



WOMEN'S VOICES FOR THE EARTH

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November 25, 2019

To the CIR:

I am writing to submit comments on the Amended Safety Assessment of Methylchloroisothiazolinone and Methylisothiazolinone to be discussed at the December 2019 meeting.

My comments include concerns over two specific issues:

- 1) The CIR SSC's QRA for these ingredients is not fully transparent in the Safety Assessment and should be clarified and amended, and it appears that there are errors in Table 3 which reports results of the QRA.
- 2) The current discussion of dermal sensitization rates of Methylchloroisothiazolinone and Methylisothiazolinone and the contribution of cosmetic product exposure to these rates is highly problematic in that it vastly underplays the recent epidemic of the problem globally, and discounts the responsibility (and ability) of the CIR to play a major role to advance public health.

1) CIR SSC's QRA for Methylchloroisothiazolinone and Methylisothiazolinone

There is one highly questionable data point presented in Table 3 which is that the highest reported maximum concentration of use in bubble baths is "0.000019 ppm". This very much appears to be an error. I have never seen any manufacturer report the presence of an intentional ingredient at such an incredibly low concentration - especially for a preservative, in which, quite obviously, this concentration would have no antibacterial efficacy whatsoever. This concentration is far below what even industry would consider a de minimus amount for any ingredient, there is no question in my mind that this number was reported in error. I believe that it is much more likely that the company reporting this concentration was reporting the actual concentration in the product, that is .000019 of the product which is equivalent to 19 ppm. And if this is the case, clearly the resulting margin of safety for bubble baths would be quite different and likely of concern. Given also that bubble bath products are predominantly used by children, and that the VCRP reports over 100 bubble bath products containing MCI/MI it would be prudent for the CIR to request and verify concentration information from bubble bath manufacturers to be better understand the actual exposure and potential risk from this product category.

Secondly, the discussion of the QRA in the safety Assessment is confusing as the text states:

"When using the exposure assumptions in this risk assessment on all reported VCRP product categories of use with the maximum concentrations of use, as set by the original CIR conclusion, of 7.5 ppm in leave-on products and 15 ppm in rinse-off products, an adequate MOS could not be assured for baby shampoo (MOS = 0.92), permanent wave (MOS = 0.13), hair tints (MOS = 0.56), skin cleansing products (0.61), or cologne and toilet waters (0.50). Table 3 summarizes the QRA results."

However, Table 3 does not in fact include these MOS numbers for baby shampoo, permanent waves, hair tints, skin cleansing products or colognes and toilet waters. In the original QRA submitted in May by the SSC, there are three tables included (Table 5, Table 6 and Table 7) which display the various MOS's calculated. The numbers mentioned above in the text come from the original Table 6, but Table 3 of this Safety Assessment only report the results found in the original Table 5. It might be helpful to either include the full QRA in the Safety Assessment - or at least include all three tables (Table 5, 6 and 7) to explain where inadequate MOS's were calculated.

Having full information on how the QRA was done, and the full results that were calculated should be important information to manufacturers who are being required to complete a QRA to assess the appropriate applicable level for their product.

2) The MCI/MI contact allergy epidemic

There is some very important contextual information missing from the MCI/MI Safety Assessment— which is that the consensus of dermatological experts around the world is that there has been an **epidemic** of sensitizations to MI and MCI/MI caused by the significant increases in the use of these chemicals in cosmetics in recent decades. The rate and speed at which MI and MCI/MI became known as significant skin sensitizers was unprecedented and caused alarm internationally. Importantly, this epidemic has largely occurred in the time since the CIR last reviewed these chemicals. This aspect is not currently mentioned in this safety assessment which appears to be a major oversight. Unlike how they are portrayed in the current draft, isothiazolinones are not just run of the mill sensitizers, but have caused an unprecedented significant epidemic of morbidity specifically due to their use in cosmetics. It is highly relevant to relay these facts in this safety assessment.

Quotes from recent papers:

"Preservative sensitivity patterns evolve with changing use patterns in products. During the last decade, the use of methylisothiazolinone (MI) at higher concentrations in both leave-on and rinse-off products has significantly increased...The epidemic of isothiazolinone sensitivity documented in Europe is now in North America."

Zirwas, M. J., Hamann, D., Warshaw, E. M., Maibach, H. I., Taylor, J. S., Sasseville, D., ... Belsito, D. V. (2017). **Epidemic of Isothiazolinone Allergy in North America**. *Dermatitis*, 28(3), 204-209. doi:10.1097/der.0000000000000288

"Methylisothiazolinone (MI) is a preservative commonly used in water-based personal care products. Increases in the allowable concentration of MI alone in these products has led to an epidemic of allergic contact dermatitis (ACD)...personal care products are the most common source of MI contact allergy"

Reeder M. Atwater AR. (2019) **Methylisothiazolinone and isothiazolinone allergy**. *Cutis*. Aug 2019, 104(2): 94-96.

“The prevalence of MI and MCI/MI contact allergy increased significantly from 2010 to 2012... Cosmetics were the most common substances causing relevant exposure found in both MCI/MI-allergic and MI-allergic patients.”

Lundov, M. D., Opstrup, M. S., & Johansen, J. D. (2013). **Methylisothiazolinone contact allergy - a growing epidemic.** *Contact Dermatitis*, 69(5), 271-275. doi:10.1111/cod.12149

This context is especially important to include in the safety assessment so that manufacturers using these ingredients fully understand the public health impact of their choices. Also, there is even more recent data which shows that a restriction and/or ban on the use of MCI/MI in cosmetics has been very successful in significantly reducing the incidence of sensitization.

In response to the growing awareness of the epidemic of sensitization to these preservatives, the European Union banned MI in cosmetics in leave on cosmetics in 2016 and implemented a limitation of 15ppm in rinse-off cosmetics. Similarly, Australia implemented regulatory restrictions on MI and eventually banned it from leave-on cosmetics as well.

There are several recent papers, (only one of which is currently included in the CIR's Safety Assessment) which demonstrate the effectiveness of these bans and restrictions on public health.

For example in a recent study of data from the European Union, **the sensitization rate to MI decreased 50% between 2015 and 2017.**

Source: Uter W, Aalto-Korte K, Agner T, Andersen KE, Bircher AJ, Brans R, Bruze M, Diepgen TL, Foti C, Giménez Arnau A, Gonçalo M, Goossens A, McFadden J, Paulsen E, Svedman C, Rustemeyer T, White IR, Wilkinson M, Johansen JD; European Environmental Contact Dermatitis Research Group. The epidemic of methylisothiazolinone contact allergy in Europe: follow-up on changing exposures. *J Eur Acad Dermatol Venereol.* 2019 Aug 16. doi: 10.1111/jdv.15875.

A study from a hospital in Spain confirmed these results, finding that

"regulatory interventions [on cosmetics] have resulted in a dramatic decrease in the prevalence of MCI and MI ACD, reaching a pre-epidemic level of 3.1% in 2019."

Source: Magdaleno-Tapial, J., Valenzuela-Oñate, C., Ortiz-Salvador, J. M., García-Legaz-Martínez, M., Martínez-Domenech, Á., Alonso-Carpio, M., ... Zaragoza-Ninet, V. (2019). Contact allergy to isothiazolinones epidemic: Current situation. *Contact Dermatitis.* doi:10.1111/cod.13396

A study in Germany reported on the *"unprecedented epidemic of MI-allergy mainly caused by its use in cosmetics"* and found that

"Comparing sensitization to MI in three periods (2009, 2013/14 and 2017/18), there was an increase to 7% in 2013 and a decrease to 3.4% in 2018."

Source: Schnuch, A., Schubert, S., Lessmann, H., & Geier, J. (2019). The methylisothiazolinone epidemic goes along with changing patients' characteristics – After cosmetics industrial applications are the focus. *Contact Dermatitis.* doi:10.1111/cod.13414

A study in Turkey found:

"In accordance with the recent reports, we also observed a decrease in the prevalence of MCI/MI and MI contact allergy from 2016 to 2018. This might be explained with the regulations made in Turkey as per European Commission cosmetics directive."

Source: Salman, A. (2018). Methylchloroisothiazolinone and methylisothiazolinone contact allergy: A retrospective cohort study from a tertiary dermatology clinic in Turkey. *Contact Dermatitis*. doi:10.1111/cod.13175

Lastly, in Australia, the sensitization rate to MI has also decreased nearly 50% between 2015 – 2017.

Source: Flury, U., Palmer, A., & Nixon, R. (2018). The methylisothiazolinone contact allergy epidemic in Australia. *Contact Dermatitis*, 79(3), 189-191. doi:10.1111/cod.13025

Meanwhile in the U.S., there are no formal regulations restricting the use of MCI/MI, but instead the CIR's recommendations have been in place since 2014 – which does not recommend against the use of MI, but requires companies to use no more than 100ppm in rinse off products and to ensure a level in leave-on products that is non-sensitizing based on a QRA. Unlike the promising epidemiological data from the EU and Australia, the U.S. has not seen declines in sensitization to MI in recent years. According to the latest data from the NACDG in 2015-16, the sensitization rates for MI and MCI **were still increasing in the U.S.**

Source: DeKoven JG, Warshaw EM, Zug KA, Maibach HI, Belsito DV, Sasseville D, Taylor JS, Fowler JF Jr, Mathias CGT, Marks JG, Pratt MD, Zirwas MJ, DeLeo VA. (2018) North American Contact Dermatitis Group Patch Test Results: 2015-2016. *Dermatitis*. 2018 Nov/Dec;29(6):297-309. doi: 10.1097/DER.0000000000000417.

While I was pleased to see that the safety assessment now includes maximum recommended concentrations, it does not appear from the US data that the CIR's prior history of recommending that manufacturers in the U.S. formulate products to be non-sensitizing based on a QRA, has been successful in limiting or reversing the rising rates of sensitization to MCI/MI.

In order to see the same promising results in the US, as have been seen in the EU and Australia, I strongly recommend that the CIR also consider a determination that MCI/MI should not be used at any level in leave-on products.

For most decisions of the CIR, gathering evidence of actual health improvements that result from regulations on ingredients is relatively rare. In this case, the data is both clear and available. And the dermatological data on sensitization to isothiazilinsones in the U.S. and elsewhere will continue to be collected every year and published. And the disparate results between countries that have implemented effective solutions to isothiazilinsones and those that have not, will become more and more evident. The CIR will be held responsible for those disparate results in the U.S. based on their decision.

We now know that an epidemic of sensitization among the current generation could potentially have been avoided if the CIR had made a different decision on MCI/MI in cosmetics back in 1992. Now that a clear and successful path to reverse the trend of increasing sensitization has been forged in the EU and in Australia, the CIR has the opportunity to make that same significant difference to the health of Americans. Making the wrong decision means thousands of additional Americans, could be unnecessarily sensitized to isothiazilinsones. This is a responsibility that the CIR must take very seriously.

Sincerely,

A handwritten signature in black ink on a light gray background. The signature reads "Alexandra Scranton" in a cursive, flowing script.

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