

Beryllium Industry Scientific Advisory Committee

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Paul Kotin, M.D.
Chairman

Martin Powers
Executive Director

Committee Members:

✓ Merrill Eisenbud
Dimitrios Trichopoulos, M.D.
Thomas Markham, M.D.
Frederick Miller, M.D.
Adrienne Rogers, M.D.

October 26, 1995

TO: BISAC
FROM: M. Powers

SUBJECT: DRAFT MINUTES OF OCTOBER MEETING

Enclosed for your review is the draft minutes of the October meeting.

Exhibit II was distributed at the October meeting.

MBP:mm

Encls

cc: Mr. Niwa
Dr. Wambach
Brush Wellman

ME002653

Blood Lymphocyte Proliferation Testing - BWI

Dr. Markham presented data showing that 42 previously abnormal test patients were retested, of which 23 were normal, nine were abnormal and 10 were pending. Dr. Miller stated he needed these BWI BLPT data for his dialogue with Dr. Parkinson and that he had earlier requested data without any reply. Dr. Markham agreed to provide the data.

Dr. Deubner questioned whether BLPT was a research or a screening test. Dr. Miller responded that its use for diagnosis and treatment made it a screening test. Dr. Markham pointed out that it was used as a screening test because NJC convinced people that the test was 95% valid. Dr. Rogers noted that BISAC had always regarded the test as research even if others treated it as a screening test. Dr. Kotin pointed out that they were not mutually exclusive and there was even a difference between experimental and research testing. Dr. Trichopoulos stated that BLPT was not a diagnostic test, despite the NJC use of it as such. Dr. Deubner requested that this issue be addressed in an organized fashion at the January meeting.

BLPT - DOE

Dr. Wambach noted that the approach and objectives of the DOE were different from those of the industry. DOE had concentrated on groups, rather than individuals. They were only duplicating abnormal tests as opposed to the industry's use of duplicate lab tests for each individual tested. Dr. Wambach presented analytical data (attached to these minutes as Exhibit II) prepared to explore whether variability in test results was the result of an individual's personal day to day variability or due to the variability of the testing lab? Dr. Miller observed that, since we don't know the answer, this underscores the need for an abnormal standard to measure against. Dr. Wambach agreed with Dr. Miller that a CABST meeting was urgently needed to address BLPT and BAL testing.

CABST

Dr. Miller reviewed the efforts to standardize the BAL, as the BLPT had been standardized earlier, and the problems encountered with Dr. Newman of NJC. It was agreed that Dr. Miller would prepare a letter to DOE proposing a protocol to be developed for a CABST meeting next Spring.

Desensitization

Dr. Miller reviewed the variety of immunologic responses, including cellular response to internal host body stimuli as well as reaction to antigens. These responses may produce harmless antibodies, e.g., hay fever, or harmful

antibodies, e.g. asthma. He noted it was possible, in some cases, to immunize the body against antibodies or to induce suppressor cells to inhibit the production of antibodies. Not enough is known of the natural history of beryllium disease, including the role of sensitization, exposure and genetic disposition to the disease to suggest prevention or inhibition as opposed to steroid treatment.

CBD Follow-up Format

Dr. Deubner briefly described the objectives of his outline, previously distributed to the Committee for review, and solicited assistance from the Committee on assembling the base line data needed to assess future activity. He acknowledged that the scope of his outline was ambitious and therefore unlikely to be available in its entirety but did represent a target he would work toward. It was agreed to explore the feasibility of the concept in the next few months and review it at the next meeting.

Miscellaneous

Dr. Kotin noted the Mauderle paper distributed to the Committee was self-explanatory and, in the absence of Mr. Niwa and Dr. Shima, discussion of the CBD experience at Reading and the Shima paper would be deferred to a later meeting.

The first day's deliberations were adjourned at 1600.

Tuesday, October 10, 1995

The meeting convened at 0800. The winter meeting dates and site of January 18 and 19, 1996 at Ocean Reef, Key Largo, Florida were confirmed.

Research Needs and Plans

Animal Models

Dr. Rogers summarized the animal data and suggested the issuance of an invitation for research proposals on a CBD model, perhaps aimed at immunologists. Dr. Miller questioned transgenic research on CBD. He observed that whereas TB affects all species, beryllium granulomata was very limited, if not unique. He also noted that human cell lines didn't look very promising, either. Dr. Kotin reminded the Committee of past consideration of a conference on animal research and suggested assembling experimental pathologists and immunologists for this purpose. After discussion it was agreed that Drs. Miller, Rogers, Deubner and Eisenbud would act as a

subcommittee to look into the extent of interest in beryllium immunology and animal experimentation on CBD and the possibilities of a conference.

Blood Cell Lines

Effects to date by Drs. Saltini and Rossman to develop blood cell lines have been unsuccessful and, as desirable as this would be, offers little hope for the future.

Genetics

Dr. Eisenbud had recommended to the DOE Genome Project that an alternative to the Saltini work be funded and suggested that perhaps it was time to reopen the subject. It was agreed that Dr. Eisenbud and Wambach should review the whole area of genetic research with Drs. Fragin and Drell at the DOE Genome Project. Dr. Miller cautioned that the legal, ethical and economic problems encountered in the BLPT program by the industry were minimal by comparison with the potential problems inherent in the genetic field.

Beryllium Copper Dermal and Inhalation Studies

Discussion of the pros and cons of further beryllium copper research resulted in a consensus that Dr. Deubner should assess the industry's needs and priorities as a guide to the Committee's deliberations.

In Vitro Sensitization

The history of this proposal was reviewed and the decision to defer the research until the Saltini genetic data at Elmore was available was confirmed.

Acid Mist Paper

Dr. Trichopoulos reported that he had evaluated the engineering data furnished to him and that the potential exposure levels in that data were too high for human endurance. Accordingly, he had made some assumptions and drafted a summary for Brush review and concurrence which he had given to Mr. Powers before the meeting. Upon receipt of Brush comments he was prepared to submit a draft of a paper to the Committee for its review. He again raised the question of authorship of the paper, which the Committee agreed to evaluate.

ACGIH Review of Beryllium Standard

Dr. Markham reported that the recommendation of the Committee would be available around the first of November.

NIOSH Nested Case Study

Dr. Markham estimated that a draft of the study would be made available for internal NIOSH review by year-end.

Mass. General Hospital

Since there has been no response to the Committee's letter of July 11, 1995, the Committee recommended that the matter be referred to outside counsel for collection or other disposition. Mr. Powers agreed to do so.

Future Meetings

It was agreed to meet on April 22 and 23, 1996 in Washington, D.C.

The meeting adjourned at 1100.

Action Items

1. Dr. Markham will provide BLPT lab data to Dr. Miller for transmittal to Dr. Parkinson.
2. Drs. Kotin, Deubner and Eisenbud and Mr. Powers will meet with Drs. Saltini and Kreiss in Denver on November 1, 1995, to review Elmore genetic data.
3. Dr. Deubner will review company issues and priorities relating to its relationship to National Jewish Center for January meeting discussion.
4. Dr. Miller will prepare a letter to DOE and a draft BAL standardization protocol for approval at a Spring meeting of CABST.
5. Drs. Deubner, Miller, Rogers and Eisenbud will form a subcommittee to evaluate a conference on the development of an animal model for CBD.
6. Drs. Eisenbud and Wambach will investigate DOE interest in funding further research on genetics, immunology and animal modeling related to beryllium.
7. Dr. Deubner will look into industry problems and priorities relating specifically to beryllium copper and report back to the Committee.