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TSCA Document Control Office (7407)
EPA East Building, Room 6428
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
1201 Constitution Avenue N.W.
Washington, DC 20460-0001

Attention: TSCA Section 8(e) Coordinator

RE: Hydrotreated C5 – OECD 422 Study in Rats by Inhalation Exposure – Submission of Supplemental Information

Dear Sir or Madam:

On January 30, 2003 the American Chemistry Council Olefins Panel (Panel) submitted a letter on behalf of certain of its members[1] pursuant to Section 8(e) of the Toxic Substances Control Act (TSCA) to inform EPA of preliminary histopathology results from an OECD 422 study that was conducted for Hydrotreated C5 in Sprague Dawley rats. The Panel now has some additional histopathology information from the same study and is submitting it as a supplement to its January 30, 2003 submission.

Hydrotreated C5 was tested pursuant to the Olefins Panel's testing plan for the C5 non-Cyclics Category under the High Production Volume Chemical Challenge Program.[2] The Hydrotreated C5 stream is a hydrotreated hydrocarbon fraction separated from pyrolysis gasoline that consists of substantial concentrations of pentenes, pentanes, and cyclopentene; a low amount of 2-methyl-2-butene (≤ 11%) and isoprene (approximately 2%); and very small amounts of other C5 dienes. CAS Registry numbers that are used by Panel members to identify Hydrotreated C5 streams include: 64742-49-0 (Naphtha, petroleum, hydrotreated light), 68410-97-9 (Distillates, petroleum, light distillate hydrotreating process, low-boiling),

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[1] The sponsor companies are BP Amoco Chemical Company, Chevron Phillips Chemical Company LP, The Dow Chemical Company, Equistar Chemicals, LP, ExxonMobil Chemical Company, The Goodyear Tire & Rubber Company, Huntsman Corporation, NOVA Chemicals Inc. and Shell Chemical Company LP.

[2] The test plan is available at http://www.epa.gov/chemrtk/olefins/olefintp.pdf.

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68602-79-9 (Distillates, petroleum, benzene unit hydrotreated depentanizer overheads), and 68603-00-9 (Distillates, petroleum, thermal cracked naphtha, and gas oil).

Additional histopathology results of the OECD 422 study were reported in a laboratory study update memorandum (attached) that described the results of additional histopathology conducted on the liver, kidney and nasal turbinates for all exposure groups in the study. The previous submission involved the finding of changes in the high dose group nasal turbinates with 3 male and 3 female rats showing minimal to slight atrophy/ disorganization of the olfactory epithelium. The additional findings on nasal turbinates reported here are minimal to slight atrophy/ disorganization of the olfactory epithelium in 3 of 12 female rats exposed to 3,000 ppm Hydrotreated C5. Nasal epithelial changes were observed in a single female exposed to 1,000 ppm Hydrotreated C5; however, this finding was not considered toxicologically significant. The nasal turbinates were also examined from male rats exposed to 3,000 and 1,000 ppm Hydrotreated C5, but no epithelial changes were observed.

A final report is not available at this time but will be forwarded when received from the laboratory.

If you have any questions, please contact me at 301 924 2006 or Elizabeth_Moran@americanchemistry.com.

Yours truly,

Elizabeth J. Moran, Ph.D.
Manager, Olefins Panel

cc: Richard H. Hefter (MC 7403)

MICROSCOPIC PATHOLOGY

Terminal animals

Treatment-related findings

Kidneys

An increase in the incidence, and severity with increasing exposure concentration, of hyaline droplets in cortical tubules was observed in all male rats exposed to Hydrotreated C5 compared to air control animals. In animals of both sexes exposed to Hydrotreated C5, and more so in the males, an increase was noted in both the incidence and severity of basophilic cortical tubules compared to air control animals.

Group		**Male**				**Female**			
Treatment		**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**
		Air	**Hydrotreated C5**			**Air**	**Hydrotreated C5**		
Exposure conc. (ppm)		**0**	**1000**	**3000**	**8500**	**0**	**1000**	**3000**	**8500**
Cortical tubules with hyaline droplets	Total	2	12c	12c	12c	0	0	0	0
	Minimal	2	2	0	0	0	0	0	0
	Slight	0	8	1	0	0	0	0	0
	Moderate	0	2	11	7	0	0	0	0
	Marked	0	0	0	5	0	0	0	0
Cortical tubular basophilia	Total	2	10b	12c	8a	0	0	1	4
	Minimal	2	6	8	7	0	0	1	4
	Slight	0	4	4	1	0	0	0	0
Number of kidneys examined		**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**

a- $p<0.05$; b – $p<0.01$; c - $p<0.001$ with Fisher's Exact Test, on total incidences only

Liver

Minimal centrilobular hepatocyte hypertrophy was observed in the male 8500 ppm Hydrotreated C5 exposure group. Single cases in the male 1000 ppm group and female 3000 ppm group are not considered toxicologically significant.

Group		**Male**				**Female**			
Treatment		**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**
		Air	**Hydrotreated C5**			**Air**	**Hydrotreated C5**		
Exposure conc. (ppm)		**0**	**1000**	**3000**	**8500**	**0**	**1000**	**3000**	**8500**
Hepatocyte hypertrophy, centrilobular	Total	0	1	0	9c	0	0	1	0
	Minimal	0	1	0	9	0	0	1	0
Number of livers examined		**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**

c- $p<0.001$ with Fisher's Exact Test, on total incidences only

Nasal Turbinates

An increase in the incidence and severity of atrophy/disorganisation of the olfactory epithelium was observed in female animals exposed to Hydrotreated C5 at 3000 ppm or 8500 ppm, and in males exposed to 8500 ppm, compared to the air control animals. The single case in a female exposed to 1000 ppm is not considered toxicologically significant.

Group		Male				Female			
Group		**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**
Treatment		**Air**	**Hydrotreated C5**			**Air**	**Hydrotreated C5**		
Exposure conc. (ppm)		**0**	**1000**	**3000**	**8500**	**0**	**1000**	**3000**	**8500**
Olfactory epithelium-atrophy/disorganisation	Total	0	0	0	3	0	1	3	3
	Minimal	0	0	0	1	0	1	1	2
	Slight	0	0	0	2	0	0	2	1
Number of nasal turbinates examined		**12**	**12**	**12**	**12**	**12**	**12**	**12**	**12**

Other Findings

In the spleen, a slightly higher incidence of extramedullary haemopoiesis was recorded in animals exposed to 8500 ppm Hydrotreated C5 compared to air control animals. This is not considered related to treatment because of the natural variation in this physiological feature and the absence of treatment-related effects in the haematological parameters on comparing the groups.

Incidental findings

All other microscopic findings were considered to be incidental and of no toxicological importance.

Conclusion

The following treatment-related changes were observed following inhalation administration of Hydrotreated C5, via whole body exposure once daily for 6 hours.

In the kidney, all male rats exposed to Hydrotreated C5 had renal cortical tubules with hyaline droplets, with an increase in severity with increasing exposure concentration. This finding correlates with the increased bodyweight adjusted kidney weights reported in all the male exposure groups. Basophilic cortical tubules were also increased in incidence and severity in all male exposure groups and the female 3000 ppm and 8500 ppm groups compared to the air control groups.

In the liver, minimal centrilobular hepatocyte hypertrophy was found at a statistically significant incidence in the male 8500 ppm group. This finding correlates with the increased bodyweight adjusted liver weights reported in the male 8500 ppm exposure group. The single cases in the male 1000 ppm group and female 3000 ppm group are not considered toxicologically significant.

In the nasal turbinates, atrophy/disorganisation of the olfactory epithelium was found in several animals in the male 8500 ppm exposure group and in the female 3000 ppm and 8500 ppm exposure groups. Although the incidences had not achieved statistical significance it is considered that they are above background level and the finding is treatment-related in these groups.

A no-effect level was not achieved in males; in females the no-effect level is 1000 ppm.

D J Bell
Pathologist
14 February 2003

S McCormick
Director of Pathology