PROJECT STATUS: MANUSCRIPT #1

Re-Evaluation of Benzene Exposure in Pliofilm Manufacture

- "Final" draft completed October 23, 1990
- Received comments on draft from Drs. Crump and Goldstein
- Hanning, Allman, Osborne interviews

IMPLICATIONS OF THE HANNING INTERVIEW

- Solvent recovery *always* used in Pliofilm manufacturing
  - made process economically feasible
  - 93% effective
- During WWII Pliofilm casting units at St. Marys converted to production of tent fabric
  - No benzene used unless scrap Pliofilm available

IMPLICATIONS OF THE HANNING INTERVIEW (cont'd)

- Masks provided to workers and required in areas where benzene was used
  - Filters on masks changed regularly
  - Workers often failed to use masks
- Casting operations were separate from other Pliofilm operations.

  Therefore, general emissions from casting operations *can not* be used to estimate exposures to other workers
- Dermal contact was appreciable

IMPLICATIONS OF THE HANNING INTERVIEW (cont'd)

- St. Marys monitored blood *monthly* while Akron monitored blood *quarterly*

- Air monitoring was done to prevent explosions, *not* for health reasons

- Much of Wilson testimony *may* have applied to other processes at Goodyear

- Kipen data appears consistent with the lack of Pliofilm manufacture at St. Marys (1942-1945)

IMPLICATIONS OF THE OSBORNE/ALLMAN INTERVIEWS

- Mixer, reactor, and neutralizer tanks vented to scrubber
  - Not on Risky diagram
- Open trough used to transport rubber hydrochloride from reactor to neutralizer
  - Exact years unknown
- Workers supplied with rubber gloves (which may not have been effective)
- General room dimensions (assists with mass balance calculations)

PHASE II

Re-Evaluation of Benzene Exposure in Pliofilm Manufacture

- New approach: time-and-motion study to quantify uptake during peak exposure periods
- Baseline exposures calculated; peak exposures in progress
- Differences between us and Crump & Allen: 1.5 x C&A; all else the same
- Conduct sensitivity analysis of linear and other models
- Funding: $113,000 spent to date
- Expected timetable: Draft revised document by March 30; Perhaps, revision needed by time of ACGIH meeting

PROJECT STATUS: MANUSCRIPT #2

Benzene-Induced Leukemia: An Examination of Disease Endpoints

- First draft of manuscript submitted October 24, 1990
- Some comments received; paper considered "not compelling"
- Detailed outline written for second draft

PROJECT STATUS (cont'd)

Benzene-Induced Leukemia: An Examination of Disease Endpoints

- Our case may not be sufficiently strong to be useful; however, choosing AML or AML + CML may not make much difference
- Awaiting further review and direction from Task Force
- Funding: $54,000 spent to date
- Timetable: Second draft will be completed 2 weeks after conference call; draft by March 1st is likely

PROJECT STATUS: MANUSCRIPT #3

Re-Analysis of the Pliofilm Cohort Using Linear and Linear-Quadratic Models

- Contract in-place with Clement International
- Awaiting development of revised Pliofilm exposure estimates
- Budget: $78,000. No expenditures to date.

SUMMARY OF DELIVERABLES/ACCOMPLISHMENTS

February 12, 1991

- Completed much of learning curve by October 1st
- Updated toxicology, industrial hygiene, and exposure information on 1940s-1960s benzene levels
- Re-examined Akron Library, Silverman Library, Industrial Health Foundation Library
- Met with Goodyear executives
- Met with Pliofilm employees
- Completed draft of publishable exposure manuscript by October 23rd
- Completed draft of unpublishable "endpoints" paper by October 24th

NECESSARY IMMEDIATE WORK

- Re-interview Hanning
- Interview Pliofilm nurse
- Interview Sakol (Akron physician) contacts
- Draw-up Pliofilm building plans (plan and overhead view)
- Look at old drawings of process
- Conduct sensitivity analysis of the "responsiveness" of the three models to changes in exposure data

POSSIBLE LONG-TERM PROJECTS

- MVK model
- Upgrade PB-PK model
- Evaluate update of Rinsky cohort
- Conduct meta-analysis of Pliofilm, Ott, Wong, etc.

POSSIBLE 1991 TASKS FOR ChemRisk INVOLVING BENZENE

February 12, 1991

Dennis J. Paustenbach, Ph.D.
Jim Jernigan, Ph.D.

Presented to the API/WSPA Benzene Task Force

POSSIBLE 1991 BENZENE PROJECTS

Task 1.0 An Evaluation of Epidemiological Studies Used to Assess the Risk of Benzene-Induced Leukemia

Task 2.0 Justification for Using the Linear-Quadratic Model for Dose-Response Extrapolation of Benzene Risk

Task 3.0 Evaluation of the Congruence of the Human Epidemiological Data with the CDHS Animal-Based *Upper* Bound Unit Risk for Inhaled Benzene

Task 4.0 Assessment of Leukemia Risk Using the MVK Model

Task 5.0 Evaluation of the Congruence of the Human Epidemiological Data with the CDHS Animal-Based *Lower* Bound Unit Risk for Inhaled Benzene

Task 6.0 Comparison of Extrapolation Models for Benzene-Induced Leukemia

Task 1.0 An Evaluation of Epidemiological Studies Used to Assess the Risk of Benzene-Induced Leukemia

Objective: Demonstrate that the Pliofilm cohort provides the most scientifically valid and precise exposure-response data for use in extrapolation modeling.

- Review and re-package Clement (1988, 1989) arguments
- Review and outline Brett et al. (1989) arguments
- Review Ott et al. (1978), Wong (1983, 1987)
- Write manuscript for journal
- Revise manuscript as suggested by journal

Estimated cost: $ 39,609

Schedule:		
	Start:	March 1, 1991
	First draft:	6 weeks after authorization
	Revised draft:	4 weeks after first draft
	Submission to journal:	As early as June 15, 1991

Task 2.0 Justification for Using the Linear-Quadratic Model for Dose-Response Extrapolation of Benzene Risk

Objective: Present evidence that a linear-quadratic model is the most valid approach for assessing the leukemia risks for the Pliofilm cohort.

- Review and re-package Clement (1988, 1989) arguments
- Review and outline Georgetown document
- Review and outline applicable sections of BIER V (1990)
- Use PB-PK data developed by Travis to pick the "break-point" on dose-response curve where it will change from quadratic to linear
- Write manuscript; present and justify each of the Clement/Georgetown recommendations
- Revise manuscript as suggested by journal

Estimated Cost: $ 48,365

Schedule:

Start:	April 5, 1991
First Draft:	6 weeks after authorization
Revised Draft:	10 days after receipt of comments
Submission to journal:	July 1, 1991 (earliest possible submission)

Task 3.0 Evaluation of the Congruence of the Human Epidemiological Data with the CDHS Animal-Based *Upper* Bound Unit Risk for Inhaled Benzene

Objective: Evaluate whether the CDHS approach is unrealistic. Determine whether the number of cancer deaths predicted by the CDHS approach is substantially higher or lower than the number observed in Pliofilm workers.

- Review and outline Clement (1990) arguments
- Write manuscript
- Revise manuscript in response to comments

Estimated cost: $ 39,041

Schedule:

Start:	March 15, 1991
First draft:	6 weeks after authorization
Revised draft:	10 days after receipt of comments
Submission to journal:	July 14, 1991 (earliest possible submission)

Task 4.0 Assessment of Leukemia Risk Using the MVK Model

Objective: Make a "first-cut" attempt in developing a cancer potency estimate using default assumptions in the MVK model and conduct a sensitivity analysis to "bracket" the data

- Assign values to the parameters b_1, b_2, b_3, b_4; provide justification for the values chosen
- Subcontract with Dr. Max Layard or Dr. Rory Connollt to evaluate the model
- Write the manuscript
- Revise the manuscript in response to comments

Estimated Cost: $ 52,244

Schedule:

Start:	August 1, 1991
First draft:	6 weeks after authorization
Revised draft:	4 weeks after first draft
Submission to journal:	Nov. 24, 1991 (earliest possible submission)

Task 5.0 Evaluation of the Congruence of the Human Epidemiological Data with the CDHS Animal-Based *Lower* Bound Unit Risk for Inhaled Benzene

Objective: Evaluate whether the CDHS approach is unrealistic. Determine whether the number of cancer deaths predicted by the CDHS approach is substantially higher or lower than the number observed in Pliofilm workers.

- Review and outline Clement arguments
- Write manuscript
- Revise manuscript in response to comments

Estimated cost: $ 40,080

Schedule:

Start:	August 16, 1991
First draft:	5 weeks after authorization
Revised draft:	10 days after receipt of comments
Submission to journal:	November 20, 1991 (earliest possible submission)

Task 6.0 A Comparison of Extrapolation Models for Benzene-Induced Leukemia

Objective: Review the evidence for using each of the following models for various leukemogenic risks posed by benzene exposure: conditional logistic regression, linear, MVK, quadratic, linear-quadratic

- Understand each model
- Evaluate fit in observable range
- Evaluate "responsiveness" to small changes in the data
- Evaluate biologic underpinnings of each model

Estimated cost: $ 43,445

Schedule:

Start:	November 15, 1991
First Draft:	6 weeks after authorization
Revised Draft:	14 days after receipt of comments
Submission to journal:	February 20, 1992 (earliest possible submission)