## LETTERS TO THE EDITOR

## **Ethyl Carbamate Formation During Urea Complexation for Fractionation of Fatty Acids**

Sir:

The October 1998 issue of the Journal of the American Oil Chemists' Society (Vol. 75, no. 10, p. 1403) contains an article by D.G. Hayes, Y.C. Bengtsson, J.M. Van Alstine, and F. Setterwall titled "Urea Complexation for the Rapid, Ecologically Responsible Fractionation of Fatty Acids from Seed Oil." The first step of this procedure involves dissolving urea in 95% ethanol at  $65 \pm 5$ °C. The formation of ethyl carbamate (EC) from the reaction of urea and ethanol (EtOH +  $NH_2CONH_2 \rightarrow EtOCONH_2 + NH_3$ ) was first reported by E. Wohler in 1845 (see Ref. 1). EC, also known as urethane, is an animal carcinogen (2,3) and has been a source of concern at the U.S. Food and Drug Administration because it has been found at ppb levels in distilled spirits, wines, and in a variety of fermented foods and beverages (4). Studies by Ough et al. (5–7) have shown that the reaction of ethanol and urea is the main contributor to EC levels in wine. Moreover, EC is listed as a hazardous material under the Comprehensive Environmental Response, Compensation and Liability Act of 1980 (CERCLA) and is included in Department of Transportation regulations which specify the manner and reportable quantity for transport of hazardous materials (8,9). We therefore question the "Ecologically Responsible" premise of the title until the authors have measured the formation of EC and determined the fate of this potent carcinogen in the system described.

## REFERENCES

 Adams, P., and F.A. Baron, Esters of Carbamic Acid, Chem. Rev. 65:567–602 (1965).

- 2. Nettleship, A., P.S. Henshaw, and H.L. Meyer, Introduction of Pulmonary Tumors in Mice with Ethyl Carbamate (Urethane), *J. Natl. Cancer Inst. 4*:309–319 (1943).
- 3. Mirvish, S.S., The Carcinogenic Action and Metabolism of Urethane and *N*-Hydroxyurethane, *Adv. Cancer Res.* 11:1–42 (1968).
- Food and Drug Administration, Urethane in Alcoholic Beverages, Federal Register 55:10816–10817 (March 23, 1990).
- Ough, C.S., E.A. Crowell, and B.R. Gutlove, Carbamyl Compound Reactions with Ethanol, *Am. J. Enol. Vitic.* 39:239–242 (1988).
- Ough, C.S., E.A. Crowell, and L.A. Mooney, Formation of Ethyl Carbamate Precursors During Grape Juice (Chardonay) Fermentation. I. Addition of Amino Acids, Urea, and Ammonia: Effects of Fortification on Intracellular and Extracellular Precursors, *Ibid.* 39:243–249 (1988).
- Ough, C.S., and G. Trioli, Urea Removal from Wine by an Acid Urease, *Ibid.* 39:303–307 (1988).
- Department of Transportation, 49 CFR Parts 171 and 172, Hazardous Substances, Final Rule. Federal Register 51:42174 (November 21, 1986).
- Dunn, A.J., A.G. Salmon, and L. Zeise, Background, in *Risks of Carcinogenesis from Urethane Exposure*, edited by A.G. Salmon and L. Zeise, CRC Press, Boca Raton, 1991.

B.J. Canas\*
M.P. Yurawecz
Food and Drug Administration
Center for Food Safety and Applied Nutrition
200 "C" St. SW, HFS-347
Washington, DC 20204

[Received December 14, 1998; accepted January 5, 1999]