

A Proposition 65 Dose Evaluation for DEHP from @@ Shoes

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1. Overview and Introduction

California’s Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65) is intended to protect California citizens and the State's drinking water sources from chemicals known to cause cancer, birth defects or other reproductive harm, and to inform citizens about exposures to such chemicals. Proposition 65 requires businesses to provide a warning before they knowingly expose anyone to a chemical that is known by the State as causing such harm. For consumer products, the warning often comes in the form a label on the product or its packaging. The warning is not required if the exposure is low enough to pose no significant risk of cancer or is significantly below levels observed to cause birth defects or other reproductive harm. For many of the chemicals for which warnings are required the State lists exposure levels (in units of micrograms per person per day, $\mu\text{g}/\text{d}$) deemed low enough to preclude the need for a warning.

The goal of this dose evaluation is aimed to determine whether certain @@ Shoes require labeling under Proposition 65, due to potential exposures to di-(2-ethylhexyl)-phthalate (DEHP) that was once contained in one part of the product.

2. Concentration of DEHP in @@ Shoes.

The Notice of Violation¹ refers to @@ shoes. These pre-walk boots are labeled as Medium size, for babies aged 6–12 months (Figure 1 -- *redacted*). The majority of the boots are constructed of polyester material that does not contain and never has contained DEHP (as confirmed by laboratory tests). The sole of the boot contains two small tread inserts of harder plastic material (Figure 2 -- *redacted*). These treads are currently made up of thermoplastic rubber (TPR), a synthetic rubber material that does not need phthalates or other plasticizers to confer the required physical properties. Tests of current production items show that the DEHP content of these treads is negligible.²

¹ 60-Day Notice of Violation # @@

² Three of these items have been tested for all six phthalates of potential toxicological interest: no phthalate other than DEHP was detected. The results for DEHP were none detected (at a lower limit of detection of 490 parts per million (ppm), 140 ppm, and 60 ppm).

Prior to 2009, however, treads of the boots were made of PVC material that could have contained DEHP. No exemplars of that production era were available for testing, but Mr. @@ indicates that an older pair of boots that he purchased in California contained 15% and 31% DEHP in the tread of the left boot and right boot. This evaluation examines potential exposures to DEHP from these boots, assuming, to be conservative, treads containing up to 40% DEHP.

3. Proposition 65 listings and “No Significant Risk” doses

The California Office of Environmental Health Hazard Assessment (OEHHA) is the agency responsible for the implementation of Proposition 65. In that role it maintains the list of chemicals “known to the State to cause cancer or reproductive toxicity,” and has established daily dose rates for many of these chemicals, below which dose the exposure is deemed to pose no significant risk of cancer or is significantly below levels observed to cause birth defects or other reproductive harm. These dose criteria are referred to as no significant risk levels (NSRLs) for carcinogens, and maximum allowable dose levels (MADLs) for chemicals causing reproductive toxicity. The latest available list and set of criteria doses is dated September 11, 2009 (OEHHA, 2009a,b).

For DEHP, the cancer NSRL is 310 µg/day, while the MADLs differ by age group and route of exposure. For oral exposure, the route of concern in this case, the MADL for adults is 410 µg/day while for infant boys it is 58 µg/day for ages 29 days to 24 months (and higher in proportion to bodyweight for older children), and 20 µg/day for neonatal infant boys (0–28 days). The relevant age range here is ages 6 months and higher, since the average user of these shoes will be aged 6 to 12 months (see labeling, Figure 1). Any exposure below the MADL of 58 µg/day (for children 29 days to 24 months) will necessarily also be lower than the cancer NSRL of 310 µg/day.

Figure 1 @@ redacted.

Figure 2 @@ redacted

4. Evaluation of DEHP exposure from treads

4.1. Methodology

To estimate potential exposures to DEHP from the treads, the approach used by the Consumer Product Safety Commission (CPSC) for exposure to diisononyl phthalate (DINP; Babich *et al.*, 2004; Greene, 2002a) is here followed, making conservative approximations where necessary, and introducing a minor correction of the CPSC procedure. A very similar approach has been used for component of DEHP exposure from toys by Bosgra *et al.* (2005).

All authors agree that the dominant potential exposure route to DEHP in toys or similar items that are mouthed by children is direct oral ingestion due to that mouthing. This route is so dominant that hand wiping followed by hand-to-mouth contact can be ignored compared with it.

Following Babich *et al.* (2004) and Greene (2002a) exposure (E , $\mu\text{g}/\text{day}$) to DEHP is estimated as³

$$E = A_s \times M_s \times \left(\frac{M_h}{M_l} \right) \times T_h \times T_d \quad (1)$$

where the terms are

- A_s area of the tread that is sucked or mouthed by the child (in units of 10 cm^2)⁴,
- M_s migration rate of DEHP as measured by a standard laboratory procedure, $\mu\text{g}/\text{min}/10 \text{ cm}^2$,
- M_h migration rate of DEHP in humans for a standardized disk of material, $\mu\text{g}/\text{min}/10 \text{ cm}^2$,
- M_l migration rate of DEHP as measured by the standard laboratory procedure for the standardized disk of material, $\mu\text{g}/\text{min}/10 \text{ cm}^2$,
- T_h time spent mouthing the tread each hour the child is awake, min/hr,
- T_d time the child is awake, hr/day.

An infant would have a difficult time attempting to mouth the tread insert on the soles of the shoes. Typically an infant or toddler mouthing a shoe would bite on the edge of the shoe;⁵ but a young child's mouth is not large enough in such a situation to reach as much on to the tread (see Figure 2). Nevertheless, to be conservative it is assumed here that a young child's mouthing could involve a semi-circle of material of diameter 4 cm, giving a total area mouthed of 6.3 cm^2 on each mouthing occasion.

CPSC (Chen, 2002) provides data on a standard laboratory migration measurement, M_s , for DINP for 25 samples⁶ of PVC (containing from 13% to 40% DINP) from soft toys, and of DEHP for 3 samples (containing 22% to 37% DEHP). For DINP the release rate ranged from 1.05 to 11.09, mean $4.2 \mu\text{g}/\text{min}/10 \text{ cm}^2$, with only a small correlation ($r = 0.2$) with DINP content. For DEHP the migration rate range in the three samples was 0.92 to $2.03 \mu\text{g}/\text{min}/10 \text{ cm}^2$; there was a high correlation ($r = 0.997$) with DEHP content, but this correlation is ignored here because of the small number of samples and high likelihood of chance correlation. Since the DINP migration rate generally exceeded (20/25 samples) the DEHP migration rate, it is here assumed that the DINP migration rate is a good surrogate, and perhaps an overestimate, of DEHP migration. The distribution of DINP migration rates is consistent with lognormal ($p = 0.78$, Shapiro-Wilk statistic).

³ This expression differs from that used by Babich *et al.* (2004) and Green (2002a) by including the A_s term. Those authors apparently failed to correct for different areas of exposure to toys, or implicitly assumed that mouthing on any toy would affect exactly 10 cm^2 on each mouthing occasion. It differs from the expression used by Bosgra *et al.* (2005) in omitting a correction for concentration of DEHP in the particular piece of PVC mouthed. As shown below, the migration rate M_h is practically independent of the concentration of DEHP in PVC, at least over the range 15% to 40%. Inserting such a correction would reduce the estimates of exposure obtained here by a factor of about two. Bosgra *et al.* (2005) apparently also failed to account for different areas of exposure for different toys.

⁴ The unit of 10 cm^2 for area is chosen to allow reporting results in the way they were originally reported.

⁵ See, for example, http://www.youtube.com/watch?v=tL9wqqs9fhM&feature=player_embedded#t=20.

⁶ Babich *et al.* (2005) and Greene (2002a) omit one of these samples.

Greene (2002a) provides copies of the individual data (obtained from the original authors) required to estimate the scaling factor M_h/M_l using a standard PVC disk used for obtaining this scaling factor contained 38% DINP. Migration rates M_h for DINP from 20 human volunteers who had been recruited to suck and bite the standard disk for 15 minutes four times over with 5 minute breaks (Meuling and Rijk, 1998) averaged $1.4 \mu\text{g}/\text{min}/10 \text{ cm}^2$ (there was no apparent variation with time in this migration rate). Babich *et al.* (2004) and Greene (2002) omitted the highest individual as being an outlier — the distribution of measurements without this outlier is indistinguishable from either normal or lognormal ($p = 0.83$ and 0.98 respectively, Shapiro-Wilk statistic). To be conservative, the outlier is here retained, with a resulting distribution that is barely distinguishable from lognormal ($p = 0.04$, Shapiro-Wilk statistic). When the standard disk was tested in the standard laboratory test, the mean migration rate M_l was $4.2 \mu\text{g}/\text{min}/10 \text{ cm}^2$ (with a distribution indistinguishable from either normal or lognormal, $p = 0.27$ and 0.18 respectively, Shapiro-Wilk statistic).

Using the mean estimates for M_s ($4.2 \mu\text{g}/\text{min}/10 \text{ cm}^2$), M_h ($1.4 \mu\text{g}/\text{min}/10 \text{ cm}^2$), and M_l ($4.2 \mu\text{g}/\text{min}/10 \text{ cm}^2$) gives an estimate for human migration rate from various PVC articles of $1.4 \mu\text{g}/\text{min}/10 \text{ cm}^2$, or $840 \mu\text{g}/\text{hr}/100 \text{ cm}^2$ for DINP migration used here as a surrogate for DEHP migration. Fiala *et al.* (undated) obtained very similar results for DINP migration⁷ from PVC teethingers containing 36% DINP. Sucking on such teethingers for 1 hour released $833 \mu\text{g}/100 \text{ cm}^2$, and for 3 hours $907 \mu\text{g}/100 \text{ cm}^2$, while chewing (as though the sheet were chewing gum) for 1 hour released $1330 \mu\text{g}/100 \text{ cm}^2$ and chewing for 3 hours released $2624 \mu\text{g}/100 \text{ cm}^2$. By comparison, Fiala *et al.* (undated) also measured $793 \mu\text{g}/100 \text{ cm}^2$ DEHP migration⁸ from PVC sheets containing 32% DEHP during 3 hours of sucking, indicating that DINP does appear to be a reasonable surrogate for DEHP.

Kiss *et al.* (2002) measured mouthing times (corresponding to T_h , but on all materials) and daily times awake (T_d) for 169 children aged from 3 to 36 months, and Greene (2002a,b) summarizes the results of those measurements. Exposure (awake) times were found to vary according to

$$T_d / \text{hours} = 9.46 + 0.0375 \times \text{Age}/\text{months} \pm 1.26 \quad (2)$$

where ± 1.26 indicates the observed standard deviation (SD; the distribution is approximately normal). Exposure times were not dependent on the sex of the child. Mouthing time T_h (min/hr) varied with the type of object considered. Mouthing of shoes was not explicitly mentioned. Mean mouthing times for the only categories described that could include mouthing of shoes are shown in Table 1. As can be seen, these categories are sufficiently broad that using them will substantially overestimate exposures from mouthing of the treads of shoes. Mouthing times were also not found to depend on sex (Greene, 2002a, Appendix).

⁷ Reported results are the means of between 3 and 10 determinations.

⁸ Reported results are the means of between 5 and 7 determinations.

Table 1 Exposure times for the categories potentially including shoes

Category	Average mouthing time, min/hour, by age			
	All ages	3-12 months	12-24 months	24-36 months
Other soft plastic ^a	0.09	0.10	0.07	0.11
Other objects ^b	2.10	2.53	2.06	1.68
^a Clothing, Furniture, Other, Unknown. A subset of Non-Pacifiers, Soft Plastic Objects, Non-food contact items; but not Soft Plastic Toys, Teethers, or Rattles.				
^b Books, clothing, carpet and furniture, non soft plastic food containers such as spoons and cups. A subset of Non Pacifiers, Soft Plastic Objects; but not Soft Plastic Food Contact Items, Soft Plastic Non Food Contact Items, Anatomy, or “Toys, Teethers and Rattles, not soft plastic”.				
	Mean exposure time at upper end of age range			
Exp time, hr.		9.91	10.36	10.81
Daily exposure time, min.		26.1	22.1	19.4

Table 1 also shows the exposure times corresponding to the upper end of the age ranges (using Equation (2)), and the resulting estimates for daily exposure time.

Greene (2002c) discusses exposure of children over the age of three, and demonstrates that their exposures are expected to be smaller than for children younger than three. The quantitative evaluation here is limited to children ages three or less for the same reasons, and because the trend found is clearly decreasing with age, whereas the MADL is increasing with age (see Section 3).

4.2. Point estimates of exposure

Conservative point overestimates of exposure may be obtained using Equation (1) from the estimates given in Section 4.1 of 6.3 cm² mouthing area, 1.4 µg/min/10 cm² DEHP migration rate from mouthing or sucking, and the daily overestimates of exposure times shown in Table 1. The results are shown in Table 2. These are overestimates primarily because of the use of the exposure times in Table 1, which include times of exposure to many other objects in addition to the treads of shoes.

Table 2 Point overestimates of daily exposure to DEHP from PVC treads

	3-12 months	12-24 months	24-36 months
	Daily exposure in µg/day		
Exposure	23	19	17

All the estimates shown in Table 2 are substantially below the MADL of 58 µg/day, and *ipso facto* lower than the NSRL of 310 µg/day.

4.3. A distributional estimate of exposure

To evaluate any possibility that the mean estimates shown in Table 2 may substantially underestimate exposures to an “average” child, distributions of all the results discussed in Section 4.1 have been approximated. Some of these distributions are variability distributions, some may be uncertainty distributions, and some undoubtedly contain components of both variability and uncertainty. However, all may be regarded as uncertainty distributions for a randomly chosen child in the relevant age range; and the resulting uncertainty distribution will necessarily be more extreme than the variability distribution for children (since the distribution will contain both variability and uncertainty). The average estimated from such a distribution will necessarily overestimate exposure of an “average” child, and the upper percentiles will overestimate the exposure at the same percentiles of the variability distribution alone.

The multiplicative form of Equation (1) indicates that the distribution of E is likely to be approximately lognormal no matter what the distributions of the individual terms on the right of the equation (provided the distribution of E is not completely dominated by a single term). Examination of the individual terms shows that lognormal approximations to their distributions are not likely to be substantially in error, so lognormal approximations to all of them were evaluated.⁹

The area mouthed at any instant will be taken as fixed at 6.3 cm^2 , since there are no measurements of this area. The area will not vary substantially — the tread insert is not amenable to crumpling to allow larger areas to be inserted in the mouth, so the mouthing area is limited to the cross-sectional area of the part of the mouth that can encompass a part of the tread.

It was pointed out above in Section 4.1 that M_s , M_h , and M_l are well approximated by lognormal distributions, and the normal distribution of Equation (2) can also be well approximated by a lognormal. Since this is an approximate and conservative estimate, only the exposure times corresponding to the upper ends of the relevant age ranges are used. Table 3 shows distributional statistics for all the variables of Equation (1) except T_h , derived from the original data for M_s , M_h , and M_l and from the arithmetic means and standard deviations given by Equation (2) for T_d .

⁹ Babich *et al.* (2004) and Greene (2002) used bootstrap simulations to account for the measured distributions. However, they did not provide the individual measurements for the 169 children observed, so it is not possible to use that method here.

Table 3 Distribution statistics for all variables except T_h

	Arithmetic scale		Natural log scale		Units on arithmetic scale
	Mean	SD	Median	SD	
A_s	0.630	0.000	-0.462	0.000	10 cm ²
M_s	4.208	2.757	1.237	0.657	μg /min/10 cm ²
M_h	1.379	0.993	0.185	0.479	μg /min/10 cm ²
M_l	4.182	0.451	1.426	0.114	μg /min/10 cm ²
T_d (12 months age)	9.910	1.260	2.286	0.127	hr/day
T_d (24 months age)	10.360	1.260	2.331	0.121	hr/day
T_d (36 months age)	10.810	1.260	2.374	0.116	hr/day

For T_h , Greene (2002a) provides the statistics on T_h for the “Other objects” category shown in Table 4. Unfortunately, Greene (2002a) does not provide statistics on the relevant combined categories; however the “Other soft plastic” category that potentially might include some mouthing of shoes (Table 1) contributes a negligible amount and will be neglected in what follows. The parameters of lognormal approximating distributions are shown in Table 5, and the statistics of the approximating distribution matching the observed statistics provided by Greene (2002a) are shown in Table 4.

Table 4 Statistics for T_h , and corresponding statistics estimated from lognormal approximations

Age Range	Mean	Median	SD	95 th percentile	99 th percentile	Number of children
	Observed (min/hr)					
3-12 months	2.53	2.14	2.13	7.83	8.08	54
12-24 months	2.06	1.36	2.02	6.59	8.99	66
24-36 months	1.68	0.7	2.59	7.14	14.31	49
Estimated by lognormal distribution (min/hr)						
3-12 months	2.66	2.09	2.08	6.53	10.47	
12-24 months	2.07	1.38	2.32	6.08	11.22	
24-36 months	1.72	0.74	3.60	6.26	15.15	

Table 5 Parameters for lognormal approximating distributions for T_h .

Age Range	Median	SD	Unit on arithmetic scale
	Natural logarithmic scale		
3-12 months	0.7380	0.6921	min/hr
12-24 months	0.3246	0.8999	min/hr
24-36 months	-0.2989	1.2969	min/hr

The parameters of the approximating distribution are maximum likelihood estimates obtained by fitting the percentiles (50th, 95th, and 99th) using the exact joint distribution for those percentiles, combined with an approximate distribution (assumed independent of the percentile distribution) for the mean. Specifically, with a sample size of n , the approximate likelihood L used for parameter estimates μ , σ for the median and SD on the natural logarithmic scale, given the values x_i for percentiles $100c_i$, $i = 1, 2, 3$ (that is, $c_1 = 0.5$, $c_2 = 0.95$, $c_3 = 0.99$, and the corresponding x_i are given in Table 4) and the value m for the mean, was

$$L \propto \varphi_1 \varphi_2 \varphi_3 \Phi_1^{r_1} (\Phi_2 - \Phi_1)^{r_2 - r_1} (\Phi_3 - \Phi_2)^{r_3 - r_2} (1 - \Phi_3)^{n - r_3} \frac{1}{\Sigma / \sqrt{n}} \varphi \left(\frac{M - m}{\Sigma / \sqrt{n}} \right)$$

where

$$\begin{aligned} \varphi(x) &= \frac{\exp(-x^2)}{\sqrt{2\pi}}; & \Phi(x) &= \int_{-\infty}^x \varphi(t) dt; & (3) \\ \varphi_i &= \frac{1}{\sigma} \varphi \left(\frac{\ln x_i - \mu}{\sigma} \right); & \Phi_i &= \Phi \left(\frac{\ln x_i - \mu}{\sigma} \right); & r_i &= \lfloor c_i n \rfloor + 1; & i &= 1, 2, 3 \\ M &= \exp \left(\mu + \frac{1}{2} \sigma^2 \right); & \Sigma &= M \sqrt{\exp(\sigma^2) - 1} \end{aligned}$$

No attempt was made to match the observed SD, since with such long-tailed distributions and small sample sizes the observed SD is very variable (and is usually lower than expected).

With the lognormal approximating distributions shown in Table 3 and Table 5, application of Equation (1) gives a lognormal distribution for overestimates of exposure E . Results are shown in Table 6; the mean estimates are very similar to the point estimates of Table 2, and even the 90th percentiles of the distribution are lower than the MADL of 58 $\mu\text{g}/\text{day}$, despite these being considerable overestimates (because of the inclusion of mouthing times of all “Other objects”). As expected (see Section 4.1 referencing the discussion of Greene, 2002c) the estimated exposure decreases with age.

Table 6 Distributional overestimates for exposure *E*

Age range	Natural logarithmic scale		Arithmetic scale				Units on arithmetic scale
	Median	SD	Median	Mean	75 th percentile	90 th percentile	
3-12 months	2.5576	1.0810	12.9	23.1	26.8	51.6	µg/day
12-24 months	2.1893	1.2239	8.9	18.9	20.4	42.9	µg/day
24-36 months	1.6089	1.5391	5.0	16.3	14.1	35.9	µg/day

5. Conclusion

An exposure evaluation was performed for DEHP from the treads of @@ shoes, on the assumption that they did at one time contain DEHP at any concentration ranging up to 40%, to assess whether they might have required warnings under Proposition 65. Using the dose estimation methods described above, the MADL (and *ipso facto* the NSRL) would not be exceeded for an average child, nor would it be exceeded even at the 90th percentile of the estimated distribution.

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