

OCTOBER 24, 1979 F.C.M.

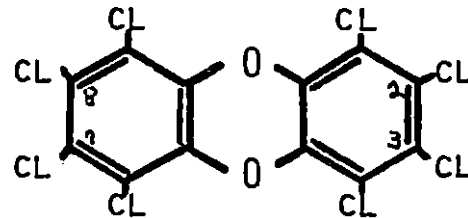
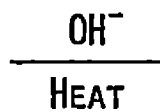
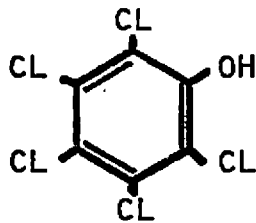
STATUS SUMMARY

DIOXINS - DIBENZOFURANES

DEFENS
ACTIVE

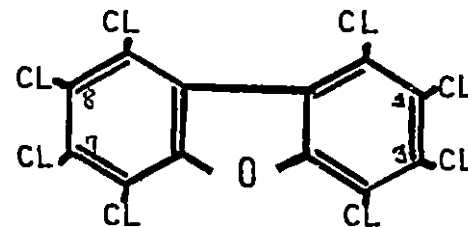
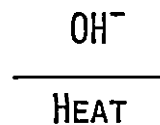
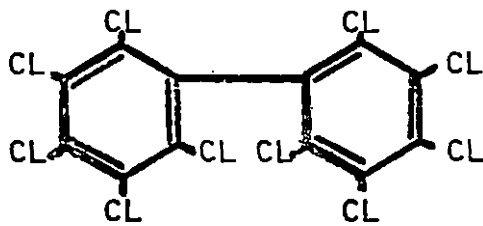


STRUCTURE



POLYCHLOROPHENOLS
PCP's

* POLYCHLORO DIBENZO-P-DIOXINS (PCDD)
(TETRA - 2,3,7,8 - TCDD)



POLYCHLORINATED BIPHENYLS
PCB's

* POLYCHLORO DIBENZOFURANES (PCDF)
(TETRA - 2,3,7,8 - TCDF)

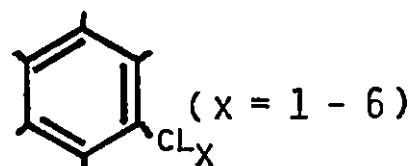
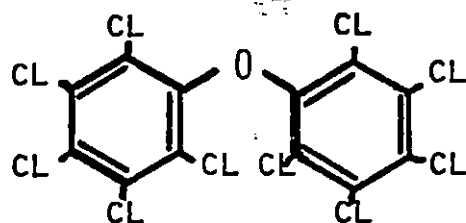
CONFIDENTIAL
SUBJECT TO PROTECTIVE ORDER.

* CONTAIN ONE OR MORE, BUT NOT NECESSARILY ALL, CHLORINE ATOMS

G02952

G001808

OTHER PRECURSORS



OTHER HALOGENATED AROMATICS - NITROCHLOROBENZENES?
CHLOROANILINES?
ETC..

CHEMISTRY - CONDITIONS

- CAN BE FORMED FROM A VARIETY OF AROMATIC CHLORINATED COMPOUNDS WITH HEAT AND TRACES OF H_2O , O_2 , COMBUSTION; CHLORINATION OF PHENOLS (BIPHENYL) AT ELEVATED TEMPERATURES CATALYZED BY ALKALI MORE LIKELY TO PRODUCE THAN OTHERS.

- OCCURENCE

- NOT YET SHOWN THAT COMBUSTION PROCESSES (POWER PLANTS, ETC. - CLAIMED BY DOW) WHERE ORGANICS AND CHLORINE CO-EXIST WILL PRODUCE MEASURABLE QUANTITIES (> 10 PPT) OF CDD OR CDF.
- PRECURSORS - PCB's, 2,4-D, 2,4,5-T, ETC., SOME OF WHICH ARE UBIQUITOUS, IN THE ENVIRONMENT, PROBABLY REQUIRED.

BIOLOGICAL EFFECTS IN ANIMALS - CDD AND CDF

SOME OF THE MOST TOXIC MATERIALS KNOWN - CARCINOGENIC,
REPRODUCTION, OTHER EFFECTS

CHLORINATED DIBENZO DIOXINS

TETRA-(2,3,7,8) TCDD	LD ₅₀	GUINEA PIG	2 µg/kg
		RAT	25-45 µg/kg
		MOUSE	115 µg/kg
DI (2,8)	LD ₅₀	GUINEA PIG	300,000 µg/kg
OCTA (1,2,3,4,6,7,8,9)	LD ₅₀	GUINEA PIG	1,000,000 µg/kg
TETRA (2,3,7,8) TCDD	CARCINOGENICITY (SEVERAL SITES)		2.1 µg/kg/DAY
	TERATOGENICITY		2.1 µg/kg/DAY

CHLORINATED DIBENZOFURANES

TETRA-(2,3,7,8) TCDF	LD ₁₀₀	CHICKS	5 µg/kg/DAY
		LIVER DAMAGE CHICKS	5 µg/kg/DAY
		HEART INFLAMATION CHICKS	5 µg/kg/DAY
		IMMUNESUPPRESSION RATS	5 µg/kg
		IMMUNESUPPRESSION GUINEA PIGS	1 µg/kg
		GENERAL TOXICITY	CA. 1/5 - 1/10 OF TCDD

MONSANTO INVOLVEMENT

FROM THE FOREGOING OUTLINE, SOME OF OUR PAST AND CURRENT INVOLVEMENTS ARE OBVIOUS:

NITRO EARLY (1949) TCP - 2,4,5-T ACCIDENT AND
 PRODUCTION TO 1969

WGK PENTACHLOROPHENOLS, CHLOROPHENOLS, PCB
 (PCP AND PCB NOW DOWN)
 POSSIBLE CHLOROBENZENES, NITRO CHLOROBENZENES,
 CHLOROANILINES, ETC.

ANNISTON PCB - EARLY 1930'S AND 1960'S - HIGH TEMP
 PRODUCTION OF HIGHER ISOMERS

ALL OF THE ABOVE INVOLVED CHLORACNE CASES.

OTHER MONSANTO PRODUCTS, RESIDUES AND EFFLUENTS CONTAINING TRACE CDD OR CDF COULD EXIST, BUT NOT YET IDENTIFIED.

6001811

HUMAN EPISODES
from
ACCIDENTAL OR OCCUPATIONAL EXPOSURE
in
MANUFACTURE/USE CHLOROPHENOLS - PCB

<u>YEAR</u>	<u>COUNTRY</u>	<u>MANUFACTURER/LOCATION</u>	<u>PRODUCTION/ PRODUCT</u>	<u>SOURCE</u>	<u>NUMBER CASES</u>
<u>1949*</u>	U.S.	Monsanto/Nitro	TCP	Accident	121 (150+)
1949	W. Germany	Nordhein, Westfalen	PCP, TCP	Occupational	17
1952	W. Germany		TCP	Occupational	60
1952	W. Germany	Boehringer	TCP	Occupational	37
1953	W. Germany	BASF/Ludwigshafen	TCP	Accident	55
1954	W. Germany	Boehringer/Ingleheim	TCP/ 2,4,5,-T	Occupational	31
1956	France	Rhone-Poulenc/ Grenoble	TCP	Accident	17
1956	U.S.	Diamond Alk/Newark	2,4-D/ 2,4,5,-T	Occupational	29
<u>1960's*</u>	Vietnam "Agent Orange"	Dow, Monsanto	2,4-D/ 2,4,5,-T	Defoliant	Unknown
1963	Netherlands	Philips-Duphar/ Amsterdam	TCP	Accident	50
1964	USSR		2,4,5-T	Occupational	128
1965-69	Czechoslovakia	Spolana/	TCP	Occupational	76
1966	France	Rhone-Poulenc/ Grenoble	TCP	Accident	21
<u>1968*</u>	Japan	"Yusho" population	PCB/PCDF	Accident	1200
1968	U.K.	Coalite/Bolsover- Derbyshire	TCP	Accident	79
1973	Austria	Linz Nitrogen Works	2,4,5-T	Occupational	50
<u>1976*</u>	Italy	ICMESA/Meda (Seveso)	TCP	Accident	135
1979	U.S.	Vertac/Jacksonville, Arkansas	TCP/ 2,4,5,-T	Occupational	16

* EPISODES WITH IMPORTANT MEDIA AND PUBLIC EXPOSURE.

G001812

SYMPTOMS - TOXICITY OF TCDD (OTHER ISOMERS?) IN MAN

CONSISTENT

CHLORACNE

INCONSISTENT OR
OCCASSIONAL

FATIGUE; LOSS OF LIBIDO

HEADACHE

HYPERPIGMENTATION (DARKENING SKIN)

IRRITABILITY (NERVOUSNESS, INSOMNIA)

ENLARGED TENDER LIVER

NEUROMUSCULAR (PAIN IN CHEST; PAIN,
WEAKNESS IN EXTREMITIES)

HIRSUTISM (EYEBROWS, TEMPLE)

HYPERLIPIDEMIA

CURRENT STATUS - FUTURE ACTIONS

NITRO -

- HEALTH STUDIES (DR. SUSKIND) COMPLETED AT NITRO IN JUNE. REPORT EXPECTED IN DECEMBER/JANUARY. EARLY RESULTS OF RESIDUAL CHLORACNE EFFECTS OBSERVED. MONSANTO MORTALITY STUDY (1949 ACCIDENT-121 CHLORACNE CASES) SHOWS NO APPARENT LONG TERM EFFECTS ON TOTAL DEATHS, CANCER OR CARDIOVASCULAR MORTALITY RATES. ADDITIONAL MORTALITY STUDIES OF CHLORACNE CASES (150+) AND 2,4,5-T WORKERS TO 1969 UNDER STUDY.

G001814

W. G. KRUMMRICH -

- DERMATOLOGY HEALTH STUDY OF FORMER PENTACHLOR AND CURRENT CHLOROPHENOL WORKERS COMPLETED OCTOBER 4-5 (DR. SUSKIND). REPORT TO BE COMPLETED OF PAST CHLORACNE EFFECTS (PENTACHLOROPHENOL) BUT NO CURRENT ACTIVE CASES NOTED.

OUTSIDE WORLD -

- AVAILABLE CURRENT DATA INDICATES THAT WHERE RESIDUAL PRECURSORS EXIST (PCB, 2,4-D/2,4,5-T, PENTACHLOR, ETC.) IN THE ENVIRONMENT, TCDD AND/OR TCDF LEVELS IN THE 10/X00 PPT. RANGE MAY BE FOUND IN THE SOIL, ANIMALS OR FISH. THERE IS NO CURRENT EVIDENCE FROM OBSERVATION AND TISSUE STUDIES IN WILDLIFE OF ANY TOXIC EFFECTS OR HEALTH HAZARD AT THESE REPORTED LEVELS.

FUTURE ACTIONS

- IT IS APPARENT THAT WE MUST DEVELOP ANALYTICAL CAPABILITIES AND KNOWLEDGE OF WHERE BIOLOGICALLY RELEVANT LEVELS OF TCDD AND TCDF EXIST TO AUTHORITATIVELY CONFIRM, REBUT OR COMMENT ON OFFICIAL STATEMENTS VALIDLY MADE ABOUT THE PRESENCE OF CDD'S OR CDF'S IN OUR PRODUCTS, FACILITIES OR EFFLUENTS.
- ALL OF OUR BASIC PROCESSES INVOLVING CHLORINATION OF AROMATIC MATERIALS MUST BE SYSTEMATICALLY EXAMINED VIA HIGH SENSITIVITY ANALYSIS FOR THEIR POTENTIAL FORMATION OF CDD'S OR CDF'S AND, WHERE FOUND, MODIFIED TO ELIMINATE OR MINIMIZE THEIR FORMATION AS BY-PRODUCTS. THIS SHOULD INCLUDE PROCESSES WHERE SOLVENTS OR BY-PRODUCTS PROVIDE UNOBTAINABLE COMBINATIONS OF CHLORINE CONTAINING MATERIALS WITH THERMAL OR MOISTURE CONDITIONS, WHICH COULD LEAD TO EXCHANGES, REARRANGEMENTS AND CONDENSATIONS TO DIOXINS OR DIBENZOFURANES.

- INCINERATOR OPERATIONS IN KEY PLANTS MUST BE EVALUATED TO DETERMINE WHETHER AND UNDER WHAT CONDITIONS CDD'S OR CDF'S ARE PRODUCED (E.G. HIGH TEMPERATURES AND LONG RESIDENCE TIMES APPEAR NECESSARY TO DESTROY TOXIC PRODUCTS).
- COMPLETE CURRENT MORTALITY AND HEALTH STUDIES UNDERWAY TO HELP DEFINE LONG TERM EFFECTS OF TCDD EXPOSURES AND CONSIDER, BASED ON CLINICAL RESULTS, WHETHER APPROPRIATE MEDICAL MONITORING FOR CDD OR CDF IS FEASIBLE AND DESIRABLE.

ANALYTICAL BACKGROUND

IT IS IMPORTANT TO UNDERSTAND THE ANALYTICAL PROBLEMS IN DETECTING TRACE (LOW PARTS PER TRILLION) CDD AND CDF IN MATERIALS, WHICH HAVE BEEN REVIEWED IN A POSITION PAPER BY DR. G. E. PAGET (6/29/79).

TO SUMMARIZE, THE LOW LEVEL DETECTION OF CDD'S AND CDF'S GENERICALLY AS A CLASS CAN BE ACHIEVED IN MANY LABORATORIES, INCLUDING MONSANTO'S. HOWEVER, FEW CAN PERFORM THE SPECIFIC 2,3,7,8-TCDD AND TCDF ANALYSIS AT HIGH SENSITIVITY (LOW PPT) WHICH REQUIRES A COSTLY, HIGH RESOLUTION GC-MASS SPECTROMETER INSTRUMENTATION ASSEMBLY, AND SOME THAT CLAIM TO BE ABLE TO DO SO ARE MISTAKEN. MONSANTO HAS JUST RECEIVED SUCH INSTRUMENTATION AND IS CHECKING IT OUT AT DAYTON. IT IS OBVIOUS ALSO THAT THE HIGH SENSITIVITY ANALYSIS IS EXTREMELY DEMANDING OF TIME (SEVERAL DAYS) AND SKILLED PERSONNEL, SUCH THAT IT MUST BE RESERVED FOR CRITICAL CIRCUMSTANCES AND CANNOT BE UNDERTAKEN ON A ROUTINE OR "QUALITY ASSURANCE" BASIS.

G001818