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J. F. BROWN JR.

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THOMAS R. CASEY, M. D.
VICE PRESIDENT AND COMPANY MEDICAL DIRECTOR

September 6, 1977

Irving J. Selikoff, M. D.
Professor of Community Medicine &
Director - Environmental Sciences Laboratory
Mt. Sinai School of Medicine
Fifth Avenue & 100th Street
New York, N. Y. 10029

Dear Dr. Selikoff:

This is to inform you that John F. Welch, Jr., Vice President and Group Executive of our Components and Materials Group, has approved the research proposals included in your communication of August 3, 1977. He has agreed to provide funds not to exceed \$94,389.00 to support the four research projects.

He would, however, like you to consider the pertinent comments of John Brown who reviewed the proposal for Dr. Welch. In order to be brief and yet accurate, the significant quotes from John Brown's communication are as follows:

Introduction:

"In essence, I believe that we are getting very close to a mutually satisfactory study; that is, one that will (a) define the health consequences (if any) of past exposure to capacitor-grade PCBs, (b) elucidate the mechanisms of capacitor-grade PCB toxicity (if any) in the human, and (c) indicate the feasibility (though not necessarily the desirability) of simple therapeutic measures to accelerate the removal of chronically-accumulated PCBs from the body. Particularly with a few minor technical modifications, I believe this could be a very worthwhile study, and I would recommend your support."

A. Mortality Study & B. Birth Defect Study

"Regarding both of these statistical studies, I believe it very important that the data reflect as far as possible not only the fact of working in a plant where the exposure to PCB was possible, but also the identity of the particular PCB to which the employee was possibly exposed. The reason for my concern here is that laboratory studies have repeatedly shown large differences between the various

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PCBs in their biological effects, and hence I believe that it may be necessary to know whether the employee's exposure was to Arochlor 1254, 1242, or 1016 in order to make any sense out of the statistics. With a bit of help from the Capacitor Department people, such information on the probable identity of the PCB involved should not be too hard to generate, once the dates and locations of employment are determined, since the overwhelming proportion of the exposure must have resulted from the practice of flood-filling, particularly of the large-volume small capacitor lines, and there does seem to be data available on when they were using which PCB in which plant. (The story seems to be that Fort Edward shifted from Arochlor 1254 to 1242 on 9/22/50 and Hudson Falls shifted from 1254 to 1242 around 1953, back again for a year in 1957, and then permanently out of 1254, except for minor special lines, around 1958. Both plants switched from 1242 to 1016 around February, 1971, I believe.) At any event, I think this sort of information should be fished out and worked into the statistical analyses."

C. Immunosuppression Study

C1. "This may be such an obvious point that Dr. Selikoff simply skipped over it in his proposal, but let me throw it in anyway. The proposed immunosuppression study would involve subjects having had widely varying levels of exposure to PCBs in the past, and varying lengths of time since exposure ceased. In order to interpret the significance of any observed immunosuppression, it would be desirable to know what sorts of PCB levels existed in the subject's blood in the past - which I presume can be determined from Dr. Wolff's earlier data - and, even more important, to know what levels were present at the time of the immunosuppression assay. Accordingly, an assay for blood PCB should be included as part of the test protocol.

C2. As we have already mentioned to Dr. Selikoff, Drs. Kaplan and Uzgis here at CRD have an ongoing program to explore the feasibility of detecting changes in the cell-mediated immune status of the body via laser-Doppler spectroscopy. We are not certain whether such studies of lymphocytes from PCB-exposed workers would be meaningful; however, if Dr. Bekesi does run across any clear indications of abnormality, we would like to be informed so that we could have a look at the mobility distribution patterns and antigen responses in the deviant cases."

D. PCB Elimination Studies

D1. "This particular study involves at least four separate experiments and the results could have bearing on several different unresolved questions. One of the less obvious of these is what it is that actually

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happens in cases of overt "PCB" (e.g., probably PCDF) poisoning, as at Yusho. One remarkable, and as yet still unexplained observation made by the Japanese was that the Yusho victims showed a markedly abnormal distribution of residual PCB isomers in their blood. This could have resulted from an abnormal activation of microsomal enzymes. If so, it might appear in the 1254-fed rats subsequently dosed with phenobarbital or 3-naphthoflavone. Accordingly, I would recommend that in these experiments there be notice made of the PCB isomer distribution patterns as well as the rate of disappearance of total PCB.

D2. I note that the proposed study will include testing of silica gel as one example of a "powerful" adsorbent. Actually, silica is a powerful adsorbent for weakly polar organic compounds only from solutions in weakly polar solvents, not from solutions in water. Unless the silica gel experiment is intended solely as a control, it might well be omitted.

D3. Any clinical use of agents to stimulate PCB elimination will require some documentation of the inability of natural processes to take care of the problem; i.e., longitudinal studies of PCB levels in Capacitor Department employees following cessation of exposure. I am somewhat disappointed to see that no specific provision for such studies is included in the proposed program. I note, however, that if the blood-PCB assays that I suggested under Section C1 be carried out, these, in conjunction with the earlier data on blood PCB levels, ought to provide the required data on at least 50 subjects, and this should be enough to indicate the trends regarding PCB persistence in chronically-exposed humans."

As we agreed by telephone, the funding arrangements will be completed by the individual(s) responsible for financial affairs at the Mt. Sinai School of Medicine and in Dr. Welch's organization. Once you have made the appropriate communication at Mt. Sinai, this person should contact Dr. Welch's designate:

James J. Costello
Manager - Group Financial Planning & Analysis
General Electric Company
1 Plastics Avenue
Pittsfield, MA 01201
Tel.: (413) 494-5432

As you are aware, I am pleased with this combined approach to a naughty problem and hope we can get started in the near future.

Sincerely,

Thomas Casey M.D.

TRC/je

c: J. F. Brown, Jr.
J. F. Welch, Jr.

bcc: H. Cross
R. L. Frigo
H. D. Pocock, M. D.

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