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RE: Comments to proposed Chapter 173-339 WAC – Cosmetic Product Restrictions (Formaldehyde in Cosmetics)

Ashland respectfully submits the following comments on the Washington State proposed Chapter 173-339 WAC restricting formaldehyde in cosmetics, in which glyoxal (CAS No. 107-22-2) has been identified. We appreciate the opportunity to comment and provide technical evidence regarding this proposal.

Ashland has a vested interest in this proposal due to potential impact to our and our customer's product portfolios.

Based on the currently available information described below, Ashland would like to respectively recommend that: (1) the definition of 'intentionally added' be further clarified, and (2) glyoxal (CAS No. 107-22-2) to be excluded from the proposed Chapter 173-339 WAC – Cosmetic Product Restrictions (Formaldehyde in Cosmetics).

Definition of 'intentionally added'

The current proposed definition of intentionally added which includes *any chemical that serves a function in the final product, manufacturing of the final product or an ingredient in the final product* broadens the scope of what is typically defined as intentionally added. Two examples to refer back to are guidance from the FDA on 'processing aids and incidental ingredients' and European Cosmetic Regulations which allow exceptions for impurities in raw materials and the manufacturing process.

The FDA defines ingredient as "any single chemical entity or mixture used as a component in the manufacture of a cosmetic product." 21 CFR 700.3(e). The FDA defines the following-

1. Incidental ingredient - substances that have no technical or functional effect in the cosmetic but are present by reason of having been incorporated into the cosmetic as an ingredient of another cosmetic ingredient.

2. Processing aids –

   i. Substances that are added to a cosmetic during the processing of such cosmetic but are removed from the cosmetic in accordance with good manufacturing practices before it is packaged in its finished form.

   ii. Substances that are added to a cosmetic during processing for their technical or functional effect in the processing, are converted to substances the same as constituents of declared ingredients, and do not significantly increase the concentration of those constituents.

   iii. Substances that are added to a cosmetic during the processing of such cosmetic for their technical and functional effect in the processing but are present in the finished cosmetic at insignificant levels and do not have any technical or functional effect in that cosmetic.

We would like to propose the State of Ecology modifies the definition and use of 'intentionally added' to align with those above provided by the FDA; allowing for 'incidental ingredients' and 'processing aids'. This allows Ashland and our customers the opportunity to continue and utilize products which comply with existing regulations.

For Ashland specifically, glyoxal is used as a processing aid in the manufacturing process. Any amounts of glyoxal remaining are residual and do not serve a purpose in the final product.

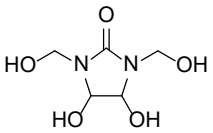
Exclusion of glyoxal (CAS No. 107-22-2) from the proposed Chapter 173-339 WAC – Cosmetic Product Restrictions (Formaldehyde in Cosmetics)

It is our understanding glyoxal was determined to be a formaldehyde releaser based on a review of literature, including *ECHA's Investigation Report on Formaldehyde and Formaldehyde Releasers* dated 15 March 2017. Ashland's team of Research and Toxicology experts have reviewed this literature and are structuring our comments from a health risk approach and misidentification of glyoxal in the referenced literature.

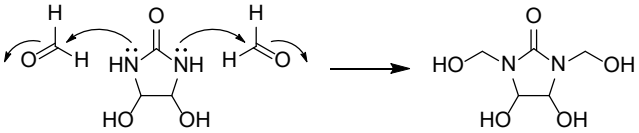
Comments on inclusion of Glyoxal (CAS 107-22-2) as a Formaldehyde Releasing Agent

Table 6 of the ECHA investigation report lists formaldehyde releasers with 'glyoxal' in their name. However, every one of them is a glyoxal compound further reacted with formaldehyde to generate "methylol" or "hydroxymethyl" groups attached to a heteroatom (O or N). Those methylol or hydroxymethyl moieties are the source of formaldehyde, not the glyoxal moiety.

For example, the first appearing compound, dihydroxydimethylolethyleneurea, methylated (CAS 68411-81-4, aka dimethylolglyoxalurea, methylated) has the structure:



It is made by adding two equivalents of formaldehyde to glyoxalurea:

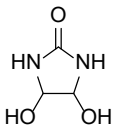


This reaction is done deliberately to make the molecule as an antimicrobial formaldehyde releaser. Over time, the reverse of the synthetic reaction occurs. The formaldehyde released reacts with something else or diffuses away, and more formaldehyde is slowly released, driven by equilibrium, until all the formaldehyde attached has been released, leaving behind glyoxalurea.

All the other "glyoxal" compounds, except one, listed in Table 6 are reaction products of glyoxal, formaldehyde and other things. As above, the source of the formaldehyde is the formaldehyde in the original synthetic reaction, not the glyoxal:

> Urea, reaction products with urea and glyoxal, CAS 296-664-6
> Urea, reaction products with urea, glyoxal and methanol, CAS 296-665-1
> Reaction product of urea, formaldehyde, glyoxal and diethylene glycol, CAS 939-056-4

The only "glyoxal" molecule listed in Table 6 that does not have formaldehyde in its synthesis is glyoxalurea (CAS 3720-97-6), which has the structure:



Over time, this molecule can equilibrate, dissociating to one molecule of urea and one molecule of glyoxal. It is our opinion that this molecule is not a source of formaldehyde and is incorrectly included in Table 6.

Comments on the perceived health risk of Glyoxal as a Formaldehyde Releasing Agent

The level (or rate) of formaldehyde being released from cosmetics containing glyoxal or formaldehyde releasing agent is very low (or toxicologically insignificant)[1] and does not have any impact to the safety/health of consumers using cosmetics containing glyoxal based on the following documented scientific facts: (1) the abundance of endogenous formaldehyde in biological systems[2, 3], (2) the rapid metabolic detoxification of formaldehyde to less hazardous chemicals[2], and (3) the efficient DNA interstrand cross-link repair system to maintain genomic stability (formaldehyde is known to cause DNA interstrand cross-link due to its highly reactive properties)[4,5].

Furthermore, it has been recently shown that formaldehyde is involved in a fundamental metabolic process in cells that enables the synthesis of nucleotides and amino acids and is present in all forms of life[6,7]. These findings change our view of formaldehyde as a toxic chemical and highlight the importance of maintaining cellular formaldehyde homeostasis to promote healthy cell growth.

Ashland is not aware of any (public) data on (1) the level of formaldehyde being released while using cosmetics containing glyoxal and (2) the consumer health risk or the adverse environmental impact due to the released formaldehyde while using cosmetics containing glyoxal.

Conclusion

In conclusion, Ashland strives to comply and support those regulations promoting safer cosmetics ingredients. We do request your consideration in reviewing our comments and recommendation related to the proposed regulation on

formaldehyde releasers in light of both the perceived health risk (of glyoxal as a formaldehyde releaser) and language used defining 'intentionally added'.

Yours sincerely,

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References

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