CONSUMER CONCERNS
*GIVE US ALL THE DATA**

I am not going to focus on public concerns about all of agricultural biotechnology but primarily on bovine growth hormone or bovine somatotropin (BST). I do this because BST is going to be the first major product in agricultural biotechnology to come out—if it is approved. There has been a lot of controversy surrounding this product, and I think there is a lot of consumer concern about BST.

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I would like to raise a couple of general issues and then spend time discussing a number of internal documents from the Food and Drug Administration (FDA)—letters and memoranda sent to companies that paints a very different picture of some of the problems with BST than what has come out publicly.

CONSUMER PERCEPTIONS OF BIOTECHNOLOGY

A number of studies have shown that consumers are very wary about new technologies and in fact, are very wary about biotechnology. In a survey that was done for the National Dairy Board in 1986, one of the conclusions was "that the strongest impression in the consumers' mind is that most problems are result of man's [sic] interference with nature, a tampering with the natural order of things for the sake of profit or convenience or both." Some of the people who have criticized the media and criticized the critics of biotechnology have tended to say that the problem with the general public is that they are very uninformed. If only they were scientifically more literate, they would understand this technology and come to accept it. I think that consumers are not as ignorant as a lot of people might think.

A study done for the National Dairy Board in 1990 asked consumers about their awareness of a number of issues and how important they felt that issue was (i.e., whether they were concerned with it or not). Two

'Edited from tape of lecture. The letters referred to were shown in slides.

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things can be seen. A large percentage of consumers were aware of both the Alar® contamination of apples and the recall of grapes from Chile because of cyanide contamination—83 and 85 percent respectively. If you look at the number of consumers, of the percent that were not concerned about those issues, among those that were aware, you find it is fairly significant—27 percent and 29 percent. When you look at other issues which I think are more important than either the Alar® scare or the recall of grapes from Chile, you see that for Salmonella in fresh poultry, drugs given to cattle, the use of hormones to increase milk in dairy cows or the antibiotics used to treat livestock that are harmful to humans—there is a smaller percent awareness of those issues in general. Yet the percentage of consumers who do nor think that issue is a problem (if they know about it) is much smaller. What this shows is that the consumers are a little bit more aware than some people give them credit for. Of those that were aware of the Alar® controversy and the recall of grapes from Chile, more than 2V2 times those people were not concerned relative to concerns over drugs given to cattle, the use of the bovine growth hormone and antibiotic questions.

WHO DO CONSUMERS TRUST?

Let us now look at who consumers tend to trust. A survey in *Dairy Today* in 1990 asked, "Who would you trust regarding BST safety?" Eighty-four percent said that they would trust consumer safety groups, 54 percent university researchers, 45 percent the American Medical Association and 34 percent the FDA. The family doctor is the number one person that consumers trust for sources of information about the safety of food. *Consumer Reports* is number two. The drug companies are at the bottom of the list. It seems as though consumers are not very trustful of the companies. They also are not trustful of FDA. Is there is a reason for that? I think that indeed there might be. In 1990 the National Dairy Board asked consumers questions after they were given information in the form of statements on BST. Only 25 percent of the consumers agreed with the statement "milk from cows treated with BST is completely safe"; 83 percent agreed with the statement "the long-term or the long run health implications of BST are not known"; only 29 percent agreed with the statement "testing has shown that the milk from cows treated with BST is completely safe"; and 63 per-

cent agreed with the statement "milk from the cows treated from BST may be harmful to humans." This survey shows there is a lot of concern out there among consumers.

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BST AND SECONDARY DRUG RESIDUES

Now, we have to ask, is this concern legitimate or is it based on not much information? If you look at the studies which have come out they have tended to say that there is not a problem with BST (i.e., with the consuming of milk and meat products from the experimental test herds). In fact, in 1986, when the FDA made the decision that there were no human health impacts and therefore permitted the marketing of milk from these experimental test animals, there was a lot of controversy. Since then there has been an article published in *Science* magazine and most recently, an Office of Technology Assessment (OTA) report came out which basically said that there is no concern for human health. Concerns are my work in this area—the main problem I have with FDA's position is the one thing they have missed—a primary human health concern with the potential for the secondary drug residues in milk. (I also have some concerns about insulin-like growth factor, but will not discuss them here.) The concern about drug residues arises when the animals treated with BST and if there is an increase in mastitis and other bacterial infections, then that could lead to increased use of antibiotics, which in turn leads to antibiotic residues in milk. This is a very important issue.

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The Government Accounting Office (GAO) late 1990 released a report which says that FDA cannot guarantee the safety of the milk supply, and that their testing procedures are highly flawed and do not pick up a lot of antibiotics. I have been told, off the record, by people from the dairy industry that they are concerned about the unregulated drug use in animal agriculture. The FDA, also off the record, admitted that there is a concern there. So our position and concern at Consumers Union is that if this technology can be shown to increase disease rates in these cattle, then that in turn potentially can lead to greater contamination in milk with antibiotic residues. If that is a significant human health concern, then how can FDA say that there are no human health effects when they have not explicitly looked at that issue? Further, the FDA has explicitly not yet discussed whether there are any health impacts on the cows.

HEALTH IMPACT ON TEST HERDS

Quoting now from the OTA report, which came out this spring, on the effects of bovine health and stress, "catastrophic effects such as the instance of ketosis (which is under production of glucose) fatty liver, crippling lameness, milk fever (which is feverish disorder following parturition), mastitis (inflammation of the udder), sickness, suffering and death have all been postulated to occur with BST." This is the important part—"however, no such effects have been observed with BST supplementation of dairy cows in any scientifically valid published study, nor have subtler health effects been in evidence." So what OTA is saying is that there is no evidence whatsoever of problems such as mastitis. Now, I tend to think that there is some evidence of such problems. I base this belief on internal documents from the FDA and other papers.

This indicates that the FDA internally knew that things like environmental assessments and health effects are not legitimate confidential business information, but was going to make people sue them to get the information out.

In a memorandum of a meeting between representatives from Monsanto and representatives from the Center for Veterinary Medicine, the first line says, "Mr. Matheson requested this meeting in order to formally request the preparation of an environmental assessment for this and all other INADs." An INAD is an Investigational New Animal Drug. An INAD had been filed by Monsanto which involved the use of recombinant DNA technology in the production of a new animal product. That new product is bovine growth hormone. By law, these environmental assessments should be done *before* an INAD is granted. The first INAD for Monsanto was granted around 1983. Did they prepare an environmental assessment? No.

The second page of this memorandum addresses the petition submitted by the Foundation on Economic Trends. In March of 1986, the Foundation on Economic Trends and sixteen other groups signed onto a petition that demanded that FDA do an environmental impact assessment on bovine growth hormone. FDA turned down their petition saying that an environmental assessment and an environmental impact statement had already been prepared. The groups then petitioned, using a freedom of information act, to get copies of the environmental assessments. FDA said, "sorry, that's trade secrets, we cannot release this." The Foundation took them to court, 2V2 years later, the documents were released. FDA had told the company that the environmental assessment and CMDs findings would re-

main in the INAD unless disclosure was required through court proceedings. This indicates that FDA internally knew that things like environmental assessments and health effects are not legitimate confidential business information, but was going to make people sue them to get the information out.

Now I am going to go on to deal with two sets of letters. They are from FDA, the first set to Eli Lilly and the second set to Monsanto. These are what are called New Animal Drug Application (NADA) incomplete letters. The way the regulatory system works, you get an INAD permit which permits you to ship a drug across state lines and gather data in farmers' fields and at universities. After that data is gathered and submitted to the agency, the company then submits a NADA asking the agency to let them sell this product and to make a given label claim. In Eli Lilly's letter of October 8, 1987, they requested approval to market a sustained release subcutaneous injectable BST with the claim of increasing milk production and improved feed efficiency. The FDA told them that the submission was incomplete, making specific comments. I want to highlight a few things in this letter that caused us to be very upset. The first thing has to do with the efficacy. In this letter, FDA talked about a serious error in the milking pattern in the Canadian trial. Critics of this research have talked about how there has been manipulation of data to show that there is not any problem or to show that the drug works. In this Canadian trial they were establishing what the optimal milking interval was for the highest producing cow. They used that milking interval with lower producing cows although it was suboptimal for them and could be detrimental to the milk yield. What the researchers said is that the cows were continually moved such that the top producers were exposed to a near ideal milking interval, while the low producers' milk yields were probably diminished due to a wide milking interval. Logically, control animals would, on average, end up with the lower producers, particularly by the end of the lactation, while BST treated cows would be among the top producers. The continual movement of cows throughout the length of the study prevented any possibility of factoring out this problem. Thus there was a bias in the way that the study that was done.

A French study commented on by FDA looked at the effect of BST on milk composition. It demonstrated no alteration or no effect on the fatty

acid content or the protein content of milk. However, FDA had to point out to Eli Lilly that this data was not very useful because just the milk yield was not changed by treatment and there were no differences between the treated cows and the experimental cows. It is not feasible to extrapolate those milk composition results to a situation where milk production was increased by BST. Again, a flawed study. The summary of sensitization studies stated that the product (milk) elicited a positive sensitization response. The same thing was brought up in the Monsanto letter. In the animal health and reproduction target animal safety section of the FDA letter to Eli Lilly, it says point blank, "We are concerned about the increased incidents and duration of mastitis and reproductive parameters in the field studies."

It is interesting that this negative result never appeared in the literature.

Now let us turn to the Monsanto letter. Again, Monsanto was trying to get FDA approval. They sent in all their data asking for approval to market this product (BST) and to make label claims of increased milk production and increased feed efficiency. All of their data that was sent in says because no statistical differences were found between treatment groups for feed efficiency, they did not bother to review the data further. That is very curious. All the data that Monsanto had sent in, as of late 1987, could not demonstrate any differences in feed efficiency. Yet if you look in the literature, there are all these studies which demonstrate increases in feed efficiency. It is interesting that this negative result never appeared in the literature.

When we go to the target animal safety section of the Monsanto letter, FDA discusses the problems with mastitis—in 3C, it says "you should address the use of gentomycin and tetracycline, which are not approved for the treatment of mastitis in dairy cattle." Critics have pointed out that internal documents leaked from Monsanto indicated that there was use of drugs which were not permitted in dairy cattle. The letter continues, "the overall conclusion for the mastitis was data presented indicates that there was an increase in mastitis at levels at which you wish to market bovine somatotropin". Responding to the reproductive data FDA says that you have compromised the usefulness of your reproductive data by the use of prostaglandins and progesterone assays. It is not possible to evaluate the effect of BST on reproduction if concurrent use of reproductive hormones in diagnostics tests masks or otherwise alters the effect of the drug. In 4B of this

letter it talks about the data indicating that the regimen outlined in their protocols was not adhered to and in 4C it indicates that the use of prostaglandins varied in time, frequency and reasons for use, and were used for unapproved claims such as metritis. "Some cows", the letter said, "received a drug that was not approved for use in dairy cattle." The overall conclusion was that "your data indicates that there are reproductive problems at the doses at which you wish to market bovine somatotropin."

Turning to injection site syndrome, FDA said that the data indicated that the severity of injection site response increases with time. In 5C it continued, "your data indicate that there may be an unacceptable level of tissue reaction with prolonged use of BST in the range of doses for which you wish approval. Lameness and displaced abomasum maybe drug related. You (Monsanto) have not established a margin of safety, nor have you established a no effect level for some of the parameters in your submission." Based on available data, this is particularly true of major clinical entities such as mastitis and reproduction. Remember, FDA is saying that Monsanto could not demonstrate a "no effect" level. The letter concludes with "if you seek approval of a range of 250 to 500 milligrams in cows or heifers, you may not even have a 1-fold margin of safety. Under current standards, this is unacceptable for an over-the-counter approval." On the last page of the letter, FDA talks about mitigation measures. They say "you should describe steps you (Monsanto) are taking, including labeling, to present sensitization by those occupationally exposed to the BST protein."

So, both of these letters, one to Eli Lilly and one to Monsanto, indicate that there seem to be problems. In fact, two weeks after the latter letter was sent, there was a meeting between Monsanto and the FDA to talk about the target animal safety portion of this NADA incomplete letter. Dr. Lehman, head of the production division of the drug section, very clearly expressed concern over the increase in days that cows were affected by mastitis during the BST treatment. Again noting that there was mastitis. Concern was also raised over injection site swelling. The use of reproductive agents was discussed. Some drugs may be used for clinical conditions; however, they also are used to get cows pregnant to cover up reproductive problems. There was a lot of concern there. About a year later, there was a memo written by Dr. Guest after meeting with the National Milk Producers Federation. In it, they are talking about how to manage the consumer

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perception. They ask that in view of the likely problems with cattle safety and the need for careful management of the cattle, should the product be prescriptioned? It was also asked whether prescriptioning BST might also give some sense of security to the consumer. My concern with a lot of these documents, and I think Consumers Union's too, is how can the OTA say that there is no evidence whatsoever that there are problems such as mastitis with BST use when, internally, it seems like FDA is saying that there are problems with mastitis and with reproduction. Unfortunately none of this data was made public.

Now, those letters that I discussed (shown as slides at the meeting) ***are*** three years old. Maybe I am willing to admit that companies have been able to overcome these problems discussed above in the last three years. But the problem I still have is why is it that none of the negative effects discussed in these letters have never made it into the literature? And if the companies and the FDA want to tell us that there is not any problem, why should we trust them?

GAINING TRUST

What I think needs to happen, if you want consumers to have some trust in what you are doing, is the data has to be made readily available. Consumers have the right to know about health impacts. I think that the data on the adverse effects of BST not being made public while all the positive data is being made public. This is of a lot of the public's concern. We would like to see all the health and safety data released to the public. I would just like to say to those other companies working on applications of biotechnology—make your data public, try to be up front with the critics.