

August 12, 2002

Lester Crawford, D.V.M., Ph.D.  
Deputy Director  
U.S. Food and Drug Administration  
Room 1471  
5600 Fishers Lane  
Rockville, MD 20857

Re: GRAS Notice No. GRN 000091; Food Additive Petition FAP 6A3930

Dear Dr. Crawford:

The Center for Science in the Public Interest previously has written to the FDA about the labeling and safety of Marlow Foods Ltd.'s Quorn-brand foods and their mycoprotein ingredient and about the inadequacy of the company's "expert" panel (which included neither an allergy expert nor a mycotoxicology expert). We would like to provide some additional information.

The *Fusarium* family of fungi produces a variety of toxins. One such toxin is deoxynivalenol (DON), also known as vomitoxin, for the obvious reason. Though that mycotoxin may not be produced by *F. venenatum*, other mycotoxins also may cause vomiting or other digestive disorders and health problems. Quorn mycoprotein is made from *Fusarium venenatum*, which can produce diacetoxyscirpenol (DAS). The U. S. added that toxin to a list of "select agents" covered under Public Law 104-132, "The Antiterrorism and Effective Death Penalty Act of 1996."

In the past several months, CSPI has received adverse reaction reports from 33 people in the U.S. and overseas (see Appendix 1). Those reports are undoubtedly just a tiny fraction of all the adverse reactions that have occurred and, if Quorn foods remain on the market, will occur in the future.

The most common adverse reaction reported to us has been vomiting, sometimes with nausea and/or diarrhea. The victims tell us that the reactions are extremely unpleasant and sometimes temporarily debilitating. One young woman vomited repeatedly, passed out, and was lucky that someone was able to bring her to the hospital where she was treated for dehydration. Another woman fainted on the toilet seat after experiencing severe vomiting and diarrhea. If they occur while someone is driving or involved in another risky activity, those severe reactions could be life-threatening. Whether the reported adverse reactions constitute "harm" (in the food-additive sense of "reasonable certainty of no harm") is a judgment call. In 1995, FDA

Commissioner David Kessler, at the FDA's Food Advisory Committee meeting on olestra, offered his personal opinion on what constitutes "harm":

... if someone is going to the bathroom all day, and there is really an effect on someone's life, that, certainly can be –I think one could argue that that is harm.<sup>1</sup>

In addition to those who experienced vomiting, nausea, and diarrhea, two people apparently experienced more traditional food-allergy hypersensitivity reactions: severe hives and facial numbness and swelling. That suggests that Quorn may be harming people through two different mechanisms.

The underlying cause(s) of the adverse reactions is not known, but may be an allergic reaction or a mycotoxin. The company claims that it maintains rigorous controls over the manufacturing process to prevent mycotoxin production, but one person who vomited told us that he had contacted the manufacturer and was told that a bad batch of Quorn might have slipped through the quality control.

Marlow Foods claims in its GRAS notification that only one in 130,000 people experiences an adverse reaction to Quorn foods, but that assertion is without foundation. (See Appendix 2.) Indeed, the company's own data submitted in support of its Food Additive Petition (FAP 6A3930) demonstrates that as many as *several percent* of people, when fed ordinary amounts of Quorn up to eight times, experience vomiting or other symptom on one or more occasions.<sup>2</sup> Some of the symptoms were severe (Pages 6709-6771):

\* Volunteer 181: "On serving the seventh meal the panellist was again nauseated by the smell and he could only eat ¼ of the meal. Two to three hours later he started sneezing and feeling unwell. This got worse until he started to vomit violently. Shortly after beginning to vomit he felt unable to draw breath. After sitting down quietly this difficulty in breathing ceased, although the vomiting continued for a further hour."

\* Volunteer 253: After consuming four test meals without ill effect, "He consumed the

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<sup>1</sup> Food Advisory Committee, Nov. 17, 1995. Transcript, P. 173.

<sup>2</sup> The test suffered from weaknesses. For instance, though subjects were supposed to consume 15 g (dry weight) of mycoprotein at a time, some consumed less. Subject 301 felt nauseated after the first mouthful of the first meal and "then only ate small portions of the seven subsequent meals" (P. 6721); subject 281 ate only small amounts of her last four meals. (P.6722) Subject 181 mistakenly was given a control food for his 6<sup>th</sup> meal. (P. 6722) Also, Table C10 (P. 6752), a summary of symptoms, omitted some subjects' symptoms (Subject 181 was nauseous at least three times, not one time; his difficulty breathing was not indicated in the "other" column.)

fifth meal in the evening and 2½ hours later was violently sick three times during ¾ hour. The following morning he felt 'queasy.' After 1½ hours from eating the sixth meal he vomited again and suffered shivering, abdominal pains and 'yellow stools.'"

\* Volunteer 260: She tolerated her first three meals with no problem, but the fourth caused, after three hours, nausea that persisted for 15 hours. "Four days later she ate her fifth test meal and after only consuming one third she felt nauseated and could not eat any more. One hour later she started to vomit violently which continued for 1½ hours and this was accompanied by severe abdominal pains. The following morning she was still experiencing severe nauseous sensations and abdominal pains but these gradually declined."

\* Volunteer 281: "This panelist experienced nausea and vomiting after her first test meal in the evening and also vomited the following morning." She experienced less or no discomfort on other occasions.

Six out of 200 (3%) people in the test group vomited a total of seven times, compared to 1 out of 100 (1%) in the control group (P. 6752). Twenty out of 200 (10%) people in the test group experienced vomiting, nausea, or stomach ache (a total of 39 times), compared to only 5 out of 100 (5%) (a total of 7 times) in the control group. The differences between test and control groups are not statistically significant; to attain statistical significance when the rate of adverse reactions is only a few percent, much larger sample sizes would be needed.

The company sought to re-test nine subjects who experienced minor or severe symptoms after eating mycoprotein (Pages 6840-6847 and elsewhere). Three of those people refused to be retested, and the researchers declined to retest a pregnant woman. Subject 251, who had vomited, was not retested. (The company also did not retest the one person who vomited in the control group.) The retest involved a maximum of four meals with mycoprotein, with one person consuming only two meals (she had adverse reactions each time) and one person consuming 15 g of mycoprotein divided into several dosages over five hours just once (no reaction). Of the five people who were rechallenged in double-blinded, controlled studies, four did not have reactions, while one did. The one who did had not experienced problems the first three times she had eaten the mycoprotein in the original study, indicating that the occurrence of reactions may depend on sensitization or other unknown factors. The company argues that only one of the original nine people was definitely, and one other possibly, sensitive to mycoprotein. However, even accepting that rosiest of pictures, two out of 200 people represents one percent of consumers experiencing vomiting after eating mycoprotein several times. That is an unacceptable percentage, especially considering the potential severity of reaction. In addition, mycoprotein caused nausea or stomach upset in other subjects.

Marlow Foods, in its GRAS notification, indicates its knowledge of the possibility that *Fusarium* can produce toxins and claims that it adjusts fermentation conditions to prevent their formation. Clearly, that is insufficient to ensure that Quorn products are safe. We urge the FDA

to consider the following three scenarios:

\* Marlow Foods may be keeping toxins at an undetectable level, but some especially sensitive individuals may be harmed by levels below the limit of detection. It is not clear on what basis the “acceptable” levels of toxins have been set.

\* Marlow Foods, despite its every effort, may not be able to exclude the presence of mycotoxins, either because of mutations in the fungi, contamination, inadequately controlled fermentation conditions, or other reason.

\* *Fusarium* may be producing unsafe levels of mycotoxins, allergens, or other toxins, other than those that the company monitors.

In any of those cases, considering that Quorn mycoprotein makes some people sick, mycoprotein cannot be considered Generally Recognized As Safe.

The FDA’s stance on existing food ingredients (for instance, sugar alcohols) that cause adverse reactions, but have not been shown to cause deaths, seems to be that ingredient labeling provides sufficient protection for consumers. We disagree. Quorn mycoprotein has been proven to cause severe digestive reactions. Those reactions have led to fainting and dehydration, which could be life-threatening. Also, one report of difficulty breathing suggests that mycoprotein might cause anaphylaxis.

Our food supply includes enough problematical ingredients already. The FDA has the authority to, and should, prevent the introduction of yet another one. While the FDA says that people who have adverse reactions can simply read the label, that is easier said than done. It always can be difficult to identify a problem ingredient – after all, consumers are not trained scientists – but that’s especially the case when, as people have told us, (a) an ingredient causes problems only intermittently (as Marlow Foods’ study noted above demonstrated), (b) eating a small portion might not elicit a reaction, (c) the presence or amount of harmful constituent might vary from lot to lot of the food, (d) people suspect that other foods caused their problems, or (e) people unwittingly eat Quorn foods at friends’ homes or at parties. One woman, a nurse, told us: “I have eaten Quorn many times and have had diarrhea and vomiting each time. As it was usually at a BBQ I put it down to alcohol. Since cooking it at home for my family, I realize it is the Quorn.” The FDA’s “labeling” strategy inevitably condemns many people to suffer severe reactions, because only after they have suffered those problems, sometimes on multiple occasions, might they know they are sensitive. That’s hardly a preventive approach to public health. Frankly, I think the American public would be shocked to learn that the FDA has given GRAS status to, and may approve as a food additive, a new substance that causes severe vomiting and other adverse reactions in some consumers.

We provided data from the 300-person feeding study, along with information about some of the adverse-reaction reports we have received, to Dr. David A. Morowitz, a Washington, D.C.,

gastroenterologist and clinical professor of medicine (gastroenterology) at Georgetown University Medical Center (Appendix 3). After reviewing it, he advised:

The data you sent me, indeed much of it anecdotal, still argues compellingly that the mycoprotein derived from *Fusarium venenatum* is almost certainly gastrotoxic and considering the ubiquity of fungal toxins, it should be deemed unsafe until known as otherwise. The perceived need for its development in Great Britain notwithstanding, the risk of its toxicity does not justify its continued use here in the United States, absent additional safety studies.

For the above reasons, we urge the FDA to revoke its acceptance of Marlow Foods' GRAS notification, deny the outstanding food additive petition, and ask the company to undertake an immediate recall before more people are harmed.

Thank you for your attention to this matter.

Sincerely,

Michael F. Jacobson, Ph.D.  
Executive Director

cc: Joe Levitt, Alan Rulis, William Hubbard, Kenneth Falci, Karl Klontz

Enclosures: Three appendices

## Appendix 2: Fraction of People Affected by Quorn

Marlow Foods maintains that vanishingly few people are sensitive to Quorn mycoprotein. Marlow's GRAS notification (page 18) states: "These figures equate to an incidence rate per the estimated number of consumers of 1 in 130,000 and 1 in 146,000." Similarly, according to CBC News, David Wilson, vice-president of Quorn Foods Inc., stated, "The adverse reaction rates are infinitesimally low, about 1 in 146,000 people — much lower than soy protein, which is about 1 in 35,000," notes David Wilson, vice-president of Quorn Foods, Inc. (4/3/02; [http://cbc.ca/stories/2002/04/02/Consumers/Quornmeat\\_020402](http://cbc.ca/stories/2002/04/02/Consumers/Quornmeat_020402); accessed Aug. 5, 2002) Marlow Foods' "expert" panel estimated that for the years 1994-1997 the incidence rate of adverse reactions ranged from 1/71,000 to 1/90,000. (Myco-protein report of the expert panel, June 1999, p. 17)

The 1/146,000 (or 1/130,000 or 1/90,000) figure is a gross underestimate of the true rate of sensitivity to Quorn for the following reasons:

\* The number assumes that everyone who experienced a reaction to Quorn realized it and contacted the company. That is a faulty assumption. For starters, Marlow Foods does nothing (in terms of labeling or advertising) to alert consumers to the possibility of adverse reactions and to encourage them to report adverse reactions. It is worth comparing the Quorn situation to the reporting of food-borne illnesses. The general public and physicians have been encouraged to report food-borne illnesses to health agencies. Nevertheless, the Centers for Disease Control and Prevention (CDC) assumes that it learns of only one out of 38 such illnesses (pers. comm., Fred Angulo, CDC). That suggests that the 1/146,000 figure should be multiplied by some factor, such as 38. Doing so would suggest that the fraction of consumers who experience adverse reactions is closer to 1/3,842.

\* Marlow Foods suggests, misleadingly, that the denominator of the 1/146,000 figure refers to individual consumers. The GRAS notification states (page 18) that the average Briton consumes "mycoprotein products an average of 7 times per year." (In addition, Marlow Foods' David Wilson told CSPI that it actually refers to servings of Quorn products (meeting, June 11, 2002). He also said that 20 million consumers have eaten a total of about one billion servings of Quorn. In other words, each consumer has eaten an average of about 50 servings.) Obviously, one person eating seven (or 50) servings of Quorn should not be considered seven (or 50) different people who might be sensitive. That suggests that the true incidence of adverse reactions is closer to 1/500 (1/3,842 [from above] divided by 7) than 1/146,000. (If the 50 servings per person is accurate, the incidence of adverse reactions is closer to 1/80.)

\* Most tellingly, in 1977, mycoprotein was evaluated in a double-blind, controlled study of 300 individuals, 200 of whom were given foods containing mycoprotein on up to eight occasions and 100 of whom (controls) were given foods that did not contain mycoprotein. Six out of 200 (3%) people in the test group vomited, compared to only 1 out of 100 in

the control group (P. 6752).<sup>1</sup> In addition, 19 out of 200 (9.5%) people in the test group experienced nausea or stomach upset, compared to only 5 out of 100 (5%) in the control group. The company rechallenged, with either a mycoprotein food (one to four test meals) or placebo, five (including three who had vomited) of the nine volunteers who had mild or severe reactions. In some cases, the dose of mycoprotein was smaller than originally used and subjects were given mycoprotein fewer times than in the original study. Despite those shortcomings, the company acknowledges that one person certainly was sensitive and another person possibly was. That, at the very least, two out of 200 people reacted adversely to mycoprotein and, quite likely, more people were sensitive, indicates that the truer fraction of individuals who might vomit is on the order of 1/100.

In sum, it is clear that the company has grossly underestimated the fraction of people who are sensitive to Quorn products.

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<sup>1</sup> A study in which 100 college students consumed 10 g of *Fusarium* mycoprotein twice a day for 30 days did not identify any problems. (Udall JN, Lo, CW, Young VR, Scrimshaw NS. The tolerance and nutritional value of two microfungus foods in human subjects. *Am J Clin Nutr* 1984;40:285-292.) The study indicates that the fungus used was *Fusarium graminearum*, however later studies found the mycoprotein actually is derived from *Fusarium venenatum*.