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Probabilistic Monte Carlo estimation for quantitative exposure assessment of lotion transfer via baby wipes usage

Swatee Dey [a, *], Gregory J. Carr [a], Lijuan Li [a], Susanna Brink [b], Shaoying Zhou [a]

[a] The Procter & Gamble Company, WHBC, 6280 Center Hill Road, Cincinnati, OH 45224, USA
[b] The Procter & Gamble Company, GmbH, Schwalbach, Germany

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ABSTRACT

Unique aspects of childhood exposure to products need childs specific exposure data. This study developed a probabilistic exposure model for lotion transfer to diapered skin through normal use of baby wipes in children up to 48 months of age. Monte Carlo simulations used baby wipe diary data from the US, Germany and the UK, body weight data from the US, and lotion transfer data from single and multiple wipes adjusting for separate diaper changes. The models predicted a declining number of wipes used/day with a reduction in lotion transfer as age and body weight increased. Experimental testing on multiple sequential wipes used on an overlapping area showed a reduction in lotion deposition by 23.9% after the first wipe. Overall, the weighted population average over the approximate diapering period of 0–36 months across the three geographies at 50th, 90th, & 95th percentiles, were between 130, 230, 260 mg/kg/day, respectively, and 150, 270, 310 mg/kg/day depending on whether a reduction due to overlap is implemented. The statistical model represents an effective strategy to determine exposure to baby wipes lotion for exposure based risk assessment.

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1. Introduction

Cleaning the diaper area is an important step in the prevention of diaper dermatitis (Stamatas and Tierney 2014; Adam, 2008). Water and a washcloth were long considered the preferred approach for cleansing during diaper changes, but the polar nature of water limits its ability to remove lipophilic substances from the skin (Adam et al., 2009). Further, water is incapable of pH buffering (Adam, 2008). As a result, baby wipes with buffered lotion have become a common means of cleansing.

The skin compatibility of baby wipes products is well established. A recent review of the literature indicated that, in studies comparing the skin compatibility of baby wipes to water-and-washcloth cleaning, baby wipes produced no difference in the incidence of diaper dermatitis (Blume-Peytavi et al., 2014). Several studies indicate that use of lotioned baby wipes compared to water- and washcloth cleaning lead to better skin barrier effects, less skin surface abrasion, improvement in diaper rash and repair of the damaged skin barrier function in compromised skin (Ehretsmann et al., 2001, Odio et al., 2001). Visscher et al. studied 131 infants in a Newborn Intensive Care Unit where two wipes formulated for sensitive skin were compared with water-and-washcloth cleaning. The wipe treatment resulted in significantly lower erythema and surface roughness (Visscher et al., 2009). In a study of skin tolerability in babies with atopic dermatitis, Adams and colleagues (Adam et al., 2009) reported that baby wipes used to clean skin during diaper changes were superior to soap or to water alone in maintaining skin pH.

As with other consumer products, manufacturers undertake extensive programs to ensure the safety of the ingredients and components of their products (Dey et al., 2014). The basic framework of risk assessment ensuring safety of an ingredient consists of: hazard identification, dose-response assessment, exposure assessment, and risk characterization (Rider et al., 2009; National Research Council, 1983). Ingredient hazard assessment and dose-response depend on the inherent biological effects of the ingredients or components of the products. Exposure assessment and risk characterization require an understanding of the type of product consumers' use, the conditions under which the individual will be exposed, and a thorough understanding of the resulting

Abbreviations: EBSA, Exposure Based Safety Assessment; FOU, Frequency of Use; UPW, Ultra Pure Water; IS, Internal standard.

* Corresponding author. 6280, Center Hill Ave, Cincinnati, OH 45224, USA.
E-mail addresses: dey.s.3@pg.com (S. Dey), Carr.g@pg.com (G.J. Carr), Li.l@pg.com (L. Li), brink.s@pg.com (S. Brink), zhou.s@pg.com (S. Zhou).

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potential local and systemic dose. Accurate exposure assessment is critical for a robust exposure based risk assessment (EBRA).

Three key variables are important for an EBRA for baby wipes: frequency of wipe use, quantified lotion exposure for each wipe use, and body weight of the child. For products intended for babies, establishing the appropriate values for each variable is especially challenging. Children gain weight rapidly after birth, especially during the first few months of life making it a challenge to determine appropriate body weight. For baby wipes the usage patterns and frequency of use change rapidly as babies grow. The amount of lotion transferred can be affected by both the type of diaper change (wet only, soiled, type of soil, etc.) and the use of multiple wipes in that diaper change, in the sense that a fresh wipe applied to skin wetted by a previous wipe may transfer less than a fresh wipe applied to dry skin.

Baby wipes manufactured by Procter & Gamble consist of a nonwoven substrate with 70% inert polymeric material (polypropylene and polyethylene fibers) and 30% cellulose. These are inert materials and have been used in diapers and feminine protection products for decades, and have a long history of safe use (Farage et al., 2004). A lotion is added to the substrate to act as a cleanser and emollient. The lotion is a watery emulsion that may contain mild surfactants, oils, pH balancing substances, skin conditioners, and moisturizers (Adam et al., 2009, Adam, 2008). Robust safety assessments for ingredients in baby wipes with lotion rely on having a clear understanding of lotion exposure (Hossain et al., 2015).

The objective of this study was to estimate the amount of lotion transferred to skin from baby wipes for quantitative exposure assessments of the lotion. Daily exposure to wipes lotion is a function of the number of wipes used, and the amount of lotion transferred from those wipes. Lotion transfer can be a particularly complex process to measure, affected by both the type of diaper change (wet only, soiled, type of soil, etc) and the serial overlapping application of wipes to skin. The approach taken here is to measure the lotion transfer from individual wipe to dry diapered skin, apply our estimates of dry skin transfer values to all wipes used in a day with respect to diaper change, both with and without a reduction due to multiple overlapping wipes. Our exposure assessment is thus built from four component distributional models: the daily usage of wipes (frequency of use), the daily number of diaper changes, the amount of lotion transferred to skin from each baby wipe and the appropriate body weight for different age groups. These four distributional models were combined into a probabilistic exposure model using Monte Carlo simulation to estimate a distribution of the daily lotion transferred (mg/kg bw/day) from the use of baby wipes. The gender, age, weight and country of residence were evaluated for their influence on the distribution of lotion transfer. Lotion transfer was estimated for children over 0–36 months of age as the approximate diapering period of life (Rai et al., 2009). Results will be applied to EBRA as part of an overall safety assessment on lotion formulations or ingredients.

2. Materials and methods

2.1. Frequency of use (FOU) distribution for wipes

A multi-center diary study was conducted in 2013 to determine the number of wipes used per day. Participants were recruited in US (N = 98), UK (N = 232) and Germany (N = 201) by using a screening questionnaire (MarketVision Research, Inc., Cincinnati, OH). Families with young children in diapers who responded that they use at least 2 baby wipes per day for diaper changes were chosen for participation. Demographic information on the children is provided in Table 1. Study participants were given a supply of 64 count Pampers® baby wipes (Procter & Gamble Co., Cincinnati, Ohio, USA) to use during the one week study. Panelists were asked to record the number of wipes used after each diaper change. Two different product versions were used in the study: the North American (NA) version with wipes measuring 180 mm × 180 mm and containing 4.1 g lotion, and the Western European (WE) version with wipes measuring 170 mm × 179 mm and containing 2.8 g lotion. The NA version was evaluated in all three geographies, and the WE version was evaluated in Germany and the UK. When the wipes usage between the two product versions was compared, there were no apparent differences in the FOU ($p = 0.913$). Therefore, data from all geographies using both wipe variants (NA and WE) was combined to estimate FOU.

Table 1
Demographic information on children in frequency of use studies.

Country	Germany	UK	US
Gender	Males/Females		
# of Participants	98/102	117/115	51/47
Proportion of children at different age groups			
0 – 11 months	36%	28%	32%
12 – 23 months	33%	34%	33%
24 – 36 months	23%	30%	24%
+37 months	8%	12%	9%

The first and last days of the subject diary count data were eliminated due to evidence that at least some of these days did not contain a complete record. Median daily totals were calculated for each household in all three studies. Regression models were fit to the median daily number of wipes as a function of age, while allowing for possible differences due to child's gender and nationality. In cases where the relationship with age appeared to be nonlinear, a smooth monotonic regression was used. Monotonic regression techniques are a type of nonparametric regression smoother in which the prediction is constrained to be increasing (or decreasing) along the entire range of data (Ramsay, 1998), which we judged to be a reasonable assumption. The wipes count data were subjected to a square root transformation to stabilize the sample variance, and the spread of the distribution around the lines was assumed to be constant across the range of ages. The diaper change frequency per day was obtained from this multi-center diary study (data not shown).

2.2. Estimation of early life body weight distribution

Body weight and age can have critical impact on exposure assessment, particularly in the first four years of life, and having a good model for the effect of age and gender on distributions of body weights is important for understanding the distribution of exposures. Data from the CDC National Health and Nutritional Examination Survey (NHANES) (Centers for Disease Control and Prevention, 2015) for 6517 children between 0 and 48 months whose body weight was measured during the years 2001–2010 were used to determine age-specific body weight distributions for male and female children separately, using the approach described by Portier and colleagues (Portier et al., 2007). Similar sources of information on body weights were not available for Germany and the UK; therefore, US-based distributions from NHANES were used for all exposure calculations.

2.3. Lotion transfer

2.3.1. Lotion transfer from single baby wipe to baby diaper area skin

Lotion transfer from wipe to baby diapered skin was measured at the Procter & Gamble Skin Lab (German Innovation Center,

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