



STATE OF NEW YORK
DEPARTMENT OF HEALTH
ALBANY

DAVID AXELROD, M.D.
COMMISSIONER

October 12, 1990

U.S. EPA, REGION II
EMER. & REM. RES. DIV.
1999 AUG 19 AM 11:29
DIRECTOR'S OFFICE

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).

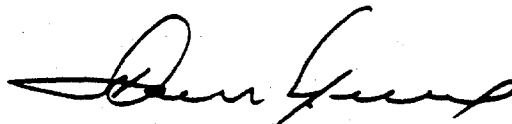
Other published studies on the reproductive and developmental effects of 2,3,7,8-TCDD in rhesus monkeys show that reproductive failure occurred in females exposed orally to 0.7 ng/kg/day for about 48 months, but did not occur in females exposed orally to 0.13 ng/kg/day for about 42 months (Schantz et 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.

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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,

A handwritten signature in dark ink, appearing to read "David Axelrod", written in a cursive style.

David Axelrod, M.D.
Commissioner of Health

Enclosure

Hon. James Benson
Acting Commissioner of Food and Drugs
U.S. Food and Drug Administration
5600 Fishers Lane
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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	Baracotti & Van Miller, 1984; Levin et al., 1988; Schantz et al., 1989
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 (1/6 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., 1983; Schantz & Bowman, 1985; Male et al., 1985; 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	Baracotti et al., 1976; Allen & Baracotti, 1976; Allen et al., 1981; Bowman et al., 1981; Bowman & Beirnaert, 1981; Schantz and Bowman, 1983; Male et al., 1985; 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

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