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International Specialists in the Environmental Sciences

July 1, 1981

Dr. John H. Craddock
Director of Product and Environmental Safety
800 N. Lindbergh Boulevard
St. Louis, Missouri 63166

Dear Dr. Craddock:

As promised, here is a copy of the talk I have given on PCBs. Enclosed you will also find a copy of the slides used at each presentation. I'm sorry that this is only an outline and therefore cannot always convey the exact thoughts I expressed, but it should five you a flavor of what I talked about.

If any of these slides interest you, please feel free to make your own copies. If you have any questions about the talk or want to discuss any of the points outlined, please call me at your convenience.

Thanks for all the help you have been and I hope sometime that I will have the pleasure of meeting you in person.

Sincerely,

Robert C. James

Robert C. James, PhD
Corporate Toxicologist

ENCL
RCJ/tlm
7/1/81

MONS 216369

recycled paper

POLYCHLORINATED BIPHENYL COMPOUNDS

(Slide 1)

I. INTROOUCTION

(Slide 2)

A. PRODUCTION

- o Polychlorinated biphenyl (PCB) compounds were first synthesized by Griefs in 1867.
- o PCBs were produced in the United States in 1929 by the Swann Chemical Company bought later in 1935 by the Monsanto Company.
- o Although as many as six companies have had registered trademarks for commercial brands of PCBs, probably most PCB mixtures have been produced in this country by the Monsanto Company.
- o It has been estimated that between 1929 and 1970 some 990 million pounds of PCBs were sold in North America alone.
- o PCBs were produced and/or imported by probably all industrialized nations in the 1950s and 1960s.

(Slide 3)

B. PROPERTIES

- o PCBs range in appearance from a clear, thin oil to a light yellow, thick liquid with boiling points of approximately 300-400°C. Having boiling points 3 to 4 times that of water, very little PCBs evaporate into the air at normal temperatures.

- o PCBs have certain physical properties which make them very useful in industry. These properties include thermal stability; resistance to oxidation by acids, bases, and other chemicals; and electrical insulation.

(Slide 4)

C. USES

- o Because of the above properties PCBs have been used extensively in the electrical industry as an insulator and coolant. They have also been used as sealants for wood or cement surfaces; as cutting oils and hydraulic fluids, as vapor suppressants for insecticides to retard their evaporation and prolong their action in soil; and in inks, carbonless duplicating paper, adhesives, immersion oil for microscopes, and plasticizers.

(Slides 5, 6, 7)

D. OCCURRENCE

- o The average air concentration in American cities in 1975 (Miami, Fort Collins, and Jackson) was 0.1 ug/m^3; this level is the currently allowable maximum concentration for PCBs in workroom air.

- o According to a 1959 report, PCB levels in workroom air in United States plants ranged from 0.2-10.5 mg/m^3. This is 2,000-100,000 times greater than today's allowable standard.

- It has been calculated that 2.2 million pounds of PCBs fall on the United States yearly in rain and particulate matter. We are constantly recycling PCBs through our environment.

- A national study in 1971-74 showed that PCBs in unfiltered water samples ranged from 0.1-3.0 ug/L (ppb).

- In 1976, it was found that the average PCB concentrations in seawater was 13 ng/L (ppt).

- PCBs were found in the fat of arctic animals (porpoises, seals, foxes, sheep, and polar bears) at concentrations ranging from 0.3-21.0 ug/g (ppm).

- A national survey in the United States during the years 1973-74 revealed that 40% of the population had PCB levels of 1 ug/g (ppm) or greater in fat tissue.

- A 1973 Finnish study revealed that 11 healthy workers employed in a capacitor factory had PCB blood concentrations of 0.07-1.9 ug/g (ppm) which was 50-100 times that of control groups.

- A Japanese survey reported the average PCB intake as 4-50 ug/person/day. This is 50 times the allowable intake via air for a worker in the United States.

(Slides 8, 9)

E. CONCERNS FOR PCB USE

- Initial concern about the health effects of PCB mixtures began in the late '30s and early '40s when production workers coming in direct contact and without proper ventilation developed chloracne and some signs of liver injury.

- In 1949, Dr. R.E. Kelly, describing a human patch test study using the technique developed by the Medical Director of The United States Public Health Service (USPHS), reported: "If the procedure recommended by the USPHS is sufficient to distinguish between chemical compounds that are innocuous when applied to the skin and other compounds that are primary irritants or sensitizers, then it would seem that Aroclor (trademark, Monsanto) has no primary irritant effect nor is it a sensitizer of high potency."

- In 1968, approximately 1,500 Japanese ingested large amounts of PCBs which had inadvertently leaked into a brand of cooking oil.

- Also in the mid '60s, a Swedish researcher investigating DDT residues in the environment found PCBs in fish. The extensive presence of PCBs in the environment was confirmed by 1970. Although PCBs are not as inherently toxic as DDT, they raise similar concerns. PCBs are fat soluble and resist degradation in animals and the environment. Therefore, even though the overall impact of PCBs on the environment was not known, its presence in the environment raised concerns about potential adverse health and environmental effects because its chemical stability would make it hard to remove once a problem was discovered.

(Slides 10, 11, 12, 13)

II. TOXICITY STUDIES IN ANIMALS

A. SYSTEMIC TOXICITY

- Toxicology is the study of adverse effects. At high enough doses every chemical in our environment is toxic, be it a chemical used in industry, as a drug, or even our vitamins and hormone supplements. This aspect was pointed out 400 years ago by PARACELSUS (1493-1541) who stated: "All substances are poisons, there is none which is not a poison. The right dose differentiates a poison and a remedy." The interesting aspect of PCBs that is often overlooked is the high doses needed to cause a toxic effect.

- The dose lethal to 50% of the animals (LD_{50}) range for rats from 4,000-14,000 mg/kg. The LD_{50} for common table salt is 4,000 mg/kg.

- The major effects of toxic concentrations of PCBs in the liver include hypertrophy (increased cell size), marked fatty infiltration, and centrilobular necrosis (cell death and degeneration).

- Exposure to the skin ranges from reddening, increased pigmentation, hair loss, chloracne, blisters, desquamation (peeling or shedding) and skin lesions.

- Other effects observed include irritation to the stomach, ulcers, anemia (less than normal number of red blood cells), decreased number of white blood cells, depression of the immune response (inability to fight infections), and prolongation of the menstrual cycle.

(Slide 14)

B. EMBRYOTOXICITY, BIRTH DEFECTS AND REPRODUCTIVE EFFECTS

- o 100-500 mg/kg/day of the Aroclors in rats (equivalent to 1 oz. liquid/day in humans) caused decreased mating performance, litter size, and survival of offspring. No birth defects were seen and the no-effect level was 50 mg/kg.

- o In monkeys, PCBs have caused irregular and prolonged menstrual cycles, resorptions, and infertility.

- o PCBs were fetotoxic in rabbits, but caused no birth defects.

- o "Karnofsky's Law"- any chemical administered at a high enough dose at the prooer stage of development to the right species will cause disturbances in embryonic development.

- o For some perspective on Karnofsky's Law it may be noted that the list of known animal teratogens (agents causing birth defects) includes: vitamin A, folic acid, insulin, steroids, androgens, estrogens, adrenalin, stress (heat, cold), and vitamin and hormonal deficiencies.

C. MUTAGENICITY

- o PCBs were tested in the Ames assay; although 4-chlorobiphenyl was mutagenic, the more chlorinated biphenyls showed little activity.

- o Aroclors did not produce chromosomal aberrations in rat bone marrow or sperm cells. They were also negative in the dominant lethal mutation test in rats.

- o No chromosomal aberrations were seen in cultured human white blood cells.

- Currently there are probably more data against caffeine as a possible mutagen than there are against PCBs.

D. CARCINOGENICITY

- The carcinogenicity data in animals concerning PCBs are controversial. Reports have been published concluding that PCBs induce neoplasms at high doses in rats and mice. However, studies by Monsanto and the 1977 National Cancer Institute study were negative. Also Dr. Pour of the Eppley Institute for Research in Cancer reviewed both the negative and the positive studies and concluded that there was no occurrence of liver cancer in either study.

(Slide 15)

III. HUMAN PCB EXPOSURE:

A. "YUSHO"

At least 1291 persons ingested large amounts of PCBs (1-2 grams) that had leaked into a brand of cooking oil. The oil contained 800-3,000 mg/kg (ppm) PCBs and required months of exposure before the onset of symptoms.

- The most common clinical features in the early phases were dermatological in nature. These symptoms included ocular discharge and swelling of the upper eyelids, extra skin growth around hair follicles, chloracne, and increased pigmentation.

- Other clinical symptoms included peripheral nerve disturbances, liver enlargement without liver injury, irregular menstruation in women, transient growth retardation in children, elevated serum triglyceride (fatty acids) levels, and bronchitis.

- Only mild birth defects were attributed to PCBs; some children were born with skin problems similar to those of the adults. The other effects included premature eruption of teeth and less than average birth size. (Note: Smoking and drinking also correlates with small birth size.)

B. OCCUPATIONAL EXPOSURES

- For the most part occupational exposure has largely caused skin symptoms only.

- The half life (time to eliminate 1/2 of the amount in the body) has been estimated at 90 days.

- Currently there is no epidemiologic evidence in studies of workers exposed to PCBs for years concluding that PCBs cause cancer in humans.

C. FDA REGULATIONS

- The following are the allowable limits of PCBs as regulated by the Food and Drug Administration.

  2.5 ppm in dairy products (on a % fat basis-whole milk-3.25% fat)
  5.0 ppm in poultry (on a % fat basis)
  0.5 ppm in eggs
  2.0 ppm in fish and shell fish
  0.2 ppm in infant food
  10.0 ppm in paper packaging materials

- Therefore, under federal regulations we can ingest and accumulate more PCBs through our food than in the workplace.

D. PERSPECTIVES ON HUMAN EXPOSURE

(Slide 16)

- Under current regulations, the allowable human exposure levels to PCBs are much lower in the workplace than in everyday surroundings. For example, total PCB intake via ingestion of food may be greater than permissible employee exposure limits.

(Slide 17)

- PCBs are less toxic than many safe over-the-counter medications.

(Slide 18)

- Vitamin A has been found to be toxic at the same level at which the highest concentration of PCBs have been found to be non-toxic in human blood.

(Slide 19)

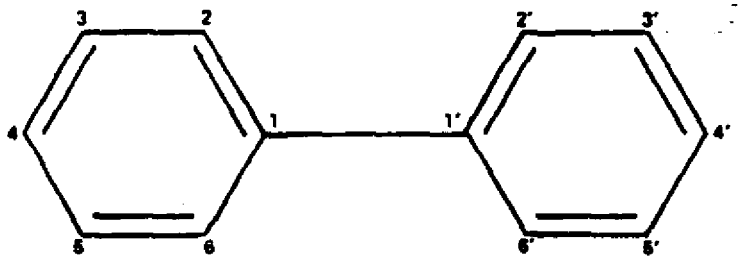
Both aldrin and DDT are more toxic than and just as persistent as PCBs, but have higher allowable exposures for the workplace. The allowable levels for vinyl chloride, a chemical proven to cause cancer in humans, are also higher.

GLOSSARY

Abbreviation	
ppm	Part per million
ppb	Part per billion
ppt	Part per trillion
mg/kg	Milligram compound per kilogram body weight
ug/kg	Microgram compound per kilogram body weight
g	1/1,000 of a kilogram
mg	1/1,000 of a gram or 1/1,000,000 of a kilogram
ug	1/1,000,000 of a gram or 1/1,000,000,000 of a kilogram
TLV	Threshold Limit Value, the highest workplace air concentration as suggested by the American Conference of Governmental Industrial Hygienists
PEL	Permissible Exposure Limit, the standard for workroom air concentrations as regulated by OSHA (Occupational Safety and Health Administration)
acute	High level short term exposure
chronic	Low level long term exposure
teratogen	Compound causing birth defects

Glossary (Cont.)

Abbreviation	
mutagen	Compound causing damage to the genetic material
embryotoxicity	Toxic effects to embryo
resorption	Indicates death of embryo



PCBs

SLIDE 1

MONS 216382

PRODUCTION

- First Synthesized In 1867 by Griefs
- First Manufactured In U.S. In 1929
- Over 1 Billion Pounds Have Been Sold In the U.S. Alone
- Produced or Imported by All Industrial Nations

SLIDE 2

MONS 216383

USEFUL PROPERTIES

- Thermal Stability
- Chemical Stability
- Good Heat Capacity
- Excellent Dielectric (Electrical Insulation)

SLIDE 3

MONS 216384

END USES OF AROCLORS BY TYPE

End use	1016	1221	1232	1242	1248	1254	1260	1262	1268
Current									
• Capacitors	x	x		x	x				
• Transformers				x		x	x		
Former									
• Heat Transfer				x					
• Hydraulics/Lubricants									
• Hydraulic Fluids			x	x	x	x	x		
• Vacuum Pumps					x	x			
• **Gas-Transmission Turbines		x		x					
• Plasticizers									
• Rubbers		x	x	x	x	x			x
• Synthetic Resins					x	x	x	x	x
• Carbonless Paper				x					
• Miscellaneous									
• Adhesives		x	x	x	x	x			
• Wax Extenders				x		x			x
• Dedusting Agents						x	x		
• Inks						x			
• Cutting Oils						x			
• Pesticide Extenders						x			
• Sealants and Caulking Compounds						x			

SLIDE 4

MONS 216385

OCCURRENCE

- 0.2.-10.5 mg/m^3 In Air at Plants-1959
- Average PCB Concentrations in Seawater Were 13 ng/L
- Average Japanese Intake Calculated to be 4-50 ug/day
- 2.2 Million Pounds of PCBs Fall on the U.S. Yearly

SLIDE 5

MONS 216386

PCB RESIDUES IN ANIMALS

Year	Species	ppm (Fat)
1971	Fish	360
1977	Cows	5.8
1973	Birds	15.3
1974	Ducks	3.3
1970	Falcons and Hawks	2-14,000

SLIDE 6

MONS 216387

PCB RESIDUES IN THE GENERAL POPULATION

Year	Country	ppm (Fat)	ppb (Blood)
1976	Finland	1.97	3-21
1974	Germany	8.3	-
1972	U.S.A.	1-2.0*	0-29
1975	Japan	2.6	3.2
1972-74	Japan	5.0	4.9

* 40% of U.S. Population > 1.0 ppm
  26% of U.S. Population 1.0-2.0 ppm
  14% of U.S. Population > 2.0 ppm

SLIDE 7

MONS 216388

PCB RESIDUES IN OCCUPATIONALLY EXPOSED

Year	Country	Occupation	ppb (Blood)
1973	Finland	Laboratory	36-63
		Capacitor Plant	75-1900
1972	Japan	Capacitor Plant	100-650

SLIDE 8

MONS 216389

PCB RESIDUES IN HUMAN MILK

Year	Country	Whole Milk (ppb)	Milk Fat (ppm)
1970	Germany	103	3.5
1972	Sweden	25	-
1973	U.S.A.	100	-
1974	Japan	30	1.2

FDA Regulation
Cow Milk — Limit 2.5

SLIDE 9

MONS 216390

TOXICOLOGY

The Study of:

(1) Chemical or Physical Agents Which Interact With
(2) Any Living System in Which a Response is Produced
(3) The Response Must be Considered Harmful or Undesirable

SLIDE 10

MONS 216391

TOXICITY RATING CHART

Rating	Probable Oral Lethal Dose for Humans*	
	Animal LD_{50}	Expected Human Dose
1. Nontoxic	15,000 mg/kg	$\geq$ 1 Quart
2. Weakly Toxic	5,000-15,000 mg/kg	1 Pint-1 Quart
3. Moderately Toxic	500-5,000 mg/kg	1 Ounce-1 Pint
4. Toxic	50-500 mg/kg	1 Teaspoon-1 Ounce
5. Extremely Toxic	5-50 mg/kg	7 Drops-1 Teaspoon
6. Supertoxic	$\geq$ 5 mg/kg	Less Than 7 Drops

* Average Adult 70 kg

SLIDE 11

MONS 216392

CROSSMATCH THE FOLLOWING CHEMICALS WITH THEIR TOXICITIES

Agents	LD_{50} (mg/kg)
Alcohol	14,000
Botulinus toxin	10,000
DDT	4,000
Dioxin (TCDD)	1,500
Iron Tablets ($FeSO_4$)	100
Nicotine	2
PCBs	1
Strychnine	0.001
Table Salt (NaCl)	0.00001

SLIDE 12

MONS 216393

ACTUAL TOXICITY AND RANKING

Agents	LD_{50}	Expected Human Dose
PCBs	14,000	1 Quart
Alcohol	10,000	1 Pint-1 Quart
Table salt	4,000	1 Pint
Iron	1,500	1 Ounce-1 Pint
DDT	100	1 Teaspoon-1 Ounce
Strychnine	2	4 Drops
Nicotine	1	1 Drop
TCDD	0.001	Less Than 1 Drop
Botulinus toxin	0.00001	Less Than 1 Drop

SLIDE 13

MONS 216394

ANIMAL TOXICITY STUDIES

Systemic	Reproductive/Fetal	Mutagen	Cancer
Liver	Resorptions	Ames Test	Mice
Skin	Litter Size	Dominant Lethal	Rats
G.I.	Survival	Chromosomal Studies	
Blood	Teratogen		
Hormonal	Karnofsky's Law		

MONS 216395

SYMPTOMS OF TOXICITY IN HUMANS

- Chloracne, Pigmentation
- Ocular Discharge
- Liver Enlargement
- Irregular Menstruation
- Growth Retardation, in Children
- Elevated Triglycerides

SLIDE 15

MONS 216396

POSSIBLE EXPOSURES TO PCBs

OSHA	FDA
	Fish
0.1 ug/m^3	2 ppm
1 ug	200-400 ug

SLIDE 16

MONS 216397

COMPARISON OF PCB TOXICITY IN HUMANS TO COMMON COMPDUNDS

Agents	Dose (grams)	Predicted Human Response
PCBs	2.0	"Yusho"
Phenylephrine (Neosynephrine, Isophrin Congespirin, Dristan)	1.0	Death
Dextromethorphan (Cough Medicines-DM Robitussin-DM)	0.5-1.0	Death
Diphenhydramine (Benadryl)	0.4-1.0	Death
Chlorpheniramine (Chlor-Trimeton, Dristan)	1.0-2.0	Death

SLIDE 17

MONS 216398

Agent	Blood Levels	Human Response
Vitamin A	3-20 ppm	Toxic
PCBs	1.9 ppm	None
PCBs	$\geq$ 1.0 ppm	None

SLIDE 18

Compound	TLV	WQC	Chronic Study	Cancer
Aldrin	250 ug/m^3	0.79 ng/l	10 ppm	yes
DDT	1,000 ug/m^3	0.24 ng/l	1-10 ppm	yes
Nitrosamine	-	8.0 ng/l	10 ppm	yes
Vinyl chloride	10,000 ug/m^3	20,000 ng/l	50 ppm	yes
PCBs	0.1 ug/m^3	0.79 ng/l	100-1000 ppm	yes/no

SLIDE 19

HONS 216400

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