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David Michaels, Ph.D., M.P.H.
Assistant Secretary of Labor for Occupational Safety and Health
U.S. Department of Labor
Occupational Safety & Health Administration
200 Constitution Avenue, N.W.
Washington, D.C. 20210

Dear Dr. Michaels,

I am writing to provide you with current information about research at the National Institute for Occupational Safety and Health (NIOSH) and the National Institute for Environmental Health Sciences (NIEHS) that addresses the respiratory toxicity of diacetyl substitutes.

At the NIOSH Workshop **Making Green Jobs Safe: Integrating Occupational Safety and Health into Green and Sustainability** held on December 16, 2009, you noted that

“...all too often, substitution is an unreachable panacea - because the safer chemical may be too expensive or may not quite fit the job's technical needs, or because we don't have enough information to know which chemicals are actually safe.”

NIOSH shares your concerns that many of the chemicals and materials used as alternatives to diacetyl for imparting butter flavor to flavoring mixtures and food products are not known to be less hazardous. For example, among the potential replacements for diacetyl, the fermentation product known as “starter mix” contains high concentrations of diacetyl itself.

Another material that adds the flavor of butter to food is acetoin, but its toxicity is incompletely investigated and it accompanies diacetyl in many of the workplaces where *bronchiolitis obliterans* occurs in workers who make or use flavorings. Acetoin toxicity is currently being investigated as part of the National Toxicology Program of the U.S. Department of Health and Human Services.

Another butter flavoring, 2,3-pentanedione, is the subject of research at both NIOSH and NIEHS. It is structurally very similar to diacetyl, since 2,3-pentanedione is a 5-carbon α -diketone and diacetyl is a 4-carbon α -diketone. This research suggests that, in rats, 2,3-pentanedione causes airway epithelial damage similar to that produced by diacetyl (Hubbs et al., 2010 [in press];¹ Morgan et al., 2010 [in press])². The research on 2,3-pentanedione will be presented at the Society of Toxicology Annual Meeting held March 7-11, 2010 and the abstracts will be published in *The Toxicologist*, Supplement to *Toxicological Sciences*.

The journal has an embargo policy, but has kindly agreed to allow us to cite the abstracts prior to publication specifically for the purpose of this communication with the Occupational Safety and Health Administration.

The issues noted above for starter distillate, acetoin, and 2,3-pentanedione exemplify the lack of evidence demonstrating the workplace safety of potential substitutes for diacetyl; and document some evidence that potential substitutes are also respiratory hazards.

We would be pleased to discuss these early findings on diacetyl substitutes with you and your staff at a mutually convenient time.

Thank you.

Sincerely,



John Howard
Director

¹ Hubbs, A. F., Moseley, A. E., Goldsmith, W. T., Jackson, M. C., Kashon, M. L., Battelli, L. A., Schwegler-Berry, D., Goravanahally, M. P., Frazer, D., Fedan, J. S., Kreiss, K., and Castranova, V. *Airway epithelial toxicity of the flavoring agent, 2,3-pentanedione*. *The Toxicologist: Supplement to Toxicological Sciences* 114, 2010 (*in press* abstract).

² Morgan, D. L., Kirby, P. J., Price, H. C., Bosquet, R. W., Taylor, G. J., Gage, N., and Flake, G. P. *Inhalation toxicity of acetyl propionyl in rats and mice*. *The Toxicologist: Supplement to Toxicological Sciences* 114 (*in press* abstract).