Message

**From:** Beck, Nancy [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=168ECB5184AC44DE95A913297F353745-BECK, NANCY]
**Sent:** 3/8/2018 12:17:50 PM
**To:** Anastasia Coots [Anastasia_Coots@cargill.com]; Morris, Jeff [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=55c34872e6ea40cab78be910aec63321-Morris, Jeff]
**Subject:** RE: Sustainable Futures TME/PMN Needs Your Attention

Anastasia,
Thank you for your note. We will look into this and get back to you.

Regards,
Nancy

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**Ex. 6**
beck.nancy@epa.gov

**From:** Anastasia Coots [mailto:Anastasia_Coots@cargill.com]
**Sent:** Thursday, March 8, 2018 4:56 AM
**To:** Morris, Jeff <Morris.Jeff@epa.gov>; Beck, Nancy <Beck.Nancy@epa.gov>
**Subject:** Sustainable Futures TME/PMN Needs Your Attention
**Importance:** High

Note: The following communication does not include confidential business information. Details regarding specific chemical identity and TME/PMN reference numbers are purposefully excluded.

Hello Jeff and Nancy,

I know from the Lynn Bergeson and the New Chemicals Coalition (NCC) that you have requested specific examples of issues or feedback with the Sustainable Futures program. We currently have a TME/PMN Sustainable Future submission that went through Focus Meeting the second week of February. The chemical fits into the Polyol Esters Category previously reviewed by EPA HPV Challenge Program in 2010 and as a category of chemicals for safe use in cosmetics as part of the Cosmetic Ingredient Review program in 2012. The initial response was a Denial based on the Human Health Assessment indicating Human Health Risk for dermal exposure based on indication of 1) blood and thyroid effects with NOAEL of 300 mg/kg/day in an oral repeat dose study available for an analogue, 2) an LOAEL of 100 mg/kg/day for developmental toxicity for one of the reactants used, and 3) skin and eye irritation based on statements in SDS. Concluding recommendations for a SNUR to address mitigation through use of PPE of gloves and safety glasses in addition to testing requirements (OECD 422 study).

We were informed of the initial response a couple of weeks ago and I was trying to get concerns from the risk assessment addressed through the PMN product manager before a final denial of the TME. However, I was informed by a phone call yesterday by the TME product manager that she was unaware of any of our on-going communications with the PMN product manager and you have already reviewed the original assessment supporting a denial.

The following is a list of specific examples that are making the Sustainable Futures program ineffective and/or need improved upon. In addition, we would still like to see our current TME/PMN issue resolved.

General Process

1) The filing of the TME/PMN jointly under the Sustainable Futures program is intended to make the review more efficient. It was not made clear to me that there were 2 separate Product Managers handling the TME and PMN separately and that I needed to address the issue of the risk assessment after the focus meeting with both managers separately.

2) We were contacted by an assigned manager to our PMN who had not reviewed our PMN and was not prepared to discuss the issue; indicated that the risk assessor had not taken into account the additional information we included in the P2 assessment; and initially just didn't seem to understand the chemistry based on comments regarding the nomenclature for esters.
3) There is a definite lack of timely communication and/or internal communication that would allow us to address issues or concerns raised by a risk assessor before the assessment gets to you for denial of a TME.
4) Specific to this TME/PMN, we had included additional information with the P2 that should have mitigated or addressed the risk assessors findings:

    a) chemical is not likely to penetrate skin based on high MW (>500 g/mol), high Pow, and low solubility, which was acknowledged in the summary by assessor as "dermal absorption is nil or poor". However, risk assessor based the risk modeling on 100% dermal absorption to derive the MOE and has based all Human Health Risk recommendations based on exposure risk through dermal absorption.

    b) The risk assessor references oral repeat tox study based on an analog indicating concern for increased blood clotting time, increased neutrophils, decreased red blood cells, increased platelets, decreased serum potassium and phosphorous, vacuolated lung macrophages, and thyroid hypertrophy and assigned a NOAEL of 300 mg/kg/day for use in modeling to derive the MOE. The study was originally concluded by study directors for the report as meeting a NOAEL of 1000 mg/kg/day based on the effects observed and indicated above where not considered significant due to lack of correlative findings or not considered adverse based on the minimal to mild severity. Study findings have been previously reviewed by other regulatory agencies and used as analogue data as supporting low or no concern findings. Additionally, when taken into account additional repeat tox studies for analogues including 422/414 studies that are available with NOAEL for hematological and systemic effects concluded no observed adverse effects for highest doses tested 1000 mg/kg/day.

    c) the reactant which is driving concerns for developmental tox with the NOAEL of 100 mg/kg/day is in fact fully reacted and any excess is removed through the process. Residuals are specified to be maintained below 0.03%. The new chemical under this submission is specific to the esters from the reaction. Any presence of the reactant greater than 0.1% is required by OSHA HazCom and the Globally Harmonized System for classification and labeling to be treated as a separate component driving hazard classification of a mixture. The reactant is included on the TSCA inventory without a SNUR. Any testing required by EPA would be with the chemical as manufactured under conditions included in the TME/PMN and would not address any concerns the risk assessor would have for subsequent manufacturers who had higher residual content of unreacted reactant. Additional 422/414 studies for analogues based on the esters with the reactant are available and endpoint data was used as our bases for weight of evidence determination of NOAEL of 1000 mg/kg/day for systemic, maternal, and developmental toxicity as summarized in our P2 assessment. A full OECD 422 study report has been published by Japan's Food and Drug Safety Center which I offered to the PMN product manager to have translated and uploaded 2 weeks ago and he said to hold off because there was indication that it was already available.

    d) Statements in SDS referenced by risk assessor as indicating concerns for skin and eye irritation which triggered a Human Health Risk finding included: "may cause minimal irritation or no effect" and "based on similar substances may be slightly irritating to eyes or skin, but not sufficient for classification" is based on valid available studies for analogues meeting OECD 404/405, Draize or similar accepted methods which results were reported for similar substance as causing slight or minimal irritation indicated by temporary redness, fully reversible within study guidelines which did not meet criteria for classification as an irritant under any current regulatory criteria (FIFRA, CPSIA/FHSA, etc). Repeat dose dermal studies for analogues indicated minimal irritation, redness, drying or flaking of skin for the category of chemicals, which when evaluated for use in cosmetics also did not indicate concern for safe use in leave-on personal care and cosmetic products. As summarized in our P2 assessment, human data is also available for use in cosmetics including use in eyeliners. Industrial uses do not indicate potential for intended repeat or prolonged contact. However, information is provided in the SDS for recognition of symptoms. In our SDS we include in Section 11. Symptoms related to physical, chemical, and toxicological characteristics: "Repeated or prolonged skin contact may cause drying, reddening, itching or cracking. Eye contact may cause temporary redness, tearing or blurred vision." All of this information was included in our TME/PMN files, however, the risk assessor concluded that the "risk to eye and skin irritation were not quantified due to lack of a suitable POD". Triggering a human health risk requiring mitigation through use of PPE. This is very difficult to accept that this was their conclusion from what was provided.

e) In the P2 assessment as part of the TME/PMN files, we included additional studies and supporting references that can be taken into consideration for weight of evidence supporting conclusions of not likely to be a human health risk

- including references for already available additional repeat toxicity studies by oral, dermal, and inhalation routes. Available OECD 422, 414 and tox studies for analogue/ester with reactant of concern which all report NOAELs for systemic, maternal, and developmental toxicity to be greater than or equal to highest doses tested, 1000 mg/kg/day. It is unclear what additional animal testing of the new chemical according to OECD 422 will provide that is not already available from existing studies with analogue or similar ester of concern.
- the attachment of EPA's 2010 HPV Screen Level Hazard Assessment for the Chemical Category which indicated that based on the review of studies available at that time in 2010 concluded no data gaps were identified.
- a 2012 Cosmetic Ingredient Review for Safe Use of the Chemical Category by an expert panel which also concluded that the chemical category including analog which triggered concern by the EPA risk assessor was determined unlikely to penetrate the skin and to be safe for the existing identified uses in leave-on personal care and cosmetic products as indicated. Specifically esters based on the reactant of concern is used as a skin conditioning agent at concentrations of up to 40% in existing consumer products regulated by FDA.

I am a strong supporter of the Sustainable Futures Program and have been working with our development team to try to address all potential foreseeable risks when developing new chemicals and provide as much readily available information as part of our submissions. However, if this information is not being used as part of the hazard assessments completed by risk assessors and/or if we are not given the opportunity address concerns raised by the risk assessor prior to final denial of the TME, then the Sustainable Futures Program will continue to be an ineffective program for making the review process more efficient.

I hope these examples help and hope to get some relief or direction on how we can provide the information that is needed.

Thank you for your time,

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