

CHEMICALS
RESEARCH
MAY 29 1979

Chemical Manufacturers Association

Record of Meeting

VINYL CHLORIDE AUDIT TASK GROUP

Experimental Pathology
Laboratories, Inc.

Herndon, Virginia

May 1-2, 1979

FR _____
OCK _____
ALL _____
DJR _____
CMS _____
WRBe _____
ATCL _____
LM _____

Dr. Z. G. Bell, Chairman, presided and opened the meeting at 3:40 p.m. The following members and guests were present:

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
V. L. Kirkland ^a .	Shell Oil Company
T. R. Torkelson	The Dow Chemical Company
J. T. Seawell	CMA Staff

a. for C. D. Kary

PRESENT BY INVITATION

W. M. Busey	Experimental Pathology Laboratories, Inc.
-------------	---

1.0 Assessment of Available Audit Data

The phase of this meeting was concerned with the evaluation of the audit data acquired to date to include data from the on-site audit session of February 19-24, 1978, the tissue inventory completed by Industrial BIO-TEST Laboratories, Inc. (IBT), and the "VINYL CHLORIDE PATHOLOGY REPORT" prepared by Experimental Pathology Laboratories (EPL). As a result of these data assessments, it was apparent that any possible additional histopathologic work would be contingent upon a complete accountability study based on the following three data categories:

14, 16, 19

DTH 000013189

- a) Total number of tissues to be saved by IBT for histopathologic study as required by the protocol,
- b) Total number of tissues examined by IBT pathologists, and
- c) Total tissues saved by IBT personnel.

2.0 Initial Observations of the Vinyl Chloride Audit Task Group. (VC-ATG) Based on Data Evaluations

The following observations were made by the VC-ATG after its evaluation of the audit and inventory data available at the beginning of this audit session:

- a) Personnel responsible for the conduct of this study are no longer with the contractor's organization and we have been informed that the organization itself will cease to exist as of January 15, 1979. This precludes verbal reconstruction of certain critical test parameters, procedures, and records.
- b) Important records which have not been audited to date include:
 - 1. Animal purchase orders
 - 2. Shipping and receiving records
 - 3. Analytical records of exposure chamber concentrations
 - 4. Randomization of test animals
 - 5. Animal weight and survival records
 - 6. Records of health, behavior, and other observations
 - 7. Logbooks

It appeared to the ATG that there was little value in auditing the documents cited above unless there were adequate pathologic materials and records available which would enable arrival at scientific valid conclusions as to tumor incidence and to dose response relationships. Therefore, as a first step, the ATG choose to concern itself with a partial audit of existing tissues, slides, blocks and records of gross and histopathologic examinations.

3.0 Tissue Accountability Study

As in the initial audit sessions, it was necessary for the ATG to divide into teams in order to cover all organs required by

the protocol for all three test animals and all test groups. Each audit section prepared an audit/tissue recapitulation based on the original tissues as stipulated in the protocol, the tissues actually examined by IBT pathologists, and total tissues saved in the form of wet tissues, tissue blocks, or slides.

Evolving from the May 1-2 audit is the following accountability summary of total tissues saved:

TOTAL TISSUES SAVED

<u>Test Animals</u>	<u>Tests Groups</u>									
	<u>UC</u>		<u>T1</u>		<u>T2</u>		<u>T3</u>		<u>T4</u>	
	<u>Total</u>	<u>%</u>	<u>Total</u>	<u>%</u>	<u>Total</u>	<u>%</u>	<u>Total</u>	<u>%</u>	<u>Total</u>	<u>%</u>
<u>Males</u>										
Rats	998	24.9	930	23.3	1061	26.5	1106	27.7	-	-
Mice	497	12.0	548	13.7	739	16.0	766	19.0	-	-
Hamsters	511	12.8	485	12.1	743	18.5	761	19.0	-	-
<u>Females</u>										
Rats	1263	32.4	853	21.9	908	23.3	970	24.9	856	21.1
Mice	402	10.0	599	15.0	942	24.0	910	23.3	-	-
Hamsters	372	9.5	406	10.0	677	17.4	454	11.4	-	-

As may be observed in the foregoing tabular studies, total tissues saved ranged from a low of 9.5% to a "high" 32.4% in any given test group. The high is 62.6% below the generally recognized minimum acceptable level.

4.0 Opinions of the VC-ATG Concerning Conduct of Study

It is the opinion of the ATG that the technical conduct of this study has been grossly deficient as indicated by the following list of partial observations:

- 1) IBT failed to save most tissues as specified in the protocol.
- 2) IBT failed to conduct histopathologic examinations of many of the tissues that were saved.
- 3) Even though all currently available (according to the IBT conducted inventory) tissues were to be examined, the number would be grossly inadequate to complete the objective of the study.
- 4) Failure to examine sufficient organs from sacrificed animals.

As an example of observation 4) presented above, of 42 male rats in the top dose level (exposure concentration of 2,500 ppm) surviving at the end of one year exposure period, only brains from nine animals were saved for histopathologic examination. Of these, only four were worked up into microscopic slides and examined. Hence, 90 per cent of the brains of those animals surviving to the most critical period were never examined.

The Task Group concluded its auditing sessions with the following recommendation which carried unanimously:

We recommend that CMA proceed with the necessary steps to have IBT rerun the entire study or refund all funds paid to IBT by CMA under the research agreement on vinyl chloride.

The ATG AGREED:

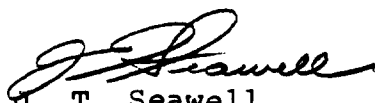
That in arriving at the recorded recommendation the ATG had in large measure been guided by the report entitled "VINYL CHLORIDE PATHOLOGY REPORT", dated January 9, 1979, prepared by William M. Busey, D.V.M., Ph.D. of Experimental Pathology Laboratories, Inc.

The ATG further AGREED:

That it concurs with Dr. Busey's recommendations as presented on pages 5 through 8 of the above-mentioned report.

The Task Group recommended that the Project Administrator write the complete final report of the Vinyl Chloride Audit Task Group. Among other important documentations, the following components are to form integral parts of the final report:

- 1) An appropriate summary of the study protocol.
- 2) Typed copies of all audit work sheets evolving from the studies of the four audit teams conducted on May 1-2, 1979.
- 3) A total tissue accountability summary to include:
 - a. Tissues required by the protocol
 - b. Tissues examined by IBT pathologist(s)
 - c. Total tissues available according to the IBT inventory completed at the request of the VC-ATG.
- 4) The report entitled "VINYL CHLORIDE PATHOLOGY REPORT", dated January 9, 1979, prepared by William M. Busey, D.V.M., Ph.D. of Experimental Pathology Laboratories, Inc.



J. T. Seawell
Project Administrator
Vinyl Chloride Research

JTS:pmt
Record Subject to Approval
May 23, 1979