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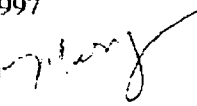
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American Petroleum Institute
1220 L Street, Northwest
Washington, D.C. 20005



memo

Date: October 2, 1997
From: Mary Paxton 
To: Benzene Task Force (BTF)
Benzene Basic Research Work Group (BBRWG)
Re: Update and Action Items from October 1 Meeting

Attached is an updated version of our issues table containing information presented at yesterday's meeting of the BTF and action items agreed upon.

For those of you who were not there yesterday, I need to inform you that I will be leaving API at the end of October. It has been a pleasure working with you.

PROJECTS AND ISSUES OF
API'S BENZENE TASK FORCE
(October 2, 1997)

Issue	Contracts	Projects/Schedule/ Status	Action Items (from 10/1/97)
Mechanism of Benzene Induced Leukemia	Richard Irons (Wayne Stillman, David Ross) University of Colorado (\$200K + \$150K,	Validation experiment on CP colony forming units successful in showing qualitative accuracy of BBRA predictions. Nature of flow cytometry subgroups. BTF comments conveyed on manuscript about diagnostic value of MPO activity for leukemia type. Stipulations for rest of 1997 money: - Start characterizing metabolism in B-cells, with emphasis on biological significance; - Start investigation of differences in metabolism & sensitivity between non-smokers & smokers; - Request quarterly reports & encourage publication. 9/30 quarterly report due	PB/MBP: convey that not report on smokers project expected 12/97 [done] clear up contract/grant issues for 1998 [ok for 1997]
Biologically-Based Risk Assessment (BBRA) Model	Tony Cox Cox Associates (\$64K from 1996; \$60K for 1997 being processed)	1996-7 projects: - Genotoxicity module; - Analysis of data from validation experiment underway; - Draft manuscript on validation of BBRA. 1997-8 projects: - Prepare for and participate in CP BBRA review WS - Convert BBRA from I-Think to Excel - Add Irons mechanism for enrichment of proliferating population to BBRA model - Convert CP model to benzene, with PBPK and cytogenetics modules - Do "model reduction" on BZ model to make its conclusions maximally robust	[remaining from 7/15] Encourage clinical validation. Chuck Ross [to NASA]: Plan symposium at ACEOM for corporate physicians [pass responsibility to someone else?]

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Peer-review WS on CP Version of BBRA	(\$17K available for travel, meeting expenses, etc.) \$4K to each of 3 non-govt main reviewers; minimal expenses for other invitees	Provide computer model and documentation to half dozen modelers; Workshop with Cox, reviewers, and other relevant parties. Cox converting BBRA to Excel; Rm 1200 reserved 12/11(day after SRA meetings in DC); Availability of key reviewers checked in late August.	TC: Write up CP BBRA + convert to Excel to share with other modelers. MBP: Make arrangements for 12/11. [12/11 now looking like problem for some of main reviewers - delay to early 1998?]
Metabolism	Rogene Henderson (Bill Bechtold) ITRI (\$126K balance from 1996)	Baldwin audit in August; method development slow, but on track; 2-dimensional re-established end of Sept; adjusting valve temperatures for optimal recovery; Generate standard curves by mid-October; Finalize protocol for exposures Exposure at ~60 ppm Exposure at ~ 6 ppm, with completion by October 1997	Monitor progress regularly (biweekly conference calls) Judy Baldwin audit in conjunction with CMA BD visit. [done although not to pt. of standard curves] Schedule site visit to OK protocol for animal study (November?)
Genotoxicity	Gary Williams (John Whysner) American Health Foundation (\$92K)	Contract signed in June. 7/29 Table of DNA adduct studies received. 9/24 Narrative on studies received (circulated for comparison to Reddy's paper for EPA comments) 10/31 Phase I draft due Review of genotoxicity literature on benzene (a) Phase I: DNA reactivity and adduct formation Literature search for all metabolites initiated (b) Phase II: Mutagenicity and clastogenicity endpoints	MBP: Clarify that they do intend to cover more than ³² P results in task on DNA binding of BZ + metabolites; give them Reddy's paper. [done]
	Gino Scarano ILSI (\$36K from 1995)	Benzene case study (along with BD and VC) of how non-tumor data could/should be used in cancer risk assessment. Benzene team (Martyn Smith, Rich Irons, and Ray Tice) to deliver draft report on Oct. 6, but unlikely any of case studies will be on schedule. ILSI will share draft with API when complete and plans to hold workshop to which API representatives would be invited.	MBP: Get timeline for work. Will there be workshop on case studies? [done]

Exposure of Pliofilm Cohort	Dennis Paustenbach (Paul Price) ChemRisk (\$12.5K legs/regs)	Outline for paper received. (ChemRisk has decided to undertake a more comprehensive Monte Carlo analysis, covering expenses above contract amount themselves.) 9/16 DP leaving ChemRisk at end '97, but will be involved in project through completion; Price says they're progressing all right.	
Update of Pliofilm Cohort	Otto Wong	Wong interested in updating mortality status for 10 years since 1987	MBP: Do we have access to cohort file in form with identifiers that could be linked to death certificates?
Chinese Epidemiology Study	Otto Wong Applied Health Sciences, Inc. (\$25K)	July 1997 JNCI publication on NCI study supports benzene associated with neoplasms other than AML, but still no risk estimates. Question: (1) accuracy of case diagnosis, (2) how low benzene exposure estimates; (3) whether confounding exposures. Proposal received from Wong and being processed. Monitor work of Qu / Chen of NYU for HEI to validate biomarkers in separate Chinese study as potential challenge to NCI expo ests.	RS: Within 2 weeks, compile list of questions + thoughts for GR to convey to Wong. Ask NCI researcher to next BTF meeting in early 1998 when Wong has framed initial questions.
Compilation of Benzene Monitoring Levels	DynCorp with oversight by IHTF	Report received documenting derivation and contents of database with appendices presenting analyses requested by IHTF; acceptability as final version will be determined at July 15 BTF meeting. Delivery of electronic database expected shortly for use by BTF members. BTF final wishes conveyed to DynCorp at end of August; final report expected beginning of October.	AJ: Have DynCorp correct text with max/min problem & provide BTF epidemiologists with electronic form of database for approval.
JHU WS on Use of Epi Data in Development of Public Health Policy	API via PM-RTS (\$10K if H&PS reprograms 10/29)	Six cases studies include PM NAAQS. 9/29 API EpiTF endorses.	
Workshop on Benzene Research Strategy		Similar to Airlie WS, Fall 1992. Aim for Summer 1998. 8/5: GG talked with Krewski; with current budget priorities couldn't sponsor in next year, but representative would attend.	CH: feel out EPA about possibly cofunding. [7/17] MBP: get list of API trained facilitators; unearth materials from 1992 WS.

European Community		Summary prepared for CONCAWE by EBSI delivered to German rapporteur in May 1996. Adapted risk assessment received by EBSI at end of September 1997, with more attention to animal tox (less to epi) and concluding that "risk reduction needed." EBSI meeting with German group in mid-Nov.	RS: provide MBP with diskette of health effects for distribution to BTF. All: comments to RS for EBSI's Nov. meeting.
U.S. EPA AEGLs - Priority Chemicals List		May 21, 1997, <i>Federal Register</i> notice that benzene among 85 chemicals on priority list for determination of acute exposure guideline (AEGL); request for data or other info.	[drop item?]
U.S. EPA Re-evaluation of potency factor	Julian Preston (\$4.5K) Vijay Reddy (\$3K)	June 30, 1997, <i>Federal Register</i> notice of release for external review of NCEA's revision of EPA's 1985 potency factor as requested by Office of Mobile Source in conjunction with CAAA in 1992. External Review Panel named (Rob Schnatter one of six members) met July 16. API submitted written comments August 29, with attachments by Vijay Reddy and Julian Preston on relative sensitivity of DNA-adduct techniques and non-linearities associated with genotoxic endpoints other than point mutation, respectively.	CH: call Sonawane for update. MBP: get comments submitted to docket.
U.S. EPA Eastmond report		9/24 JV inadvertently found May 1997 EPA document by Eastmond addressing nature of hematopoietic tumors produced by various classes of agents (including BZ) + relevance of rodent models to human response. Why not considered in potency review? 10/2 Document pulled from EPA Website.	MBP: review? by Irons? [10/2 Irons interested; sent to him when he couldn't get from Web]
California		WSPA requesting review from CARB; OEHA then makes decision whether to do review 9/97 OEHHA released draft document on BZ's potential as a DART (reproductive and developmental toxicant under Prop 65); recommend listing as repro (but not devel) - indicates regulatory level higher than that for cancer; WSPA will handle any response.	