On March 27, 1981, I attended a conference of the MTBE study group. The purposes of this meeting were to review the status of the pre-study work for Phase I of the MTBE toxicity studies, review the studies with the third party auditor Tracer-Jitco and to review any protocol changes made to the planned teratology and reproduction studies.

Highlights of the discussion are given below:

**General**

1. ARCO has sent technical material to the laboratory for use in the inhalation studies. Analytical information on the material is available and will be sent out by API.

2. Although not present, Ben Thomas of Shell sent a message that Shell has been involved in the contamination of a township’s drinking water with DPE (disopropyl ether) and 100 ppb MTBE. According to Ben, approximately 20% of all underground gasoline storage tanks leak, leading to the possibility of ground water contamination. This ground water contamination may have to be considered when long term testing is considered. It might also make the NTP rat study of TBA in the drinking water more applicable.

To date, Shell and ARCO are the only ones with MTBE in gasoline.

**Reproduction – Teratology Studies**

A question arose over what supplier to obtain rats from. Bio/dynamics has a history of SDA virus. Charles River’s Kingston facility, the original supplier, is supposedly SDA free. If animals were ordered from Kingston, they were likely to develop SDA symptoms after arrival. The group considered ordering animals from CR’s Portage facility, where animals would already have been exposed to SDA.

The decision was made to stay with Kingston since Bio/dynamics has been getting animals from there for the last nine months and has not experienced any problems. To insure the animals will be SDA-free when the exposure begins, animals will be acclimated for three weeks.
The concentrations of MTBE given in the justification document which were said to produce narcosis were questioned by C. Conaway. I said I would check them.

Details of the study monitoring by Tracer-Jitco will be sent to members by API.

The dates of the reproductive studies depend on when the nine-day probe study is completed.

At my suggestion, a complete water analysis will be done in the middle of the teratology study. This is required by GLP's.

Metabolism Studies

The methods development segment of the metabolism studies is completed. It has been found that the majority of MTBE is eliminated via the lungs within an hour after dosing in the aqueous soluble phase.

Since problems were encountered with hemolysis when MTBE was given I.V., future studies will use the I.P. method of dosing.

Nine-Day Inhalation Study

Prestudy work with the chambers and analytical methods has been completed. The material is being atomized without heating to consistently generate levels of 100, 300, 1000 and 3000 ppm.

Chamber concentrations will be analyzed using I.R. For future studies, an online GC analysis will be available. Analysis will be done automatically every 15 minutes for 100, 300, and 1000 ppm and manually every 4 hour for 1000 ppm.

Bio/dynamics recommends eliminating the charcoal grab samples of chamber concentration. This was accepted by the group since the accuracy of these samples is questionable.

Tracer-Jitco will monitor the study once during early exposures and the day of necropsy. C. Kerwin, of Phillips Oil will also monitor the study during the necropsies.

Mr. Van Dyke of Bio/dynamics raised a point which deserves further consideration. The metabolic studies which have shown most of the MTBE blown off in the first hour have been done in an unsaturated atmosphere. However, all the toxicity studies will be done in atmospheres in which MTBE concentration is quite high, preventing MTBE from being eliminated so rapidly or completely. This may change the pharmacokinetic profile of
MTBE and result in the metabolic studies not giving an accurate profile of MTBE's fate in the air. Mr. Van Dyke felt the group may want to do future metabolic work in an MTBE saturated atmosphere. However, the group felt the planned metabolic studies should be completed before considering Mr. Van Dyke's suggestion.

It would appear that the unsaturated atmosphere in the metabolic studies more closely approximates the atmosphere workers will be exposed to.

Overall, I think the planned MTBE studies are moving along very well. If we could be assured of receiving accurate and regular progress reports from Dr. J. Ridlon, I do not think our presence would be necessary at the group meetings since ARCO seems adequately represented by Dr. Ridlon.

cc: J. A. Budny
RNR: mp