STATE OF NEW YORK
DEPARTMENT OF HEALTH
ALBANY

DAVID AXELROD, M.D.
COMMISSIONER

b-PCB

October 12, 1990

Dear Commissioner Benson:

The U.S. Food and Drug Administration (FDA) has set a 2 ppm tolerance level for PCBs and a 25 ppt advisory level for 2,3,7,8-TCDD in fish. However, new toxicological studies raise concerns about the potential human health risks from PCB and 2,3,7,8-TCDD exposure and the adequacy of the current tolerance and advisory levels.

A series of published studies on the toxicity of Aroclors 1016, 1248 or 1254 in rhesus monkeys indicate that mild dermal, developmental or immunological effects may occur at chronic oral doses of 5-7 ug/kg/day (Table 1). Department of Health staff calculated that the margin of exposure between 5 ug/kg/day and the intakes of 60-kg women consuming average amounts of fish (14.3 grams/day, Javitz, 1980; US EPA, 1989) at 2 ppm PCBs is 10. The margin of exposure is substantially lower (3.6) for women consuming above average amounts of fish (42 grams/day at the 95 percentile, Javitz, 1980; US EPA, 1989). Our concern over these low margins of exposure is heightened by epidemiological studies linking PCB exposure to low birthweight and behavioral anomalies (Fein et al., 1984; Gladen et al., 1988; Jacobson et al., 1983, 1984a, 1984b, 1985; Rogan et al., 1986; Taylor et al., 1984, 1989) and a preliminary report (Arnold et al., 1987). These studies suggested that chronic doses of 5 ug Aroclor 1254 kg/day interfered with normal reproduction in rhesus monkeys (see Tryphonas et al., 1989, for discussion of the immunological effects of Aroclor 1254 in the same monkeys).

Other published studies on the reproductive and developmental effects of 2,3,7,8-TCDD in rhesus monkeys show that reproductive failure occurred in females exposed orally to 0.7 ng/kg/day for about 48 months, but did not occur in females exposed orally to 0.13 ng/kg/day for about 42 months (Schantz et al., 1986; Bowman et al., 1989a,b). Moreover, subtle behavioral alterations were reported in juveniles born to females exposed to either dose (Schantz and Bowman, 1989). Daily intakes of 2,3,7,8-TCDD for 60-kg women consuming 14.3 or 42 grams of fish per day containing 25 ppt 2,3,7,8-TCDD provide margins of exposure of 22 and 6.5, respectively, over the daily dose ingested by female rhesus monkey which gave birth to offspring with behavioral alterations.

I request that you review these data and evaluate the need for (1) a downward revision of the FDA tolerance level for PCBs in fish, and (2) the promulgation of a FDA tolerance level for 2,3,7,8-TCDD (and other PCDDS/PCDFs) in fish. Based on the potential for a similar mechanism of toxicity for PCDDs and PCDFs, I'm also requesting your guidance on incorporation of toxicity equivalency factors into the development of an advisory or a tolerance level for PCDDs/PCDFs in fish.

What advisory, if any, would the FDA suggest as appropriate to protect women of childbearing age from the potential adverse reproductive effects of PCBs in fish? This request arises because of the new toxicological information, the likelihood that some populations have easy access to affordable fresh fish (e.g., those living near the ocean or large bodies of water) and could consume higher than average amounts of fish. Also, recent sampling shows that the average levels of PCBs in fish (e.g., bluefish) commercially available in some areas is about 1 ppm. If an advisory is warranted for women of child-bearing age, how should the states address the inconsistency of basing a health advisory on commercially available fish?

Sincerely,

David Axelrod, M.D.
Commissioner of Health

Enclosure

Hon. James Benson
Acting Commissioner of Food and Drugs
U.S. Food and Drug Administration
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Chronically Exposed to Diets Containing Aroclors 1016, 1248 or 1254.

Aroclor	No. of Females/Dose	Duration of Exposure	Dose Levels (ug/kg/d)**	Parameters	Study
1016	7	87 weeks	7, 30	offspring: low birthweight at high dose only; hyperpigmentation about hairline at both doses; no behavioral effects at 14 or 48 months at low dose; behavioral effects at 14 months and perhaps 48 months at high dose	Barsotti & Van Miller, 1984; Lev-[illegible] et al., 1988; Schantz et al., 19[illegible]
1248	5	66-102 weeks	6, 13	offspring: no effect on birthweight at either dose; no overt signs of toxicity at low dose but mild dermatological lesions and hyperpigmentation during nursing at high dose; post-weaning mortality (1/8 with signs of PCB toxicity at high dose; behavioral effects at 12 months at both doses; no behavioral effects at 14 months at high dose or at 40 and 48 months at low dose	Bowman et al., 19[illegible] Schantz & Bowman, 1985; Male et al., 1986; Schantz et al., 1989
1248	8	16-21 months	90, 190	adults: dermal, eye and reproductive toxicity at both doses offspring: fetotoxicity; dermal and internal organ toxicity during nursing; behavioral toxicity (low dose only tested) during first 6 years of life	Barsotti et al., 1976; Allen & Barsotti, 1976; Allen et al., 19[illegible] Bowman et al., 19[illegible] 1981; Bowman & Beirmaimus, 1981; Schantz and Bowma[illegible] 1983; Male et al 1986; Levin et al 1988; Schantz et al., 1989
1254	4	27-28 months	200	adults: severe dermal, eye and internal organ toxicity	Tryphonas et al., 1986a,b
1254	16	23 months	5, 20, 40, 80	adults: dose-dependent reduction in antibody levels to sheep red-blood cells starting at lowest dose	Tryphonas et al., 1989

**female dose

References

Allen, J.R. and D.A. Barsotti. 1976. The effects of transplacental and mammary movement of PCBs on infant rhesus monkeys. Toxicology. 6: 331-340.

Allen, J.R., D.A. Barsotti and L.A. Carstens. 1980. Residual effects of polychlorinated biphenyls on adult nonhuman primates and their offspring. J. Toxicol. Environ. Health. 6: 55-66.

Arnold, D.L., F. Bryce, K. Karpinski, J. Mes, H. Tryphonas, J. Truelove and Z.Z. Zawidzka. 1987. Toxicity of polychlorinated biphenyls (Arcolor 1254) in adult monkeys as a consequence of continous exposure and in infant monkeys exposed during pregnancy and nursing. Paper presented at 30th Annual Meeting, Canadian Federation of Biological Societies. Winnipeg, Manitoba.

Barsotti, D.A. and J.P. Van Miller. 1984. Accumulation of a commercial polychlorinated biphenyl mixture (Aroclor 1016) in adult rhesus monkeys and their nursing infants. Toxicology. 30: 31-44.

Barsotti, D.A., R.J. Marlar and J.R. Allen. 1976. Reproductive dysfunction in rhesus monkeys exposed to low levels of polychlorinated biphenyls. Fd. Cosmet. Toxicol. 14: 99-103.

Bowman, R.E. and M.P. Heironimus. 1981. Hypoactivity in adolescent monkeys perinatally exposed to PCBs and hyperactive as juveniles. Neurobehav. Toxicol. Terat. 3: 15-18.

Bowman, R.E. and M.P. Heironimus and J.R. Allen. 1978. Correlation of PCB body burden with behavioral toxicology in monkeys. Pharmacol. Biochem. Behav. 89: 49-56.

Bowman, R.E., M.P. Heironimus and D.A. Barsotti. 1981. Locomotor hyperactivity in PCB-exposed rhesus monkeys. Neurotoxicology. 2 251-268.

Bowman, R.E., S.L. Schantz, M.L. Gross and S. Ferguson. 1989a. Behavioral effects in monkeys exposed to 2,3,7,8-TCDD transmitted maternally during gestation and for four months of nursing. Chemosphere. 18: 235-242.

Bowman, R.E., S.L. Schantz, N.C.A. Weerasinghe, M.L. Gross and D.A. Barsotti. 1989b. Chronic dietary intake of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) at 5 and 25 parts per trillion in the monkey: TCDD kinetics and dose-effect estimate of reproductive toxicity. Chemosphere. 18: 243-252.

Fein, G.G., J.L. Jacobson, S.W. Jacobson, P.M. Schwartz and J.K. Dowler. 1984. Prenatal exposure to polychlorinated biphenyls: Effects on birth-size and gestational age. J. Pediatrics. 105: 315-320.

Gladen, B.C., W.J. Rogan, P. Hardy, J. Thullen, J. Tingelstad and M. Tully. 1988. Development after exposure to polychlorinated biphenyls and dichlorodiphenyl dichloroethene transplacentally and through human milk. J. Pediatr. 113: 991-995.

Jacobson, J.L., P.M. Schwartz, G.G. Fein and J.K. Dowler. 1984a. Prenatal exposure to an environmental toxin: A test of the Multiple Effects Model. Dev. Psychol. 20: 523-532.

Jacobson, J.L., G.G. Fein, S.W. Jacobson, P.M. Schwartz and J.K. Dowler. 1984b. The transfer of polychlorinated biphenyls (PCBs) and polybrominated biphenyls (PBBs) across the human placenta and into maternal milk. Am. J. Public Health. 74: 378-379.

Jacobson, S.W., J.L. Jacobson, P.M. Schwartz and G.G. Fein. 1983. Intrauterine exposure of human newborns to PCBs: Measure of exposure. In: PCBs: Human and Environmental Hazards. D'Itri, F.M. and M.A. Kamrin (eds.). Boston: Butterworth. pp. 311-343.

Jacobson, S.W., G.G. Fein, J.L. Jacobson, P.M. Schwartz, J.W. Dowler. 1985. The effect of intrauterine PCB exposure on visual recognition memory. Child Dev. 56: 853-860.

Javitz, H. 1980. Seafood Consumption Data Analysis. Final Report. Menlo Park, CA: SRI International.

Levin, E.D., S.L. Schantz and R.E. Bowman. 1988. Delayed spatial alternation deficits resulting from perinatal PCB exposure in monkeys. Arch. Toxicol. 62: 267-273.

Mele, P.C., R.E. Bowman and E.D. Levin. 1986. Behavioral evaluation of perinatal PCB exposure in rhesus monkeys: Fixed-interval performance and reinforcement-omission. Neurobehav. Toxicol. Terat. 8: 131-138.

Rogan, W.J., B.C. Gladen, J.D. McKinney, N. Carreras, P. Hardy, J. Thullen, J. Tinglestad and M. Tully. 1986. Neonatal effects of transplacental exposure to PCBs and DDE. J. Pediatr. 109: 335-341.

Schantz, S.L. and R.E. Bowman. 1989. Learning in monkeys esposed perinatally to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). Neurotoxicol. Teratology. 11: 13-19.

Schantz, S.L., N.K, Laughlin, H.C. Van Valkenberg and R.E. Bowman. 1986. Maternal care by rhesus monkeys of infant monkeys exposed to either lead or 2,3,7,8-tetrachlorodibenzo-p-dioxin. Neurotoxicology. 1: 637-650.

Schantz, S.L., E.D. Levin, R.E. Bowman, M. Heironimus and N.K. Laughlin. 1989. Effects of perinatal PCB exposure on discrimination-reversal learning in monkeys. Neurotoxicol. Terat. 11: 243-250.

Schantz, S.L. and R.E. Bowman. 1983. Persistent locomotor hyperactivity in offspring of rhesus monkeys exposed to polychlorinated or polybrominated biphenyls. Soc. Neurosci. Abstr. 9: 423.

Taylor, P.R., C.E. Lawrence, H.-L. Hwang and A.S. Paulson. 1984. Polychlorinated biphenyls: Influence on birthweight and gestation. Am. J. Public Health. 74: 1153-1154.

Taylor, P.R., J. Stelma and C.E. Lawrence. 1989. The relation of polychlorinated biphenyls to birthweight and gestational age in the offspring of occupationally exposed mothers. Am. J. Epidemiol. 129: 395-406.

Tryphonas, H., S. Hayward, L. O'Grady, J.C.K. Loo, D.L. Arnold, F. Bryce and Z.Z. Zawidzka. 1989. Immunotoxicity studies of PCB (Aroclor 1254) in the adult rhesus (Macaca mulatta) monkey - Preliminary report. Int. J. Immunopharmac. 11: 199-206.

Tryphonas, L., S. Charbonneau, H. Tryphonas, Z. Zawidzka, J. Mes, J. Wong, and D.L. Arnold. 1986a. Comparative aspects of Aroclor 1254 toxicity in adult cynomolgus and rhesus monkeys: A pilot study. Arch. Environ. Contam. Toxicol. 15 159-169.

Tryphonas, L., D.L. Arnold, Z. Zawidzka, J. Mes, S. Charbonneau and J. Wong. 1986b. A pilot study in adult rhesus monkeys (M. mulatta) treated with Aroclor 1254 for two years. Toxicol. Pathol. 14: 1-10.

U.S. Environmental Protection Agency (US EPA). 1989. Exposure Factors Handbook. EPA/600/8-89/043. Washington, DC: Office of Health and Environmental Assessment.

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