

subject to the requirements of this AD. For helicopters that have been modified, altered, or repaired so that the performance of the requirements of this AD is affected, the owner/operator must use the authority provided in paragraph (c) to request approval from the FAA. This approval may address either no action, if the current configuration eliminates the unsafe condition, or different actions necessary to address the unsafe condition described in this AD. Such a request should include an assessment of the effect of the changed configuration on the unsafe condition addressed by this AD. In no case does the presence of any modification, alteration, or repair remove any helicopter from the applicability of this AD.

Compliance: Required as indicated, unless accomplished previously.

To detect cracks that could lead to delamination of the tail rotor blade Kevlar tie-bar (Kevlar tie-bar), loss of tail rotor control, and subsequent loss of control of the helicopter, accomplish the following:

(a) Within 10 hours time-in-service (TIS) after the effective date of this AD, and thereafter at intervals not to exceed 250 hours TIS, inspect each Kevlar tie-bar for a crack or delamination in accordance with paragraph B, Operational Procedure, of Eurocopter France Service Bulletin 05.00.34, Revision 3, dated November 14, 1996.

(b) If any delamination or cracking is found during any of the inspections required by paragraph (a) of this AD, remove the blade and replace it with an airworthy blade before further flight.

(c) An alternative method of compliance or adjustment of the compliance time that provides an acceptable level of safety may be used if approved by the Manager, Rotorcraft Standards Staff, Rotorcraft Directorate, FAA. Operators shall submit their requests through an FAA Principal Maintenance Inspector, who may concur or comment and then send it to the Manager, Rotorcraft Standards Staff.

Note 2: Information concerning the existence of approved alternative methods of compliance with this AD, if any, may be obtained from the Rotorcraft Standards Staff.

(d) Special flight permits may be issued in accordance with sections 21.197 and 21.199 of the Federal Aviation Regulations (14 CFR 21.197 and 21.199) to operate the helicopter to a location where the requirements of this AD can be accomplished.

Note 3: The subject of this AD is addressed in Direction Generale De L'Aviation Civile (France) AD 92-185-33(B)R4 dated December 4, 1996.

Issued in Fort Worth, Texas, on February 28, 1998.

Eric Bries,

Acting Manager, Rotorcraft Directorate,
Aircraft Certification Service.

[FR Doc. 98-6496 Filed 3-12-98; 8:45 am]

BILLING CODE 4910-13-M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 184

[Docket No. 89G-0393]

Direct Food Substances Affirmed as Generally Recognized as Safe; Egg White Lysozyme

AGENCY: Food and Drug Administration, HHS.

ACTION: Tentative final rule.

SUMMARY: The Food and Drug Administration (FDA) is issuing a tentative final rule to amend its regulations to affirm that egg white lysozyme enzyme preparation, when labeled by the common or usual name "egg white lysozyme" to identify its source, is generally recognized as safe (GRAS) for use in preventing late blowing of cheese caused by the bacterium *Clostridium tyrobutyricum* during cheese production. This action is in response to a petition submitted by Fordras S.A. (formerly SPA-Società Prodotti Antibiotici S.p.A.). FDA has tentatively concluded that this use of the egg white lysozyme enzyme preparation is GRAS only when the ingredient statement for both bulk and packaged food that contains cheese manufactured using egg white lysozyme includes the common or usual name "egg white lysozyme" to identify the source of the protein. To give interested persons an opportunity to comment on this condition of use required for GRAS status, FDA is issuing this tentative final rule.

DATES: Submit written comments by May 27, 1998.

ADDRESSES: Submit written comments to the Dockets Management Branch (HFA-305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1-23, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: Linda S. Kahl, Center for Food Safety and Applied Nutrition (HFS-206), Food and Drug Administration, 200 C St. SW., Washington, DC 20204, 202-418-3101.

SUPPLEMENTARY INFORMATION:

I. Background

In accordance with the procedures described in § 170.35 (21 CFR 170.35), SPA-Società Prodotti Antibiotici S.p.A., now Fordras S.A., Milan, Italy, submitted a petition (GRASP 9G0355) requesting that egg white lysozyme used to inhibit the bacterium *C. tyrobutyricum* to prevent late blowing of cheese during production be affirmed as

GRAS as a direct human food ingredient. FDA published the notice of filing for this petition in the **Federal Register** of October 27, 1989 (54 FR 43861), and gave interested persons until December 26, 1989, to submit written comments.

II. Standards for GRAS Affirmation

Under § 170.30 (21 CFR 170.30), general recognition of safety may be based only on the views of experts qualified by scientific training and experience to evaluate the safety of substances directly or indirectly added to food. The basis of such views may be either: (1) Scientific procedures, or (2) in the case of a substance used in food prior to January 1, 1958, through experience based on common use in food. General recognition of safety based upon scientific procedures requires the same quantity and quality of scientific evidence as is required to obtain approval of a food additive regulation and ordinarily is based upon published studies, which may be corroborated by unpublished studies and other data and information (§ 170.30(b)). General recognition of safety through experience based on common use in food prior to January 1, 1958, may be determined without the quantity or quality of scientific procedures required for approval of a food additive regulation, but ordinarily is based upon generally available data and information concerning the pre-1958 history of use of the substance.

FDA has evaluated Fordras S.A.'s petition on the basis of scientific procedures to whether the petitioned use of egg white lysozyme enzyme preparation to prevent the late blowing of cheese caused by the bacterium *C. tyrobutyricum* during cheese production is GRAS. In evaluating the petition, FDA considered published and unpublished data and information relating to the identity of, characteristic properties of, and estimated dietary exposure to the enzyme component (i.e., lysozyme) of the petitioned enzyme preparation (Refs. 1 through 7). FDA also considered that the source of the petitioned enzyme preparation, egg white, has been safely consumed by humans as a source of food protein throughout recorded history, and, therefore, is GRAS (§ 170.30(d)), and that the methods used for extracting lysozyme from the egg white source do not ordinarily alter the chemical identity and characteristic properties of enzymes (Ref. 8). FDA also considered published scientific review articles (Refs. 1 and 2) and a generally available trade association bulletin (Ref. 7) discussing the use of egg white lysozyme enzyme preparation for its

technical effect of preventing late blowing of cheese contaminated with *C. tyrobutyricum* as well as generally available information documenting that this intended use of the petitioned enzyme preparation has been approved in several European countries (Refs. 9 through 13). Finally, FDA considered generally available and accepted information relating to processing aids used in the manufacture of the enzyme preparation and generally available and accepted specifications for food-grade enzyme preparations (Ref. 14).

III. Safety Evaluation

When present as a contaminant in milk used for cheesemaking, the pasteurization-resistant bacterium *C. tyrobutyricum* ferments lactate to produce carbon dioxide, hydrogen, and volatile organic acids. This fermentation causes a defect in cheese manufacture known as "late blowing," which is typified by abnormal levels of open texture accompanied by undesirable odors and flavors. Late blowing can be a serious economic problem in the manufacture of several varieties of cheese (Refs. 1, 2, and 7).

The contamination by *C. tyrobutyricum* of milk used for cheesemaking, although reducible by good husbandry and hygienic milking practices, is unavoidable. Although treatment with certain chemical agents has been shown to be effective against the problems raised by this contamination, treatment with lysozyme enzyme preparation has been found to be the most effective method of managing the late blowing of cheese contaminated with *C. tyrobutyricum* (Refs. 1 and 2).

A. The Enzyme Component

Enzymes are proteins or conjugated proteins (i.e., a protein that contains a nonamino acid moiety such as a carbohydrate) produced by plants, animals, and microorganisms that function as biochemical catalysts (American Heritage Dictionary of the English Language). Most enzymes are very specific in their ability to catalyze only certain chemical reactions; this high degree of specificity and strong catalytic activity are the most important functional properties of enzymes (Ref. 15).

The Commission on Enzymes of the International Union of Biochemistry has devised a systematic strategy for naming enzymes. This system combines a naming system and a numbering system. For most enzymes, the systematic name is derived from the names of the substrate, product, and type of reaction. The systematic number is based on the

class and subclasses to which the enzyme belongs. The systematic name of lysozyme is peptidoglycan *N*-acetylmuramoylhydrolase. Its systematic number is EC No. 3.2.1.17 and its Chemical Abstracts Service Registry Number (CAS Reg. No.) is 9001-63-2.

Lysozyme was first discovered by A. Fleming, who identified lysozyme as an antibacterial enzyme present in nasal mucus membrane (Ref. 3). Subsequently, it was learned that the antibacterial activity of lysozyme occurs because of its ability to catalyze the hydrolysis of the structural polysaccharide peptidoglycan present in cell walls of certain bacteria (Ref. 2). Lysozyme activity has been shown to be present in bacteria, fungi, plants, and almost all animal tissues, with the highest levels found in secretions (including milk, mucus, saliva, and tears) and eggs. Lysozyme is believed to function in all of these organisms and tissues as an endogenous antimicrobial substance (Refs. 1 and 2).

Lysozyme was the first enzyme to have the details of its three-dimensional structure published (Ref. 4), and it has become one of the best characterized of all enzymes, serving as an example for studies of enzyme mechanism and molecular evolution (Refs. 5 and 6). Lysozymes from various organisms are very similar to one another. Egg white lysozyme differs very little in structure, amino acid sequence and composition, catalytic mechanism, and substrate specificity from the enzyme found in human milk, saliva, mucus, and tears (Refs. 3 and 6).

The petitioner provided two published scientific review articles (Refs. 1 and 2) that discuss the use of egg white lysozyme in cheese and other food. The petitioner also provided a generally available trade association bulletin (Ref. 7) that focuses on the use of egg white lysozyme for its technical effect of preventing late blowing in cheese. This bulletin describes the late blowing defect and how it arises, traditional chemical control measures (other than the use of lysozyme) to reduce the problem, and the increasing interest in using lysozyme as a replacement for traditional chemical control measures. In addition, the petitioner provided generally available information documenting that this intended use of the petitioned enzyme preparation has been approved in several countries, including Denmark, France, Germany, Italy, and Spain (Refs. 9 through 13).

FDA considered the estimated dietary exposure to lysozyme for the proposed use in cheese (Refs. 16 and 17).

Lysozyme accounts for approximately 3.5 percent of the total protein of domestic hen egg whites (Ref. 7). Whole eggs contain lysozyme at a level of approximately 3,300 parts per million (ppm). The petitioner reported that cheese manufactured using egg white lysozyme enzyme preparation contains a maximum of 400 ppm of lysozyme, or at least 8 times less than eggs on a weight basis. FDA has estimated a long-term mean intake of lysozyme to be 74 milligrams per person per day (mg/p/d) for consumers of eggs and 3.8 mg/p/d for consumers of cheese; the respective 90th percentile intakes are estimated to be 163 mg/p/day and 8.1 mg/p/day. Egg whites from which lysozyme is extracted will be subsequently consumed in other food uses. Thus, there will be no long-term net increase in lysozyme intake by the general population because egg whites without lysozyme will replace egg whites in current use that contain lysozyme (Ref. 16). On a per eating occasion basis, lysozyme intake for cheese consumers may be 16 mg on average, or 22 mg at the 90th percentile level. For comparison, a per eating occasion lysozyme intake for egg consumers may be 264 mg on average, or 416 mg at the 90th percentile level. Thus, lysozyme intake per eating occasion due to cheese consumption may constitute 5 to 6 percent of lysozyme intake due to egg consumption (Ref. 17).

In general, issues relevant to a safety evaluation of proteins such as the enzyme component of an enzyme preparation are potential toxicity and allergenicity (Ref. 18). Proteins derived from egg whites do not raise toxicity concerns because egg whites have been safely consumed by humans as a source of food throughout recorded history without any reports of toxicity. However, proteins derived from egg whites do raise allergenicity concerns because, as with many common foods, there have been reports that consumption of egg whites can cause an allergic reaction in certain individuals, particularly children (Ref. 19). Therefore, FDA considered the question of whether the lysozyme component of egg whites is allergenic.

In evaluating this question, FDA considered a report of an *in vitro* study of the binding of antibodies to specific egg proteins, where the antibodies were derived from the serum of patients known to be allergic to eggs (Ref. 20). This report suggests that lysozyme was an allergen for some individuals who became sensitive to egg whites. Although this study does not establish that ingestion of egg white lysozyme in cheese will actually cause a clinically

significant allergic reaction in such sensitive individuals, FDA is not aware of any data or information that would refute the study's inference that egg white lysozyme may be allergenic. Accordingly, FDA is proposing labeling, as discussed below, to alert the sensitive population to the presence of egg white lysozyme in cheese.

A related question is whether egg white lysozyme, when present in cheese, is capable of inducing an allergic response in susceptible individuals who have not previously consumed egg whites, e.g., because their customary diet excludes eggs. This question is no different than for any other food containing egg white when consumed by individuals with unknown susceptibility to eggs. The proposed label declaration would provide such individuals with the same protection as that provided by other egg-containing products with ingredient labeling. Thus, individuals who experience an allergic reaction to lysozyme-containing cheese could identify egg white lysozyme as a possible cause of the reaction.

B. Enzyme Source, Manufacturing Methods, and Processing Aids

Commercial preparations of lysozyme are derived from domestic hen egg whites using ion exchange methods and selective precipitation to isolate a highly purified protein fraction that contains mainly lysozyme but also may contain small amounts of other egg white proteins. Consistent with the agency's finding in its GRAS affirmation of microparticulated protein product (55 FR 6384, February 23, 1990), FDA finds that egg whites have been safely consumed by humans throughout recorded history and, therefore, are GRAS (§ 170.30(d)). The agency evaluated the methods used to isolate the enzyme lysozyme from egg whites. These methods are based on generally available and accepted principles of protein purification (Ref. 8). Such methods, if appropriately selected, do not ordinarily alter the chemical identity and characteristic properties of enzymes. Therefore, these methods do not materially change the quality, utility, functionality, or safety of enzymes. Moreover, the retention of the antibacterial activity that is characteristic of egg white lysozyme when egg white-derived lysozyme enzyme preparation is used in cheese evidences that lysozyme in the manufactured enzyme preparation remains unaltered from the lysozyme in egg whites. This is corroborative evidence of the fact that the methods used to isolate lysozyme from egg

whites do not materially change the quality, utility, functionality or safety of the enzyme lysozyme.

Enzyme preparations used in food processing are usually not chemically pure but contain, in addition to the enzyme component, materials that derive from the enzyme source. As mentioned above, egg white lysozyme enzyme preparation may contain small amounts of other egg white proteins. A related question is whether such proteins that may be present in the enzyme preparation are allergenic. Even if present, other source-derived proteins would not be a concern because the proposed label declaration for egg white lysozyme would alert individuals who are sensitive to egg whites to the possible presence of other proteins derived from egg whites.

In addition to source-derived materials, enzyme preparations used in food processing usually contain materials that derive from the manufacturing methods used to generate the finished enzyme preparation. The egg white lysozyme enzyme preparation that is the subject of this document complies with the general requirements and additional requirements for enzyme preparations in the Food Chemicals Codex, 4th ed. (Ref. 14). The egg white lysozyme enzyme preparation that is the subject of this document may contain substances that are added to the enzyme preparation, such as preservatives, stabilizers or diluents, and trace amounts of processing aids that are used in its preparation. These substances must be acceptable for general use in foods (Refs. 14 and 15).

C. Labeling as a Condition of Use

Egg whites are known to be an allergenic food source, particularly in children (Ref. 19). There is a literature report (Ref. 20) indicating that lysozyme may in fact have been an allergen for some individuals who became sensitive to egg whites. Although the reported *in vitro* study does not establish that ingestion of egg white lysozyme in cheese will actually cause a clinically significant allergic reaction in such sensitive individuals, FDA is not aware of any data or information that would refute the study's inference that egg white lysozyme may be allergenic. Therefore, FDA concludes that there is insufficient information in the current record to determine whether the ingestion of egg white lysozyme elicits an allergic response when consumed by individuals who are sensitive to egg whites. Accordingly, as discussed below, FDA is proposing labeling to alert such individuals to the presence of egg white lysozyme in cheese. Such

labeling also would alert the sensitive population to the possible presence of source-derived proteins other than lysozyme in the enzyme preparation.

Under section 409(c)(1) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 348(c)(1)), FDA is authorized, in approving the use of a food additive, to list the conditions under which the additive may be safely used. These conditions may include any labeling requirements that the agency deems necessary to ensure the safe use of the additive. Similarly, under § 184.1(b)(3) (21 CFR 184.1(b)(3)), in affirming a substance as GRAS, FDA is authorized to set forth the particular conditions of use, including labeling, under which there is general recognition among qualified experts that the use of the substance is safe. After careful review of the evidence on the use of egg white lysozyme enzyme preparation in preventing late blowing in cheese, FDA has tentatively concluded that such use is GRAS only when the conditions of its use include a declaration on the label or labeling of the presence of egg white lysozyme in both bulk and packaged food containing such treated cheese. Therefore, this tentative final rule (§ 184.1550(c)(1)) establishes that the declaration of egg white lysozyme enzyme preparation by the common or usual name "egg white lysozyme" is a condition of use required for GRAS status, so that consumers who are allergic to egg white products can be alerted to the presence of the egg white-derived enzyme in treated cheese.

D. Summary and Conclusions

The petitioner provided published data and information relating to the identity of, characteristic properties of, and estimated dietary exposure to the enzyme component (Refs. 1 through 7). The source of the petitioned enzyme preparation, egg white, has been safely consumed by humans as a source of food protein throughout recorded history, and, therefore, is GRAS (§ 170.30(d)). The petitioner provided generally available information showing that the methods used for extracting lysozyme from the egg white source do not ordinarily alter the chemical identity and characteristic properties of enzymes (Ref. 8). Moreover, there is corroborating evidence that the extraction of egg white lysozyme does not change its chemical identity or characteristics because the antibacterial activity of egg white lysozyme is retained. FDA concludes that the methods used to manufacture egg white lysozyme enzyme preparation do not change the safety for food use of the enzyme lysozyme and that toxicological

studies are not necessary to establish the safety of lysozyme or other source-derived proteins that may remain in the manufactured enzyme preparation. FDA also concludes that there will be no net increase in dietary exposure of the general population to the commonly consumed enzyme lysozyme due to the proposed use in cheese because lysozyme will simply be transferred from eggs to cheese (Ref. 16).

The petitioner also provided generally available and accepted information relating to processing aids used in the manufacture of the enzyme preparation and generally available and accepted specifications for food grade enzyme preparations (Ref. 14). FDA concludes that substances added to the egg white lysozyme enzyme preparation or potential residues of processing aids used in the manufacturing process do not present a basis for concern about the safety of the egg white lysozyme enzyme preparation.

The petitioner provided published scientific review articles (Refs. 1 and 2) and a generally available trade bulletin (Ref. 7) that discuss the use of the egg white lysozyme enzyme preparation in cheese and other food, including its use for the intended effect of preventing late blowing of cheese contaminated with *C. tyrobutyricum*. The petitioner also provided generally available information documenting that this intended use of lysozyme has been approved in several European countries (Refs. 9 through 13). FDA concludes that generally available and accepted data and information establish that lysozyme will achieve the intended technical effect of preventing late blowing in cheese contaminated with *C. tyrobutyricum*.

Finally, information in the petition and otherwise available to FDA raises the question of whether the lysozyme component of egg whites is allergenic. FDA is proposing labeling to alert individuals who may be sensitive to egg whites to the presence of egg white lysozyme in cheese, including the possible presence of other source-derived proteins that may be present in the enzyme preparation.

IV. Comments

FDA received two comments in response to the filing notice. One comment expressed agreement that lysozyme is GRAS for use in preventing late blowing in cheese and supported the affirmation of GRAS status by the agency.

One comment stated that use of lysozyme as a food preservative may lead to selection of lysozyme-resistant strains of the bacterial food poisoning

agents *Listeria monocytogenes* and *C. botulinum*, rendering one of the body's main defense mechanisms useless against resistant strains. The comment likened the potential selection of lysozyme-resistant strains of bacteria to the selection of penicillin-resistant bacteria as a result of its widespread use. The comment pointed out that the body could not readily substitute the lysozyme naturally present in secretions such as tears and saliva for another antimicrobial.

The mechanism of action of lysozyme involves hydrolysis of the structural peptidoglycan present in cell walls of susceptible bacteria. Therefore, development of resistance to lysozyme would require that a bacterium develop a variant of peptidoglycan that is resistant to the action of lysozyme. Development of such a variant peptidoglycan is, in principle, possible. However, as already discussed, lysozyme activity has been shown to be present in bacteria, fungi, plants, and almost all animal tissues. If such relative ubiquity has not resulted in the clinically significant selection of lysozyme-resistant bacteria to date, the use of lysozyme in those cheeses that are susceptible to late blowing is unlikely to favor selection of lysozyme-resistant bacteria and adversely affect the public health. Moreover, FDA is not considering lysozyme for use as a widespread food preservative. Rather, FDA is considering the narrow question of whether the use of lysozyme in preventing late blowing in cheese is generally recognized as safe. FDA disagrees that this limited use in cheese is analogous to the widespread use of antibiotics such as penicillin and the subsequent selection of antibiotic-resistant bacterial strains. Therefore, FDA concludes that the use of lysozyme in preventing late blowing in cheese does not raise concerns about the selection of lysozyme-resistant strains of *L. monocytogenes* or *C. botulinum*.

V. Specifications

The agency finds that, because the potential impurities in the egg white lysozyme preparation that may originate from the source or manufacturing process do not raise any basis for concern about the safe use of the preparation, the general requirements and additional requirements for enzyme preparations in the monograph on Enzyme Preparations in the Food Chemicals Codex, 4th ed. (1996), which are being incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51, are adequate as minimum criteria for food-grade egg white lysozyme enzyme preparation.

Lysozyme assay can be performed using a method entitled "Lysozyme hydrochloride, Microbiological Determination," which is included in the petition (Ref. 21) or by using any appropriate validated method.

VI. Conclusions

The agency has evaluated all available information and finds, based upon the published information about the manufacturing methods used in the preparation of egg white lysozyme enzyme preparation, and published data and information about the identity and characteristic properties of egg white lysozyme, that the enzyme component of egg white lysozyme enzyme preparation is unaltered from the lysozyme found in the commonly consumed food, eggs. The agency also finds, based upon generally available and accepted information, that when the preparation is manufactured in accordance with § 184.1550(c), the source, egg whites, and the manufacturing process will not introduce impurities into the preparation that may render its use unsafe. Further, the agency finds, based upon published information, that egg white lysozyme enzyme preparation will achieve its intended technical effect of preventing late blowing in cheese contaminated with *C. tyrobutyricum*. Therefore, the agency tentatively concludes, based upon the evaluation of published data and information, corroborated by unpublished data and information, that the egg white lysozyme enzyme preparation described in the regulation set out below is GRAS for use by the general population in preventing late blowing in cheese.

To give interested persons an opportunity to comment on the proposed label declaration that is a condition of use required for GRAS status, FDA is issuing this tentative final rule under 21 CFR 10.40(f)(6). FDA will review any comments that are relevant to this condition of use and that are received within the 75 day comment period and will respond accordingly to these comments in the **Federal Register**.

VII. Environmental Considerations

The agency has carefully considered the potential environmental effects of this action. FDA has concluded that the action will not have a significant impact on the human environment, and that an environmental impact statement is not required. The agency's finding of no significant impact and the evidence supporting that finding, contained in an environmental assessment, may be seen in the Dockets Management Branch

(address above) between 9 a.m. and 4 p.m., Monday through Friday.

VIII. Analysis of Economic Impacts

A. Benefit-Cost Analysis

FDA has examined the impacts of this tentative final rule under Executive Order 12866. Executive Order 12866 directs Federal agencies to assess the costs and benefits of available regulatory alternatives, and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety effects; distributive impacts; and equity). According to Executive Order 12866, a regulatory action is "significant" if it meets any one of a number of specified conditions, including having an annual effect on the economy of \$100 million, adversely affecting in a material way a sector of the economy, competition, or jobs, or if it raises novel legal or policy issues. FDA finds that this tentative final rule is not a significant regulatory action, as defined by Executive Order 12866. In addition, it has been determined that this final rule is not a major rule for the purpose of congressional review.

The primary benefit of this action is to remove uncertainty about the regulatory status of the petitioned substance. FDA is tentatively affirming the GRAS status of egg white lysozyme in cheese only when the ingredient statement of the bulk and packaged food that contains the cheese includes the common or usual name of the substance, i.e., "egg white lysozyme." The labeling requirement will add a small cost to the future use of the petitioned substance, and therefore, is not a significant action under the Executive Order 12866.

FDA has examined the impacts of this tentative final rule under the Unfunded Mandates Reform Act of 1995 (UMRA) (Pub. L. 104-4). A written statement under section 202(a) of the UMRA is not required for this rule because the rule does not impose a mandate that results in an expenditure of \$100 million or more by State, local, and tribal governments in the aggregate, or by the private sector, in any 1 year.

B. Regulatory Flexibility Act

FDA has evaluated this tentative final rule under the Regulatory Flexibility Act. The Regulatory Flexibility Act (5 U.S.C. 601-612) requires Federal agencies to consider alternatives that would minimize the economic impact of their regulations on small entities.

FDA believes that this tentative final rule is not likely to have a significant

economic impact on a substantial number of small entities. However, the agency seeks comment on this tentative conclusion. First, FDA is tentatively affirming the GRAS status of egg white lysozyme in cheese only when the ingredient statement of the bulk and packaged food that contains the cheese includes the common or usual name of the substance, i.e., "egg white lysozyme." This labeling requirement will impose only minimal costs to the future use of the petitioned substance. Second, FDA has information that the petitioner does not currently sell egg white lysozyme in the United States (Refs. 22 and 23). Moreover, FDA is not aware of any manufacture or use of cheese containing egg white lysozyme in the United States. If no small entities are currently manufacturing or using cheese containing egg white lysozyme, the proposed labeling requirements would not impose any cost to small entities. However, because FDA does not have any information on whether other entities in the United States are manufacturing or using cheese containing egg white lysozyme, FDA is unable to conclude, in this tentative final rule, that there will be no significant economic impact on a substantial number of small entities. Therefore, the agency seeks comment on the manufacture or use, by any small entity, of cheese containing egg white lysozyme. In its final rule, the agency will, based on any relevant comments received, determine whether there is a significant economic impact on a substantial number of small entities.

IX. References

The following references have been placed on display in the Dockets Management Branch (address above) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. Carini, S., G. Mucchetti, and E. Neviani, "Lysozyme: Activity Against Clostridia and Use in Cheese Production—A Review," *Microbiologie Aliments Nutrition*, 3:299-320, 1985.
2. Procter, V. A., and F. E. Cunningham, "The Chemistry of Lysozyme and Its Use as a Food Preservative and a Pharmaceutical," *CRC Critical Reviews in Food Science and Nutrition*, 26:359-395, 1988.
3. Fleming, A., "On a Remarkable Bacteriolytic Element Found in Tissues and Secretions," *Proceedings of the Royal Society*, 93:306-317, 1922.
4. Blake, C. C. F., D. F. Koenig, G. A. Mair, A. C. T. North, D. C. Phillips, and V. R. Sarma, "Structure of Hen Egg-White Lysozyme," *Nature*, 206:757-783, 1965.
5. Kuhara, S., E. Ezaki, T. Fukamizo, and K. Hayashi, "Estimation of the Free Energy Change of Substrate Binding in Lysozyme-

Catalyzed Reactions," *Journal of Biochemistry*, 92:121-127, 1982.

6. Malcolm, B., K. Wilson, B. Matthews, J. Kirsch, and A. Wilson, "Ancestral Lysozymes Reconstructed, Neutrality Tested, and Thermostability Linked to Hydrocarbon Packing," *Nature*, 345:86-89, 1990.

7. "The Use of Lysozyme in the Prevention of Late Blowing in Cheese," *Bulletin of the International Dairy Foundation*, No. 216, 1987.

8. Chaplin, M. F., and C. Bucke, *Enzyme Technology*, Cambridge University Press, New York, NY, pp. 66-72, 1990.

9. Denmark Ministry of Agriculture Circular on Approved Enzymes for Cheese, Journal nr. 10.1.5-18/83, January 13, 1984.

10. French Republic Ministry of Agriculture Service Note 5236, April 21, 1987.

11. Federal Republic of Germany, Bundesgesetzblatt Nr. 56, pp. 2103-2107, November 22, 1985.

12. Official Gazette of Italian Republic, General Series n. 23, October 4, 1986.

13. Spanish Ministry of Health and Consumption, General Direction of Public Health, General Sanitary Register, File n. 8826, June 20, 1983.

14. Monograph on "Enzyme Preparations," Food Chemicals Codex, National Academy Press, Washington, DC, 4th ed., pp. 133-134, 1996.

15. Pariza, M. W. and E. M. Foster, "Determining the Safety of Enzymes Used in Food Processing," *Journal of Food Protection*, 46:453-468, 1983.

16. Memorandum dated March 20, 1990, from Food and Color Additives Review Section, FDA, to Direct Additives Branch, FDA, "Use of Lysozyme to Prevent the 'Late Blowing' of Cheese."

17. Memorandum dated August 5, 1996, from Chemistry Review Branch, FDA, to Biotechnology Policy Branch, FDA.

18. Kessler, D. A., M. R. Taylor, J. H. Maryanski, E. L. Flamm, and L. S. Kahl, "The Safety of Foods Developed by Biotechnology," *Science*, 256:1747-1749 and 1832, 1992.

19. Crespo, J. F., C. Pasqual, A. Ferrer, A. W. Burke, J. M. Diaz Pena, and M. M. Esteban, "Egg White-specific IgE Level as a Tolerance Marker in the Follow-up of Egg Allergy," *Allergy Proceedings*, 15:73-76, 1994.

20. Anet, J., J. F. Back, R. S. Baker, D. Barnett, R. W. Burley, and M. E. H. Howden, "Allergens in the White and Yolk of Hen's Egg: a Study of IgE Binding by Egg Proteins," *International Archives of Allergy and Applied Immunology*, 77:364-371, 1985.

21. Lysozyme Hydrochloride, Microbiological Determination.

22. Letter dated November 25, 1996, from John B. Dubeck, Keller and Heckman, to Linda Kahl, FDA.

23. Letter dated February 28, 1997, from John F. Foley, Keller and Heckman, to Linda Kahl, FDA.

List of Subjects in 21 CFR Part 184

Food ingredients, Incorporation by reference.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under

authority delegated to the Commissioner of Food and Drugs and redelegated to the Director, Center for Food Safety and Applied Nutrition, it is proposed that 21 CFR part 184 be amended as follows:

**PART 184—DIRECT FOOD
SUBSTANCES AFFIRMED AS
GENERALLY RECOGNIZED AS SAFE**

1. The authority citation for 21 CFR part 184 continues to read as follows:

Authority: 21 U.S.C. 321, 342, 348, 371.

2. Section 184.1550 is added to subpart B to read as follows:

§ 184.1550 Egg white lysozyme.

(a) Egg white lysozyme (CAS Reg. No. 9001-63-2) is the enzyme peptidoglycan *N*-acetylmuramoylhydrolase (EC No. 3.2.1.17) obtained by extraction from egg whites. The enzyme catalyzes the hydrolysis of peptidoglycan in the cell walls of certain bacteria including *Clostridium tyrobutyricum*.

(b) The ingredient meets the general requirements and additional requirements for enzyme preparations in the monograph on Enzyme Preparations in the Food Chemicals Codex, 4th ed. (1996), which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, and may be examined at the Center for Food Safety and Applied Nutrition's Library, 200 C St. SW., rm. 3321, Washington DC, or at the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(c)(i) The ingredient is used in cheeses, as defined in § 170.3(n)(5) of this chapter, in accordance with § 184.1(b)(3) at levels not to exceed current good manufacturing practice.

(2) The affirmation of the use of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following conditions of use:

(i) The ingredient is used as an enzyme as defined in § 170.3(o)(9) of this chapter.

(ii) Current good manufacturing practice utilizes a level of the ingredient sufficient to prevent the late blowing of cheeses caused by the bacterium *Clostridium tyrobutyricum* during cheese production.

(iii) The ingredient statement for both bulk and packaged food that contains cheese manufactured using egg white lysozyme shall include the common or usual name "egg white lysozyme" to identify the source of the protein.

Dated: March 3, 1998.

L. Robert Lake,

Director, Office of Policy, Planning and Strategic Initiatives, Center for Food Safety and Applied Nutrition.

[FR Doc. 98-6571 Filed 3-12-98; 8:45 am]

BILLING CODE 4160-01-F

**FEDERAL COMMUNICATIONS
COMMISSION**

47 CFR Part 73

[MM Docket No. 98-29, RM-9190]

Radio Broadcasting Services; Indian Wells, CA

AGENCY: Federal Communications Commission.

ACTION: Proposed rule.

SUMMARY: This document requests comments on a petition for rule making filed on behalf of Professional Broadcasting, Inc. requesting the allotment of FM Channel 238A to Indian Wells, California, as that community's first local aural transmission service. Coordinates used for this proposal are 33-42-04 and 116-14-47. Indian Wells, California, is located within 320 kilometers (199 miles) of the Mexico border, and therefore, the Commission must obtain concurrence of the Mexican government to this proposal.

DATES: Comments must be filed on or before April 27, 1998, and reply comments on or before May 12, 1998.

ADDRESSES: Secretary, Federal Communications Commission, Washington, DC 20554.

In addition to filing comments with the FCC, interested parties should serve the petitioner's counsel, as follows: John R. Feore, Jr., M. Anne Swanson and Kevin P. Latek, Esqs., Dow, Lohnes and Albertson, 1200 New Hampshire Avenue, NW., Washington, DC 20036-6802.

FOR FURTHER INFORMATION CONTACT: Nancy Joyner, Mass Media Bureau, (202) 418-2180.

SUPPLEMENTARY INFORMATION: This is a synopsis of the Commission's Notice of Proposed Rule Making, MM Docket No. 98-29, adopted February 25, 1998, and released March 6, 1998. The full text of this Commission decision is available for inspection and copying during normal business hours in the FCC's Reference Center (Room 239), 1919 M Street, NW., Washington, DC. The complete text of this decision may also be purchased from the Commission's copy contractor, International Transcription Service, Inc., 1231 20th

Street, NW., Washington, DC 20036, (202) 857-3800.

Provisions of the Regulatory Flexibility Act of 1980 do not apply to this proceeding.

Members of the public should note that from the time a Notice of Proposed Rule Making is issued until the matter is no longer subject to Commission consideration or court review, all *ex parte* contacts are prohibited in Commission proceedings, such as this one, which involve channel allotments. See 47 CFR 1.1204(b) for rules governing permissible *ex parte* contacts.

For information regarding proper filing procedures for comments, See 47 CFR 1.415 and 1.420.

List of Subjects in 47 CFR Part 73

Radio broadcasting.

Federal Communications Commission.

John A. Karousos,

Chief, Allocations Branch, Policy and Rules Division, Mass Media Bureau.

[FR Doc. 98-6514 Filed 3-12-98; 8:45 am]

BILLING CODE 6712-01-P

**FEDERAL COMMUNICATIONS
COMMISSION**

47 CFR Part 73

[MM Docket No. 98-28; RM-9234]

**Radio Broadcasting Services;
Meyersdale, PA**

AGENCY: Federal Communications Commission.

ACTION: Proposed rule.

SUMMARY: The Commission requests comments on a petition filed by Douglas M. Dasdorf proposing the allotment of Channel 253A at Meyersdale, Pennsylvania, as the community's second local FM transmission service. Channel 253A can be allotted to Meyersdale in compliance with the Commission's minimum distance separation requirements at city reference coordinates. The coordinates for Channel 253A at Meyersdale are North Latitude 39-48-42 and West Longitude 79-01-36. Since Meyersdale is located within 320 kilometers (200 miles) of the U.S.-Canadian border, concurrence of the Canadian government has been requested.

DATES: Comments must be filed on or before April 27, 1998, and reply comments on or before May 12, 1998.

ADDRESSES: Federal Communications Commission, Washington, DC 20554. In addition to filing comments with the FCC, interested parties should serve the petitioner, his counsel, or consultant, as