American Petroleum Institute
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TO: Toxicology Committee

FROM: Mark S. Swanson/Edward M. Vernot

DATE: September 9, 1987

SUBJECT: Minutes of the October 28-30, 1986 Toxicology Committee Meeting

The minutes of the October Toxicology Committee Meetings of last year are enclosed.

API Annual Health and Environmental Meeting
Toxicology Group
S.C. Lewis, Ph.D.
Chairman

Intercontental Hotel
Houston, Texas

October 28-29-30, 1986

Members Present

W. D. Broddle
P. H. Craig
P. Garvin
G. C. Granville
T. H. Keenan
M. L. Lakin
S. Lovre
C. Parker
R. Roth
S. L. Schmitt
C. A. Schreiner
C. Skisak
F. B. Thomas

Others Present

F. F. Aurelius
B. Ballanfant
P. W. Beatty
D. Z. Bradfield
M. Butler
R. J. Capion
C. E. Cummings
K. Dillie
T. Donaugh
J. Doyle
B. Duchie
M. J. Duffy
A. A. Elfarra
M. W. First
L. Golberg
R. Hanson
C. Herrin
D. R. Hitchcock
R. Joyner
B. N. Kightlinger
W. J. Koehl
J. Levine
C. D. Perna
E. Rodriquez
C. S. Ryan
R. C. Russell
R. A. Scala
T. R. Scovel
J. Sepesi
D. E. Strothers
J. Yermatoff

API Staff Present

R. T. Drew
C. E. Holdsworth
S. H. Kneiss
R. P. Strieter
M. S. Swanson
S. M. Swanson
E. H. Vernot

28 October 1986 - 1:30 - 5:00 P.M.

S. Lewis asked for discussion items from this morning's issue meetings. B. Ballanfant said that the overview of benzene toxicology given by B. Thomas was interesting to him because of the stages in the myeloproliferative syndrome which could be associated with specific chromosomal changes. Chromosomal mapping might address the relationship between acute myleogenous leukemia and benzene exposure.

Florida Rule on Benzene in Groundwater

W. Duchie explained the approach which had been taken by the Florida Petroleum Council to respond to the Florida Regulation on benzene in groundwater.

The report concluded that the Florida standard of 1 ppb is overly conservative and that human benzene intake resulting from 25-30 ppb would be insignificant compared to that from other sources of benzene.

P. Craig emphasized that before chronic drinking water studies were performed, it would be important to identify the active metabolite(s), and investigate the pharmacokinetics of benzene in the mammalian system. The changes in metabolism, distribution and elimination as functions of dose would require description before credible risk assessment could be performed.

B. Thomas noted that carcinogenicity was not the only endpoint in benzene toxicology. For instance, effects on the immune system were also important. He also observed that intermittent exposures were more effective than continuous in eliciting benzene toxicity and carcinogenicity. This made understanding the pharmacokinetics even more important in selection of dosing regimens.

L. Golberg commented that if other endpoints than carcinogenicity were selected, a 2-year study might not be necessary. One ought to be able to learn if dose-rate is a significant element in bone marrow toxicity.

B. Ballanfant observed that it might be possible to do chromosomal analyses during such a study.

C. DiPerna inquired whether redirection of the proposed drinking water study to accentuate metabolism and pharmacokinetics might be advantageous. He also suggested that analyses similar to that done in Florida might be useful in future rule-making situations.

1987 Projects

S. Lewis noted that the agenda for 1987-88 programs had been planned and approved. An important charge was to react to regulatory or other needs with consultation support. The toxicology committee is satisfied that the projects are in strong condition as indicated in the project status reports which have been distributed. Reprogramming funds were transferred into PS-62, methods development, to validate short-term initiation/promoting testing, leading to economies of scale in an expanded program.

IARC Monographs

IARC is developing monographs on crude oil, gasoline, diesel fuel, heating fuel and occupational expsoures in refining. These are scheduled for completion in March, 1988. In order to aid CONCAWE in providing information to IARC, an ad hoc group chaired by R. Scala has been formed to expedite getting unpublished API and industry data into peer-reviewed literature.

Benzene Pilot Study

Concerning the benzene in drinking water pilot study, the PS-7 Task Force should be charged with deciding whether a change of direction to emphasize pharmacokinetics is beneficial. If a change of direction is approved, HEGC will be informed, and the change should be formalized in a letter from B. Thomas to S. Lewis and R. Drew. B. Thomas stated that an approach could be scheduled at a Task Force meeting late this year or early next year. He asked what the schedule was for developing '88 proposals.

S. Lewis replied that HEGC will give guidance of funding for benzene issues in November. He thought that B. Thomas might consider what directions in research appeared most productive.

29 October 1986 - 3:30 - 5:00 P.M.

Opening Remarks S. Lewis opened the meeting with a summary of the status of the Toxicology Committee budget for 1986. As of October, 1.41 million of the approved 1.5 million 1986 budget has been committed. An additional 117k has been reprogrammed into the Initiation/promotion Short-term Dermal Bioassay project (PS-62) to increase from 5 to 10 the number of samples to tested in this project. This reprogramming will allow greater economy of scale as well as allowing this project to achieve its goals in the absence of 1987 funds. For the status of other ongoing projects committee members were referred to the progress reports.

IARC Monographs It was announced that IARC will be gathering information for the development of Monographs on petroleum materials for 1988. Plans include the development of separate monographs for materials including crude oil, gasoline, jet fuel, fuel oil, and diesel fuel, along with a monograph on occupational exposure (refining). For the most part, IARC will be considering only articles and reports from peer reviewed literature. The need to get both API and industry research into the appropriate literature was emphasized. An ad hoc committee has been formed to facilitate publication of API/industry reports. One method being planned is to hold a symposium to expedite this process.

Mogas

Refueling Rules

J. Levine - although new refueling controls were planned for ozone reduction, EPA has introduced the issue of cancer risks into the subject, estimating a decrease of 55 cancer deaths (from 77 to 22) per year due to gasoline exposure by the change from stage II to on-board refueling canisters.

S. Kneiss noted that new epidemiological information may influence API's position on gasoline.

Possible Research Directions, 0-145°C Sample

S Lewis commented that R. Scala has submitted a proposal to R. Drew to consider new research, specifically a chronic bioassay using the 0-145°C fraction of gasoline. J. Levine gave the following reasons for carrying out this study:

1. This is a data gap in assessing exposure effects.
2. 0-145°C sample is a better surrogate for actual exposures than gasoline samples.
3. Light ends are less carcinogenic than whole gasoline

S. Lewis said that the reasons for doing the study were probably more regulatory than scientific.

J. MacGregor stated that assessing dermal exposure as part of the total exposure at the pump was important.

S Lewis said that the ICMG should consider the issue with specific attention to:

1. Suitability of 0-145°C sample.
2. Relevance from regulatory and litigative standpoints.
3. Importance of dermal exposure.
4. Implications and impact of study results (positive, negative etc.)

Male Rat Kidney - CIIT Work

P. Craig introduced the subject of CIIT work on kidney effects of gasoline components. This is of high scientific quality and impressive to EPA.

It was noted that funding for the CIIT work was not included in the '87 budget.

S. Lewis commented that CIIT would carry on work on male rat nephropathy. However, in the absence of funding from API, they would probably choose non-petroleum-related compounds to work with. He suggested that ICMG consider the CIIT work in prioritizing programs. Susan Schmitt is the person to contact on status of CIIT work.

Reproduction Study

S. Lewis brought up the proposed reproduction study using the 0-145°C fraction as a sample.

J. MacGregor stated that industry should address the gap in information on reproductive toxicology.

S. Lewis felt that there was no compelling evidence that gasoline may be a reproductive toxin. Results from repro studies do not indicate effects on reproductive organs. R. Drew said that J. Budny had written a letter recommending that a reproductive study be carried out. R. Drew responded with a letter suggesting taking the request through normal channels. If not approved by HEGC, then independent support could be considered.

RCRA Issues S. Lewis reviewed topics from the RCRA Issues Group Meeting for which toxicology support is needed. Listed below are brief descirptions of these issues and the chairperson or contact for each of the workgroups:

Land Disposal Ban A list of materials identified in waste samples at production sites is being developed by Rocky Mountain. Toxicology support is needed to review this list and identify materials of concern with respect to human health hazard. Potential human health hazards from production sites are important since loss of the current RCRA hazardous waste exclusion could cost the industry 15 billion dollars in capitaol expenditures and another 5 billion dollars annually in operating costs. Chairperson: Harold Yates (Exxon).

Proactive Research on RCRA Reauthorization An ad hoc group chaired by Earl Arp has been formed to develop proactive research proposals to deal with this issue. Specific areas of concern include air emission from land farming and overall exposure at hazardous waste sites. The application of current clean air standards vs 8 hour TLV's to these emissions should be examined. Toxicology support could be useful in answering questions about the health effects potential of specific agents relevant to emissions. Workgroup chair/contacts are Brian Harney (Mobil) and Wayne Kachel (Exxon).

Health Effects Advisory Documents These documents figure prominantly in air and water regulations and initiatives under RCRA. It may be in our interests to challenge them. More are emerging and the need to challenge them will require toxicology support. Chairperson: Colin Grieves (AMOCO).

TCLP's An additional 30 compounds are being added to the list for TCLP's. Help is needed to evaluate the new list for purposes of developing reasonable health-based standards on those relevant to the petroleulm industry. Chairperson: W. Clark, (Texaco).

Unbudgeted 1987 HEAD funds (200 K) are available to handle "regulatory response" for these issues.

30 October 1986 - 1:30 - 3:30

S. Lewis opened the meeting (see prior remarks from 10/28 and 10/29) with a brief status update on the 1986 budget. Members were referred to the Progress Reports for specific details on other projects. The status of the 1987 budget was described as follows: 350 K is allocated for benzene research. Of this, 100 K was for a pilot study on benzene in drinking water for which redirection was suggested during the October 28 meeting in favor of pharmacokinetics. The remaining 1987 budget of 1.2 million is allocated for the C-9 test rule research.

C. Cummings outlined health effects-related needs of the CERCLA issues group. Four basic needs were described as follows:

Listing of Hazardous Substances: The Agency for Toxic Substances and Disease Registry (ATSDR) and EPA must list and develop toxicological profiles on 100 substances in 1987 found most commonly at NPL Superfund sites and posing the most significant potential health threat. If adequate health effects data are not available to profile a substance, ATSDR must assure initiation of a research program to determine health effects under TSCA (section 4) and if necessary, FIFRA. Over the next 3 years 175 additional substances must be identified and profiled. Once listed, ATSDR has 3 years to develop profiles.

Reportable Quantities: Quantities requiring reportable releases will be established for 200 substances. The CERCLA Issues Group will need assistance in the form of health effects concerns for evaluation of these substances in order to set quantities.

Hazard Ranking System: A revised hazard ranking system will be promulgated to rank NPL sites according to relative health hazard. The revised ranking system will take into account the toxicity of substances identified at the site, health effects evaluations of each site (based on qualitative and quantitative assessment of each site, contents, and surrounding community risks). Production sites could be affected by this legislation.

Clean-up Standards for Sites: Cleanups are required to meet Federal and or State environmental laws "where applicable, relevant or appropriate." This includes the Federal Clean Air Act, Solid Waste Disposal Act, Safe Drinking Water Act, Clean Water Act, and TSCA among others. Cleanups must also meet recommended maximum concentration levels (RMCL) under the Safe Drinking Water Act where groundwater is involved. The RMCL's for some substances such as carcinogens are "zero." The RMCL's have already been set for many substances believed to be present in NPL sites but not yet listed. The EPA criteria for classification of carcinogens is similar to IARC. One need pointed out would be to develop a positon on which RMCL's currently interpreted as zero could be changed to a quantifiable levels. Thus the major focus perhaps should be on that of impacting on the policy of establishing and regulating current water standards.

S. Lewis asked that Toxicology Committee assistance be requested in writing from the CERCLA Issues Group when the first listing of substances from NPL sites is published. Upon request, the chairperson of the the Toxicology Committee will then solicit support to help in the selection and evaluation of relevant substances and submission of profiles to EPA. It was mentioned that a new agency has been created to develop these profiles (ATSDR) and that in some cases, insufficient data may trigger test rules under TSCA Section 4. It was also pointed out that the best chance of positive impact on the development of profiles will be to supply data on listed substances prior to the development of profiles by the agency.

Questions were asked about the EPA method of ranking NPL waste sites. C. Cummings stated that the method used by EPA is not complex and can be performed using no more than a desk top calculator. S. Lewis pointed out that the aforementioned regulatory response will be limited to a support and consultant level in view of the level of funds available (1987 Toxicology Committee budget).

TSCA Issues

R. Roth noted that immediate support was needed in C9 and C6 test rule making. If HEGC approves the proactive testing of generic streams, a great deal of routine testing will be required. Also, a new ITC-candidate list will be published soon. Any petroleum-related compounds will be identified to the Toxicology Committee by the TSCA Issues Group.

R. Fensterheim said that EPA should be given information identifying the relevant generic stream for each material designated. R. Roth said that, in view of the CIIT studies of male rat hydrocarbon nephropathy, bioassay studies of generic streams may utilize another species. S. Lewis agreed that there was an ongoing need for elucidation of the male rat kidney effects to clarify induction of cancer in male rats. He suggested that relevant data from CIIT be given to R. Scala who is chairing the ad hoc committee for IARC data communication.

R. Roth introduced the subject of TSCA test guidelines which become available for comment each year. Early input to the agency may correct some methodological deficiencies. We are particularly interested in neurotoxicity and mutagenicity guidelines. S. Lewis said that the Toxicology Committee would coordinate the selection of consultants who can evaluate the guidelines and propose improvements.