Chemical Manufacturers Association

VINYL CHLORIDE PROJECT PANEL

Washington Hilton
Georgetown West

March 18, 1980

11:00 a.m.

PROPOSED AGENDA

1. Introduction and Purpose of the Meeting

2. Background Information on Industrial BIO-TEST research project and an audit of this study by Experimental Pathology Laboratory

3. Disposition of Busey Report

4. Additional treatment and disposition of Industrial BIO-TEST data and tissues

5. Termination of Industrial BIO-TEST Contract and legal claim

6. Other follow-up work

Manufacturing Chemists Association

Record of Meetings

TASK GROUP FOR AUDIT OF VINYL CHLORIDE CHRONIC INHALATION STUDY

Industrial BIO-TEST Laboratories, Inc. Decatur, Illinois
Sheraton Inn Decatur, Illinois

February 19-24, 1978

Dr. Bell presided and convened the meetings with the following in attendance at the respective meetings described below:

Industrial BIO-TEST Laboratories Meeting

MEMBERS PRESENT

Z. G. Bell, Chairman	PPG Industries, Inc.
T. J. Benya	Ethyl Corporation
G. K. Hatfield	Diamond Shamrock Corporation
R. K. Hinderer	The BFGoodrich Company, Chemical Division
C. D. Kary	Shell Oil Company
T. R. Torkelson	The Dow Chemical Company
J. T. Seawell	MCA Staff

GUESTS PRESENT

W. M. Busey	Experimental Pathology Laboratories, Inc.
P. Churukian	Industrial BIO-TEST Laboratories, Inc.
J. W. Goode	Industrial BIO-TEST Laboratories, Inc.
W. J. Koretke	Industrial BIO-TEST Laboratories, Inc.
D. C. Lindberg	Industrial BIO-TEST Laboratories, Inc.
J. H. Mennear	Industrial BIO-TEST Laboratories, Inc.
R. Rhudy	Industrial BIO-TEST Laboratories, Inc.
R. J. Roman	Industrial BIO-TEST Laboratories, Inc.
D. J. Sullivan	Industrial BIO-TEST Laboratories, Inc.
I. Te Vault	Industrial BIO-TEST Laboratories, Inc.
M. Vlaovic	Industrial BIO-TEST Laboratories, Inc.

Controls
Group TE I - 50 ppm
Group TE II - 200 ppm
Group TE III - 2500 ppm
Group TE IV* - 2500 ppm

*Rats only, special cage conditions for this test group.

4) There were 2,500 test animals.

5) Inhalation exposures were initiated and terminated as follows:

Species	Initiated	Terminated
Mice	September 10, 1973	June 10, 1974
Rats*	September 10, 1973	September 10, 1974
Hamsters	September 10, 1973	September 10, 1974

6) The last interim report on this research project issued on September 23, 1975. No additional data or reports subsequent to this date were available to the Task Group.

7) On Monday morning, February 20, 1978 it was learned that final shipments of VC test documents, organ and tissue evidence from IBT, Northbrook to IBT, Decatur were completed on Friday, February 17, 1978. There were available to the Audit Task Group, only gross inventories of the shipment components.

8) No summaries or detailed inventories were available on the:

   a. Status of necropsy sheets or reports

   b. Status of histopathology readings

   c. Wet tissues inventoried or catalogued

- Analysis of the test agent and exposure chamber concentrations and investigations of possibilities of stratified flow in the test chambers.

- Test animals - test facilities' procedures for quarantined, randomization, identification, and environment. Possible deviations from these procedures -

Execution of Study:

- Frequency of observations of animals for possible abnormalities.

- Clinical laboratory test conducted.

- Recording of clinical observations in bound laboratory notebooks with appropriate signatures and initials of investigators.

- Nature of test conducted on animals found dead.

Necropsies (Gross Pathology):

- Were necropsies performed on all animals?

- Examination of animals found dead and subject to postmortem autolysis.

- Supervision of examination by Board Certified Pathologist.

- Organs described and weighed.

- Descriptive data on all lesions observed.

- What wet tissues and tissue blocks were preserved and were these clearly identified or labeled and recorded?

- Where are wet tissues and histopathologic slides stored and under what storage conditions?

- Pathology - examination of prepared slides
- Number of tissues being prepared
- Organs selected for histopathologic study

Team 2 - General Laboratory Audit

Audit Parameters

- Body weights
- Organ weights
- Analytical chemical data
- Clinical chemical data
- Hematological data - blood parameters
- Clinical observations
- Air flow in exposure chambers
- Records of concentrations of test chemical in exposure chambers
- Cross checks of necropsy sheets with behavioral sheets

Team 3 - Audit and Review of Mortality Data and Reported Lesions

Audit Parameters

All recorded and/or reported mortality data.

. Individual weights) _ _ weight change data
Organ weight) relevant to both

Exposure Chamber Data

. Concentrations of test chemical

. Computer printouts

. Detailed records of down-times and reasons for, duration of

. Checks for stratified flow in chamber(s)

. Number of full exposure days

. Criteria used to determine a full exposure day

Team 2 - Research Procedures up to and Including Necropsy

Audit Parameters

. Laboratory Notebooks -

Type
System of recording entries
Tie-in with computer entries and printouts

. Types of observations recorded

. Mortality incidences

. Mortality curves

. Records of postmortem autolysis

. Clinical observations

. Mortality Curves Versus Calendar Incidences

Comparative summations of:

Animals found dead versus day of week
Animals sacrificed versus day of week
Records of all tissues saved

Possible Target Organs and Organs of Major Concern, e.g.,

Brain	Lungs
Heart	Mammary Gland
Kidneys	Spleen
Liver	Stomach

. Tissue Blocks

Preparation procedure
Preservation
Inventory records - by test animal number

2.4 Audit Plan III

This plan was designed on the basis of findings evolving from the general assessment and review of research documents and materials conducted on February 20, 1978.

The results of the general assessment survey conducted during the morning of February 20, 1978 showed clearly that Plan III would have to be used. Detailed audits based on the original necropsy/histopathology sheets for each control and test animal would have to be conducted and the tissues histopathologically read and/or retained for each test animal would have to be recorded on master audit sheets showing each of the possible 38 organs of each test animal from which tissues reportedly had either been taken, or for which histologic slides had been prepared, or from which wet tissues had been preserved.

The organization of this audit plan is as follows:

Team 1- Histopathology

Audit Team 1, Members

Dr. W. M. Busey
Dr. G. K. Hatfield
Drs. D. J. Sullivan and M. Vlaovic and members of the IBT histopathology and necropsy staffs

Areas Audited and Work Performed by Audit Team 1

. Inventory of tissues examined microscopically

Audit Team 3, Members

Dr. Z. G. Bell
Dr. C. D. Kary
Dr. D. J. Sullivan, Dr. M. Vlaovic,
Mr. W. J. Koretke, Ms. I. Te Vault,
and members of IBT staff

Areas Audited and Work Performed by Audit Team 3, Test Animals - Hamsters

The areas audited and investigations conducted by Audit Team 3 are covered by the descriptive work titles shown under this comparable section under Audit Team 2.

Audit Team 4, Members

Dr. T. R. Torkelson
Mr. J. T. Seawell
Dr. D. J. Sullivan, Dr. M. Vlaovic,
Mr. W. J. Koretke, Ms. I. Te Vault,
and members of IBT staff

Areas Audited and Work Performed by Audit Team 4, Test Animals - Rats

The areas audited and the investigations performed by Audit Team 4 are covered by the descriptive work titles shown under this comparable section under Audit Team 2. However, Audit Team 4 reviewed all research entries under "Gross Pathological Observations" and "Histological Observations" for Controls, Test Group I, II, III, and IV. The fourth test group for this species of test animal was included in this exposure series to enable comparison with animals subjected to comparable test conditions in the laboratories of Dr. Cesare Maltoni.

Test Group 4 audited gross and histopathological data for 900 test animals, 38 organs per animal, or a total of 34,200 organ

3.1 Phase I - An Inventory of All Wet Tissues, Tissues in Blocks, and Histologic Slides

The Task Group was unanimous in its recommendation that IBT complete the following at the earliest possible time:

1. A complete inventory is to be made of:

   A. All wet tissues in preservative in plastic containers are to be inventoried by opening each container and specifically identifying all tissues present.

   B. All tissues in blocks with specific identification of each tissue therein.

   C. All histologic slides with a complete identification and listing of each tissue for each animal.

   D. A histopathology sheet is to be used for recording all entries evolving from inventories under A., B., C. above.

   E. Summary sheets similar to those developed by the Audit Task Group, i.e., 50 animals per sheet/38 organs per animal, are to be used when preparing data summaries.

2. Arrange in order all animals as to the days on test at death by:

   A. Species

   B. Group

   C. Exposure level

   D. Sex

   E. Animal numbers

Item 2 - At this stage, the IBT pathologist and members of the Audit Task Group will proceed according to Phase 1, Step 4 (of section 3.1) described above.

3.3 Procedure to Govern Reading of Histologic Slides

Only one pathologist should be assigned tissue examinations. By no means should different pathologists histologically examine animal tissues from the same species. Further, IBT should use a consistent code of findings when summarizing histopathologic data.

4.0 Concluding Comment by Dr. John H. Mennear, Technical Director, IBT, Decatur

Dr. Mennear stated that he fully recognized the importance of this study and concluded by saying that he wanted to get it completed as promptly as possible.

J. T. Seawell
Project Manager
Vinyl Chloride Research

JTS:ec
Record Subject to Approval
March 31, 1978