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Screening-level human health risk assessment of toluene and dibutyl phthalate in nail lacquers

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ABSTRACT

Toluene and dibutyl phthalate (DBP) are found in many consumer products, including cosmetics, synthetic fragrances, and nail polish. In 2012, the California Environmental Protection Agency evaluated 25 nail products and found that 83% of the products that claimed to be toluene-free contained toluene at concentrations ranging up to 190,000 ppm, and 14% of the products that claimed to be DBP-free contained DBP at concentrations ranging up to 88,000 ppm. We conducted a preliminary, screening-level analysis of the potential toluene and DBP-related health risks to consumers and professionals based on the medium and maximum concentrations of toluene and DBP presented in the 2012 report and evaluated dermal and inhalation exposure to a salon patron, nail technician, and home user. We concluded that the maximum toluene concentration for the technician and home user scenarios exceeded the California MADL, but the estimated air concentrations did not exceed the Federal or Cal OSHA PEL. The MADL for DBP was exceeded for all user scenarios at both the median and maximum concentrations. Using these highly conservative assumptions, exposures above regulatory limits could possibly occur during routine use of nail products; further research is needed in order to evaluate potential human health risks.

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1. Introduction

Some beauty and health care products sold in the United States contain chemicals that can cause adverse health effects at sufficiently elevated exposures. The United States Food and Drug Administration (FDA), for example, recently reported an average lead concentration of approximately 1 ppm in 420 lipstick samples in two separate studies (Hepp, 2012). Novick et al. (2013) reported concentrations of the skin sensitizer 1,2-benzisothiazolin-3-one (BIT) ranging from 0.0075% to 0.035% in sunscreen, laundry detergent, dish soap, and spray cleaners. In addition, until recently, many hair straightening products contained formaldehyde, a chemical that can cause dermal and respiratory irritation, as well as more serious effects (Pierce et al., 2011).

Beauty and health care products (and their labels) are not regulated under the Federal Food, Drug, and Cosmetic Act (FDCA), and thus an assessment of the potential health risks associated with their use is typically not required by any regulatory agency (USFDA, 2014). In many instances in which a "post-market" health risk assessment of such products was conducted, the findings often indicated that the chemical concentrations in the product were too low to pose a significant health hazard. Recent quantitative assessments of exposure to lipstick lead and sunscreen sensitizers, for example, have determined that these products would be unlikely to pose a consumer risk, even under worst-case user assumptions (Monnot et al., 2015; Novick et al., 2013). On the other hand, a recent study found that airborne formaldehyde levels associated with hair straighteners were actually highest in products that claimed to be "formaldehyde-free" (Pierce et al., 2011), and the airborne formaldehyde concentrations measured in a salon under simulated hair straightening applications has the potential to produce formaldehyde concentrations that meet or exceed current occupational exposure limits.

Nail polish and nail polish removers are sold in liquid form, and often contain a mix of volatile compounds, such as acetone, butyl acetate, formaldehyde, and toluene, as well as non-volatile compounds, such as dibutyl phthalate (DBP) (Cal/EPA, 2012). DBP is used as a binder in nail polish to improve the longevity of the lacquer, and toluene is a common solvent used in nail products. In the U.S., domestic nail polish sales continue to rise, climbing 59% from 2010 to 2011, 32% in 2012, and 19% in 2013 (Groden, 2013). Excluding gel and acrylic polish applications, traditional nail polish manicures and pedicures comprise approximately 40% of the total number

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of services performed in a beauty salon (BBM, 2013). With increasing demand for new products and services, nail polish manufacturers are developing products with a greater variety of colors and finish.

Concerns have been raised regarding the presence of certain chemicals in nail polish products, (e.g., DBP, toluene, and formaldehyde, which has have termed "the toxic trio" by some in the cosmetic industry) (Breskey, 2013). Because of the potential developmental toxicity of DBP, for example, the use of DBP in cosmetics, including in nail polishes, has been banned in the European Union since 2004 (European Commission, 2004). More recently, many U.S. companies have also opted to voluntarily remove DBP from nail lacquers, and, similarly, many companies have chosen to remove toluene from their nail products and advertise their products as "toluene free" (Blum, 2014).

There are approximately 120,000 fulltime licensed nail technicians in California, the vast majority of whom are women of reproductive age, and often not native English speakers (Cal/EPA, 2012). In 2011, the Department of Toxic Substances Control (DTSC), under the California Environmental Protection Agency (Cal/EPA), measured toluene and DBP concentrations in nail polish products available in the San Francisco Bay Area (Cal/EPA, 2012). Both of these compounds are regulated by the State of California as developmental toxicants under Proposition 65. Analysis of 35 samples from six randomly chosen nail polish distributors indicated that toluene was detected in 23 samples ranging up to 190,000 ppm, and DBP was detected in 10 samples ranging up to 88,000 ppm. Although the DTSC noted that many of the products that were labeled as being free of toluene and/or DBP did in fact contain one or both chemicals, they did not conduct a quantitative assessment of exposure and potential developmental health risks to salon workers or patrons.

A few studies (e.g., Gjolstad et al., 2006; McNary and Jackson, 2007), measured airborne toluene concentrations in nail salons and determined that the exposures did not pose a health concern to the nail technicians. These studies, though, did not identify the toluene sources, nor were the salon products themselves identified; whether these findings are applicable to a salon setting in which nail products are heavily used, then, remains unclear. Also, to our knowledge, no attempts have been made to assess exposures and risks for salon patrons or home users.

The objective of this paper, then, is to provide a preliminary, screening-level analysis of the potential toluene and DBP-related health risks to consumers and professionals (e.g., home users, nail technicians, and nail salon customers) who use nail polish products. Using the measured chemical concentrations reported by the DTSC, inhalation and dermal doses of toluene and DBP are estimated for a variety of product use conditions. These exposures are characterized via comparisons with several different regulatory benchmarks, including the Proposition 65 Maximum Allowable Dose Level (MADL) values that have been established specifically for protection against developmental effects. Highly conservative exposure assumptions are employed to ensure that potential risks are not under-estimated. The results are interpreted with respect to the need for additional research and the conduct of a refined risk assessment analysis.

2. Methods

2.1. Identification of comparative exposure benchmarks for toluene and DBP

2.1.1. Toluene

Toluene is often used as a solvent in paints, lacquers, coatings, adhesives, inks, and pharmaceutical and cosmetic products (Huff, 1990; IARC, 1999). Although toluene is not considered carcinogenic, adverse effects to the central nervous system (CNS), cardiovascular, hematopoietic, reproductive, and respiratory systems, as well as to the liver, kidneys, skin, and sensory organs have been reported after exposure to high concentrations. Toluene was listed in 1991 under Proposition 65 as a chemical known to the State of California to cause reproductive toxicity, and the established MADL of 7000 μg/day for toluene is based on protection against adverse developmental effects (Cal/EPA, 2013; Cal/EPA, 2014). The MADL is partially based on a study published by the International Research and Development Corporation (IRDC) in 1985, as detailed by the Office of Environmental Health Hazard Assessment (OEHHA) in 1999 (Cal/EPA, 1999). In that study, female rats were exposed to 1, 100, 500, and 2000 ppm toluene in air for six hours per day, 80 days from the time prior to mating, through lactation. A significant reduction of fetal weights from dams exposed to 2000 ppm toluene was reported; no such responses were observed at the lower exposures, and, therefore, a developmental no-observed-adverse-effect level (NOAEL) of 500 ppm was established. The absorbed dose for 500 ppm toluene in air for six hours per day exposure was estimated to be 112.5 mg/kg-day (API, 1985) based on an assumption that 50% of the inhaled toluene was absorbed systemically. This weight-normalized dose (112.5 mg/kg-day) is equivalent to approximately 7000 μg/day. The toluene MADL of 7000 μg/day represents the internal dose of toluene that the state of California believes should not be exceeded on any single day. An uncertainty factor (UF) of 1000 is used when establishing the MADL, in order to account for any variation or uncertainty in the calculation.

OSHA set the 8-hour time-weighted average (TWA) PEL for toluene at 200 ppm, based on protection against neurological effects studies. In 2012, the Division of Occupational Safety and Health (DOSH), better known as Cal/OSHA, lowered its PEL for toluene from the existing 50 to 10 ppm (CAL/OSHA, 2011, 2012) to provide more worker protection against neurologic effects, such as impaired color vision, hearing, and decreased performance in neurobehavioral analysis.

The US EPA reference concentration (RfC) of 5 mg/m^3 (1.23 ppm) for toluene is based on neurological effects reported in occupationally-exposed workers (USEPA, 2014). The RfC was calculated from an average adjusted NOAEL of 34 ppm divided by an UF or 10 for human variability. The RfC is EPA's estimate of an airborne toluene concentration that is likely to be without an appreciable risk of adverse health effects over a lifetime of daily exposure for the general population (including susceptible subgroups).

In summary, for the purposes of this analysis, we employ several different toluene exposure benchmarks: (1) the Cal EPA MADL, which is based on protection against developmental effects in the children of pregnant women; (2) the OSHA and Cal/OSHA PELs, which are based on protection against CNS effects in workers; and (3) the US EPA RfC, which is based on protection against CNS effects in the general population. The MADL is an absorbed (internal) dose, while the PELs and the RfC are expressed as air concentrations.

2.1.2. DBP

DBP is not considered to be a carcinogen in human or animal models, and was therefore classified by the US EPA as Group D (not classifiable as to human carcinogenicity) (ATSDR, 2001; USEPA, 2013). Developmental effects, including reduced fetal weight, decreased number of viable litters, and birth defects (neural tube defects) have been reported in mice exposed orally to high concentrations of DBP. Reproductive effects, such as decreased spermatogenesis and testes weight, have also been reported in oral animal studies (ATSDR, 2001; Huff, 1990; OSHA, 1994). The Proposition 65 MADL for DBP is 8.7 μg/day, and is based on developmental effects observed in an oral rat study by Lee et al. (2004), in which dietary maternal exposure during pregnancy and the lactation period adversely affected reproductive system development in male and female rat offspring. Since the developmental and reproductive effects observed in pups were mediated by maternal exposure, the DBP MADL was calculated based on maternal exposure and a human female body weight of 58 kg (Cal/EPA, 2007). As with all MADLs, a UF of 1000 was used to assure a large margin of safety. DBP is nearly completely absorbed following oral administration in rats (NTP, 2003). Thus, the DBP MADL can also be considered to be an absorbed dose (Cal/EPA, 2007).

Comparative exposure benchmarks for toluene and DBP are described below, and summarized in Table 1.

2.2. Exposure assessment

Toluene exposure from a nail polish application was assumed to occur through both dermal and inhalation routes, while DBP exposure was estimated to occur exclusively through the dermal pathway. DBP has low volatility with a vapor pressure of 3×10^{-5} mm Hg at room temperature (Kemppinen and Gokcen, 1956), and is not expected to pose an inhalation hazard under the scenarios examined in this paper. Toluene is more volatile, with a vapor pressure of approximately 28.5 mm Hg at 25 °C (Ambrose, 1993; Lide, 1993).

Three exposure scenarios were considered: a salon patron receiving a manicure in a professional salon, a nail technician performing a manicure in a salon, and a home user performing a self-manicure. An exposure estimate was conducted using

Table 1
Exposure benchmark values for toluene and DBP.

Chemical	Benchmark value
DBP	8.7 μg/day (Proposition 65 MADL)
Toluene	7000 μg/day (Proposition 65 MADL)
	200 ppm (OSHA TWA PEL)
	10 ppm (Cal/OSHA TWA PEL)
	5 mg/m^3 or 1.23 ppm (US EPA reference RfC)