

DRAFT
MINUTES OF BISAC MEETING
NOVEMBER 2 AND 3, 1994
DENVER, COLORADO

Wednesday, November 3

The meeting convened at 0900. In attendance were the full committee and two representatives of the industry, Messrs. Rosek and Stock of Brush Wellman. Mr. Skoch serves as Brush Wellman liaison with BISAC.

In response to the Chairman's request for comments on the recently distributed minutes of the July meeting, the following revisions were proposed:

1. Page 2, line nine should read "0.3 micrograms".
2. Page 3, delete last sentence of second full paragraph.
3. Page 3, first paragraph Wayne Anderson should read "Wayne Sanderson."

Subject to the foregoing revisions, the minutes of the July meeting as circulated were approved for adoption.

The Chairman, noting that Mr. Harnett, CEO of Brush Wellman, would be attending the meeting later in the morning, suggested deferring discussion of the NIOSH meeting until his arrival.

NIOSH Case Control Study

Dr. Trichopoulos reported on his telephone conversation with Dr. Sanderson of NIOSH concerning the case control study. He felt that Sanderson was receptive to our concerns about matching the date of entry between cases and controls and offered to contact Dr. Trichopoulos further on the study, although, noting that NIOSH was running behind schedule on the project. There has been no contact to date.

BaCl₂ Skin Test Data and ITRI Study

Dr. Markham had distributed progress reports on the two studies shortly prior to the meetings. Data in both reports, though tentative, showed an irritant reaction to copper, as well as to beryllium copper. Dr. Markham reported that ITRI was attempting to obtain a copper powder for use as an aerosol.

The skin test data evoked a number of questions that were not answerable by the preliminary report, most notably,

what controls were used and what reaction did the controls experience? Dr. Markham said he expected further clarification from the researchers on these questions.

Schuller Corp. Presentation

Dr. Kotin reported a telephone conversation with Dr. Hesterberg in which the latter indicated that recent test developments had raised questions that required resolution prior to addressing the applicability of such work to beryllium. As a result both had agreed to defer the presentation until some later date.

Dr. Trichopoulos inquired about the objective of the proposed research on beryllium copper. In response, Dr. Miller noted that while scientists in general accepted that there were significant differences in human and animal carcinogenicity, regulatory agencies in general did not. It was necessary, therefore, to provide these regulators with data on animals for commercially compelling reasons even though there might be little or no scientific value in the data.

Mr. Rosek described the history of cancer regulatory efforts in Europe noting that animal data was relied upon heavily and where industry initiative and discretion in the application of these regulatory directives was severely limited.

CASBT

Dr. Markham presented data showing discordance between initial samples split between Cleveland Clinic Foundation (CCF) and National Jewish Center (NJC). Of 15 CBD cases, initial reports of CCF would have missed 4 and NJC would have missed 7. The data showed continuing use of borderline as a category, despite the unanimous laboratory agreement to discontinue the use of that terminology.

Dr. Miller then summarized data provided by Dr. Littlefield of OHSU in which samples split between laboratories showed the following:

National Jewish - Pennsylvania Hospital

Agreed	29
Disagreed	59

National Jewish - Specialty Labs

Agreed	6
Disagreed	28

Specialty Labs - Pennsylvania Hospital

Agreed 10
Disagreed 12

Of 303 individuals previously tested as normal, 11 subsequently retested as abnormal, of which 2 were diagnosed as CBD. Dr. Miller noted that there were two scenarios possible. Either they were missed in the initial testing (false negative) or they had changed from normal to abnormal.

He noted the ORISE approach to testing was to split samples only on the retesting of individuals originally testing as abnormal, whereas the Brush approach was to randomly split initial testing samples. Recognizing that the ORISE population included a large number of people with dubious exposure histories there was a logic to the ORISE approach but the possibility of false negatives, or lost cases, dictated a preference for the Brush approach.

Mr. Harnett had joined the meeting during the CABST presentation and raised question as to management's responsibility to sensitized employees. In the ensuing discussion it was pointed out that there were opposing pressures on management to counsel on one hand there was clearly a responsibility to counsel such employees on the potential risk of continuing exposure in the workplace. On the other hand, legislation and court cases clearly showed an intent to preclude any attempt by management to force employees out of the workplace for health reasons.

Dr. Markham summarized the current status of the Brush Ohio BLPT experience as follows:

	Total	Normal	Abnormal
St. Clair	148	139	6
Elmore	627	575	52

Of these, 15 were confirmed as CBD and 23 were in some stage of evaluation.

In response to Mr. Harnett's question as to the future direction of this effort, the Committee recommended analysis of the current data and continued observation of the sensitized and CBD cases that continue to be occupationally exposed. It was also recommended that the company review its current policy statement to see if some redefinition was in order.

NLEHS Meeting

Dr. Eisenbud reviewed the development of the meeting concept and the reasoning behind going to NLEHS for support, how the addition of OSHA and NIOSH had resulted in losing control of the meeting agenda, and the delays and confusion resulting from NLEHS (Jamason) incompetence. Despite everything that had happened, however, he felt that participation by everyone who would attend would be helpful for damage control if not for any other reason. Drs. Miller, Rogers and Trichopoulos had already declined in writing. Dr. Kotin and Mr. Povera argued against participation by BLSAC or Brush Wellco. After considerable discussion Mr. Harnett decided the Brush representatives should attend the meeting as participants, rather than merely as observers.

Duke University Report

Dr. Eisenbud presented graphs showing CBD cases cumulatively by year of first exposure and by year of diagnosis. He described difficulties encountered in trying to find data on total employees exposed during these periods. Dr. Trichopoulos noted that this lack of denominator, which he felt should be many years of exposure rather than total employees, together with changes in diagnostic criteria and differential time of follow-up, made the data difficult to interpret in a meaningful way. Dr. Eisenbud stated that the data shows that sensitization and disease continue to exist despite all efforts to reduce exposures.

Thursday, November 4, 1984

The meeting reconvened at 0730. The chairman identified diagnosis of CBD as the next topic on the agenda. In the course of the ensuing discussion Dr. Trichopoulos suggested that a paper be published in an appropriate journal defining the criteria for CBD. Dr. Miller stated his experience with convening a knowledgeable but disinterested panel to review and define the criteria. At 0800 Drs. Kreiss and Repscher joined the group.

Tucson Study

Dr. Kreiss reviewed the questionnaire and interview procedures that preceded the study, and the taking of blood for BLPT and genetic testing. She noted that at the time of the Tucson meeting there were two samples abnormal in only one lab that were now identified as blood abnormal with no granulomata but with immunological changes. In her response to a question from Dr. Miller as to whether, in her opinion, an individual who tested abnormal once, but on all subsequent tests shows normal, is indeed sensitized,

she answered yes. Dr. Miller went on to query whether to label an individual as sensitized is to imply a greater degree of risk. She again answered yes, noting a greater Rocky Blot 3 of 6 sensitized individuals had gone on to develop CBD. Dr. Miller stated he had reviewed all the BLPT data and was concerned about the number of false positives and false negatives. Dr. Kreiss concurred that she, too, was concerned. She attributed the problems in the National Jewish lab to albumin difficulties and expressed the hope it had been corrected.

She stated that 127 of 137 total employees had provided samples for genetic testing. Of this 127, 5 had CBD and 8 were sensitized. Forty-one of the 127 had the genetic marker (32%) whereas 4 of the 5 CBD cases had it (80%) and 5 of the 8 sensitized had it (62.5%). Thus the marker was not present in 20% of the CBD cases and 37.5% of the sensitized employees.

Noting the higher percentage of machinists with CBD and sensitization Dr. Kreiss stated that exposure factors remain an important element in assessing risk and opportunities for reducing risks. She also stated that workers exposed to beryllium oxide appeared to have a more virulent form of CBD.

In response to a question, Dr. Kreiss expressed some uncertainty about Dr. Saitini's intent to test the Elmore workforce, saying that his interest appeared to be on a basis, as opposed to epidemiological, research. She felt that the use of a consent form for genetic testing had led to a "sense of expectation" on the part of the Tucson workforce. In response Dr. Markman stated that a meeting between Dr. Saitini and the Tucson workforce had been scheduled for November 14.

This statement led to extensive discussion as to the appropriate manner of communicating information, such as the results of genetic testing and the implication of that testing, to the workforce involved as well as to other plant populations at risk. It was agreed to cancel the November 14, 1994 Tucson meeting and to rethink the whole issue with greater input to, and feedback from, BSAAC.

(Note: At the NIEHS Beryllium Conference on November 10, 1994, in response to a question by Mr. Powers about the status of in vitro testing, Dr. Ojo Amala stated that he thought the purpose of the November 14 meeting in Tucson had been to obtain blood samples for in vitro tests but, since that meeting had been canceled, his study is now on hold.)

Dr. Rapscher's Presentation

Dr. Rapscher noted that he was a practicing clinician more than he was a researcher and reviewed his past experience with CBD, primarily at Coora and at Rocky Flats. He felt that there were problems with the diagnosis and treatment degree of concern.

1. BLPT testing.

He was concerned about the value of the test in general but was particularly concerned about its use at National Jewish Center.

2. The significance of a single granuloma in the sub-mucosa area.

Dr. Miller noted that Brush cases had fibrosis and granulomata. Dr. Rapscher said he was not seeing this in Colorado cases.

3. Separation of disease and sensitization.

He felt that the distinction here was being blurred by terminology that failed to clearly differentiate between them.

4. Overtreatment of the disease.

He felt that excessive or unnecessary use of steroids or other overtreatment stemmed from exaggeration of the prognosis of the disease.

5. Prognosis distortion.

This, in turn, he felt was the result of non-CBD limitations, e.g., heart disease.

6. Automatic use of biopsy to confirm abnormal BLPT.

He agreed that from a research perspective it was desirable to know whether blood sensitized individuals were also abnormal on lavage and/or had granulomata. From a clinician's perspective, however, he questioned whether the risk of invasive procedure was justified in order to make a diagnosis that would not affect treatment.

At the conclusion of Dr. Rapscher's presentation the meeting was then adjourned.

Action Items

1. Eisenbud, Skoch, Markham and Kolanz would attend the NIEHS meeting as participants. Rosek and Powers would attend as observers.
2. Markham would cancel the Tucson meeting on November 14, 1994. Brush would reassess its BLPT-CBD policy and program.
3. Salini would be contacted at the NIEHS meeting regarding testing the Elmore workforce.