Monsanto

FROM (NAME & LOCATION): E. S. Tucker - R&D Laboratories - So. Second St. - St. Louis

DATE: August 20, 1969

SUBJECT: REFERENCE SAMPLE - BUREAU OF FISHERIES; MONSANTO SAMPLE #2084

REFERENCE:

cc: R. E. Keller - So. Second
M. W. Farrar - So. Second
W. R. Richard - GO
E. P. Wheeler - GO

TO : C. R. Campbell - Pensacola
Tuck Dean - Pensacola

We have completed the analysis of the exchange water sample #2084 and I have included with this memo a Xeroxed copy of the complete run calculations and calibration curve.

Three 250 ml aliquots were taken from the 5 pint bottle and analyzed directly after extraction with hexane and concentration to a specific volume. Sample #201-1 was taken prior to shaking the bottle vigorously, samples #201-2 and #201-3 after. The material extracted is as they reported - Aroclor 1254. Their reported concentration of 274 ppb agrees well with our duplicate analysis, #201-2 and #201-3, which were 270 ppb and 269 ppb, respectively. In sample #201-1, we found 17.2 ppb Aroclor 1254 indicating that most of the Aroclor 1254 is adsorbed by the particulate matter present.

We also have received the fish samples and the other water samples which we talked about. We analyzed one of the larger Bluegills (65.37g) and found 133 $\pm$2 ppm Aroclor 1254.

We will report the results of our analysis of the other samples as soon as they are completed.

Scott Tucker

db
Encl.

MONS 206941

IM-10 REV 11-65

AUG 1969

Monsanto

FROM (NAME & LOCATION): C. R. Campbell - Pensacola — Textiles Division

DATE: August 13, 1969

SUBJECT: Stream Pollution

REFERENCE:

cc: B. T. Dean
J. E. Lipe
Elmer Wheeler
C. E. Rannefeld
F. S. Riordan, Jr.

TO: D. W. Brubaker - Pensacola

B. T. Dean and I met with Drs. T. S. Hopkins, Chairman, Department of Biology, University of West Florida and Tom Dukes, Head of the Bureau of Commercial Fisheries, U. S. Department of Interior on August 8, 1969 at the University. Dr. Dukes reported finding residues identified as Aroclor 1254 in various marine life in the area and increasing concentrations rising to 41ppB at our outfall. Specifically, PCB residues were reported as follows:

Our Outfall	41 ppB
Highway 90 Bridge	0.5 ppB
Dead Menhaden (Mulat Bayou)	12 ppm
Escambia Bay Flounder's Liver	76 ppm

He reported finding these residues in oysters in East Bay, and, in fact, this was where PCB was originally found in this area on February 4, 1969 although a monitoring program has been in effect since January 5, 1968. Dr. Dukes further stated that he did not believe that PCB was involved in any of the recent fish-kills but that he was concerned with its possible effect on shrimp's breeding and migratory habits.

His people had conducted a 96-hour test on shrimp at the 42 ppb level of PCB in which they experienced a mortality rate of 50%. Dr. Dukes invited us to visit his lab and to observe their techniques and data and also requested that we analyze one of their samples as a cross-check.

J. A. Lubkowitz and I visited Dr. Dukes at the Bureau of Fisheries on August 12, 1969. Again Dr. Dukes expressed his belief that PCB was not a factor in the recent fish-kills. He gave us a personal tour of his facilities which were quite impressive. The analysis of PCB was conducted by Alfred Wilson and the work seemed sound. The procedures on water involved an extraction using petroleum ether-acetonitrile mixtures and concentration of same. Wilson has chromatographed the extract residue using a number of different columns and had available various Arochlor isomer mixes for comparison. His VPC results were superimposable on Archlor 1254 standards. He has some confirmation using thin layer chromatography techniques and had checked for irreversible absorption on the VPC columns by hexane injection between sample analysis. As a non-expert in the field, I would guess that the results are probably valid.

IN-10 REV. 11-68

This laboratory is conducting research and analysis on pesticide residues for the Eastern half of the United States. We were shown a test on juvenile shrimp of 18-day duration, evaluating the effect of PCB at the 5 ppb level. Eighteen of twenty-five shrimp were dead in the test batch as of today while all of the twenty-five controls were living. An additional series of samples had been taken in the Escambia River. One from our outfall had been analyzed at 274 ppB. Dr. Dukes gave us a 5-pint bottle of the same sample for a crosscheck. I will forward this sample to Scott Tucker, Organic Division for analysis.

While I believe that Dr. Dukes will proceed cautiously and objectively; I believe that he will continue his close scrutiny of our estuary system and that we should proceed with all haste to determine the validity of his findings and act accordingly.

C. R. Campbell

/bps

MONS 206943

file

MITSUBISHI MONSANTO CHEMICAL COMPANY

FROM LOCATION : Tokyo

cc: Mr. H. S. Bergen *

DATE : July 24, 1969

SUBJECT : CHLORINATED BIPHENYL TOXICITY

REFERENCE :

TO : Dr. R. Emmet Kelly *
St. Louis, Mo.

Dear Emmet:

Attached is an English language translation of a recent newspaper article from the MAINICHI JOURNAL, dated July 24, 1969.

This is associated with the exposure to contaminated rice bran oil. You will recall the much more detailed medical summary which was forwarded to you in May.

John
J. R. Durland

JRD:fu
Encl.*

THE MAINICHI July 24, 1969

The reported two deaths among the rice bran oil patients are suspected to have been caused by malfunction of the pituitary and suprarenal systems. The reported causes of their deaths, both acute heart failures, seem to have been caused by the suprarenal malfunction. Their autopsies revealed atrophy of the suprarenal body or suggested disturbance of the function. If this function is disturbed, there is a high posibility that a heart failure occurs all of a sudden.

There had been complaints from some of the oil disease patients of some acute abdominal pains or sudden chill of the body, which are often related to suprarenal system disorders, while the organ is a fat tisue and can be suspected to have collected Kano-Chlor* (the organic chlorine in question) there. The committee, therefore, has decided to run more examinations of all the patients not only at their skin conditions but with more weight on internal conditions including blood and urine analyses and check-up of the total circulartory system.

*chlorinated biphenyl

TY:yf

MONS 206945

AUG 4 1969

UTAH STATE UNIVERSITY · LOGAN, UTAH 84321
COLLEGE OF AGRICULTURE

DEPARTMENT OF
ANIMAL SCIENCE

July 30, 1969

Dr. Elmer P. Wheeler
Manager, Environmental Health
Monsanto Company
800 North Lindbergh Boulevard
St. Louis, Missouri 63166

Dear Dr. Wheeler:

Thank you for the information in your letter of July 16. Your research project underway with polychlorinated biphenyls is impressive and I will be very interested to learn some of the forthcoming results. Regarding the question of "no effect" levels for induction of hepatic microsomal enzymes, our data may be useful to you and we would have no objection to providing you with copies of our manuscripts when they are ready.

One aspect of our study concerns the magnitude of residue storage in adipose tissue and qualitative changes in the stored material relative to that fed. I do not intend to pursue this deeply but will make an effort to provide reasonably quantitative interpretations. Perhaps I could compare notes with you on these points before we make our presentations.

I regret that you cannot provide pure isomers of the various biphenyls since our investigations of structure vs. activity would be considerably more enhanced by having pure isomers to study. Should your plans mature to visit in laboratories working with PCB materials we will be pleased if you can arrange to visit with us.

I have another question, somewhat related, which I will pose to you in the hope that you can direct it to the proper individual at Monsanto. We are making an extensive study of structure-activity relationships of hepatic enzyme inducing agents in the general class of diphenyl methane derivatives. I have been told that Monsanto has an interesting cyclopropane analogue of DDT [1-cyclopropyl-1,1-bis(parachlorophenyl)-methane], an experimental insecticide. We would appreciate a 1-5 gram sample of analytical reference grade to include in our studies if that could be arranged.

Thank you for your assistance.

Sincerely yours,

Joseph C. Street
Professor

JCS:jw

MONS 206946

July 16, 1969

Joseph C. Street
Professor, Dept. of Animal Science
College of Agriculture
Utah State University
Logan, Utah 84321

Dear Professor Street:

Dr. Cummings Paton has asked me to reply to your letter to him of July 3.

We are extremely appreciative of your thoughtfulness in informing us of the paper which you have submitted for the next meeting of the American Chemical Society. As you can imagine, we are very interested in learning of new research efforts that are underway concerning the polychlorinated biphenyls.

I am sorry that we can not provide at this time pure isomers of the various chlorinated biphenyls. We are investigating the possibility of separation techniques since a number of laboratories and agencies have asked us for pure isomers. In our own rather extensive sampling and analytical program, we are using the technical materials for reference.

Perhaps you would be interested in learning that we have a number of toxicity and research projects underway. These include two year chronic feeding studies in rats and dogs; three generation rat reproduction studies; studies with chickens to determine possible toxicity effects on the birds, egg production, hatchability of eggs, viability of chicks, egg shell thickness and calcium and phosphorus content. The above studies include three dietary levels and controls. In the case of the rat work sufficient numbers have been included to allow sacrifice of a significant number at three months, six months and twelve months.

MONS 206947

We have discussed with our toxicological consultants the question of undertaking studies relating to the induction of hepatic microsomal enzymes. For the time being we have decided that more toxicity data based on the usual parameters for establishing a "no effect" level would be helpful.

We learned recently of one study abroad where chickens fed a diet containing 100 ppm of 60% chlorinated biphenyl for a year showed no gross effects. Unfortunately, the study was not as comprehensive as we have undertaken and would not include the parameters mentioned above in connection with our studies with chickens.

I expect that some time this summer Dr. Robert E. Keller, Manager of Applied Sciences for our Organic Chemistry Division, and I will attempt to set up an itinerary to allow visits to those scientists who have contacted us about the PCB situation. We obviously would hope to include a visit with you and will write you further as our plans develop.

Very truly yours,

Elmer P. Wheeler
Manager, Environmental Health

EPW:ju

c.c. Dr. Cummings Paton

b.c. R. E. Keller
W. R. Richard

UTAH STATE UNIVERSITY · LOGAN, UTAH 84321
COLLEGE OF AGRICULTURE

DEPARTMENT OF
ANIMAL SCIENCE

July 3, 1969

Dr. Cummings Paton
Organic Division Development
Monsanto Chemical Company
800 North Lindberg Boulevard
St. Louis, Missouri 63166

Dear Dr. Paton:

Through collaboration with Dr. Francis A. Gunther, University of California-Riverside, I obtained samples of the Arochlor products from your company which have been studied for effectiveness in induction of hepatic microsomal enzymes. The enclosed abstract which summarizes our work to date, has been submitted for the program of the Pesticide Division, American Chemical Society for its next annual meeting. Dr. Gunther asked that I keep you informed of our studies, hence this letter.

My primary interest in studying substituted biphenyls has been in connection with a sizable endeavor to identify significant structure-activity relationships in compounds capable of inducing hepatic microsomal enzymes. We had earlier investigated a considerable series of bridged and unbridged diphenyl compounds involving a variety of substituent groupings. The activities of the Arochlors seem to fit reasonably well with that predicted on the basis of our earlier studies, allowing for the crude composition of the Arochlor products. We are most anxious to obtain pure compounds in the chlorinated biphenyl family and would appreciate any assistance you and your company might be able to provide in obtaining such.

In regard to the possible significance of PCB materials in the environment, I am presently fairly openminded. I am impressed with the potency of the higher members of the Arochlor family as enzyme inducers. However, I am by no means committed to the view that this is a serious hazard in itself to the health of any organism including the wildlife species that have been the subject of so much recent concern because of pesticide residues. The scientific questions remaining in this area are extremely complex and much more research information is needed before a clear understanding emerges. Toward that end the continued assistance of your company will be most appreciated and, of course, acknowledged in our presentations and publications.

Sincerely yours,

Joseph C. Street
Professor

JCS:jw

MONS 206949

COMPARATIVE EFFECTS OF POLYCHLORINATED BIPHENYLS AND ORGANOCHLORINE PESTICIDES IN INDUCTION OF HEPATIC MICROSOMAL ENZYMES. J.C. Street, F.M. Urry, D.J. Wagstaff, and A.D. Blau. Dept. of Animal Science, Utah State University, Logan, Utah 84321

Polychlorinated biphenyls (PCBs) are of interest because of their recent identification with residues of organochlorine pesticides in tissue samples of fish and certain birds where their presence causes some interference with routine GLC analysis of the pesticide residues. Moreover, some PCB products have been reported to induce liver microsomal enzymes, as do many organochlorine pesticides. The microsomal enzyme inducing activity of a series of PCB products (Arochlors) has been evaluated and compared to that of many organochlorine pesticides. The 10 products ranged from 21 to 68 percent chlorine and included two chlorinated triphenyls. Female rats were fed the test products at levels of 50 and 100 ppm in the diet for 15 days. Microsomal enzyme activity was assayed with liver homogenates using p-nitroanisole, aniline, EPN and progesterone as substrates. In addition, indirect measurements of hexobarbital and dieldrin metabolism, in vivo, were made. Administration of each PCB product induced metabolism of all substrates; the amount of stimulation measured increased regularly with percentage chlorination of the product. Products containing over 50% chlorine were as potent in enzyme induction as DDT, heptachlor epoxide and other highly active pesticides. Since certain hazardous aspects of pesticide residues in the environment toward wildlife may derive from their induction of hepatic microsomal enzymes, the presence and equally high activity of some PCB materials in mixed residues is of greater significance than merely a source of analytical interferences.

MONS 206950