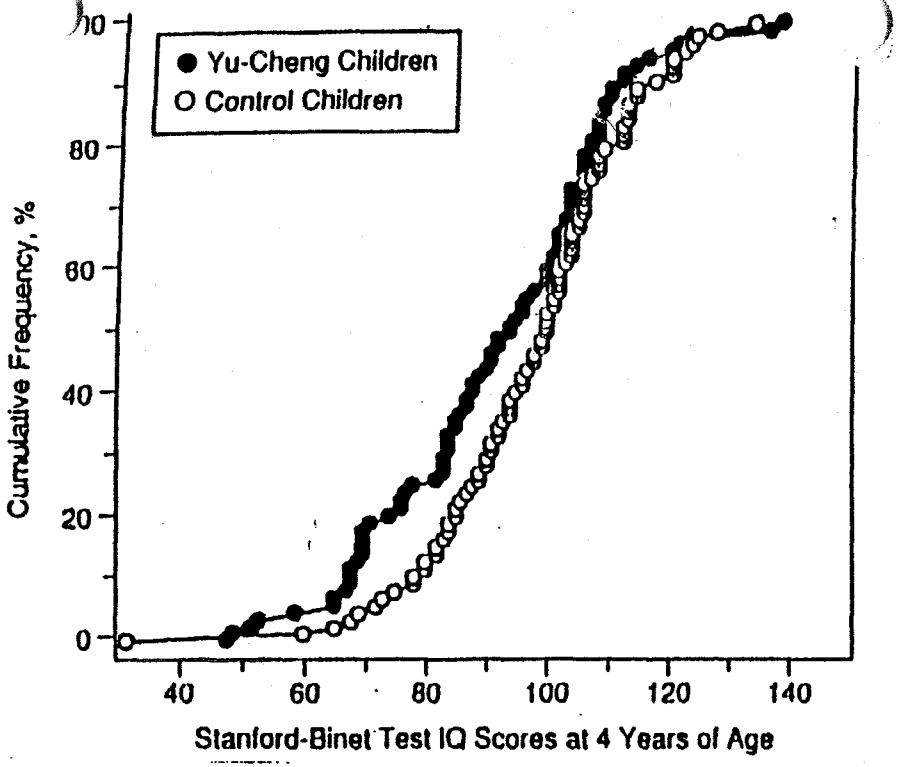
ATTACHMENT 3
4-8

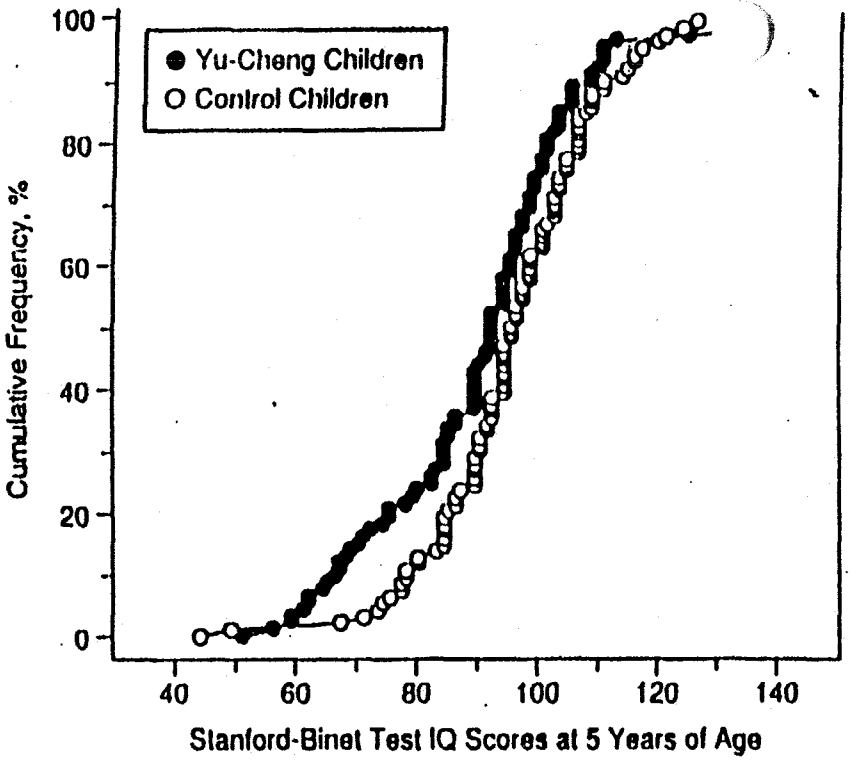
PCBS, P4501A1 POLYMORPHISM AND BREAST CANCER RISK

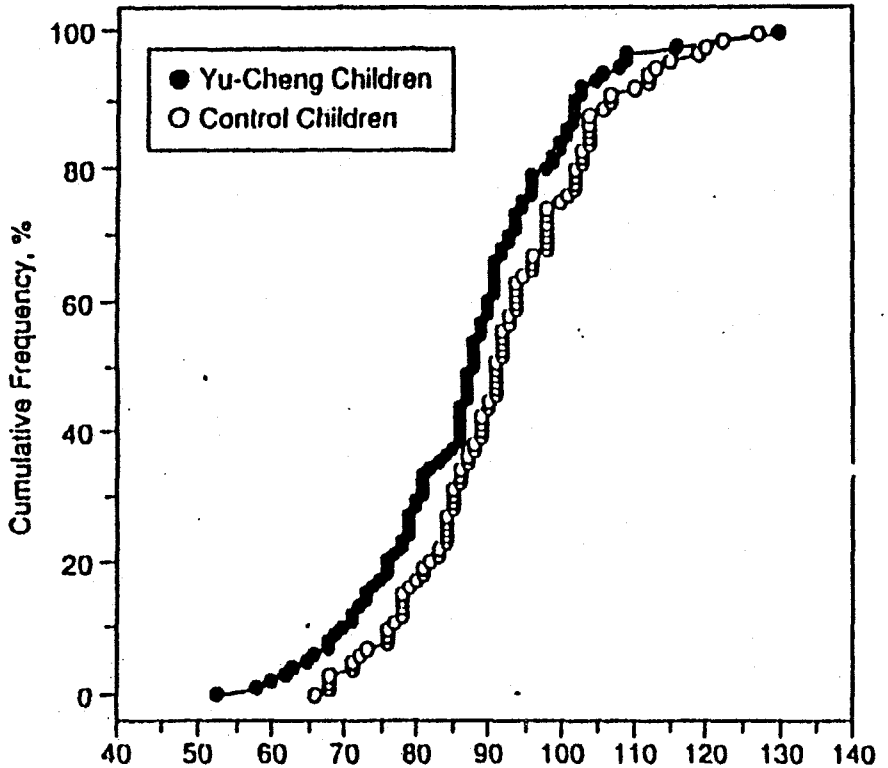
	Odds Ratio
Low PCBs	1.0
High PCBs	1.27 (0.76-2.14)
Polymorphism	1.79 (0.91-3.55)
High PCBs + Polymorphism	2.9 (1.18-7.45)

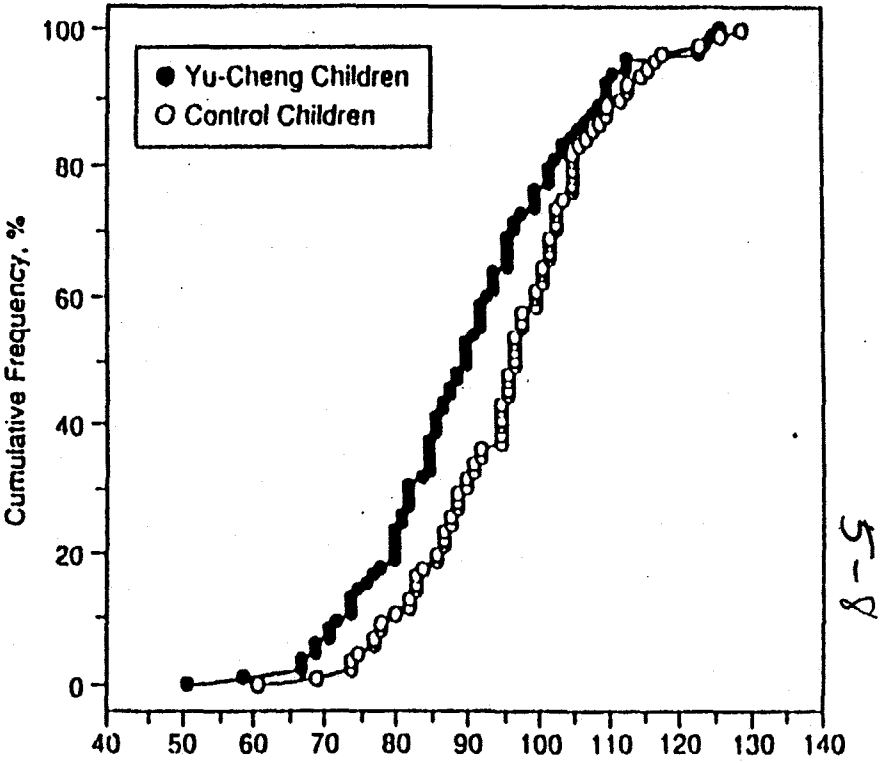
Moysich et al., 1999.

(1)









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ATTACHMENT 5
5-8

Lake Michigan Study Shows Intellectual Impairment

- Assessment at age 11 (212)
  - » 167 fish eaters and 45 nonfish eaters
- Results
  - » One child was mental retarded
  - » Poorer short term memory
  - » Most highly exposed children had a 6.2 point in IQ
  - » They were also 1 year behind in reading
  - » Fish eaters childern were all at the lower end of the normal range of intelligent

Oswego Newborn & Infant Development Project

- Behavioral effects of neonates who's mothers consumed Lake Ontario fish.
- High Fish eaters (>40 lb.) Low Fish eater (<40 lb.) Controls had never eaten L.O. fish. (Self report)
- Cord blood/breast milk were taken for PCB analysis
- Infants in the high exposure group
  - » abnormal reflexes
  - » less mature autonomic responses
  - » less developed attention to visual and auditory stimuli
  - » delayed habituation

Behavioral Impairment Produced by Low-Level Postnatal PCB Exposure in Monkeys

Deborah C. Rice[1]

Toxicology Research Division, Bureau of Chemical Safety, Food Directorate, Health Protection Branch, Health Canada, Ottawa, Ontario, Canada

The preponderance of evidence in humans suggests that polychlorinated biphenyl (PCB)-induced behavioral deficits result from prenatal exposure rather than exposure through breast milk, although a recent study reported lower psychomotor scores during infancy associated with PCB concentration in breast milk. In the current study, monkeys were dosed from birth to 20 weeks of age with a PCB congener mixture representative of the PCBs found in human breast milk. Blood and fat levels of PCB-exposed monkeys at the end of the dosing period were within the range observed in the general human population, while levels in control monkeys were below averages observed in humans in industrialized countries. Behavioral assessment on a series of tasks was performed when monkeys were between 2.5 and 5.0 years of age. Robust deficits were observed on spatial delayed alternation, fixed interval, and differential reinforcement of low rate performance. No group differences were observed for the number of errors on a series of nonspatial and spatial discrimination reversal tasks. Behavioral deficits included retarded learning, perseverative behavior, and inability to inhibit inappropriate responding. These results have implications for the potential contribution of exposure to PCBs through breast milk to behavioral impairment.

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ATTACHMENT 3
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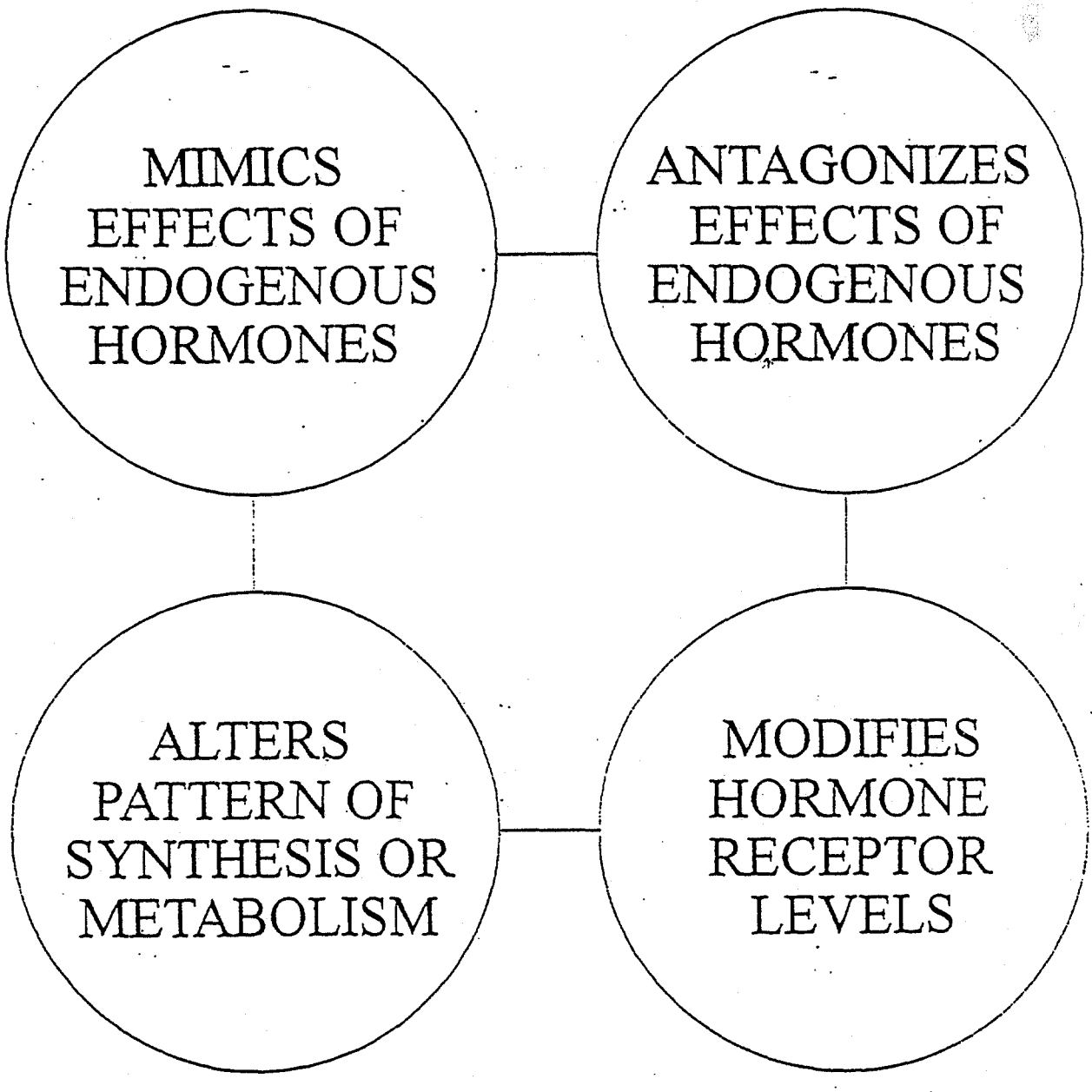
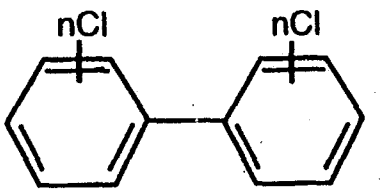
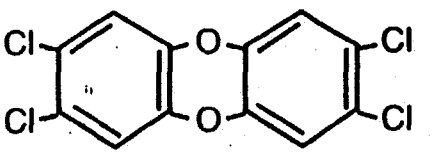
ENDOCRINE DISRUPTORS

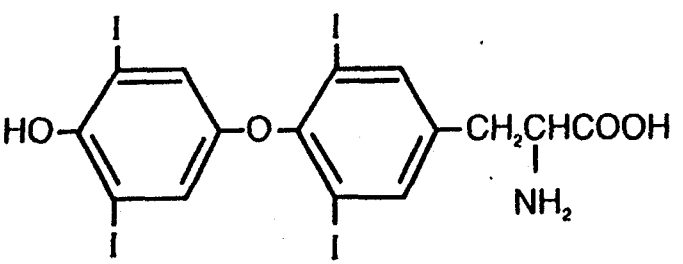




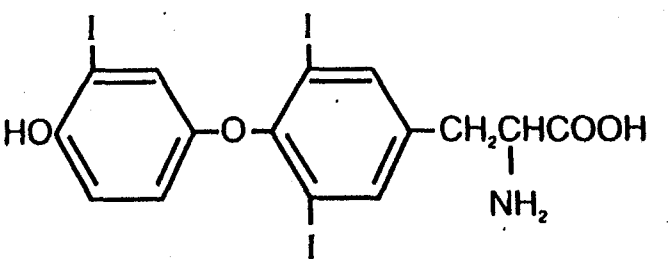
PCBs



DIOXIN (TCDD)



THYROXINE (T4)



T3

Possible Endocrine Disruptive Effects of Environmental Contaminants Mediated by Sex Steroids

Feminization of males
Masculinization of females
Decreased fertility
Reduced sperm counts in males
Reduced conception in females
Increased spontaneous abortions
Increased birth defects of the reproductive system
Hypospadias
Cryptorcharism
Small genitalia
Vaginal and uterine abnormalities
Altered sexual preference
Cancer of breast, prostate, testis
Endometriosis and fibroids

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ATTACHMENT 4

Report on Dr. Ian Nesbit's Findings on EPA's Human Health Risk Assessment

Rich Schiafo
Environmental Associate

Hudson River PCBs Reassessment
Community Interaction Program
Steering Committee Meeting
Saratoga Springs
Tuesday, October 26, 1999

Good Evening. My name is Rich Schiafo, from Scenic Hudson. As many of you know, Scenic Hudson is a regional, non-profit environmental organization that has been protecting the natural, historic and cultural resources of the Hudson Valley for 35 years.

Scenic Hudson has an EPA Technical Assistance Grant for the Hudson River PCB Superfund site. The brief comments I have tonight have been prepared by Dr. Ian Nisbet, our Technical Advisor, of I.C.T. Nisbet & Company, under the TAG program. Dr. Nisbet was invited to attend this meeting but was unable.

Dr. Ian Nisbet is a professional risk assessor and has specialized in the use of risk assessments since the early 1980's. Dr. Nisbet has published numerous professional papers on risk assessment and has presented papers at the First World Conference on Toxicology and Environmental Health (Washington, 1982), the First World Conference on Primary Prevention and Cancer (Belgium, 1986), and has authored a book entitled "Chemical Hazards to Human Reproduction" (Noyes Data Corporation, 1983). Dr. Nisbet is also an expert on PCBs and has written several major reviews of the scientific data on PCBs.

The comments submitted by Dr. Nisbet are as follows:

Scenic Hudson and its subcontractor, I.C.T. Nisbet & Company, have reviewed the Phase 2 Report: "Further Characterization and Analysis, Volume 2F - Human Health Risk Assessment. Hudson River PCBs Reassessment RI/FS (hereafter, the "HHRA"). Although we are familiar with the methods used for risk assessment and most of the data and sources cited in the HHRA, we have not attempted to check every source or every

calculation. Our review is limited to assessing the completeness of coverage of the available literature, the reasonableness of the assumptions made in the calculations, the inclusion of appropriate qualifications and statements of uncertainty, and the clarity of presentation. With these limitations, we offer the following general evaluation of the HHRA:

Generally, we find this document to be a thorough, clear, and reasonable assessment of the baseline risks posed to the general population by the presence of PCBs in the sediments of the Hudson River at present and foreseeable levels. The exposure assessment uses existing data on PCB contamination in an appropriate way, incorporates results from an up-to-date and acceptable model of contaminant fate and transport, and analyzes data on the target populations and their activities in a thorough and reasonable way. In particular, we commend USEPA for its thorough review of the available data on angling habits and its application of these data to the Hudson River population. We have already commented that the toxicological profile for PCBs is out of date and we have urged USEPA to complete its updates of the cancer and non-cancer toxicity of PCBs as soon as possible. As stated in our earlier comments, we believe that incorporation of recent new data on the effects of PCBs will lead to increases in both the estimated magnitudes of risk and the degree of certainty in those risks. With that exception, we believe that the information on toxicity of PCBs was appropriately incorporated into the risk assessments and that the estimates of risk in the HHRA are reasonable and scientifically defensible. We especially commend USEPA for the inclusion of the Monte Carlo analysis. The assumptions made in this analysis and the sources for estimates of uncertainty and variability are reasonable and clearly stated. The results of the Monte Carlo analysis provide substantial support for the central-tendency and RME estimates of risk, which otherwise would remain uncertain and subject to debate. Finally, we find the presentation clear and transparent, with explicit statements of the way in which the assessment is carried out, its scope, and the assumptions incorporated into it, and the degree of uncertainty in the results. Although the report is not free of technical jargon, it does a good job in reducing it to a minimum and explaining the technical terms that must be used. Overall, this report will be very useful to Scenic Hudson for its primary task of explaining the tortuous process of risk assessment to the public.

ATTACHMENT 5
1-4

Letters to the Editor

Readers are invited to submit letters for publication in this department. Submit them to: The Editor, Journal of Occupational and Environmental Medicine, PO Box 370, Bryn Mawr, PA 19010. Letters should be typewritten and double spaced and should be designated "For Publication."

Evidence of Excess Cancer Mortality in a Cohort of Workers Exposed to Polychlorinated Biphenyls

To the Editor: To further explore previously reported excesses in cancer-specific mortality in workers who have been occupationally exposed to polychlorinated biphenyls (PCBs), Kimbrough et al[1] reported a retrospective cohort mortality study of 7075 male and female workers exposed to PCBs during the capacitor-manufacturing process at two General Electric (GE) plants in upstate New York. Kimbrough et al concluded that the study results failed to show any association between occupational PCB exposure and cancer-related mortality. We interpret their study findings differently. Although limitations in the study approach (outlined below) tend to dilute any excesses in cancer mortality resulting from PCB exposure, the findings *still* suggest a relationship between PCB exposures and excess cancer in humans.

First, this study demonstrated once again that modern industrial workers are healthier than the general population. Known as the "healthy worker effect" (HWE), this bias results in standardized mortality ratios (SMRs) that are considerably less than expected (eg, SMR < 90) for all mortality and cancer mortality[2-4] when workers are compared with a general population. Consistent with the HWE bias, Kimbrough et al found that all cancer mortality was significantly below that expected in male hourly workers (SMR = 81), male salaried workers (SMR = 69), and female salaried workers (SMR = 75). However, despite the HWE, female hourly workers had elevated SMRs for all cancer mortality (SMR = 110) and for three (intestinal [SMR = 157], rectal [SMR = 169], and melanoma [SMR = 144]) of the six cancers of a priori interest. Melanoma mortality was also elevated for male hourly workers (SMR = 130). Although the elevations in cancer-specific SMRs did not achieve statistical significance, they were consistent with elevations found in other studies of PCB-exposed workers.[4-6] Given the HWE, these elevations are particularly noteworthy.

Second, when looking at cancer mortality rates, it is customary to include a latency period to adjust for the time lag between exposure and clinical evidence of disease (or, in this study, cancer death).[7] However, Kimbrough et al included a latency period only for all cancer mortality and for intestinal cancer mortality among female hourly workers. When female hourly workers with at least 20 years of follow-up were evaluated (ie, with a sufficient latency period), the SMR for all cancers increased from 110 to 117* ($P = 0.058$). The SMR for intestinal cancers increased from 157 to 189, thus becoming statistically significant ($P < 0.05$).

Third, proper assessment of exposure should have accounted for the dates (calendar years) of employment, the intensity of exposure for each type of job, and the specific Aroclor PCB used. For example, in the earlier years of plant operation (1946 to 1954), any exposures would have been to Aroclor 1254, whereas exposures in the 1970s would have been to the less toxic Aroclor 1016.[8,9] Industrial hygiene procedures at the plant probably improved over time as well. Therefore, length of employment alone was an inadequate surrogate of exposure and a likely source of exposure misclassification bias that could have led to an underestimate of effect and distortion of exposure-response relationships.

Kimbrough et al assembled the largest cohort of hourly PCB workers studied to date, including a large number of female workers. However, most of the hourly workers had exposures that were comparable with exposures among the general US population. From the data provided, it appears that approximately one fourth of the person-years contributed by male hourly workers, and approximately 10% of the person-years contributed by female hourly workers, were contributed by workers who had been employed for at least 6 months in high-exposure jobs. Only 112 (3.8%) male hourly workers and 12 (0.5%) female hourly workers were employed exclusively in high-exposure jobs. The majority of the hourly workers never worked in high-exposure jobs. Only a small percentage of hourly workers had evidence of PCB exposure that was appreciably greater than that of the US population. Therefore, relatively small elevations in cancer mortality would be expected for this group, even if PCB cancer potency were alarmingly high.

Fourth, although one of the goals of this study was to evaluate six specific cancers of a priori interest (ie, melanoma, liver, rectal, gastrointestinal tract, brain, and hematopoietic cancers), the study focused almost entirely on all cancer mortality. In planning the study, the researchers should have realized that the size and age distribution of the hourly work-

*Note: There is an error in Table 6 of the study report. The SMR for "all cancers" in female hourly workers with ≥20 years' latency over all lengths of employment should be "117," not "96" as reported.

TABLE 1
Calculations of Statistical Power to Detect Varying Standardized Mortality Ratios (SMRs) for the Six Cancers of A Priori Interest

Cancer	Expected Number	SMR = 150	SMR = 200	SMR = 300
Male hourly workers				
Melanoma	3.8	12%	35%	80%
Liver	2.5	9%	24%	62%
Rectum	3.4	14%	37%	80%
GI*	14.0	36%	85%	100%
Brain	5.1	15%	44%	89%
Blood	14.1	37%	86%	100%
Female hourly workers				
Melanoma	2.0	8%	22%	55%
Liver	2.2	12%	28%	65%
Rectum	1.6	10%	22%	52%
GI*	12.7	36%	83%	100%
Brain	3.7	11%	32%	78%
Blood	10.5	32%	77%	100%

* GI, Gastrointestinal tract.

force would result in poor statistical power to evaluate the cancers of a priori interest. Table 1 shows the expected number of deaths for each of these cancers for male and female hourly workers and the resulting statistical power for SMRs from 150 to 300, using the study's method for determining statistical significance (ie, the 95% confidence interval). Because of the biases in the study and the low percentage of highly exposed workers, an SMR of 150 might be as high as would be expected for these cancers. As seen in Table 1, for an SMR of 150, the study had less than a one in five chance of obtaining a statistically significant result for four of the six cancers. Given the sample size and the numbers of expected cancers, the study did not have sufficient statistical power (>80%) to detect an SMR of 300 for most of the cancers of interest.

Kimbrough et al examined and reported SMRs for categories of increasing length of employment and years of latency only when "... there was an elevated total SMR with two or more observed deaths and for which the lower boundary of the 95% confidence interval (CI) was 90 or above."[1] The impact of this decision can be seen in Table 2. Given

TABLE 2
Number of Observed Deaths and the SMR Required for ≥90 as the Lower Limit of the 95% Confidence Interval

No. of Deaths	SMR
2	744
3	437
4	331
5	278
6	245
7	224
8	209
9	197
10	188
11	180
12	174
13	169
14	165
15	161
16	157
17	154
18	152
19	150

the biases mentioned previously, it is understandable that just one of the six a priori cancers met these requirements. Furthermore, accounting for a latency period should be a prerequisite for calculating any adult cancer SMR. Otherwise, the SMR is biased toward or below 100. For all six cancers of a priori interest, analyses accounting for latency and for length of employment should have been done and presented, allowing the reader to decide whether or not the results were meaningful.

In summary, the Kimbrough et al study suffered from HWE bias, failure to account for latency, exposure misclassification, potentially insufficient dosage differences between exposed and comparison groups, and poor statistical power. Nevertheless, the study did find excesses in three of the six cancers of interest. Future research should include analyses made with internal comparisons (to minimize biases from HWE) of sufficient numbers of highly exposed workers, as well as analyses accounting for cancer latency periods. This might require an additional decade or more of follow-up on this cohort and the addition of exposed workers from other PCB plants (eg, workers at the Massachusetts plant included in Brown[5]), before a definitive statement about the association between PCB exposure and specific cancers can be made.

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Barbara A. Slade, M.
Richard A. Canady, PhD
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Division of Health Studies/ Division of Health Assessment and Consultation
Atlanta, GA

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ATTACHMENT 5
2-4741

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To the Editor: We were glad to see the recent article on mortality among workers exposed to polychlorinated biphenyls.[1] At a time when fewer and fewer companies are funding occupational epidemiological studies, we commend the sponsor, General Electric, for this initiative. The completeness of case ascertainment was outstanding. In addition, this report was a model of clear writing and clear display of results.

However, two issues, sample size and exposure, raise significant concern. First, the study population was very small. Over 7000 workers contributed over 200,000 person-years of observation, more than in prior PCB mortality studies. But when attention is restricted to those workers with high exposure, moderate- to long-duration employment, and adequate person-time after a latency period, the numbers are dramatically reduced. For example, only one third of the cohort worked for longer than 5 years. (We note in passing that Table 2, the source of these data, shows 7178 workers in the upper panel and 7075 workers in the lower panel, a disparity the authors do not explain.) Similarly, less than one fourth of the cohort was classified as highly exposed, and the median period of high exposure was less than 2 years. Although data are not presented to support exact calculations, it appears that fewer than 10 cancers of any type, and more typically fewer than three, were expected in any sex-salary stratum with high exposure, more than a year of employment, and more than 20 years of latency. Could this be why the article is conspicuously silent on the issue of statistical power?

The problem of small number could have been addressed. A company as large as GE presumably had other capacitor plants and could have supported a multisite study. Alternatively, an industry-wide study would have been informative, as we have seen in the semiconductor, rubber, petrochemical, automobile, and other industries. Indeed, we wonder why restricting a cancer mortality study to only two plants should not be viewed as a willful effort to avoid a positive finding.

The second major concern lies with exposure assessment. As with many historical cohort studies, the authors created a matrix to characterize each individual's exposure. If the designated "high exposure" jobs did not actually entail high exposure, then misclassification occurred and could have introduced substantial bias toward the null. Were the exposures accurately assessed?

The article makes reference to a readily available way to validate the exposure assessment: serum PCB levels obtained during the 1970s on a sample of several hundred cohort members. Where are these measurements? Did the authors check their exposure assignments against the past serum measurements? If not, why not? If so, why was this comparison not reported?

Another difficulty with exposure in this article is the admixture of various types of PCBs. More carcinogenic forms, such as Aroclor 1254, were used in the early years, and less carcinogenic forms, such as Aroclor 1016, were used later. By combining the two rather than focusing on the early exposures, the authors may have obscured a true effect.

Overall, these concerns significantly limit the conclusions that can be drawn from the study. The authors conclude that their results "would suggest a lack of an association." This conclusion is overstated. These results do offer some evidence that PCBs are not highly potent carcinogens causing relative risks above 10 or 20, a conclusion that was already fairly well established. But they provide little reassurance that PCBs do not double or triple the risk of some cancers after significant exposure.

For this reason, we were especially concerned that the results of the study were not interpreted and presented more carefully. The authors might have noted, in their conclusion, that PCBs are serious health hazards irrespective of carcinogenicity,[2] with effects that include decreased birth weight,[3] neurodevelopmental abnormalities,[4–8] and interference with both estrogen[9] and thyroid[10] hormone function. Accordingly, even negative findings in a cancer study would not reassure us of safety. That omission in the *JOEM* article, in turn, may have contributed to overtly misleading journalistic coverage, such as the *New York Times* headline: "Study Finds Little Risks [sic] From PCB's."[11]

The authors of this study note that our knowledge of PCB health effects is "limited." On the path to a more complete understanding, the current study results represent a great leap sideways.

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The Authors Reply: Thank you for giving us the opportunity to reply to the letters by Bove et al and Frumkin and Oris commenting on our mortality study of PCB-exposed capacitor workers.[1] We disagree with the statement by Bove et al that "... limitations in the study approach tend to dilute any excesses in cancer mortality resulting from PCB exposure. . . . " These assertions are speculative and not supported by the data. Although some degree of misclassification in observational studies is unavoidable, it is usually not possible to determine whether this misclassification is differential or non-differential. Furthermore, non-differential misclassification does not always result in bias toward the null hypothesis. Neither the type nor the effect of the misclassification can be determined by Bove et al. In our article, we do, however, discuss at length the measures taken to limit misclassification, and we feel strongly that we were successful in doing so.

Bove et al assert that the healthy worker effect (HWE) results are an underestimate of the SMRs for all-causes mortality and cancer mortality. This is partially true. The HWE is most pronounced for cardiovascular deaths and thus affects all-causes mortality.[2] It has much less of an effect on cancer deaths.[3]

The presentation by Bove et al of the all-cancers SMRs and selected cancer-specific SMRs without confidence intervals (CIs) gives incomplete information and is misleading. Had the confidence intervals been reported, the lack of significance for these SMRs would have been immediately obvious to the reader. Bove et al selected the female hourly employees' all-cancers SMR of 110 (95% CI, 93 to 129), intestinal cancer (SMR = 157; 95% CI, 96 to 242), rectal cancer (SMR = 169; 95% CI, 46 to 434), melanomas (SMR = 144; 95% CI, 30 to 421), and melanomas in male hourly employees (SMR = 130; 95% CI, 42 to 303). Notably absent from this list of SMRs considered by Bove et al are the male hourly SMRs for intestinal and rectal cancer (SMR = 57; 95% CI, 25 to 112; and SMR = 87; 95% CI, 18 to 255, respectively).

Bove et al suggest that the male all-cancers SMRs of 81 (hourly employees; 95% CI, 68 to 97) and 69 (salaried employees, 95% CI, 52 to 90) are largely due to the HWE. A careful examination of Table 4 in our article suggests that the statistically significantly low all-cancers SMRs in both the hourly and salaried males result primarily from the lower than expected lung cancer SMR hourly workers: 42 observed/ expected; SMR = 77; 95% CI, 56 to 104; and for salaried workers: 12 observed/29.6 expected; SMR = 41; 95% CI, 21 to 71).

The statement by Bove et al that these elevations were consistent with elevations found in other studies of PCB-exposed workers is not correct.[4–6] In addition to the three studies cited by Bove et al, there is the Bertazzi cohort and its update by Bertazzi et al[7] and Tironi et al.[8] The results of the Brown[4] and Sinks et al[5] studies are inconsistent with each other. The Loomis et al[6] study of utility workers, not capacitor workers, did report an elevation in melanomas in some subsets of the cohort that were presumed to have had exposure to PCBs while working outdoors. Exposure to sunlight was not adequately accounted for by Loomis et al.[6] Brown and Jones[9] and Brown[4] found an excess of liver and re cancers. Neither Sinks et al[5] Loomis et al[6] reported such increases. Sinks et al[5] reported a non-significant elevation in brain and nervous system cancers. Neither Brown and Jones,[9] Brown,[4] Bertazzi et al,[7] or Tironi et al[8] found an elevation in brain cancer. These inconsistencies were discussed in our article.

Bove et al state that we only included a latency-period analysis for all cancers and for intestinal cancer. This was done primarily because of space limitations. Cumulative exposure and latency tables were computed and evaluated for many other causes of death, including all of the cancers of interest. The interpretation by Bove et al that the intestinal cancer SMR increases to a significant level for women with ≥20 years of latency ignores the importance of examining the trend associated with latency and length of employment. Furthermore, it might be worth n ing that for women employed for 10

years or longer with a latency period ≥20 years, the SMR was 100. The individual category–specific SMRs cannot be interpreted as meaningful without examination of the trend across cumulative exposure categories. Although the intestinal cancer SMR for latency ≥20 years was significantly elevated, there was no significant trend indicating an increase in risk with cumulative exposure or latency, as discussed in our article. Furthermore, comparison with the regional population resulted in a much-reduced SMR (SMR = 120; 95% CI, 74 to 186) for intestinal cancer in female hourly workers. The regional comparison is more representative because higher rates of intestinal cancer are observed among the white population of the northeastern part of the United States.

Bove et al raise concerns about our exposure assessment. Several factors need to be recognized when assessing the propriety of our exposure assessment and our use of length of employment as a surrogate of exposure. Workers accumulate PCB body burdens over time, which persist for many years even after their occupational PCB exposure is discontinued. To suggest that PCB body burdens among capacitor workers were comparable to those found in the general population is unjustified and is not supported by previously published data.[10–13] The fact that workers in capacitor plants had significantly higher body burdens than the general population has been demonstrated in other capacitor plants.[14] As reported in our article, average serum PCB levels in the general population between 1976 and 1979 were 5 to 7 parts per billion (ppb; μg/L).[14] Geometric mean serum PCB levels in GE workers in 1979 (2 years after PCBs were no longer used) were 277 ppb (μg/L) reported as Aroclor 1242 and 55 ppb (μg/L) reported as Aroclor 1254. In 1983, 5 years after termination of the use of PCBs, geometric mean serum levels were 116 ppb (μg/L) for Aroclor 1242 and 34 ppb (μg/L) for Aroclor 1254. In 1988, the geometric mean serum PCB levels were 90 ppb (μg/L) quantitated as Aroclor 1242 and 32 ppb (μg/L) quantitated as Aroclor 1254.[15] Workers preferentially retained the more persistent congeners so that the gas chromatographic pattern of their body burden gradually approached that observed in the general population, with primary retention of the more highly chlorinated, poorly metabolized congeners.[12] The half-lives of the major PCB congeners retained in these workers were as follows: for 2,4,4′ trichlorobiphenyl, 1.4 years; for 2,4,4′5 tetrachlorobiphenyl, 3.2 years; for 2,3′,4,4′,5 pentachlorobiphenyl, 5.8 years; and for 2,2′,4,4′,5,5′ hexachlorobiphenyl, 12.4 years.[16] Even though different commercial mixtures of PCBs were used in the capacitor plants, the congeneric composition on a qualitative basis is similar.[17] Production began in 1946 with the highly chlorinated Aroclor 1254, and small amounts of Aroclor 1254 were used in the plant at least through 1971.

The statement that length of employment alone was an inadequate surrogate for exposure and a likely source of exposure misclassification bias leading to an underestimation of the effect and a distortion of the exposure-response relationship is not supported by the toxicokinetics of PCBs, nor is it an accurate representation of the data analyses conducted on our cohort and reported in the article.

Bove et al report that the majority of hourly workers never worked in a high-exposure job, when in fact 1268 of the 2984 male hourly employees (42.4%) did work in a high-exposure job. Only 13.8% of the female hourly employees worked in a high-exposure job, not an uncommon occurrence in an industrial setting. To suggest that the remaining portion of the cohort experienced PCB exposure similar to that of the general population is not an accurate representation of the facts. This is presented in the exposure-assessment section of our article.

Bove et al state in the opening sentence that although the goal of the study was to evaluate six specific cancers, we focused almost entirely on all-cancers mortality. Table 4 in the article presents SMRs and 95% CIs not only for the six cancers of interest but for 32 other causes of death, including 15 additional cancers. The issue of statistical power is raised by Bove et al and two tables were provided. These tables were not properly referenced nor was the methodology used to generate these calculations explained. It is unclear why an SMR of 150 should be considered the "highest expected" for these cancers, when previous publications on smaller cohorts reported statistically significant SMRs well above 150. Our study was an attempt to evaluate these earlier observations in a larger study with a longer follow-up period.

Bove et al question the decision to limit the latency by length of employment calculations to cancers with more than two observed cases and a lower boundary of the 95% CI of 90 or above. This decision was made by the investigators to limit the multiple comparison problem and to provide more meaningful data, rather than to obscure data. Additionally, the lack of presentation of data should not be interpreted as the data not having been analyzed. All six a priori cancers of concern were examined carefully; however, publication space is limited and presenting a table of latency by cumulative exposure for liver cancer, for instance, with two deaths was deemed unwarranted.

In their summary statement, Bove et al dismiss our study findings because of the HWE effect, failure to account for latency, exposure misclassification, potentially insufficient dosage differences between exposed and comparison groups, and poor statistical power, yet they still insist that we did find excess cancer risk for three of the six a priori cancers of interest and give credence to those findings. It is inconceivable to the

investigators of this study how Bove et al, given this litany of problems, were able to differentiate the impact and direction of these biases with such certainty and specificity.

The authors take exception to the tone of the letter by Frumkin and Orris and find statements such as "conspicuously silent" and "willful effort to avoid a positive finding" inflammatory and suggest that such statements do little to advance the understanding of PCBs and cancer risk.

Most of the issues raised by Frumkin and Orris have been addressed earlier. Their suggestion to include more capacitor plants to increase power has merit, however. The General Electric Company had only the two facilities in upstate New York (Hudson Falls and Fort Edward) where capacitors were made using PCBs.

Frumkin and Orris question whether high-exposure jobs actually entailed high exposure and raise concerns about misclassification. The exposure misclassification suggested by Frumkin and Orris is highly improbable, given the distinction between jobs with direct dermal and inhalation exposure and those with only inhalation exposure to PCB air levels in the plant, as explained and referenced in our article. Additionally, the characterization of this bias as substantial is unwarranted and is an overstatement of the potential effect. Assignment of exposure for specific job categories was done before determination of vital status. At both plants, workers were located in the same building, and the same air-ventilating system served the entire building. We verified the physical layout by conducting a walk through the building and by talking to present and former employees. Many workers had different jobs in the different exposure categories (high, undefinable, and low). All workers, including those in low-exposure jobs, had significantly higher exposures than the general population, on the basis of PCB serum levels reported by Lawton et al,[11] Brown et al[15,16] and Brown.[18]

The PCB blood levels (from 194 and 290 workers) mentioned by Frumkin and Orris were of limited value in validating an exposure job matrix for 7075 workers. Although the job histories and the exposure assignment did confirm that workers in high-exposure jobs had high PCB blood levels, these workers were selected either because of their known high-exposure job[11] or they were self-selected.[10] The high-exposure jobs were readily identified by plant personnel and were confirmed by PCB air-level readings and PCB blood levels. Misclassification of jobs into the high-exposure category or misclassifying high-exposure jobs as lower-level exposure jobs was extremely unlikely.

Frumkin and Orris suggested that PCBs are serious health hazards, irrespective of carcinogenicity, with effects that include decreased birth weight, neurodevelopmental effects, and interference with thyroid and estrogen hormone function. It has not been shown that PCBs interfere with estrogen-hormone function in humans. Studies conducted to examine the effects of PCBs in infants and children have been critically reviewed[19-25] or could not be supported.[26] Results from thyroid function tests performed in infants were within the normal range. Furthermore, Koopman-Esseboom et al[27] stated, "The mean dioxin-like PCB toxic equivalent levels and the mean total PCB and dioxin toxic equivalent levels of the neurological normal infants were significantly higher ($p = 0.04$ for both) compared with the levels of the neurologically (mildly or definitely) abnormal infants. There was no relationship between the TT3 (serum total triiodothyronine), TT4 (serum total thyroxine), FT4 (free thyroxine), and TSH (thyroid stimulating hormone) levels in maternal, umbilical, or infant plasma (collected in the second week after birth) and the results of the neonatal neurological examinations. We conclude that overt abnormalities found in the neonatal period are not caused by either direct effects of PCB or dioxin exposure or lowered thyroid hormone levels." According to the National Center for Health Statistics,[28] birth weight is affected by education of the mother, mother's age, birth order, interval between births, gender, inadequate prenatal nutrition, alcohol consumption, smoking, lack of prenatal care, incidence of elective induction, contraceptive utilization, out-of-wedlock births, metropolitan areas (lower), and race. The body size of the parents and maternal illnesses such as diabetes also play a role. These many variables exemplify the difficulties of appropriately designing studies to examine a single factor affecting birth weight. Given these uncertainties and the published criticisms of studies reporting "other health effects of PCBs," it has not been conclusively shown that PCBs cause other "serious" health problems in humans.

We disagree with the final comment by Frumkin and Orris that this study was a great leap sideways on the path to a more complete understanding of the health effects of PCBs. The issue of PCBs and potential health effects has been a significant public health concern for more than 30 years. The lack of consistent findings in the previous cohort studies was assumed to have resulted from small cohort sizes and short follow-up periods. Given the disparate findings in these smaller capacitor cohorts, the appropriate next step was to assemble a larger cohort of PCB-exposed workers and examine them throughout a longer follow-up period. The fact that we were unable to confirm any of the previously reported findings is important and adds to the knowledge about PCBs and health effects. The assumption that a negative study does not provide valuable information imposes significant restrictions on the scientific process and the ability to ade-

ATTACHMENT 5
4-4

quately and objectively assess all data.

Errata: The correct number of female salaried workers with a length of employment of 10 to <15 years in Table 2 is 27; 5.8% is the correct percentage. In Table 6, line 2, last column, total SMR for ≥20 years of latency should be 117. The total number of workers in the upper panel of Table 2 should be 7075.

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Investigation of Elevated Urine Beta-2-Microglobulin in a Cohort of Cadmium Workers

To the Editor: Prior to the issuance of the 1993 Occupational Safety and Health Administration Cadmium Standard, urine testing for beta-2-microglobulin (β_2m) was not frequently performed. Testing for β_2m was an esoteric laboratory test performed only on workers whose cadmium levels had been found to be elevated. The Cadmium Standard mandated that all employees exposed to greater than 2.5 $\mu g/m^3$ cadmium dust or fumes be tested at least annually for urine β_2m, as well as for blood cadmium (CdB) and urine cadmium (CdU). At a nickel-cadmium battery manufacturing facility, approximately 1000 employees, some of whom had been exposed to cadmium and some of whom had not, were evaluated for β_2m levels, most for the first time.

Elevated β_2m was defined as a β_2m level higher than 300 $\mu g/g$ creatinine[1]; expectations were that approximately 10% of workers with cadmium levels higher than 10 $\mu g/L$ blood or 10 $\mu g/g$ creatinine would also show an elevated β_2m level.[2,3] Because 54 employees had such elevated cadmium levels in 1993, it was expected that approximately five or six would also show elevated β_2m levels. It was not known how many employees with other conditions