Public Health Issues Concerning the Use of BST

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It is a pleasure to be here and to be given the opportunity to speak to this group on the safety of Bovine Somatotropin and the role of the FDA in making that determination.

I would like, first, to congratulate you. The work you do in the individual states to help protect the consumers and the milk industry is especially important today. Milk enjoys one of the best reputations in the animal-food industry for providing a safe and nutritious product to the American consumer. Safeguarding that reputation is an important part of what you do and what is done at the FDA.

Before I get into the specific subject of Bovine Somatotropin, I'd like to acquaint you with the FDA's Center for Veterinary Medicine, specifically its responsibilities. The Center is one of several in the FDA responsible for the regulation of food and drug products. It is comprised of approximately 250 employees with responsibility for regulating products used by the animal health and production industries. Its primary purposes are: to evaluate proposed and marketed animal drugs, feed additives and marketed devices for safety and effectiveness; to direct surveillance and compliance programs relating to the proper use of marketed animal drugs, feeds, and devices; to coordinate the veterinary medical aspects of FDA inspection programs; to provide veterinary medical opinions, hearings, and court cases; and to evaluate potential environmental impacts of actions the FDA takes or products it approves.

In order for you to understand how the FDA is arriving at the decisions it is making about Bovine Somatotropin, I'd like to be more specific about evaluation and approval of new drugs for use in animals. The FDA through its Center for Veterinary Medicine evaluates data about new drug products to assure that the drug is safe and effective and that the consumer and the environment are adequately protected from potentially harmful residues. It does not take that responsibility lightly. I have personally been involved in the program and believe that animal drugs are among the most thoroughly evaluated consumer products in the world.

The drug approval process, as outlined in the Federal Food, Drug and Cosmetic Act and in the FDA's regulations, involves two stages: the Investigational New Animal Drug (IND) stage and the New Animal Drug (NADA) stage.

To begin the process that leads ultimately to approval or non-approval of a new drug product, the Center closely regulates the investigational phases of a proposed new drug's development prior to the company submitting a new animal drug application. The investigational phase includes both basic and applied research in the laboratory and clinical research conducted as field trials.

The law requires that investigational drugs being tested for safety and efficacy be registered with the FDA at the time they are being shipped in interstate commerce, that is, prior to them being shipped across state boundaries, including to other countries. If they are intended for food-producing animals, an additional requirement must be met that any food derived from the animals be considered safe by the FDA before the food is allowed for either human or other animal consumption. Therefore, it is not uncommon for the Center to have assessed to some degree the safety of drug residues even prior to the review of an application requesting commercial marketing of the new drug product.

For a company to be able to investigate the effects of a new drug, it must submit information to the FDA as to the identity of the chemical, any information being supplied to investigators, the name and address of each investigator receiving the drug, the approximate number of animals being treated, when the experiments will take place, and the dose, duration of administration and route of delivery of the drug. As mentioned before, the company or investigator must receive FDA authorization to market any food taken from animals being administered investigational drugs. Scientific data must be supplied to achieve this authorization. The amount and extent depends on how many animals are involved, how many will be used for food, the toxic properties of the drug, and how long the drug is withdrawn from the animal before meat or milk is marketed for food.

Only after these requirements have been met, can a drug firm study a new drug in food producing animals. In addition, the Center encourages the drug developer to submit protocols for the studies they intend to undertake. In this way the FDA can assure that the data will address major safety and effectiveness concerns. The Center is currently working closely with the companies developing

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BST on the kinds of studies appropriate for this drug.

I should also point out that apart from the review and authorizations the FDA conducts at its headquarters in Rockville, MD, there are also FDA field offices throughout the U.S. At headquarters direction, inspections of ongoing investigations are performed. These inspections help assure that the company is complying with all the requirements for the approval process. The Center has conducted inspections on most of the pivotal BST trials currently ongoing in this country.

Before an application for marketing a new product is filed, the drug firm must conduct laboratory and clinical investigations to establish safety and efficacy of the product. Effectiveness data includes two or more well controlled studies proving the product will work as labeled. In addition, separate dosing studies are performed to determine the optimum level of effectiveness. These data are required in several different geographic regions of the country to access the effectiveness of the drug under different management, nutritional and environmental conditions.

In the case of drugs for food-producing animals, the application must usually contain data on toxicity of the drug in laboratory animals including data to determine whether the drug could cause cancer or reproductive effects in man. In addition, information is required describing how the drug is broken down in the animal's body, the kinds and amounts of residues remaining, and a laboratory assay method to detect such residues in food.

A common misconception about the FDA is that the FDA does the testing that determines the approvability of a new drug product. The law requires the manufacturer of the new drug to show that the drug is safe and effective, through the submission of substantial evidence from well controlled studies. The drug company or an independent testing laboratory conducts the studies and then the FDA determines whether the requirement for substantial evidence has been met. Only in rare cases does the Agency conduct any testing.

It is also important to understand that the FDA does not simply approve an animal drug in terms of the substance itself. The agency regulates drug products. A product consists of the drug substance combined with other ingredients in a particular dosage form or in a feed premix, and labeled for specific claims or uses. Studies are conducted on the specific product in a specific form for use in a specific species for a specific purpose.

Now, having given some background on our approval process, I would like to discuss the current investigational process for BST and the FDA's role in the development of this drug.

Since BST is a product of the new biotechnology age, it is undergoing intense scrutiny—by the FDA, by pharmaceutical companies, by the scientific community, by Congress, and by consumer groups.

Scientists have known for over 50 years that bovine growth hormone naturally produced in the pituitary gland of cows is one of the factors affecting the quantity of milk dairy cows produce. Bovine growth hormone influences an array of physiological processes so that more nutrients from feed are specifically directed toward milk synthesis. Lactating cows compensate for the extra nutrients and energy used to make milk by eating more. Overall efficiency of milk production is enhanced because the feed energy needs required to maintain the other physiological activities of the cow are not simultaneously increased. Theoretically, fewer cows can produce the same amount of milk with less feed than would be required for a larger number of untreated animals.

Dairy experts doubt that BST will reach 100 percent use once it is approved. Not all dairy farmers will buy it and many of those who do may administer the hormone to only a portion of the herds, at least for the first few years. Various company officials involved in BST research predict that by the mid 1990's, about half of U.S. dairy herds will be receiving BST. This estimate is based on experience with other dairy industry innovations, such as artificial insemination. "Forty-five years after its introduction, 30 percent of dairy cows are now artificially inseminated with genetically selected semen." The president of the National Dairy Herd Improvement Association made this statement in June 1986 testimony before the House Agriculture Subcommittee on Livestock, Dairy, and Poultry. (Dr. Neal Jorgensen, Associate Dean for Agricultural Research at the University of Wisconsin, Madison, said at the same hearing, "In Wisconsin, for example, only 62 percent of our cattle are bred artificially...") It was predicted that it would take about 10 years for most dairy producers to adopt BST.

BST is currently undergoing clinical testing and is considered an investigational new animal drug subject to all of the requirements and oversight previously discussed. At this stage of the approval process, information about a drug is proprietary to the companies submitting the data to the FDA. Because of the broad interest in BST, however, the companies have disclosed more information than is normally available at this early phase of the approval process.

As you know, the FDA has authorized the consumption of milk and meat derived from cows treated experimentally with BST. That authorization was not made until studies to prove human safety had been conducted and provided to scientists at the Agency.

There are three possible decisions regarding requests for authorization to market food derived from animals treated during investigational stages of the drug approval process.

1. Authorization to market food products derived from experimentally treated animals is denied. This occurs when information on the toxicity of potential residues resulting from the test drug or on elimination of residues from the tissues is inadequate to support such authorization.

2. Authorization to market food products is approved but is based on a withdrawal period following treatment. This occurs when information on the toxicity of potential residues of the test drug and/or its elimination from the tissues of treated animals is adequate to assure that when withdrawal periods are observed, no harmful residues will be present in human food derived from the experimentally treated animals.

3. Authorization to market food products is approved without a requirement for a withdrawal period. This occurs when the sponsor has demonstrated that no residues occur following treatment and/or that such residues represent no risk to humans consuming the food products from the treated animals.

As I indicated earlier, it is common for the FDA to require drug withdrawal periods before food from animals treated with experimental drugs may be consumed. In the case of BST, FDA scientists have determined from the data submitted by the companies and by review of the scientific literature that animals treated with BST can be safely consumed without a withdrawal time. This decision is based on evidence demonstrating that BST is not active as a hormone in humans, even if injected directly into the body. All mammals produce somatotropin in the pituitary gland. While the chemical composition of somatotropin is similar in all species, the amino acid sequence is different. This difference causes the hormone to be species specific. In addition to the species specificity, BST is a protein and is deactivated when consumed through the digestive system. A third factor in the decision to consider the milk safe for human consumption is the evidence that milk from animals treated with BST appears to be similar in composition to that of cows not treated with BST. Some BST does occur naturally in the milk and meat of dairy cows not treated with a BST product.

Milk from cows injected with BST is also being marketed in the United Kingdom. The Milk Marketing Board has announced that there are no restrictions on the sale of milk from cows treated with BST in the United Kingdom or from other countries. The Board also has stated that BST found in cows treated with BST is not greater than that found in non-treated cows and that it is impossible to distinguish between milk from cows treated with BST and those not treated.

For all these reasons, the FDA had concluded that the current scientific evidence is such to establish the safety of milk from treated cows during the investigational phases of the approval process. Given that no evidence appears to change that opinion, it appears highly likely that human food safety will not pose any obstacle to final approval of BST for commercial use. However, as part of the requirements to show safety of individual BST products, the FDA is requiring that all manufacturers conduct studies to demonstrate that their particular product is not absorbed if ingested. These studies are conducted in laboratory animals with drug levels considerably above those expected to be found in milk or meat in order to provide an assurance that the specific BST product will be safe. If these studies confirm what is expected with these products, it is highly likely that further food residue safety data would not be required prior to FDA approval of this product for lactating dairy cattle.

Another issue which is being considered by the Agency before approval of BST products is that of long-term efficacy and safety of the product to the treated cows. Short term studies have confirmed that the drug can increase milk production up to 40 percent with no adverse animal health effects. Long term studies have yet to be completed and evaluated.

Much of the debate about the use of BST by the dairy industry has concerned the possible economic effects of the drug. These considerations are, of course, germane to the industry itself, but are not relevant to whether the products are approved or not approved by the FDA. The FDA evaluates new products strictly on the grounds of safety, effectiveness and potential environmental impacts. Economic aspects are not within the scope of the Food, Drug and Cosmetic Act and are not taken into consideration when the FDA is considering approval of a new product for use in animal species. The FDA's regulatory responsibilities are not involved with the free market determination of economic risks and benefits. Any action to stop the approval and marketing of these products on the grounds that they offer no clear economic benefit would require congressional action on these specific products or to change the existing laws.

This audience is well aware, I am sure, that new technologies have brought significant improvements on the production efficiency and safety of products from the dairy industry. Milk pasteurization, dairy herd improvement programs, herd genetics and breeding programs, animal drugs to synchronize estrus, superovulation, embryo transplantation, artificial insemination techniques, and new animal drugs to treat and control mastitis are all examples of new technologies which have had a part in transforming the dairy industry into what it is today. The use of bovine somatotropin to increase the efficiency of milk production is another such new product of technology. To date, it appears that no health or environmental issues have emerged that are likely to keep BST products from FDA approval.

The FDA's mission remains the same: to ensure that the nation's pharmaceutical and biological products are safe and effective and that the food supply is safe and nutritious. The law requires that our review of any new drug product, including drugs made through recombinant DNA technology such as BST, focus on whether that product is safe and effective for its intended use. The Center for Veterinary Medicine's scientists work diligently to carry out that responsibility. It is my belief that they do it as well as it can be done.