

December 26, 2006

Frank W. Foote, Esq.
Director, Regulations and Rulings Division
Alcohol and Tobacco tax and Trade Bureau
P.O. Box 14412
Washington, DC 20244-4412

By FAX: 202-927-8525

Re: TTB Notice No. 62 (71 FR 42329)

Dear Mr. Foote:

On behalf of the two major lysozyme producers Fordras S.A. and Neova Technologies, and their North American suppliers, Scott Laboratories and Lallemand, respectively, we welcome the opportunity to comment on your very important and relevant allergen labeling proposal.

Lysozyme is an enzyme derived from the white of hens' eggs and is also present in many plants and animals, including human tears and saliva.¹

Lysozyme has proven to be an effective substitute for sulfur dioxide in preventing malo-lactic fermentation carried out by spoilage lactic acid bacteria. Therefore, the availability and use of lysozyme has reduced the need for, and use of, sulfites in winemaking. Furthermore, lysozyme has the desirable property of inhibiting bacterial contaminants in wine like *Lactobacillus sp.* and *Pediococcus sp.*² that produce biogenic amines (histamine and tyramine) which can cause headache and facial flushing.

TTB Proposal Notice 62 (71 Federal Register 42329)

We applaud the Tax and Trade Bureau's (TTB) initiative regarding allergen labeling in beverage alcohol products. The proposal is certainly consistent with the Food Allergen Labeling and Consumer Protection Act of 2004 (FALCPA) and is an excellent forum to address the possibility of allergens being present in beverage alcohol products at a level resulting in an allergic response in sensitive individuals. We look forward to working with the TTB on this very important rulemaking project.

Christine A. Rogers, Ph.D. Petition dated April 10, 2004 and Her Comment to TTB Notice 41

Notice 62 (71 FR 42330) refers a number of times to Christine Rogers' April 10, 2004, petition to change the regulations to require labeling of all ingredients and substances used in the production of alcohol beverages.

In her petition, Dr. Rogers states, in part,

“Normally I avoid exposures to egg through diligent examination of food labels. However, on several occasions I have started to drink a glass of wine (only 2-3 sips are needed) and I suddenly become aware that I am having gastro-intestinal allergic symptoms. These last 3-4 hours and are very disruptive. On a few occasions I have later phoned the winery and confirmed that indeed they used egg protein in processing of the particular wine I was drinking. Therefore the residual amount of egg in the wine after processing is sufficient to induce allergic reactions.”

Dr. Rogers presented no data in support of her conclusion that her symptoms resulted from residual egg protein in the wine. Furthermore, it would be very useful had Dr. Rogers inquired as to the quantity egg white used in processing the wine, the kind of wine, and processing which may have occurred subsequent to the egg white fining. In any event, there are a number of other possible wine constituents which can cause such symptoms, including biogenic amines.^{3,4} The point being there may have been no

residual egg in this wine after processing.

Furthermore, in her June 23, 2005, comment to TTB Notice 41⁵, Ms. Rogers states, in part,

“I can also attest to the fact that egg allergic individuals can react to lysozyme in cheese (I have done so on a number of occasions) and for me egg lysozyme could not and should not be “generally regarded as safe”, although it may be for the majority of the population.”

For someone who normally “avoids exposures to egg through diligent examination of food labels,” this behavior appears to be inconsistent as the United States Food and Drug Administration requires lysozyme, when used in cheese production, be labeled.⁶ Cheese is another food product containing biogenic amines.⁷ Therefore, Dr. Rogers’ symptoms may very well be a result of biogenic amine intolerance and not lysozyme.

In the interest of objective scientific decision making, we suggest TTB consider only data from a double-blind, placebo control tests and not anecdotal observations. Indeed, anecdotal observations offer little or no help, and often confuse the making of sound, unbiased decisions and we believe anecdotal observations have no place in objective rulemaking. After all, there is a tremendous burden of proof required of petitioners for allergen label exemption. TTB should hold all parties in rulemaking to these same standards.

Regulatory Implementation Date

As TTB may recognize, it will take a considerable period of time to prepare an allergen label exemption petition. We are attempting to gather sufficient data for TTB to make the most informed decision possible. Toward this goal, we are working in three areas of study; clinical trials of persons known to be allergic to lysozyme; improved analytical methodology for the detection of minute levels of residual lysozyme in wine; and developing processing techniques which will remove residual lysozyme from wine, if any is present.

Clinical Studies

First, we are experiencing difficulty finding adults who are allergic to lysozyme. Egg allergies are primarily a childhood problem and fortunately most allergic individuals “out grow” their allergies to lysozyme.^{8,9} Indeed, Fordras and Neova initiated an *in-vivo* clinical study in France to assess the allergenicity of lysozyme in wine when it is consumed by people known to be allergic to egg proteins, and more specifically to lysozyme. The necessary series of approvals was obtained from “official ethical committees” in order to carry out this type of clinical study.

The protocol of the study involved a double-blind, placebo control protocol to be carried out with wine containing lysozyme and wine not containing lysozyme. The clinical studies were to be carried out in four French hospitals on a panel of adult patients known to be allergic to egg proteins and more specifically to lysozyme. This is where the problem gets complicated.

Among the panel of patients who are regularly evaluated by these four French hospitals for their known allergy to eggs, only one was considered to be allergic to lysozyme, i.e., IgE corresponding to lysozyme have been detected in his blood serum. This does confirm this allergy is very rare.

Dr. Catherine Pecquet, M.D (Hôpital Tenon, Centre d'allergologie, 4 rue de la Chine, 75970 Paris cedex 20, France) subsequently advised us that the lysozyme sensitive individual ex-patriated from France leaving no lysozyme sensitive patient to participate in the clinical study.¹⁰

We hope to pursue these clinical studies at another venue, if we can find enough adults allergic to lysozyme to provide for a statistically significant study.

Analytical Methodology

Second, we are in the process of refining analytical methodology specific for lysozyme analyte with an eye toward lower detection limits. After refinement, we will seek recognition of the methodology by an international wine organization.

Lysozyme Removal Processing

Third, we are currently evaluating processing steps which will remove any residual lysozyme from wine. Present data shows no residual lysozyme remains in red wine due to relatively high levels of polyphenolic compounds¹¹. However, with the possibility of residual in lysozyme treated white wine, we are very interested in pursuing practical measures for the removal of residual lysozyme from wine.

Also, TTB has 180 days to evaluate exemption petitions and if there is no decision after 180 days, the petition is deemed denied unless an extension of time is mutually agreed upon by the appropriate TTB officer and the petitioner.¹² Therefore, some of these decisions may take an extended amount of time. Further, we feel implementing the allergen labeling requirement before TTB makes decisions on the exemption petitions may mislead the consumer if allergen information appears on beverage alcohol labels one day and not the next. This would be very confusing, indeed.

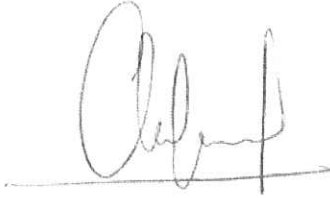
In view of the above, and considering the TTB interim rule provides for producers, bottlers, and importers of wine, distilled spirits, and malt beverages to voluntarily implement allergen labeling,¹³ we are requesting a lengthy implementation date of 3 to 4 years from the publication of the final rule in the Federal Register.

Disclosure Statement Protocol

As an alternative to "Contains," we would prefer disclosure statements to be the alternative proposed in Notice 62, i.e., "Processed with:" Further, we feel the proposed requirement to label "fish," "milk," or "eggs," as the case may be, very misleading. Indeed, a label stating "Contains: fish" could imply to many consumers that fish swam or otherwise came in contact with the wine. Similar implications with "Contains: eggs" or "Contains: milk." In view of this, we suggest TTB consider a protocol which includes the term protein. Protein, as you know, is the primary allergen in these food products. An example would be "Processed with fish protein," instead of "Processed with fish."

Thank you very much for considering our comments. We look forward to working with the TTB and others on this very important rulemaking initiative.

Sincerely yours:

A handwritten signature in black ink, appearing to read 'Gilles Lagarde', written over a horizontal line.

Gilles Lagarde, Executive V-P, Neova Technologies

A handwritten signature in black ink, appearing to read 'Adalberto Villa', written in a cursive style.

Adalberto Villa, Fordra, S.A.

A handwritten signature in black ink, appearing to read 'Richard Degré', written in a cursive style.

Richard Degré, V.P. Lallemand, Inc.

A handwritten signature in black ink, appearing to read 'Zachary S. Scott', written in a cursive style.

Zachary S. Scott, Scott laboratories, Inc.

References:

1. 63 FR 12422, FDA Tentative Final Rule re: GRAS Egg White Lysozyme
2. Gerbaux, V., Meistermann, E., Cottureau, Ph., Barriere, C., Cuinier, C., Berger, J.L., Villa, A. (1999), Use of Lysozyme in Enology, Bulletin O.I.V., 72:348-373.
3. Gotz, M., (1996) Pseudo-allergies are due to histamine intolerance, Wien Med Wochenschr; 146(15):426-430.
4. Wante, F., Gotz, M., Jarisch, R. (1993) Histamine-free diet: treatment of choice for histamine-induced food intolerance and supporting treatment for chronic headaches. Clin. Exp. Allergy, 23(12):982-985.
5. Rogers, Christine A., Comment 91, TTB Notice 41 (70 FR 22274)
6. 21 CFR 184.1550(c)(2)(iii)
7. Valsamaki K.; Michaelidou A.; Polychroniadou A (2000), Biogenic amine production in Feta cheese, Food Chemistry, 71(2):259-266.
8. Heine, RG, Laske, N., Hill, DJ. (2006) The diagnosis and management of egg allergy, Curr Allergy Asthma Rep, 6(2):145-152.
9. Mine, Y., Rupa, P. (2004), Immunological and biochemical properties of egg allergens, World's Poultry Science Journal, 60(3):321-330.
10. Dr. Catherine Pecquet M.D., Personal Communication, November 22, 2006.
11. Restani P, Beretta B, Ballabio C, Galli CL, Poiesi C, Bertelli, A, Evaluation by SDS-PAGE and Immunoblotting of Residual Antigenicity in Lysozyme-Treated Wine: A Preliminary Study, unpublished data 2006.
12. 71 FR 42267 – TTB Notice 62, proposed rule 27 CFR 4.32b(b).
13. 71 FR 42260 – Treasury Decision TTB- 53.