WOMEN'S VOICES FOR THE EARTH

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September 12, 2018

To the CIR:

I am writing to provide additional comments to supplement the previous comments I have submitted on the CIR panel's assessment of parabens. Women's Voices for the Earth is very concerned about the potential health impacts of parabens, particularly on women's health. We appreciate the opportunity to comment and your careful consideration of the information provided.

There are several issues that should be addressed in the next draft of the safety assessment on parabens:

1) There is new research indicating significant hazards to sperm motility from the levels of parabens commonly found in vaginally applied cosmetic products. The research indicates that paraben-containing cosmetics applied vaginally prior to intercourse have the potential to adversely affect sperm. In addition, earlier research indicates that exposure to paraben-containing cosmetic products used vaginally, increased the adherence of Candida to vaginal epithelial cells, increasing the potential for yeast infections. It is important for the CIR to examine the safety of parabens used in vaginally applied cosmetic products, such as douches, vaginal moisturizers and vaginal deodorant suppositories in light of this research.
2) I previously commented that the CIR's prior claim that parabens do not accumulate in the body is outdated, and not supported by more recent research which finds parabens considerably more persistent and accumulative than previously believed. It is unclear if this previous language (which is currently included in the draft safety assessment but in italics) will remain in the final version or if it is just there for reference in the draft and will be removed. It is important not to include former language from previous assessments if the scientific understanding has changed, so as to avoid confusion.
3) The vast majority of the literature that has measured paraben exposure with respect to the use of cosmetic products has concluded that the use of cosmetics or personal care products is the most significant source of paraben exposure, much greater than the contributions from food or pharmaceuticals. The current draft assessment however, still includes language implying that non-cosmetic sources of parabens may be significant. This language should be corrected to reflect the most current information.
4) Table 4 on particle size ranges of parabens should include data on all the parabens included in the report, not just the four currently listed. This data is available from the ECHA database for all the parabens included in this report. Of note, the ECHA data indicate that for propylparaben, 37.8% of particles are smaller than 10 microns in diameter, the CIR's established level of concern for inhalation. This information contradicts the summary claim found in the report that 95-99% of particles have diameters greater than 10 microns and are thus unlikely to be inhaled deeply.

5) The calculation used to derive a MOS for parabens needs to be updated to reflect more conservative product usage amounts and more conservative absorption rates that are consistent with data included in other sections of the assessment.

1.) **Parabens in vaginally applied cosmetics**

There are two recent studies on parabens used in vaginally applied cosmetic products that indicate hazards to human health.
The first is a 2018 study which examined the impacts of cosmetic products (vaginal moisturizers and lubricants) which contain parabens on sperm motility. The study found that the levels of parabens found in these consumer products led to oxidative stress and DNA damage that resulted in significant impacts to sperm motility and viability. The researchers concluded:

""The fact spermatozoa may spend several hours stored in cervical crypts during the early stages of sperm transport to the egg means that exposure to mM concentrations of parabens for several hours as a consequence of the topical application of vaginal lubricants is a realistic situation."
"Given that the permitted concentrations (SCCP, 2005) of methylparaben (0.4% 26 mM) and propylparaben (0.19% 10 mM) are well above the concentrations shown to be damaging to human spermatozoa in this study, the use of these preservatives in commercial products should be re-evaluated and couples should be made aware of their potential for harm in a reproductive context."
Samarasinghe SVAC et. al. (2018) Parabens generate reactive oxygen species in human spermatozoa. Andrology. 2018 May 2. doi: 10.1111/andr.12499.

The second study, from 2009, found that vaginal products containing parabens altered the expression of virulence-related genes in Candida glabrata, a vaginal yeast pathogen. Specifically, exposure to paraben-containing vaginal consumer products (including a test of Massengill douche for example) increased the adherence of Candida glabrata to human vaginal epithelial cells. Testing with vaginal products that did not contain parabens, did not show this effect.

Mundy RD and Cormack B (2009) Expression of Candida glabrata adhesins following exposure to chemical preservatives. J Infect Dis. 2009 June 15; 199(12): 1891–1898. doi:10.1086/599120.

Adherence of Candida to vaginal epithelial cells is a significant issue in women's health. As explained in the following study:
"'"Adherence has been shown to play a central role in the pathogenesis of many microbial infections. The adherence to various surfaces represents the first step in the mechanisms of pathogenesis and suggests means of controlling infection at an early stage."
El-Din A, Al-Basri H and El-Naggar M. (2012) Critical factors affecting the adherence of Candida albicans to the vaginal epithelium. Journal of Taibah University for Science. Vol. 6, pp 10-18. 2012.

Our research of currently available products indicates that in addition to vaginal moisturizers and lubricants, parabens can also found in other vaginally-applied cosmetics including douches, feminine washes and vaginal deodorant products.

We ask the CIR to address the specific health impacts of parabens in cosmetic products that are administered vaginally in the safety assessment.

2) <u>Bioaccumulation of parabens</u>

I previously commented that the CIR's prior claim that "parabens do not accumulate in the body" is outdated, and not supported by more recent research which finds parabens considerably more persistent and accumulative than previously believed. It is unclear if this previous language (which is currently included in the draft safety assessment but in italics) will remain in the final version or if it is just there for reference in the draft and will be removed. It is important not to include former language from previous assessments if the scientific understanding has changed, so as to avoid confusion.

Specifically the italicized sections of the draft assessment marked "Previous Discussions" contain most of the outdated language regarding bioaccumulation and excretion. These sections should be removed from the final draft so as not to cause confusion. Also, once removed, it would be helpful for the CIR safety assessment to include new summary language in the discussion of the ADME section which better reflects the CIR"s current understanding of the potential for parabens to be stored in the human body over time.

Currently the Discussion section states:

> "*The Panel adopted that the parabens are relatively lipid soluble compounds, they would tend to bioaccumulate in the lipid fraction of the biological tissues. Recent studies have showed the presence of parabens in breast, adipose, and placenta tissues. However, the metabolism, the excretion and the pharmacokinetics of the parabens made accumulation in the body not an issue*."

It is very unclear how the Panel was able to come to the conclusion from the data presented that "made accumulation in the body not an issue".

As I have commented before, parabens have long been understood both byb the CIR and others to be transient in the body, both metabolized and eliminated quickly. New research has found that this is not always the case, and that impacts on health should be considered from exposure to parabens which are retained in the body and which build up over time.

This change in thinking is best described by a 2018 study which assessed measured parabens in human adipose tissue. The researchers conclude:

> "*Urinary concentrations of non-persistent environmental pollutants (npEPs) are widely assessed in biomonitoring studies under the assumption that they are metabolised and eliminated in urine. <u>However, some of these chemicals are moderately lipophilic, and their presence in other biological matrices should also be evaluated to estimate mid/long-term exposure to npEPs and its impact on human health</u>."*
> and

> "*To the best of our knowledge, this study is among the very first to contribute evidence on the distribution and predictors of environmental phenols and parabens in adipose tissue from an adult cohort, showing the widespread presence of certain npEPs in the fat compartment. We consider these results of special interest to public health, given the increasing importance of adipose tissue as a biologically-active matrix, highly relevant in the development of chronic diseases.*"

(Source: Artacho-Cordón F et.al. (2018) Environmental phenols and parabens in adipose tissue from hospitalized adults in Southern Spain. Environ Int. 2018 Jun 29;119:203-211. doi: 10.1016/j.envint.2018.05.052.)

Similarly a 2015 study found high concentrations of parabens in human adipose tissue indicating bioaccumulation of parabens in humans can occur from chronic exposure over time. The researchers state:

> *"Environmental phenols and heterocyclic aromatic compounds are thought to be excreted completely from the body. However, relatively high concentrations of these chemicals found in human adipose tissues compared to the levels reported in urine suggest that,* ***bioaccumulation can occur from chronic daily exposures****. For some environmental phenols with endocrine disrupting activity, concentration as high as ~5000 ng/g (for BP-3) and 17,400 ng/g (for parabens including p-HB) were found in human adipose and these values were close to their effective concentration reported in in vitro experiments…"*

In addition, the researchers found a positive correlation between paraben levels in fat tissue and age of the subject indicating an accumulation over time.

> *"…a positive correlation between donor's age and CΣparabens (within the 75th percentile of adipose concentrations; n = 15) was observed (Fig. 2),* ***which suggests bioaccumulation in human adipose fat****."* (emphasis added)

(Source: Wang L, Asimakopoulos AG, Kannan K. (2015) Accumulation of 19 environmental phenolic and xenobiotic heterocyclic aromatic compounds in human adipose tissue. Environ Int. 2015 May;78:45-50. doi: 10.1016/j.envint.2015.02.015. Epub 2015 Mar 10.)

It is surprising that in direct contrast to the above mentioned study, the current draft assessment's discussion section states:

> "Some studies indicated that no correlations were found between parabens concentration in tissues and age groups of subjects, thereby suggests no bioaccumulation."

I was unable to find any references in the draft assessment to studies which measured both paraben concentration in tissues and age groups of subjects other than the Wang study mentioned above (which comes to the conclusion that correlations were found between paraben concentrations in tissues and

suggested that bioaccumulation can occur. This statement should be removed from the Discussion session unless multiple studies which back up this claim can be added to the assessment.

To further confirm this newer thinking on parabens, bioaccumulation and bioconcentration of parabens has also been noted in numerous recent wildlife studies, where animals highest on the food chain are commonly found to have the highest levels of parabens in the tissues sampled. For example:

"*In this study, accumulation profiles of six parabens and their metabolites were determined in 254 tissue (including liver, kidney, egg, and plasma) samples from 12 species of fish and seven species of birds collected from inland, coastal, and remote aquatic ecosystems. In addition, liver and kidney tissues from black bears were analyzed. Methyl paraben (MeP) was found in a majority of the tissues, with the highest concentration (796ng/g (wet weight [wet wt])) found in the liver of a bald eagle from Michigan. 4-Hydroxy benzoate (HB) was the major metabolite, found in 91% of the tissue samples analyzed at concentrations as high as 68,600ng/g, wet wt, which was found in the liver of a white-tailed sea eagle from the Baltic Sea coast.*"

> Xue J, Kannan K. (2016) Accumulation profiles of parabens and their metabolites in fish, black bear, and birds, including bald eagles and albatrosses. Environ Int. 2016 Sep;94:546-553. doi: 10.1016/j.envint.2016.06.015.
>
> "*The widespread exposure of humans to parabens present in personal care products is well-known. Nevertheless, little is known about the accumulation of parabens in marine organisms. In this study, six parabens and four common metabolites of parabens were measured in 121 tissue samples from eight species of marine mammals collected along the coastal waters of Florida, California, Washington, and Alaska. Methyl paraben (MeP) was the predominant compound found in the majority of the marine mammal tissues analyzed, and the highest concentration found was 865 ng/g (wet weight [wet wt]) in the livers of bottlenose dolphins from Sarasota Bay, FL. 4-Hydroxybenzoic acid (4-HB) was the predominant paraben metabolite found in all tissue samples. The measured concentrations of 4-HB were on the order of hundreds to thousands of ng/g tissue, and these values are some of the highest ever reported in the literature. MeP and 4-HB concentrations showed a significant positive correlation ($p < 0.05$), which suggested a common source of exposure to these compounds in marine mammals. Trace concentrations of MeP and 4-HB were found in the livers of polar bears from the Chuckchi Sea and Beaufort Sea, which suggested widespread distribution of MeP and 4-HB in the oceanic environment.*"

Source: Xue J, Sasaki N, Elangovan M, Diamond G, Kannan K. (2015) Elevated Accumulation of Parabens and their Metabolites in Marine Mammals from the United States Coastal Waters. Environ Sci Technol. 2015 Oct 20;49(20):12071-9. doi: 10.1021/acs.est.5b03601.

Similarly, the current safety assessment claims "*"Little or no unchanged paraben is excreted in the urine*." This claim is also outdated and is contradicted by newer data included in the current assessment which states:

"Free and conjugated parabens and their known, non-specific metabolites, p-hydroxybenzoic acid and p-hydroxyhippuric acid, were detected in the urine samples…17.4 %, 6.8 %, 5.6% of the doses of Methylparaben, Isobutylparaben and Butylparaben, respectively, were excreted in the urine; about 16% and 6% of Isobutylparaben and Butylparaben were excreted as 2OH-iso-butylparaben and 3OH-n-butylparaben, respectively; less than 1% was excreted as ring-hydroxylated metabolites "

Clearly when 17.4% of methylparaben is excreted as free parabens in the urine, the statement that "little or no unchanged paraben is excreted in the urine" is incorrect.

3.) **Personal care product use is the most significant contributor to paraben exposure**

The vast majority of the literature that has measured paraben exposure with respect to the use of cosmetic products has concluded that the use of cosmetics or personal care products is the most significant source of paraben exposure, much greater than the contributions from food or pharmaceuticals. The current draft assessment however, still includes language implying that non-cosmetic sources of parabens may be significant. This language should be corrected to reflect the most current information.

Specifically, the discussion section of the draft safety assessment currently states:

"*The high levels of Methylparaben and Propylparaben observed in tissues could be due to the fact that they are the most common compound used as preservative not only in cosmetics and hygiene products, but also in food, beverages, pharmaceuticals household pesticides, cleaning products, paints, pet supplies, and paper products."*

First, this statement is misleading, as it implies that parabens are the most common compound used as a preservative in food, beverages, pharmaceuticals, household pesticides, cleaning products, paints, pet supplies, and paper products. This is patently untrue, and should be deleted. Parabens are used as preservatives in these other products, but are certainly not the most common preservative used in any of these industries by any measure.

Secondly, this statement contradicts data included in other parts of the assessment. With respect to paraben exposure from food for example, the CIR safety assessment clearly states:

"…estimates for exposure to Methylparaben and Propylparaben via food are at last 25-fold lower than the estimates for aggregate exposure resulting from dermal exposure to cosmetic products."

Thus the contribution to body burden from foods is almost negligible compared to the contribution from cosmetic products, so the high levels of methylparaben and propylparaben observed in tissues are extraordinarily unlikely to be "due to the fact" that parabens are used as preservatives in food.

With respect to pharmaceuticals, the Estimate and Refinement of Aggregate Exposure section of the safety assessment states:

"*In addition to cosmetic and personal care products, parabens are also widely used in drugs and foods… The Dutch National Institute for Public Health and the Environment (RIVM) conducted an exposure assessment inconsideration of the aggregated exposure to parabens via three major sources: PCPs, foods, and medicinal products. For Methylparaben, adding exposures results in an aggregate exposure estimate of 3.0 mg/kg/day for both adults and children. The estimate for medicinal products contributes 70 - 74% of this value, while the contribution of food is less than 1%. For Propylparaben, adding the exposures results in an aggregate exposure estimate of 1.2 mg/kg/day for both children and adults; 64 - 72% of the exposure is from medicinal products, and less than 1% from food*."

Again these statements are highly misleading as they imply that the RIVM report claims that medicinal products contribute 64-74% of the aggregate exposure of parabens. What is missing from this section is the very important information that the RIVM report has very little confidence in the data on medicinal products (which were derived from a single study conducted in China.) In contrast the synopsis of the RIVM report states:

"*Exposure via personal care products has been examined in some detail and generally seems to be the greatest contributor to total exposure. Exposure via food appears to be negligible. Too little information is available for an acceptable estimate of exposure via medicines."*

Truly, scientists across the board, understand cosmetic products to be the most significant determinants of paraben exposure. This is confirmed in numerous studies showing the enormous increases in paraben levels in bodies of people who regularly use cosmetic products compared to those who do not – differences of up to 1000%. It is impossible to ignore the preponderance of data and continue to claim that a majority of paraben exposure could be due to other non-cosmetic factors.

Below is a summary of recent research indicating that personal care product use is the most significant predictor of paraben exposure:

"*Use of hair products, deodorants, face and hand creams were significantly associated with higher urinary levels of parabens…In the present study, we investigated both food consumption and use of PCPs as separate determinants of exposure. Use of body and face creams, deodorants and hair products were associated with higher concentrations of most parabens in both mothers and children… None of the environmental phenols showed a clear pattern with any of the food groups consumed in the present study…* ***Body and face creams, deodorants and hair products were the main determinants of urinary parabens*** *and BP-3."*

Sakhi AK, Sabaredzovic A, Papadopoulou E, Cequier E, Thomsen C. (2018) Levels, variability and determinants of environmental phenols in pairs of Norwegian mothers and children. Environ Int. 2018 May;114:242-251. doi: 10.1016/j.envint.2018.02.037

*"Overall, **use of 10 PCPs** within 6 h prior to collection explained at least 70% of the weighted score. These included cologne/perfume, deodorant, suntan/sunblock lotion, hand/body lotion, aftershave, other hair care products, mouthwash, conditioner/crème rinse, hairspray/hair gel, and liquid soap/body wash, which **explained at least a 254% and up to a 1,333% increase in MEP and the three parabens urinary concentrations.**"*

*"**For the three parabens, the strongest predictors were use of suntan/sunblock lotion (66–156% increase) and of hand/body lotion** (79–147% increase). Hairspray/hair gel, shaving cream, aftershave, mouthwash, and deodorant were moderate predictors for parabens. Liquid soap/body wash use was a strong predictor only for butylparaben (86%)."*

Nassan FL, Coull BA, Gaskins AJ, Williams MA, Skakkebaek NE, Ford JB, Ye X, Calafat AM, Braun JM, Hauser R. (2017) Personal Care Product Use in Men and Urinary Concentrations of Select Phthalate Metabolites and Parabens: Results from the Environment And Reproductive Health (EARTH) Study. Environ Health Perspect. 2017 Aug 18;125(8):087012. doi: 10.1289/EHP1374.

"*Girls who reported using makeup every day vs. rarely/never had higher urinary concentrations of monoethyl phthalate (MEP) (102.2 ng/mL vs. 52.4 ng/mL, P-value: 0.04), methyl paraben (MP) (120.5 ng/mL vs. 13.4 ng/mL, P-value < 0.01), and propyl paraben (PP) (60.4 ng/mL vs. 2.9 ng/mL, P-value < 0.01). Girls who reported recent use of specific makeup products, including foundation, blush, and mascara, had higher urinary concentrations of MEP, mono-n-butyl phthalate (MBP), MP, and PP… **Our findings suggest that personal care product use is associated with higher exposure to certain phthalates, parabens, and other phenols in urine**. This may be especially relevant in adolescent girls who have high use of personal care products during a period of important reproductive development*."

Berger KP, Kogut KR, Bradman A, She J, Gavin Q, Zahedi R, Parra KL, Harley KG. (2018) Personal care product use as a predictor of urinary concentrations of certain phthalates, parabens, and phenols in the HERMOSA study. J Expo Sci Environ Epidemiol. 2018 Jan 9. doi: 10.1038/s41370-017-0003-z.

*"…Women who used lotion had BP concentrations 111% higher (95% confidence interval (CI): 41%, 216%) than non-users, whereas their MBP concentrations were only 28% higher (CI: 2%, 62%)… **We observed a monotonic dose-response relationship between the total number of products used and urinary paraben** and phthalate metabolite concentrations."*

Braun JM, Just AC, Williams PL, Smith KW, Calafat AM, Hauser R. (2014) Personal care product use and urinary phthalate metabolite and paraben concentrations during pregnancy among women from a fertility clinic. J Expo Sci Environ Epidemiol. 2014 Sep-Oct;24(5):459-66. doi: 10.1038/jes.2013.69.

"*"Compared with individuals who reported "Never" using mouthwash, individuals who reported daily use had significantly elevated urinary concentrations of mono-ethyl phthalate, methyl and propyl parabens, and BP3 (28%, 30%, 39%, and 42% higher, respectively).* ***Individuals who reported "Always" using sunscreen had significantly higher urinary concentrations*** *of triclosan, methyl, ethyl, and propyl parabens, and BP3 (59%, 92%, 102%, 151%, and 510% higher, respectively)* ***compared with "Never" users of sunscreen****."*

Ferguson KK, Colacino JA, Lewis RC, Meeker JD. (2017) Personal care product use among adults in NHANES: associations between urinary phthalate metabolites and phenols and use of mouthwash and sunscreen. J Expo Sci Environ Epidemiol. 2017 May;27(3):326-332. doi: 10.1038/jes.2016.27

"A statistically significant difference was demonstrated between serum parabens in women who used lipstick containing these substances compared with those not using this cosmetic (p = 0.0005 and 0.0016, respectively), and a strong association was observed between serum parabens and lipstick use (Spearman correlation = 0.7202)."

Tahan GP, de Kássia Souza Santos N, Albuquerque AC, Martins I. (2016) Determination of parabens in serum by liquid chromatography-tandem mass spectrometry: Correlation with lipstick use. Regul Toxicol Pharmacol. 2016 Aug;79:42-8. doi: 10.1016/j.yrtph.2016.05.001. Epub 2016 May 3.

"The use of lotions in the previous 24 h was associated with 80−110% higher levels of parabens (BP, EP, MP, and PP). Users of shampoo, conditioner, and cosmetics (makeup and eye makeup) also had urinary BP concentrations 72−84% higher compared to nonusers. Soap use in the past 24 h was also significantly associated with higher PP and MP concentrations in urine. **Women who were categorized as "High Product Category Users" had between 100 and 200% higher parabens concentrations compared to "Low Product Category Users"**.

Fisher M et.al. (2017) Paraben Concentrations in Maternal Urine and Breast Milk and Its Association with Personal Care Product Use. Environ Sci Technol. 2017 Apr 4;51(7):4009-4017. doi: 10.1021/acs.est.6b04302

4) Particle Sizes of additional parabens should be included in Table 4

Table 4 on particle size ranges of parabens should include data on other parabens included in the report, not just the four parabens currently listed: Sodium Methylparaben; Ethylparaben; Sodium Ethylparaben; Sodium Propylparaben. Specifically:

For example, particle size data can also be found for:

Methylparaben

https://echa.europa.eu/registration-dossier/-/registered-dossier/14310/4/6

Propylparaben:

https://echa.europa.eu/registration-dossier/-/registered-dossier/13890/4/6

Butylparaben

https://echa.europa.eu/registration-dossier/-/registered-dossier/25335/4/6

Isopropylparaben

https://echa.europa.eu/registration-dossier/-/registered-dossier/19482/4/6

Isobutylparaben

https://echa.europa.eu/registration-dossier/-/registered-dossier/17752/4/6

4-hydroxtbenzoic acid:

https://echa.europa.eu/registration-dossier/-/registered-dossier/15944/4/6

Of note, the ECHA data indicate that for propylparaben, 37.8% of particles are smaller than 10 microns in diameter, the CIR's established level of concern for inhalation. This information contradicts the summary claim found in the report that 95-99% of particles have diameters greater than 10 microns and are thus unlikely to be inhaled deeply. This statement should be corrected.

5. **The Margin of Safety (MOS) Calculation should be more conservative.**

The calculation used to derive a MOS for parabens needs to be updated to reflect more conservative product usage amounts and more conservative absorption rates that are consistent with data included in other sections of the assessment.

Currently the calculations in the safety assessment are:

> *Systemic exposure dose (SED, Butylparaben) = 17.76 g/day of product x 0.4 % use concentration ÷ 60 kg person x 50 % absorption x 1000 mg/g conversion factor = 0.59 mg/kg/day*
>
> *MOS (adult, Butylparaben) = NOAEL/SED = 160 mg/kg/day / 0.59 mg/kg/day= 270*

Systemic exposure dose (SED, multiple parabens) = 17.76 g/day of product x 0.8 % use concentration ÷ 60 kg person x 50 % absorption x 1000 mg/g conversion factor = 1.18 mg/kg/day

MOS (adult, multiple paraben) = NOAEL/SED = 160 mg/kg/day / 1.18 mg/kg/day= 135

These calculations use an estimate of 0.4% use concentration of Butylparaben, and a 0.8% use concentration for multiple parabens. These numbers come from the regulatory limits applied in the EU in which no more than 0.4% butylparaben and no more than 0.8% cumulative parabens are allowed in products. Those regulatory limits however, do not apply in the United States. According to the VCRP data included in the safety assessment, the maximum reported use rate for butylparaben is 0.5% (not 0.4%). Therefore 0.5% (or higher) would be a more appropriate conservative use rate for exposure in the United States.

Similarly, for a use rate for cumulative parabens, 0.8% seems low. Unfortunately the VCRP data as reported does not provide data on levels of parabens used cumulatively in products. However, the data does show us that the maximum concentration of use of methylparaben is 0.9%, the maximum for propylparaben is 0.7%, the maximum for ethylparaben is 0.65% etc. We know that these parabens are used in combination in products, and cannot rule out that they would be used at these maximum concentrations together. The current use of 0.8% for combined parabens is not a conservative estimate for concentration of use and should be increased to get a more accurate margin of safety.

Secondly, the calculations currently use an estimated absorption rate of 50%. However, the safety assessment cites a risk assessment study published by Procter & Gamble researchers (Cowan-Ellsberry and Robison 2009) which supports the use of a conservative absorption rate of 80%. Specifically, the study states:

> *"The measured extent of dermal penetration and metabolism [of parabens] in these studies is somewhat variable ranging from 15% to 75% probably due to matrix effects, differences in animals used and other experimental artifacts. Therefore, we chose 80% as a conservative estimate of the amount of the parabens either as parent or metabolite penetrating the skin. This is consistent with the guidance that has recently been outlined for estimating exposure to materials which occur at low levels in cosmetic products."*

Source: Cowan-Ellsberry CE and Robison SH. Refining aggregate exposure: example using parabens. Regul Toxicol Pharmacol. 2009;55(3):321-329.

The CIR calculations should also reflect this more reasonable conservative estimate of absorption.

Lastly, the recent draft reflects a change in the calculations from using a NOAEL of 1,000 mg/kg/day to a NOAEL of 160 mg/kg/day. The recommendation to use this lower NOAEL came from George Daston , a Procter and Gamble researcher. While I am sure Dr. Daston is highly respected in his field, it cannot be ignored that his employer, Procter and Gamble would be significantly affected financially by a decision of the CIR that current usage of parabens does not result in an appropriate margin of safety. The conflict of interest is there. Given that, the draft assessment should be especially transparent on the

justification of the panel to use the NOAEL of 160 mg/kg/day rather than the more conservative NOAEL of 10 mg/kg/day form the Boberg study or even the NOEL of 2 mg/kg/day used by the European researchers. Currently the safety assessment briefly summarizes possible reasons for not using these other more conservative values, but doesn't give specifics. The wording used currently unfortunately gives the impression that Procter and Gamble has made the decision for the CIR to use a less protective level, rather than the panel themselves. Additional information specifying the individual reasons that the other two possible NOAEL/NOEL values were dismissed, would alleviate what currently appears to be a conflict of interest.

Thank you for the opportunity to comment on this safety assessment and appreciate the careful consideration of these comments by the Panel and staff of the CIR.

Sincerely,

Alexandra Scranton
Director of Science and Research
Women's Voices for the Earth