Endosulfan’s Effects: Omissions and Flawed Data

The main objective of the Endosulfan Manufacturers and Formulators Welfare Association in India is disseminating scientific facts concerning the use of endosulfan. Because endosulfan is used in several countries, the association watches for global news and information relevant to endosulfan.

Members of the Endosulfan Manufacturers and Formulators Welfare Association are of the strong opinion that Saiyed et al. (2003) omitted significant information in their published report “Effect of Endosulfan on Male Reproductive Development.” Consequently, to unintiated readers the article presented an alarming picture of endosulfan, a pesticide registered for use in over 70 countries for more than 40 years.

Saiyed et al. (2003) failed to mention the origin of their study. In fact, their study is an integral part of an epidemiologic study submitted to the government of India in 2003, “Report of the Investigation of Unusual Illnesses Allegedly Produced by Endosulfan Exposure in Padre Village of Kasargod District” [National Institute of Occupational Health (NIOH) 2003]. After studying this report and other related studies, an expert group appointed by the government of India categorically concluded in February 2003 that “there is no link established between use of endosulfan in PCK [Plantation Corporation of Kerala] plantations and health problems reported in Padre village” (Central Insecticides Board and Registration Committee 2003). The government of India has since accepted this conclusion.

Epidemiology is a science of proving association and not causation. Therefore, we consider the conclusion of Saiyed et al. (2003) that their “study results suggest that endosulfan exposure may delay sexual maturity and interfere with hormone synthesis in male children” to be unscientific, uncalled for, and objectionable.

Saiyed et al. (2003) failed to mention the fact that, besides endosulfan, a host of other pesticides were also used in both exposed and control study areas. The comment by EHP’s Science Editor, Jim Burkhart, in the press release dated 1 December 2003 (EHP 2003) that “decades of spraying this pesticide [endosulfan], and only this pesticide” is therefore erroneous.

The authors failed to mention the actual quantity of endosulfan aerially applied in the cashew plantation block closest to Vaninagar school (exposed group), which was 105 g active ingredient (ai)/acre/year. This rate should be compared with the permissible seasonal application rates elsewhere, including the United States, where 1,000 g ai/acre/year is often exceeded.

Saiyed et al. (2003) failed to take into consideration the fact that the interval between annual aerial applications was nearly 11 months and that the aerial applications were made 5–6 months ahead of monsoon rains. All this must be weighed against the known half-life of endosulfan in conditions in India (30–50 days).

In the proceedings of the expert group, the experts on epidemiology and residue science raised serious objections to the study design, sample selection, and residue analysis adopted by the NIOH (2003).

Endosulfan residue levels reported by Saiyed et al. (2003) in blood samples are 1,000 times greater than the residue levels reported in water samples by the authors in the original report submitted in India (NIOH 2003). The scientific properties of endosulfan do not support this phenomenon. Also, two studies by Kerala Agricultural University (State of Kerala 2001) that preceded the article by Saiyed et al. (2003) did not find endosulfan residues in water in Padre village.

There are a few representative omissions and flaws in the article by Saiyed et al. (2003). Knowing the reputation and professional excellence of EHP, I appreciate the chance to address these problems here.

The author declares a competing financial interest because he is retained as executive secretary to the Endosulfan Manufacturers and Formulators Welfare Association of India.

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Endosulfan’s Effects: Inaccurate Data

We would like to address problems with the article “Effect of Endosulfan on Male Reproductive Development” by Saiyed et al. (2003). Our comments are based on extensive discussions with several experts and decision-making bodies on the subject.

First, Saiyed et al. (2003) described the results from a report first submitted in India in July 2002 by the National Institute of Occupational Health (NIOH 2002). We noted with interest that Saiyed et al. (2003) did not include additional or new data in the article beyond what was presented in the original report (NIOH 2002). Consequently, there was no need for discussing the results again.

The original NIOH report (NIOH 2002) was submitted to an expert panel of Indian scientists appointed by the Government of India. The results of this review were reported to the Indian Central Insecticides Board and Registration Committee in April 2003. The committee was highly critical of the overall conduct of the study and concluded that “there is no link established between use of endosulfan in PCK [Plantation Corporation of Kerala] plantations and health problems reported in Padre village” (Central Insecticides Board and Registration Committee 2003). This was further endorsed at a subsequent meeting of the Registration Committee in September 2003. The Indian scientists who reviewed this report evidently had some major advantages of additional information that were not available to the reviewers of the article by Saiyed et al. (2003). Namely, they had access to all of the data, they could consult the authors, and they clearly comprehended the local situation in the region of India under consideration. Therefore, they found that the NIOH study (NIOH 2002) failed to prove what appeared to be an apparently flawed hypothesis.

Referring to the statement by the Central Insecticides Board and Registration Committee (2003), the Minister for Agriculture reiterated in the Indian parliament that “The [Government] of India also constituted an expert committee and based on its recommendations decided that the use of endosulfan be continued as per provisions of Insecticides Act 1968 as there is no link established between the use of endosulfan in PCK plantations and health problems in Padre village.”

In their article in EHP, Saiyed et al. (2003) emphasized the premise that the geographical area studied was unique, with only a single pesticide used over a long period of time. Unfortunately, this is not correct; local records show that several pesticides were applied in this area. Furthermore, what is
also apparent from local records is that several of the same pesticides were also commonly used in the control area. Thus, the scientific value of this study is questionable.

For sexual maturity rating (SMR) and hormone levels, the results presented by Saiyed et al. (2003) displayed a relatively poor correlation with age; this is not enough to clearly describe a positive correlation. There are two additional confounding factors: a) small sample size (small number of subjects and only one blood sample per subject), which was recognized by the authors, and b) Saiyed et al. (2003) did not mention the normal biological ranges for either SMR or hormone levels in such a population. For example, serum hormone levels are highly variable and, without reference to what would be considered a normal range, the authors cannot confidently claim that the apparent changes they described were caused by pesticide exposure. This is evident in the last paragraph of the article, in which Saiyed et al. (2003) concluded that “long-term follow-up of the children is essential to understand the implications.” As a measure of endosulfan exposure, the authors described serum levels of endosulfan and endosulfan sulphate. There are a number of interesting paradoxes with these results. The first is that endosulfan was not used in the area, as described in the article, for 10 months before the study started. Given the rapid biodegradation and subsequent clearance of endosulfan in this type of environment, it is surprising that endosulfan was discovered in these samples. To further confound this, the levels of endosulfan, again as described by Saiyed et al. (2003), were $\geq 0.03$ ppb in water and $\geq 0.3$ ppb in pond sediments, well below the levels in the serum samples. Endosulfan is rapidly cleared from the body and does not bioaccumulate; thus, the serum levels are clearly at odds with those found in water samples, including those of the control samples. It should also be added that the water levels of endosulfan described by Saiyed et al. (2003) are well below the maximum recommended by the U.S. Environmental Protection Agency (EPA).

The distance between PCK plantations and Vaninagar school is about 3 km. The amount of endosulfan applied in the PCK plantation block closest to Vaninagar school was about 105 g active ingredient (ai)/acre/year, whereas the permissible application rates authorized by the U.S. EPA are $> 1,000$ g ai/acre/season. Saiyed et al. (2003) did not include this fact in their article.

In the area described by Saiyed et al. (2003), aerial application was carried out by helicopter at a height of about 10 feet above cashew tree plantations. It is highly unlikely that the sprayed endosulfan would drift away all the way to the Vaninagar school area 3 km away. Also, the interval between annual aerial applications was about 11 months. Endosulfan is likely to undergo significant degradation during this period.

In this area, it is highly unlikely that significant amounts of endosulfan would have translocated with rainwater runoff during monsoon rains, which normally occur 5–6 months after aerial application. Under typical conditions in India, significant degradation of endosulfan would have occurred.

The endosulfan residue levels Saiyed et al. (2003) reported in blood samples were 1,000 times higher than those reported in water samples. Based on the physicochemical properties of endosulfan, such a finding is highly unlikely.

Finally, the reproductive effects of endosulfan reported by Saiyed et al. (2003) are inconclusive.

We are concerned with the comment made by EHP’s Science Editor, Jim Burkhart, in the press release dated 1 December 2003 (EHP 2003):

“Decades of spraying this pesticide, and only this pesticide, on the village provided a unique opportunity to analyze its impact. Although the sample size is somewhat limited, the results are quite compelling. Calling the results “compelling” has caused significant paranoia among users of endosulfan and the general public. A number of pesticides were in use around Padre village for many decades, so it was not correct to state that only one pesticide was used. In conclusion, we hope we have shown that the article by Saiyed et al. (2003) does not contribute to the knowledge on the behavior of endosulfan or to the research to determine the cause of health problems of the people in Padre village. In view of the foregoing facts, we believe that EHP should reevaluate their review of the article by Saiyed et al. (2003).”

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Endosulfan’s Effects: Saiyed’s Response

I would like to respond to the comments of both Abraham and Indulkar about the origin and results of our study (Saiyed et al. 2003). On the basis of media reports of unusual illnesses in Padre village, we were asked by the National Human Rights Commission to investigate these illnesses and determine if they were linked to endosulfan exposure. These reported illnesses consisted of birth defects, growth- and development-related problems in children, neurologic disorders, epilepsy, allergic disorders, cancers, and high rates of suicide. On the basis of our site visit, study of the topography of the area, the report of the Regional Remote Sensing Service Centre (Nageswara Rao PP, personal communication), and information from the Plantation Corporation of Kerala (PCK), we determined that we had a unique opportunity to study various health effects of long-term exposure to endosulfan on human health.

Our study (Saiyed et al. 2003) had two components: a) an investigation of growth- and development-related parameters, such as physical growth (height and weight), skin-fold thickness, IQ, study of behavioral problems and scholastic performance, sexual maturity rating (SMR), and an estimation of sex hormones, in schoolchildren exposed to the aerial spray of endosulfan; and b) an investigation of diseases, such as neurologic and psychiatric disorders, infertility, and allergic disorders, in the adult population, which was carried out through secondary data collection from parents of the children.

In our report submitted to the National Human Rights Commission, [National Institute of Occupational Health (NIOH) 2002], we reported a higher prevalence of birth defects in both male and female children, lower mean SMR and serum testosterone levels in male children of similar age, a higher prevalence of scholastic backwardness, and neurobehavioral problems in children who had been exposed to endosulfan through aerial treatment of fields (NIOH 2002). We suggested a possible link between endosulfan exposure and these problems, which has been reported in a number of published animal experimental studies, for example, endosulfan-related birth defects (Food Machinery and Chemical Corporation 1980;
Correspondence

García-Rodríguez et al. 1996; Gupta et al. 1978; scholastic development (Lakshmana and Raju 1994; Paul et al. 1994); and reproductive effects in males (Dalsenter et al. 1999; Sinha et al. 1997, 2001). We submitted our report to the Registration Committee at their request. The eight-member expert committee, which included two major stakeholders of endosulfan in the country, was set up by the Registration Committee to examine our report along with the report of the Kerala Agriculture University (KAU) and the Fredrick Institute of Plant Protection and Toxicology (FIPPAT). The committee raised issues, many of which are also mentioned in the letters from Abraham and Indulkar, and remarked that “the findings of the NIOH study are not in conformity with the known and accepted properties, chemistry and toxicology of endosulfan” (Dubey 2003). The committee concluded that the study did not establish a link between endosulfan exposure and the health problems in Padre village. The decision of the committee was not unanimous.

One of the important components of any scientific investigation is dissemination of information to other scientists through publication of the results in a suitable journal; therefore, we submitted a manuscript covering part of the study to EHP. The opinion of the expert committee and their deliberations in no way affected our right of scientific communication. Our study was scientifically planned, designed, and carried out by a team of experts, which included epidemiologists, physicians, pediatricians, medical toxicologists, statisticians, analytical chemists, and biochemists, who have years of experience in conducting such studies and have many publications to their credit. Our article (Saiyed et al. 2003) was based on a portion of the results of the study in children. Some of the other parameters related to growth and development will be communicated at a later date.

Both Abraham and Indulkar comment that several pesticides were used in the area, so endosulfan cannot be blamed for the reported health problems. Based on the topographic study of the area, we were concerned about what was sprayed on the cashew plantation, which covered a very large area on the hills; we believed that compounds sprayed on the plantation would run off into streams used by residents of the village downhill from the plantation. We asked the PCK, the owners of the cashew plantation, to give us information on all pesticides that were sprayed in the study area. On 20 August 2001, PCK informed us that since 1980 they had aerially sprayed endosulfan (0.1% of 35% emulsifiable concentrate) twice a year almost every year. They did not mention the use of any other pesticides. In their letters, Abraham and Indulkar mention the use of other pesticides in the area; this probably refers to the valley where there are small farms that are owned by the local families. The major crop in this valley and in the control area is areca nut, for which Bordeaux mixture (copper sulfate and lime) is used. The small family farms in the valley and in the control village had a similar crop pattern; therefore, we can assume localized ground use of pesticides. This type of localized pesticide use is unlikely to cause significant widespread exposure. Our conclusions (Saiyed et al. 2003) were based on the comparison of the control and study areas on the basis of aerial exposure; therefore, the use of other pesticides, if similar in both the study and control areas, would not affect our conclusions. The issue of finding endosulfan in serum samples of the control population was adequately addressed in the “Discussion” of our article (Saiyed et al. 2003).

In their letters, Abraham and Indulkar comment that downward movement of the pesticides could start only at the onset of monsoons 5–6 months after exposure, by which time no endosulfan would remain because it biodegrades rapidly. The NIOH and three other agencies carried out endosulfan analyses at varying times (January 2001–August 2001) and reported significant amounts of endosulfan in various environmental media. First, the Centre for Science and Environment, New Delhi (a nongovernment organization), analyzed biological and environmental samples for endosulfan residues in January 2001. 1 month after the last aerial spray of endosulfan carried out on 26 December 2000. The results showed that the concentration of endosulfan in three water samples was 7–51 times higher than the maximum residue limit (MRL) (Joshi 2001). Very high levels of endosulfan were reported in samples of human blood, human milk, vegetables, spices, cow’s milk, animal tissues, cashews, cashew leaves, and soil. In one of the soil samples, the concentration of endosulfan was 391 times higher than the MRL.

Second, the KAU, Thrissur District (Kerala), India, studied endosulfan levels in soil (n = 4), plants (n = 5), water (n = 5), and sediment (n = 1) in the pond in the valley on 19 February 2001 using an HPLC–spectrophotometric detector technique. They reported endosulfan in soil (3,815 ppb on PCK plantation), 55 ppb in the mid-hills, and 315 ppb in the sediment in the pond (Mathew S, personal communication). They also reported 507–858 ppb endosulfan in cashew leaves. Their report clearly demonstrated downward movement of endosulfan from hills to the pond water (Figure 1). (Mathew S, personal communication).

Third, FIPPAT, Padappai, India, carried out sampling between March and May 2001 in cashew leaves (n = 28), human blood (n = 112), water (n = 30), and soil (FIPPAT 2001). The authors reported up to 3,430 ppb endosulfan in cashew leaves, 1–11 ppb in soil, and no endosulfan in blood or water samples. On examination of the report (FIPPAT 2001), we noted large peaks of alpha- and beta-endosulfan in some chromatographs of soil, leaf, and blood samples that they had not mentioned. We reported this discrepancy to the expert committee and requested action.

The results of the studies by the Centre for Science and Environment in January 2001 (Joshi 2001), the KAU in February 2001 (Mathew S, personal communication), and FIPPAT (2001) in March–May 2001 clearly indicate significant translocation of endosulfan from the hills to the valley and its persistent nature.

Abraham and Indulkar both noted a discrepancy in our article (Saiyed et al. 2003) between endosulfan levels in serum and water. They both assume that the endosulfan exposure occurred only through water, which is not correct. Endosulfan adheres to the soil particles; runoff water then carries the endosulfan attached to soil particles from leaf surfaces and the ground during the first few rainfalls. Also, winter rains are common in this area of India. This view is largely supported by the KAU study (Mathew S, personal communication), which showed high levels of endosulfan (315 ppb) in pond sediment in the study village. Endosulfan attached to soil particles can enter the body.
through the dermal route, more so in a hot and humid climate (excessive sweating), and through ingestion, particularly in children, who commonly have hand-to-mouth behavior. Endosulfan attached to the soil particles can also be translocated through other environmental media.

Indulkar raised several points about the results of our article (Saiyed et al. 2003). He incorrectly stated that we found poor correlation of SMR and hormone levels with age; our correlations are shown in Tables 2 and 3 of our article (Saiyed et al. 2003). He also complained that we had not compared the ranges of SMR and hormone levels in our study groups to normal ranges, but we did not consider it necessary because we were comparing the groups with each other. Also, Indulkar’s points about the wide variability of hormone levels and small sample size were discussed and clarified in our article.

Both Abraham and Indulkar stated that endosulfan cannot travel a distance of 3–4 km and that it biodegrades quickly. The long half-life of endosulfan in soil is well known and was mentioned in our “Discussion” (Saiyed et al. 2003). The U.S. Environmental Protection Agency (EPA 2002) reported that endosulfan is a volatile and persistent cyclodiene pesticide that can migrate over a long distance through various environmental media such as air, water and sediment. Once endosulfan is applied to crops, it can either persist in soil as a sorbed phase or be removed through several physical, chemical and biological processes. Recent studies suggest that secondary emissions of residual endosulfan continue to recycle in the global system while they slowly migrated and are redeposited via wet deposition in the Northern Hemisphere. The occurrence of endosulfan in remote regions like the Great Lakes, the Arctic and the mountainous areas is well documented. Endosulfan can also enter the air as adsorbed phase or suspended particulate matter, but this process does not appear to be a major contributor to long range transport like volatilization.

The information provided above further supports the comment made by Jim Burkhart, EHP Science Editor, that decades of spraying this pesticide, and only this pesticide, on the village provided a unique opportunity to analyze its impact. Although the sample size was somewhat limited, the results are quite compelling.

We stand by the conclusions in our article (Saiyed et al. 2003).

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Defining Wetlands
I read with interest David J. Tenenbaum’s article about constructed wetlands in the January 2004 issue of EHP (Tenenbaum 2004). While I noted his caveat that “their design remains a bit of an uncertain art,” I think he should have gone further to ensure that engineers do not immediately embrace constructed wetlands as a panacea for waste treatment and decontamination.

I also find myself increasingly unsettled by articles such as this one as potentially and inadvertently capitalizing on the opinion of the populace that wetlands are good places—a widespread view these days (deservedly so) because of excellent advocacy by government agencies and environmental nongovernmental organizations such as Ducks Unlimited.

Although the sewage treatment facilities promoted in the article (Tenenbaum 2004) may resemble wetlands, they are far from the real thing, or at least as far as the term is generally understood. In fact, I noted that later in the article Tenenbaum turned his attention to wetland restoration projects. In my experience, these again generally involve real wetlands, so to speak. Thus our wetland contrivances, enhancements, or other more utilitarian versions are more fairly not referred to as “restoration” for the straightforward reason that the former condition of these sites, the target for restoration, did not include sewage treatment.

The waste treatment benefits from constructed wetlands are clear, and Tenenbaum (2004) is to be commended for pointing this out as well as the uncertain risks. We cross the line, however, when we pitch constructed wetlands without mentioning the caveat that these surrogate ecologic features are intended to become contaminated (per heavy metal sinks, for example) and that this will impair other uses for these facilities, including use as habitat for species that rely on wetlands and cannot discern the real from the fake. Nature’s way advises us to be responsible about our waste generation at the source and not to dress up the end-of-pipe solution.

The author declares he has no competing financial interests.

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PHALATE EXPOSURE AND EARLY THELARCHE
Several years ago Colón et al. (2000) reported higher levels of phthalates, particularly di-(2-ethylhexyl) phthalate (DEHP) in serum from 41 girls experiencing premature breast development (thelarche) as compared to 35 age-matched controls. These data seem puzzling for at least two reasons. First, in light of the pharmacokinetic properties of phthalates, the reported blood levels are very high when compared to more recent exposure information, and, second, toxicologic evidence shows that phthalates do not act like estrogens under conditions, nor do they affect female sexual development and maturation in rodents. Despite these concerns, the study by Colón et al. (2000) is one of the few studies that has compared chemical exposures with sexual development and, as a consequence, it is now being cited by authors developing...
phthalate). In a pharmacokinetic study in marmosets (Kessler et al. 2004), oral doses of 30 and 500 mg/kg resulted in peak MEHP concentrations of 8 and 66 µM, approximately 20 times greater than the peak DEHP levels at equivalent doses. In contrast, the average MEHP level of 3 ppb reported by Colón et al. (2000) was more than two orders of magnitude below the reported average DEHP level. The only imaginable situation that might produce such anomalous results is if the blood samples had been taken immediately after direct introduction of DEHP into the blood stream. This is theoretically possible, but the reported levels still seem unlikely. The only way in which significant levels of unmetabolized phthalates may enter the blood stream is by way of medical devices including blood bags, tubing, and other medical equipment (e.g., Food and Drug Administration (FDA) 2001). DEHP is the primary phthalate plasticizer for such vinyl medical devices. However, as shown in an assessment by the FDA (2001), only critical-care procedures could produce blood levels that begin to approach the levels reported by Colón et al. (2000). Further, in blood, DEHP is rapidly metabolized with a biological half-life in humans of < 6 hr (e.g., Peck and Albro 1982). Thus, assuming medical treatment to be the explanation for the high DEHP/MEHP ratio reported by Colón et al. (2000), the measured blood levels imply intensive care procedures performed in the few hours proceeding the blood collection. However, given the circumstances this seems unlikely.

In the study by Colón et al. (2000), the blood samples were taken from children after referral to pediatric clinics, that is, after premature thelarche had been observed. Because phthalates are rapidly metabolized and excreted, the blood level data, if not the result of laboratory contamination, could only have reflected exposures occurring shortly before the blood was drawn. For the hypothesized link between phthalate exposure and early breast development to be supported, one would have to assume that these point estimates were indicative of a pattern of exposure that had persisted for an extended period of time. But, as shown above, the conditions leading to the reported blood levels are so unusual that they cannot reflect an extended exposure profile. Analytical difficulties seem a more likely explanation to reconcile the data reported by Colón et al. (2000) with the extensive body of information on phthalate pharmacokinetics.

The second general reason why an association between phthalate exposure and the early onset of puberty in girls is puzzling and seems unlikely is that it is not supported by the toxicologic data. There is a hypothesis that premature thelarche is a consequence of unintentional exposure to estrogen or estrogen-like substances (e.g., Li et al. 2002; Tiwary 1998). It has been reported that some phthalates, although not DEHP, can bind and activate the estrogen receptor under in vitro conditions (e.g., Jobling et al. 1995; Soto et al. 1995); however, subsequent work has shown that this is an artifact of the testing conditions.

As described above, under in vivo conditions the phthalates are rapidly metabolized to the corresponding monoesters, but these metabolites are not active under in vitro conditions (Brady et al. 1998; Harris et al. 1997; Picard et al. 2001). In rats and mice, phthalates are inactive in uterotrophic assays and do not induce vaginal cornification (Kanno et al. 2003; Zacharewski et al. 1998). Similarly, in longer-term studies phthalates do not influence age at vaginal patency or estrous cyclicity and do not otherwise influence sexual development or behavior in female rats (Moore 2000). Some phthalates produce effects in male rats, apparently as a result of alterations in testosterone synthesis (Parks et al. 2000), but these alterations do not produce estrogen-like effects in female rats (Gray et al. 1999; Moore et al. 2001; Mylchreest et al. 1998, 1999). With respect to female reproductive development, the only effect that has been described in rats relates to histologic changes in the ovary that occur at very high doses (Loyekamp-Swan and Davis, 2003; Loyekamp-Swan et al. 2003).

These changes seem to be caused by inhibition of aromatase activity in the granulosa cells. Aromatase inhibition reduces conversion of testosterone to estradiol and produces what is effectively an antiestrogenic effect under these circumstances. However, this seems unlikely to have any public health implications, partly because the doses required in rodents are much higher than those to which humans are exposed and also because the aromatase inhibition is dependent on activation of the peroxisome proliferator-activated receptor α (PPARα). In other situations, there is evidence that PPARα-dependent effects exhibit profound species specificity, with rodents being very sensitive and humans being much less sensitive, if not refractory (e.g., Klaunig et al. 2003).

In summary, the purported relationship between phthalate exposure and early thelarche (Colón et al. 2000) seems highly unlikely, in part because the reported exposure levels do not seem plausible given other information on phthalate exposure, and also because phthalates do not influence the timing of female sexual development in laboratory studies.
The author wrote this letter in his capacity as chairman of the Toxicology Research Task Group of the Phthalate Esters Panel, a trade association representing the phthalate industry. He certifies that his freedom to design, conduct, interpret, and publish research was not compromised by any controlling sponsor as a condition of review and publication.

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Correction
Karmas et al. detected errors in their article “Backward Estimation of Exposure to Organochlorines using Repeated Measurements” [Environ Health Perspect 112:710–716 (2004)]. In Table 1, values in the equations for the proposed regression model were incorrect. The correct equations for Table 1 are as follows:

For estimation of 1970s values from 1980s values,

\[
PCB_{70\text{(estimate)}} = PCB_{80} \times 0.565 + (\varphi_{80} - 0.163) + (\alpha \times 0.106)
\]

For estimation of 1980s values from 1990s values,

\[
PCB_{80\text{(estimate)}} = 10^{(0.193 + (\log_{10} PCB_{90} \times 0.781) + (\varphi_{90} \times 0.049) + (\tau_{90} - 0.145))}
\]

Also, in Figure 3, there should not be a measurement for the year 2010. The authors apologize for the errors.