PLAINTIFF'S EXHIBIT

CAP-742

A/C Pipe Producers Association

Internal Correspondence

TO Board of Directors
International Affairs Committee

FROM J. F. Welch, Vice-President

DATE August 17, 1984

SUBJECT U.S. National Institute of Environmental Health Sciences (NIEHS) - Asbestos Feeding Studies

REF: (1) JFW correspondence, U.S. Environmental Protection Agency (EPA) - Advance Notice of Proposed Rulemaking on National Drinking Water Regulations
(2) JFW correspondence, same title, April 30, 1983

ACTION REQUIRED: Review for information

Reference (1) mentions the reported finding of "nodules" in rats fed chrysolite in the National Toxicology Program (NTP) animal studies.

NTP Draft Technical Report on the Toxicology and Carcinogenesis Studies of Chrysotile Asbestos in F344/N Rats

Enclosed are excerpts from the report. To summarize, oral administration of "short range" chrysotile did not cause any overt toxicity and neoplastic or nonneoplastic disease. These results are consistent with NTP studies feeding amosite and crocidolite asbestos to rats and hamsters.

In male rats fed "intermediate range" (IR) chrysotile, however, benign neoplasms called adenomatous polyps were observed in the large intestine. The incidence of these neoplasms was not statistically significant when compared to the control group (not fed asbestos) in this study. When the incidence is compared with all male control groups in NTP's oral asbestos studies, it is considered highly significant. Thus, the report concludes that there is some evidence of carcinogenicity in male rats fed intermediate range chrysotile.

In the section entitled "Discussions and Conclusions," NTP interprets the significance of these findings. Five important observations are made: (1) adenomatous polyps are benign neoplasms, (2) no malignant neoplasms were observed in this study (or any of the other oral asbestos studies), (3) the polyps did not progress to carcinomas even though, (4) this was a lifetime study that allowed progression to malignancy. Finally, no gastrointestinal tumors were observed in female rats in the same experiment.

Discussions with NTP Staff

On July 27, 1984, NTP's Board of Scientific Counselors peer reviewed the draft technical reports of the chrysotile feeding studies. According to Dr. E. E. McConnell, Project Officer, the Board determined that the polyps were "absolutely related to exposure to intermediate range chrysotile." Unfortunately, the Board did not address the question of why neoplasms were induced by IR chrysotile but not induced by amosite and crocidolite of comparable fiber dimensions in the same test animals. McConnell went on to say, "It's real. The neoplasms are definitely treatment-related. These results probably would not have been detected in a study involving a smaller number of animals (e.g. Smith, et al) and indicate that ingested asbestos certainly is not a rip-roaring carcinogen." He said that the Donham animal study, in which an asbestos dosing level of 10% resulted in a "trend toward increased colon lesions," suggested that neoplastic

response might occur but did not do so with statistical significance. The larger number of animals in this NTP study permitted this "trend" to develop fully, in his judgement.

Public Health Significance

When questioned about the point, McConnell stated that the current findings "meant very little with regards to human health." He said (not a direct quote), "From a public health standpoint, we obviously know that inhaled asbestos is carcinogenic. Ingested asbestos is probably not much of a public health threat, especially since many of the fibers in water are much shorter than IR chrysotile. The dosing levels in these studies were 160,000 to 16 billion times greater than the projected level of possible human exposure. I'm not going to lose any sleep worrying about drinking water coming out of A/C pipe."

After the peer review meeting, McConnell discussed the Board's conclusions with NTP Director Dr. David Rall. Rall concurs with McConnell's views, including the public health implications.

Staff Analysis

It would have been highly desirable for all the NTP studies to show no evidence of carcinogenicity with all fiber types, size ranges, and animal species and sexes. The current findings demonstrating "some evidence of carcinogenicity" blemish what previously was a strong, consistent body of animal toxicology studies showing no carcinogenic effects from ingested asbestos.

It is not known whether EPA will share NTP's views about the public health implications of these findings. If anything, they complicate the question of whether asbestos in drinking water should be regulated and may well slow down the Agency's decision-making process. For example, the Office of Drinking Water may reraise the issue with the EPA Science Advisory Board. The matter definitely will be discussed at the next meeting of the National Drinking Water Advisory Council.

Staff plans to issue an A/C Advisory on this NTP study and McConnell's comments so that undue significance is not imparted to the findings. If you have any questions, please do not hesitate to call.

JFW/bwm

Enclosure

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Board Draft, 7/84

NTP TECHNICAL REPORT

ON THE

TOXICOLOGY AND CARCINOGENESIS STUDIES

OF

CHRYSOTILE ASBESTOS

(CAS NO. 12001-29-5)

IN F344/N RATS

(FEED STUDIES)

E. E. McConnell, D.V.M.
(Chemical Manager)

NATIONAL TOXICOLOGY PROGRAM
P.O. Box 12233
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NOTICE

This is not a final report. Until this DRAFT is reviewed and approved by the Technical Reports Review Subcommittee of the NTP Board of Scientific Counselors, this DRAFT does not represent the official position of the National Toxicology Program.

NTP TR 295

NIH Publication No. 84-2551
NTP-83-173

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
National Institutes of Health

NOTE TO THE READER

These studies are designed and conduct to characterize and evaluate the toxicologic potential, cluding carcinogenic activity, of selected chemicals in laboratory animals (usually two species, rats a mice). Chemicals selected for testing in the NTP Carcinogenesis Program are chosen primarily on t bases of human exposure, level of production, and chemical structure. Selection per se is not an indica of a chemical's carcinogenic potential. Negative results, in which the test animals do not have a grea incidence of cancer than control animals, do not necessarily mean that a test chemical is not a carcinog inasmuch as the experiments are conducted under a limited set of conditions. Positive resu demonstrate that a test chemical is carcinogenic for animals under the conditions of the test and indic that exposure to the chemical has the potential for hazard to humans. The determination of the risk humans from chemicals found to be carcinogenic in animals requires a wider analysis which exter beyond the purview of this study.

Five categories of interpretative conclusions were adopted in June 1983 for use in the Technical Repo series to specifically emphasize consistency and the concept of actual evidence of carcinogenicity. F each definitive study result (male rats, female rats, male mice, female mice), one of the following quin will be selected to describe the findings. These categories refer to the strength of the experimental e dence and not to either potency or mechanism.

- Clear Evidence of Carcinogenicity is demonstrated by studies that are interpreted as showin chemically related increased incidence of malignant neoplasms, studies that exhibit a st stantially increased incidence of benign neoplasms, or studies that exhibit an increased incider of a combination of malignant and benign neoplasms where each increases with dose.

- Some Evidence of Carcinogenicity is demonstrated by studies that are interpreted as showin chemically related increased incidence of benign neoplasms, studies that exhibit marginal creases in neoplasms of several organs/tissues, or studies that exhibit a slight increase in t common malignant or benign neoplasms.

- Equivocal Evidence of Carcinogenicity is demonstrated by studies that are interpreted showing a chemically related marginal increase of neoplasms.

- No Evidence of Carcinogenicity is demonstrated by studies that are interpreted as showing chemically related increases in malignant or benign neoplasms.

- Inadequate Study of Carcinogenicity demonstrates that because of major qualitative or qua titative limitations, the studies cannot be interpreted as valid for showing either the presence absence of a carcinogenic effect.

Additionally, the following concepts (as patterned from the International Agency for Research on Canc Monographs) have been adopted by the NTP to give further clarification of these issues:

> The term *chemical carcinogenesis* generally means the induction by chemicals of neoplasms usually observed, the earlier induction by chemicals of neoplasms that are commonly observed, the induction by chemicals of more neoplasms than are generally found. Different mechanis may be involved in these situations. Etymologically, the term *carcinogenesis* means induction cancer, that is, of malignant neoplasms; however, the commonly accepted meaning is the inducti of various types of neoplasms or of a combination of malignant and benign neoplasms. In the Tec nical Reports, the words *tumor* and *neoplasm* are used interchangeably.

This study was conducted under contract to the National Institute of Environmental Health Scienc National Toxicology Program. The study described in this Technical Report has been conducted unc NTP health and safety requirements and/or guidelines for toxicity studies. Individual toxicology testi contractors are required to demonstrate corporate health and safety programs in compliance with N chemical health and safety requirements and to meet or exceed all applicable Federal, state, and lo health and safety regulations.

Although every effort is made to prepare the Technical Reports as accurately as possible, mistakes m occur. Readers are requested to identify any mistakes so that corrective action may be taken. Furth anyone who is aware of related ongoing or published studies not mentioned in this report is encouraged make this information known to the NTP. Comments and questions about the National Toxicolo Program Technical Reports on Toxicology and Carcinogenesis Studies should be directed to Dr. J. E. Hu National Toxicology Program, P.O. Box 12233, Research Triangle Park, NC 27709; 919-541-3782.

These NTP Technical Reports are available for sale from the National Technical Information Servi U.S. Department of Commerce, 5285 Port Royal Road, Springfield, VA 22161, 703-487-4650. Sin copies of this Technical Report are available without charge (and while supplies last) from the N Public Information Office, National Toxicology Program, P.O. Box 12233, Research Triangle Park, 27709

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TABLE B2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR + PW IR
ENDOCRINE SYSTEM (Continued)					
#PANCREATIC ISLETS	(87)	(124)	(249)	(175)	(99)
ISLET-CELL ADENOMA	2 (2%)	1 (1%)	6 (2%)	1 (1%)	4 (4%)
ISLET-CELL CARCINOMA	4 (5%)	1 (1%)	7 (3%)	1 (1%)	3 (3%)
REPRODUCTIVE SYSTEM					
*MAMMARY GLAND	(88)	(125)	(250)	(175)	(100)
CARCINOMA, NOS	1 (1%)		3 (1%)		1 (1%)
ADENOMA, NOS	6 (7%)	2 (2%)	21 (8%)	5 (3%)	11 (11%)
ADENOCARCINOMA, NOS	5 (6%)		9 (4%)	1 (1%)	4 (4%)
FIBROADENOMA	49 (56%)	36 (29%)	128 (51%)	41 (23%)	58 (58%)
CHONDROMA					1 (1%)
*VULVA	(88)	(125)	(250)	(175)	(100)
FIBROSARCOMA, INVASIVE			1 (0%)		
*CLITORAL GLAND	(88)	(125)	(250)	(175)	(100)
CARCINOMA, NOS		5 (4%)	16 (6%)	4 (2%)	4 (4%)
SQUAMOUS CELL CARCINOMA	1 (1%)		2 (1%)		
*VAGINA	(88)	(125)	(250)	(175)	(100)
FIBROMA		1 (1%)			
FIBROSARCOMA			1 (0%)		
ENDOMETRIAL STROMAL POLYP					1 (1%)
ENDOMETRIAL STROMAL SARCOMA			2 (1%)		
ENDOMETRIAL STROMAL SARCOMA, INVASIVE				1 (1%)	
#UTERUS	(87)	(125)	(249)	(175)	(99)
PAPILLARY ADENOCARCINOMA					1 (1%)
PAPILLARY CYSTADENOMA, NOS					1 (1%)
LEIOMYOMA	2 (2%)		1 (0%)		
ENDOMETRIAL STROMAL POLYP	13 (15%)	7 (6%)	22 (9%)	15 (9%)	10 (10%)
ENDOMETRIAL STROMAL SARCOMA	1 (1%)	2 (2%)	2 (1%)	2 (1%)	1 (1%)
#CERVIX UTERI	(87)	(125)	(249)	(175)	(99)
FIBROMA			1 (0%)		
LEIOMYOSARCOMA				1 (1%)	
ENDOMETRIAL STROMAL POLYP	1 (1%)				1 (1%)
ENDOMETRIAL STROMAL SARCOMA			3 (1%)	1 (1%)	
ENDOMETRIAL STROMAL SARCOMA, INVASIVE				1 (1%)	1 (1%)
#UTERUS/ENDOMETRIUM	(87)	(125)	(249)	(175)	(99)
CARCINOMA, NOS			1 (0%)		
PAPILLARY CARCINOMA				1 (1%)	
ADENOMA, NOS			1 (0%)	4 (2%)	
PAPILLARY ADENOMA				1 (1%)	
#OVARY	(87)	(125)	(249)	(174)	(99)
PAPILLARY ADENOCARCINOMA			1 (0%)		
THECOMA	1 (1%)				
GRANULOSA-CELL TUMOR	1 (1%)		4 (2%)	1 (1%)	2 (2%)

BLE B2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR + PW IR
RVOUS SYSTEM					
CEREBRUM	(87)	(125)	(250)	(175)	(100)
ASTROCYTOMA	1 (1%)				
BRAIN	(87)	(125)	(250)	(175)	(100)
CARCINOMA, NOS, INVASIVE	4 (5%)	1 (1%)	13 (5%)	1 (1%)	1 (1%)
GRANULAR-CELL TUMOR, NOS					1 (1%)
GLIOMA, NOS					1 (1%)
ASTROCYTOMA	1 (1%)		5 (2%)	1 (1%)	1 (1%)
SPINAL CORD	(88)	(125)	(250)	(175)	(100)
OLIGODENDROGLIOMA			1 (0%)		
CIAL SENSE ORGANS					
EYE	(88)	(125)	(250)	(175)	(100)
FIBROMA			1 (0%)		
EYELID	(88)	(125)	(250)	(175)	(100)
SQUAMOUS CELL CARCINOMA	1 (1%)				
EAR,	(88)	(125)	(250)	(175)	(100)
SQUAMOUS CELL CARCINOMA				1 (1%)	
ZYMBAL GLAND	(88)	(125)	(250)	(175)	(100)
SQUAMOUS CELL PAPILLOMA		1 (1%)		2 (1%)	
SQUAMOUS CELL CARCINOMA	1 (1%)	14 (11%)	7 (3%)	26 (15%)	2 (2%)
ADENOMA, NOS				1 (1%)	
SARCOMA, NOS, INVASIVE					1 (1%)
SCULOSKELETAL SYSTEM					
MAXILLA	(88)	(125)	(250)	(175)	(100)
SQUAMOUS CELL CARCINOMA			1 (0%)		
FEMUR	(88)	(125)	(250)	(175)	(100)
OSTEOSARCOMA	1 (1%)				
SKELETAL MUSCLE	(88)	(125)	(250)	(175)	(100)
RHABDOMYOSARCOMA					1 (1%)
ABDOMINAL MUSCLE	(88)	(125)	(250)	(175)	(100)
MIXED TUMOR, INVASIVE				1 (1%)	

TABLE B2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR + PW IR
BODY CAVITIES					
*MEDIASTINUM	(88)	(125)	(250)	(175)	(100)
MUCINOUS CYSTADENO-CARCINOMA, METASTATIC				1 (1%)	
*ABDOMINAL CAVITY	(88)	(125)	(250)	(175)	(100)
LEIOMYOSARCOMA	1 (1%)				
*ABDOMINAL WALL	(88)	(125)	(250)	(175)	(100)
MIXED TUMOR, INVASIVE				1 (1%)	
*MESENTERY	(88)	(125)	(250)	(175)	(100)
SQUAMOUS CELL CARCINOMA, INVASIVE					1 (1%)
MIXED TUMOR, INVASIVE				1 (1%)	
ALL OTHER SYSTEMS					
*MULTIPLE ORGANS	(88)	(125)	(250)	(175)	(100)
ADENOCARCINOMA, NOS, METASTATIC		1 (1%)			
ALVEOLAR/BRONCHIOLAR CARCINOMA, METASTATIC			1 (0%)		
PAPILLARY ADENOCARCINOMA, METASTATIC			1 (0%)		
CORTICAL CARCINOMA, METASTATIC			2 (1%)		
C-CELL CARCINOMA, METASTATIC	1 (1%)				
MUCINOUS CYSTADENO-CARCINOMA, METASTATIC		6 (5%)		10 (6%)	
SIGNET RING CARCINOMA, METASTATIC		1 (1%)		4 (2%)	
SARCOMA, NOS		1 (1%)			
MIXED TUMOR, METASTATIC		1 (1%)			
CARCINOSARCOMA, METASTATIC		1 (1%)			
OSTEOSARCOMA, METASTATIC	1 (1%)				
THORACOLUMBAR REGION					
OSTEOSARCOMA	1				
PERINEUM					
FIBROSARCOMA			1		
LOWER LEG					
OSTEOSARCOMA	1				
FOOT					
FIBROMA			1		
ADIPOSE TISSUE					
MUCINOUS CYSTADENOCA, METASTATIC				1	
MIXED TUMOR, INVASIVE				3	
BROAD LIGAMENT					
LEIOMYOMA			1		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE B2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE LIFETIME FEED STUDY OF INTERMEDIATE-RANGE (IR) CHRYSOTILE ASBESTOS (Continued)

	CONTROL (UNTR)	DMH	IR	IR + DMH	IR + PW IR
BODY CAVITIES					
*MEDIASTINUM	(88)	(125)	(250)	(175)	(100)
MUCINOUS CYSTADENO-CARCINOMA, METASTATIC				1 (1%)	
*ABDOMINAL CAVITY	(88)	(125)	(250)	(175)	(100)
LEIOMYOSARCOMA	1 (1%)				
*ABDOMINAL WALL	(88)	(125)	(250)	(175)	(100)
MIXED TUMOR, INVASIVE				1 (1%)	
*MESENTERY	(88)	(125)	(250)	(175)	(100)
SQUAMOUS CELL CARCINOMA, INVASIVE					1 (1%)
MIXED TUMOR, INVASIVE				1 (1%)	
ALL OTHER SYSTEMS					
*MULTIPLE ORGANS	(88)	(125)	(250)	(175)	(100)
ADENOCARCINOMA, NOS, METASTATIC		1 (1%)			
ALVEOLAR/BRONCHIOLAR CARCINOMA, METASTATIC			1 (0%)		
PAPILLARY ADENOCARCINOMA, METASTATIC			1 (0%)		
CORTICAL CARCINOMA, METASTATIC			2 (1%)		
C-CELL CARCINOMA, METASTATIC	1 (1%)				
MUCINOUS CYSTADENO-CARCINOMA, METASTATIC		6 (5%)		10 (6%)	
SIGNET RING CARCINOMA, METASTATIC		1 (1%)		4 (2%)	
SARCOMA, NOS		1 (1%)			
MIXED TUMOR, METASTATIC		1 (1%)			
CARCINOSARCOMA, METASTATIC		1 (1%)			
OSTEOSARCOMA, METASTATIC	1 (1%)				
THORACOLUMBAR REGION					
OSTEOSARCOMA	1				
PERINEUM					
FIBROSARCOMA			1		
LOWER LEG					
OSTEOSARCOMA	1				
FOOT					
FIBROMA			1		
ADIPOSE TISSUE					
MUCINOUS CYSTADENOCA, METASTATIC				1	
MIXED TUMOR, INVASIVE				3	
BROAD LIGAMENT					
LEIOMYOMA			1		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED