June 12, 2003

Elmer Rauckman, Ph.D., DABT
Consulting Toxicologist
BPPB Consortium
1201 Anise Court
Freeburg, IL 62243

Dear Dr. Rauckman:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for gamma-Butyrolactone posted on the ChemRTK HPV Challenge Program Web site on January 30, 2003. I commend The BPPB Consortium on behalf of the gamma Butyrolactone Consortium for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that The BPPB Consortium on behalf of the gamma Butyrolactone Consortium advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

-*S*-

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: W. Penberthy
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission:
gamma-Butyrolactone

Summary of EPA Comments

The sponsor, the Gamma-Butyrolactone Consortium, submitted a test plan and robust summaries to EPA for gamma-butyrolactone dated December 30, 2002. EPA posted the submission on the ChemRTK HPV Challenge Web site on January 30, 2003. The sponsored substance is gamma-butyrolactone, CAS No. 96-48-0.

EPA has reviewed this submission and has reached the following conclusions:

1. Physicochemical Properties. The data provided by the submitter are adequate for the purposes of the HPV Challenge Program.

2. Environmental Fate. The data provided by the submitter are adequate for the purposes of the HPV Challenge Program.

3. Health Effects. Adequate data were provided for all health effects endpoints for the purposes of the HPV Challenge Program. The submitter needs to include robust summaries for the reproduction organ evaluations from the two NTP repeated-dose toxicity studies.

4. Ecological Effects. Adequate data were provided for aquatic invertebrates and algae. The submitted acute fish toxicity data are inadequate and testing is needed for this endpoint.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA Comments on the gamma-Butyrolactone Challenge Submission

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility)

Adequate data are available for the purposes of the HPV Challenge Program.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity)

Adequate data are available for the purposes of the HPV Challenge Program.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

Adequate data were provided for all health effects endpoints for the purposes of the HPV Challenge Program. The submitter needs to provide separate robust summaries for the evaluation of reproduction organs from the two NTP repeated-dose toxicity studies.

Reproductive Toxicity. Evaluation of reproduction organs from the two NTP repeated-dose toxicity studies adequately address this endpoint. However, the submitter needs to submit this information in reproductive toxicity robust summaries. The submitted summaries for the other two studies do not adequately address the endpoint. Specifically, the study on ovulation by Beattie et al. used a non-standard exposure route

(intraperitoneal injection). Also, an evaluation of testicular effects in rats exposed to the test material in the drinking water study was assigned a reliability code of 4 (not assignable) because of reporting omissions and inconsistencies.

Ecological Effects (fish, invertebrates, and algae)

Fish. The available study is inadequate to satisfy the endpoint and the submitter needs to perform an acute fish toxicity study in accordance with OECD Guideline 203. The study duration of 48 hours is inadequate. The duration should be 96 hours.

Invertebrates and Algae. The data provided for daphnia and green algae are adequate. However, the submitter needs to provide some missing data elements in the robust summary for algae.

Specific Comments on the Robust Summaries

Ecological Effects

Algae. The submitter needs to provide test substance purity and statistical methods used. The submitter also needs to clarify whether the reported 96-hour IC_{50}/IC_{20} values were based upon measured or nominal concentrations.

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.