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CONTAINS NO CBI

RHÔNE-POULENC

FYI-OTS-0692-0851

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June 15, 1992

Federal Express #3346645256

TSCA Document Processing Center (TS-790)
Room 201 East Tower
Attn: Section 8(e) Coordinator
Office of Toxic Substances
U. S. Environmental Protection Agency
401 M Street, SW
Washington, DC 20460

RE: TSCA 8(e) Docket - FYI Notification

Dear Sir or Madam:

Enclosed is a copy of the summary from the draft final NTP reports on Coumarin (CAS No. 91-64-5) and dihydrocoumarin (CAS No. 119-84-6). These reports will be presented at the Peer Review Meeting to be held at RTP on June 23 and 24, 1992.

Rhône-Poulenc is submitting there summaries FYI as we could not determine whether or not EPA had been informed of these studies. The draft final NTP reports will be out next week and EPA can get a copy from NTP or we will be glad to furnish a copy if requested.

Sincerely,

Charles E. Moyer, Jr.
Director, Product Safety

S. Mooney
RECEIVED
7/10/92

CEMjr/rc

Enclosures
REF. 92-069L.EPA

Summary of the 2-Year Carcinogenesis and Genetic Toxicology Studies of Coumarin

Male F344/N Rats	Female F344/N Rats	Male B6C3F$_1$ Mice	Female B6C3F$_1$ Mice
Doses			
0, 25, 50, or 100 mg/kg in corn oil by gavage	0, 25, 50, or 100 mg/kg in corn oil by gavage	0, 50, 100, or 200 mg/kg in corn oil by gavage	0, 50, 100, or 200 mg/kg in corn oil by gavage
Body weights			
Dosed groups lower than controls	High-dose group lower than controls	Dosed groups similar to controls	High-dose group lower than controls
2-Year survival rates			
28/50, 9/50, 2/51, 0/50	29/50, 38/50, 36/50, 30/50	43/50, 47/50, 42/50, 37/51	33/50, 40/50, 42/51, 28/51
Nonneoplastic effects			
Liver: cytologic alterations (0/49, 0/50, 28/51, 29/50); fibrosis (0/49, 3/50, 41/51, 42/50); necrosis (1/49, 13/50, 38/51, 40/50); bile duct hyperplasia severity grades (1.6, 1.8, 2.2, 2.1) Forestomach: ulcer (7/48, 24/50, 35/51, 34/50) Parathyroid gland: hyperplasia (3/41, 20/47, 31/49, 29/47) Nephropathy severity grades (2.0, 3.1, 3.7, 3.6)	Liver: fibrosis (0/50, 0/50, 1/50, 12/50); necrosis (3/50, 3/50, 4/50, 15/50); degeneration (0/50, 0/50, 8/50, 30/50); bile duct hyperplasia severity grades (1.2, 1.3, 1.3, 1.5) Forestomach: ulcer (1/48, 1/49, 6/50, 9/48) Nephropathy severity grades (1.2, 1.4, 1.8, 2.3)	Liver: syncytial alteration (0/50, 6/50, 35/50, 47/51); centrilobular hypertrophy (1/50, 2/50, 23/50, 44/51); eosinophilic focus (6/50, 15/50, 13/50, 15/51)	Liver: syncytial alteration (0/50, 0/49, 2/51, 19/50); centrilobular hypertrophy (0/50, 0/49, 0/51, 17/50); eosinophilic focus (4/50, 20/49, 20/51, 9/50)
Neoplastic effects			
Kidney: renal tubule adenoma (standard evaluation – 1/49, 2/50, 2/51, 1/50); renal tubule adenoma (step section evaluation – 0/49, 4/50, 5/51, 4/50)	Kidney: renal tubule adenoma (standard evaluation – 0/49, 0/50, 0/50, 2/49); renal tubule adenoma (step section evaluation – 0/49, 0/50, 1/50, 1/49)	Lung: alveolar/bronchiolar adenoma (14/50, 8/50, 14/50, 24/51); alveolar/bronchiolar adenoma or carcinoma (combined) (14/50, 9/50, 15/50, 25/51)	Lung: alveolar/bronchiolar adenoma (2/51, 5/49, 7/49, 20/51); alveolar/bronchiolar carcinoma (0/51, 0/49, 0/49, 7/51); alveolar/bronchiolar adenoma or carcinoma (combined) (2/51, 5/49, 7/49, 27/51) Liver: hepatocellular adenoma (8/50, 26/49, 29/51, 12/50)
Uncertain findings			
None	None	Forestomach: squamous cell papilloma (2/50, 8/50, 2/50, 0/51)	Forestomach: squamous cell papilloma (1/52, 5/50, 2/51, 2/51)
Level of evidence of carcinogenic activity			
Some evidence	No evidence	Some evidence	Clear evidence

Genetic toxicology

Salmonella typhimurium gene mutation:	Positive with S9 in strain TA100; negative with and without S9 in strains TA1535, TA1537, and TA98
Sister chromatid exchanges Chinese hamster ovary cells *in vivo*:	Positive without S9
Chromosomal aberrations Chinese hamster ovary cells *in vivo*:	Positive with S9
Sex-linked recessive lethal mutations *Drosophila melanogaster*:	Negative when administered by feed or injection
Micronuclei in mice peripheral blood:	Negative at 13 weeks

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