

DRAFT

Minutes of January, 1996
BISAC Meeting
Key Largo, Florida

Thursday, January 19

The meeting was convened at 0800. A list of attendees is appended to these minutes. Minutes of the October 1995 meeting were approved subject to written comments previously submitted. The Chairman welcomed the Committee's guests and noted that Dr. Trichopoulos was in New York to receive this year's award from Sloan-Kettering Institute for his work on passive smoking and would join the group on the following day. In accordance with this change, the original agenda was modified to defer his acid mist presentation until Friday and to begin the meeting with Dr. Kreiss' report on her study of the Elmore, Ohio plant of Brush Wellman, a draft copy of which had been distributed to the Committee prior to the meeting.

ELMORE SURVEILLANCE STUDY REPORT

Subsequent to the study of the Brush ceramic operations at Tucson, NJC was given a contract by Brush to study the Elmore, Ohio plant. Dr. Kreiss reviewed the history of this study beginning in late 1992 and through the following three years until submission of the draft report under discussion. Dr. Deubner noted that several teams at Brush were reviewing the report preparatory to employee notification of the findings. Dr. Miller expressed disappointment that earlier BISAC criticism of NJC reporting practices were ignored in this report, citing, as examples, the use of "borderline" as a test classification, the effect of lab technician ideocyncrasies on test results and the reclassification of employees after conclusion of the study. Dr. Kreiss defended the last example as necessary to avoid misleading results from comparison of Dr. Saltini's genetic data with data on "sensitized" employees. Dr. Rogers suggested recasting the data with strict adherence to the study protocol.

A discussion of the limitations of the BLPT ensued, including the desirability of retesting "normals" to avoid false negatives. Industry representatives expressed concern, from a management point of view, about the relevance of the BLPT data to the worker and the lack of precision in the terminology utilized. At least one BISAC member felt the criticism was valid -- that there was a need to clarify the meaning of the data being generated.

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Dr. Kreiss expressed concern about laboratory differences in biopsy procedures, noting that Table 3 of the study showed the percentage of abnormals having granulomata increased with the increase in the number of biopsies. Dr. Miller stated that he had canvassed a number of pathologists and the consensus was that 4-6 biopsies were required and that 6 was a recommended number. Dr. Deubner stated that a standard biopsy report, showing at least the minimal information needed for evaluation, was necessary and he felt that BISAC should establish such a report. Dr. Kreiss observed that genetic susceptibility and occupational process exposure appeared to be equal risk factors for CBD.

Dr. Kreiss reported that the genetic testing at Elmore showed that while 80 % of the CBD cases had the GLU - 69 marker only about 40% of the sensitized employees had the marker, comparable to the 44% in the control population. It appears that the GLU-69 allele is sensitive to granulomatous response but not to an antigen presentation itself. This would further suggest the influence of other genes in the total disease development process.

SCREENING, SURVEILLANCE AND CASE-FINDING

Prior to the meeting Dr. Deubner had prepared and distributed a proposed program of medical surveillance for Brush Wellman and a set of conceptual definitions differentiating between screening, surveillance and case-finding.

Under the proposed surveillance program, pulmonary function testing would be mandatory for annual tests and voluntary for quarterly tests. The new program would change X-ray tests from annually to every 3 years, on a voluntary basis, with baseline and exit X-rays only being mandatory. The Committee was fully supportive of these proposed changes with some members questioning the need for any routine pulmonary function tests.

The proposed classifications of beryllium pulmonary granuloma (BPG) absent symptoms and CBD with symptoms was not as well received, raising questions about creating new categories of disease and further confusion between terms evidencing exposure and terms evidencing disease.

Dr. Deubner described the internal Brush organizational set up for evaluation of health-related issues, including the proposed surveillance program.

INDUSTRY-BISAC INTERFACE

A. BRUSH WELLMAN-BISAC INTERFACE

Dr. Deubner identified three areas of interest, i.e.,

1. Scientific leadership and funding.
2. Interested science, e.g. regulatory matters
3. Internal policy guidance.

He recommended a more formal recognition of BISAC and industry roles in decision-making. Mr. Skoch recommended prioritization of projects as a BISAC function.

B. NGK-BISAC IINTERFACE

Mr. Niwa described the historical and current role of NGK in beryllium production including the union-management aspects. He pointed out that the surveillance program carried out by Mass General Hospital was a provision of the union contract. NGK processed no metal or ceramics, only beryllium alloys and the occupational hazards were quite different from those of Brush. He shared Ms. Abeles concern that the BLPT program had too many uncertainties for introduction into other beryllium producer-user plants at this time.

C. CERADYNE-BISAC INTERFACE

Ms. Duffy cited the industry need for clarification and standardization of terms, definitions, processes and of diagnosis of disease.

D. CBL-BISAC INTERFACE

Ms. Abeles stressed the need for recognition of the practical aspects of the health problem, clarification of the BLPT confusion and the existence of a tool for pre-selection of employees.

E. DOE-BISAC INTERFACE

Dr. Wambach pointed out the dual role of DOE as a beryllium user and as a Federal Health Agency. The former provided a commonality of interest with the industry in addressing employee health concerns while continuing to recognize the latter in assessing the validity of data and the need for consensus forming.

BISAC SELF ASSESSMENT - PAST

Dr. Eisenbud observed that a few years ago he felt that at last we might be seeing the end of the tunnel on CBD. Today that light is less clear. He reviewed the history of the disease, the derivation of the standard, the drop off in cases, the concern that the standard was too stringent, the reappearance of cases, the concern that the standard is not stringent enough and the emergence of immunological testing at about the same time as the creation of BISAC in 1990. He identified what he assessed as positive and negative actions by the Committee in its first five years of existence. Among the former, he cited:

1. Resolution of differences between NJC and Pennsylvania Hospital
2. Standardization of BLPT labs.
3. Saltini's research
4. Rossman's research
5. Specialty labs' research
6. Coordination of DOE-BISAC activities

On the negative side he cited:

1. Lack of monitoring of projects
2. Lack of information on new CBD cases.
3. Lack of attention to industrial hygiene aspects of CBD control.

BISAC SELF ASSESSMENT - FUTURE

Dr. Kotin suggested the development of an analysis comparable to the old military "Pert Chart" to assess our disappointments and identify what happened and why. He compared the limitations of clinical research versus epidemiologic research vs animal experimentation in the understanding and control of CBD.

Dr. Rogers noted that, absent a line of reliably positive human blood cells, an animal model was the only alternative and despite the acknowledged difficulty of finding such a model we had to proceed in that direction.

Considerable discussion of the need for, and the logistics of conducting, a workshop on the dual needs of a line of T-cells and an animal model for CBD then ensued. During the course of this discussion it was agreed that the Committee invite Dr. Frazier of DOE's Genome Project to attend the April BISAC meeting. Details of a proposed workshop to explore with invited scientists the possible avenues of investigation were discussed. At this point, the meeting was adjourned for the day.


Friday, January 19, 1996

The meeting was reconvened at 0800. Dr. Kotin noted that Dr. Trichopoulos was not present when Dr. Keiss' report on Elmore had been discussed and invited Dr. Trichopoulos to comment on the draft report. Dr. Trichopoulos suggested that his comments were too detailed to be reviewed in Committee but that he would be available to work with Dr. Keiss in Boston at her convenience.

GENETIC TESTING FOLLOW-UP

Dr. Deubner referred to Tab D of the agenda, a discussion drafted by Dr. Saltini for presentation to the Elmore workforce. Dr. Miller expressed the opinion that the draft was far too detailed for that purpose. Dr. Keiss stressed that the Elmore employees were waiting for word on the results of the study. Dr. Kotin instructed Mr. Powers to include this item on the April meeting agenda.

ACID MIST PAPER



Dr. Trichopoulos stated that the classification of beryllium as a human carcinogen was really a scientific scandal but that, in spite of its absurdity, the classification will be extremely difficult to change, given the normal human tendency to perpetuate error rather than admit to it. The proposed acid mist paper gave everyone a chance to correct the error without losing face if they were willing to do so. The Committee discussed the evidence of BeSO₄ exposure and agreed that the number of acute disease cases attributed to Be SO₄ by De Nardi was adequate evidence of such exposure. The addition of Beryllium fluoride as a further confounder was suggested but the consensus was that this would confuse the issue and add nothing to the argument. After discussing the publication of the paper and its authorship, it was agreed that it would be submitted to JOM with the entire BISAC Committee listed as authors.

CABST - BAL AND BIOPSY PROTOCOLS

Dr. Miller described the current status of the review of BAL and BIOPSY procedures. He noted problems with 7th day harvesting, with 100 as a dosage maximum and with less than six biopsies for diagnosis. He also noted that the presence of macrophages complicated the BAL analysis. Dr. Miller will prepare a draft protocol for circulation and approval at the April meeting of CABST. It was agreed to set aside April 22-24 for meetings, with priority given to CABST to select one of those days for its meeting. The remaining two days would be devoted to BISAC.

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CLEVELAND CLINIC PROPOSAL

The Committee reviewed the proposal submitted by Dr. Barbara Barna of the Cleveland Clinic and determined that, while the 56 biopsies are a valuable resource and should be carefully utilized, the Committee priorities would not justify supporting the proposal at this time.

MEETING SCHEDULE

It was agreed to meet in Washington, D. C. on April 22-24, with one day devoted to CABST and two days to BISAC.

The summer meeting was scheduled for July 22-23 in Boston. A proposal was made to arrange for meeting on Sunday. This was favorably received but deferred until the Fall meeting for implementation.

(NOTE: Subsequent to the meeting a schedule conflict developed and, by telephone canvass of the members, the meeting date for July was changed from July 22-23 to Sunday, July 21 and Monday, July 22, 1996 at the Guest Quarters Hotel in Cambridge, Mass.)

INDUSTRIAL HYGIENE

It was agreed that Dr. Eisenbud would develop a statement of industrial hygiene needs for review and discussion at the April meeting. Dr. Rogers suggested that the Committee address BISAC interest in two areas:

1. The validity of evaluating risk factors in small worker populations (re: Dr. Kreiss' reports on Tucson and Elmore).
2. How to relate workplace beryllium exposures to individual employees.

RESEARCH NEEDS

Dr. Wambach noted that DOE would be conducting a review of research needs and, in recognition of the desirability of coordinating the DOE and industry interests, he would keep Drs. Rogers and Miller informed of the DOE schedules.

The discussion of a workshop, to explore the feasibility of an animal model or developing a line of abnormal human cells, that had been started on the previous day was resumed. Dr. Rogers had prepared a rough budget estimate of \$50,000 based upon some ten invitees. At this point, Dr. Trichopoulos suggested, in lieu of the workshop approach, a procedure that he felt would be more productive. He suggested a letter be sent to selected candidates with recognized expertise, but with no beryllium experience, inviting them to suggest a proposed program of research to address our needs. We would suggest BISAC provide seed money and indicate our prior success in obtaining long term support if the preliminary research warranted such funding. BISAC could review all proposals and, if a conference was deemed advisable, it would be focused on specifics. After discussing the concept it was agreed to follow the suggestion and Dr. Miller agreed to draft the invitation letter.

The meeting was adjourned at noon.

ACTION ITEMS

1. BISAC will initiate development of a standard report on biopsy for CDB with definition of minimal data necessary for evaluation.
2. BISAC will invite Dr. Frazier of DOE to the April BISAC meeting.
3. Dr. Miller will draft a letter inviting selected researchers to submit proposals for animal model or cell line development research.
4. Mr. Powers will list a discussion of notification to Brush employees on the agenda for the April meeting.
5. Dr. Trichopoulos will be available to meet with Dr. Kreiss in Boston at her convenience to review her proposed Elmore paper.
6. Dr. Deubner will coordinate review of the acid mist paper and submit to JOM for publication.
7. Dr. Miller will draft a protocol on BAL for review and approval at CABST meeting in April.
8. Mr. Powers will notify Dr. Barna that BISAC will not recommend approval of her proposal.
9. Dr. Eisenbud will prepare a list of industrial hygiene needs for the April meeting.

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January 1996 BISAC Meeting
List of Attendees

Barbara Abeles	Consolidated Beryllium Ltd.
David Deubner	BISAC
Linda Duffy	Ceradyne
Merril Eisenbud	BISAC
Paul Kotin	BISAC
Kathleen Kreiss	National Jewish Center
Frederick Miller	BISAC
Yasuhito Niwa	NGK Metals Inc.
Martin Powers	BISAC
Adrienne Rogers	BISAC
Daniel Skoch	Brush Wellman
Dimitrios Trichopoulos	BISAC
(Friday Only)	
Paul Wambach	U. S. Department of Energy