

2010 SAB REVIEW OF TCDD: COMMENTARY by GARY KAYAJANIAN,
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This is the fourth SAB TCDD Review NCEA has requested. In the initial, 1988 Review, the SAB accepted the NCEA proffer from the Kociba life time feeding study in rats, that at mid and high dose (3300 and 25,600 parts per trillion (ppt)) TCDD (the technical abbreviation for 2,3,7,8-tetrachloro-para-dioxin) caused a significant increase in liver cancers in females. NCEA made the policy-based claim that TCDD was a possible human carcinogen, but the low human health risk associated with the finding did not spur the Administrator to act.

In 1995, the SAB entertained NCEA claims drawn from a NIOSH study of cancer mortality in chemical workers exposed to contaminant levels of TCDD which showed a significant increase in total cancers. NCEA and the NIOSH investigators [see Fingerhutt et al. (1991), a contemporary NIOSH Report, and plant specific mortality tables] failed to reveal the identity and levels of other chemicals in the plants. NCEA made the claim that TCDD was a human carcinogen responsible for up to one-in-a-thousand deaths; none of the unrevealed chemicals in the plants were assumed to contribute to the cancer excess Fingerhutt reported. The SAB rejected the cancer classification claim, and, therefore, NCEA's cancer mortality assessment. Let me enumerate why. [1] My assessment of the Kociba rat data showed that [a] at the most relevant exposure endpoint --low dose (540 ppt) -- [b] in both sexes, TCDD significantly ($p < .01$) reduced the most relevant cancer endpoint -- total cancers. So, I found TCDD was an anti-carcinogen in male and female rats. [2] I asked two separate follow-up questions, which really are asked and answered together. Is TCDD an anti-carcinogen in humans? If it is, at what step in cancer creation does TCDD act -- initiation, promotion, or cancer cell replication? The first ten years of the prospective Italian study of low exposure men and women exposed to TCDD (and many other unidentified chemicals) when a nearby chemical plant exploded provided an answer to both questions. (See, Bertazzi et al., 1993.) Uterine cancers in the second five years following exposure showed a very significant decrease ($p < .0002$) from the expected and found levels in the first five years. So, TCDD was an anti-carcinogen, and, based on the timing of the decrease in expected cancers, a promoter blocker. Total cancers in women were significantly reduced over the ten years of the study (no first five, second five year breakouts were provided by Bertazzi). [3] Some of the men's cancer mortality in the NIOSH occurred over the first five and second five years following exposure to TCDD. Total cancer mortality was significantly reduced in the second five years compared to the first five years -- the pattern expected of a promoter blocker.

Earlier this decade, NCEA utilized a 1999 follow-up to the 1991 NIOSH study, to renew its TCDD cancer claim to the SAB, this time associated with an increased mortality claim. Steenland used paper records in eight of the twelve plants to

estimate TCDD levels in arbitrary units. All but one of the excess cancers in these eight plants were found in three plants -- the two high exposure plants with virtually identical TCDD exposure and the lowest exposure plant with an expected 3 ppt TCDD level. The cancer classifications found in excess in the highest exposure plants should have been similar, if not identical, if TCDD caused them; however, the cancer patterns were different, so TCDD could not have caused them -- other chemicals known to NIOSH but publically unidentified by them caused those excess cancers. In the low exposure plant, the virtual absence of TCDD caused, that is the presence of other chemicals, caused the plant's excess cancers. The SAB informed NCEA that its classification of TCDD as a carcinogen was without merit. Two other factors may have played into the SAB decision. [1] My showing that the [Operation Ranch Hand] airmen exposed to the highest levels of TCDD thirty years earlier (a body burden over 123 ppt) in Southeast Asia showed a significant (greater than forty percent) reduction of cancer incidence compared to matched unexposed veterans. [2] The SAB observation that Agency regulators were not forthcoming with the first SAB Review Committee when they failed to disclose the true nature of the most relevant Kociba data. The clear implication of the rebuke was that had these data been revealed, no initial classification of TCDD as a possible human carcinogen would have been approved by the SAB in 1988.

In looking forward to the fourth SAB review of TCDD data, I notice a different landscape of SAB members, a new DFO, and different SAB management from the days of my involvement in the second and third SAB review of TCDD. Most have my observations on TCDD data have been published under my name in refereed journal articles; earlier SAB reviewers were aware of them. I suspect the new SAB reviewers are unaware of my TCDD work, because (and I am not surprised) none of my articles are cited in NCEA's latest TCDD document. At least, my patent [No 6,444,698], describing TCDD as a potent cancer prevention chemical should have merited citation and discussion by NCEA. In any case, many of the issues, factual presentations and, especially, modelling the NAS and NCEA raise become irrelevant to solving health concerns EPA has imputed to TCDD, because they can not explain away the repeated observations that at low levels of exposure above background in men and women TCDD is a potent total cancer anticarcinogen: any cancer modelling that fails to incorporate the J-shape of the dose response curve is unresponsive to real human data. In brief, this fourth SAB review should not recommend adverse regulation of TCDD, because at the most relevant of exposures/body burdens above background TCDD reduces total cancer incidence in men and women.

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