There is a growing demand from consumers, members of industry, and law enforcement officials for authentic information concerning the chemicals that appear in our food. The dairy industry and milk sanitarians are concerned particularly with antibiotics (as well as other substances) which have been detected in milk supplies and in products manufactured from milk. These are basic foods consumed throughout our lifetime and their safety is of prime importance to the public health. My comments will outline the problem of antibiotics in dairy products, the cause of the problem, and the steps which have been taken by the Food and Drug Administration designed to obtain authentic information regarding the problem and to minimize or eliminate the problem.

Very large amounts of antibiotics are used in the treatment of mastitis in milk producing cows. It is estimated that more than 75 tons of these potent drugs are used yearly in the treatment of this widespread infection. The greater proportion of infected cows are treated by udder infusion and a variety of drug products are available for this purpose. Penicillin is used in the greatest volume, since this drug is quite effective in those cases caused by streptococci, particularly Streptococcus agalactiae, the organisms responsible for most cases of streptococcal mastitis. There are other variants. As a result, other antibiotics such as dihydrostreptomycin, the tetracyclines, neomycin, bacitracin and the sulfonamides are used for treatment and prophylaxis. Treatment usually consists of a single tube or syringe full of the preparation for each infected quarter but as many as four treatments at 12-hour intervals may be necessary per quarter. Thus, with a single treatment an animal treated with a combination preparation may be administered 500,000 or more units of penicillin, 500 milligrams of dihydrostreptomycin, 500 milligrams of neomycin and one or more grams of one or more sulfonamide drugs. If the infection is severe, the animal may receive as much as four times these amounts within a 48-hour period.

By regulation, mastitis preparations must carry a warning in their labeling to the effect that "milk from treated quarters should be discarded or used for purposes other than human consumption for at least 72 hours after the last treatment." Comments on recent modification of this warning will be made later.

When the antibiotic drug used is effective, the clinical response is quite dramatic and a marked change in the appearance of the milk, teat, and udder takes place within 24 hours. However, the disappearance of the signs of infection and reduction in inflammation is not a guarantee the infection is eliminated. This can be determined only by a thorough bacteriologic examination of the milk. A favorable change of appearance in the milk or infected quarter is no guarantee that the drugs infused have been completely absorbed, or eliminated. Experimental evidence points to the contrary. It is necessary to milk infected cows twice daily for a period of at least three days to be sure that the great bulk of the drugs has been milked out. Experience has shown that substantially the entire amount of infused antibiotic is eliminated by regular milking over a period of three days. Excluding the possibility of illegal addition of antibiotics to milk as a preservative, failure
to follow the caution in the labeling of mastitis preparations, concerning discarding milk from treated animals, is largely responsible for antibiotic residues in our milk supply.

As long ago as 1948 it was noted that in some instances milk from cows treated for mastitis intra-mammary infusion contained enough drug to inhibit cheese starter cultures even though mixed with large quantities of antibiotic-free milk. Sometimes this resulted in serious economic loss. The cheese industry has largely eliminated this difficulty by insisting that their suppliers discard the milk of treated cows for three or more days following treatment, and by testing the milk for penicillin or other antibiotics.

The Food and Drug Administration has conducted three nation-wide surveys to determine the incidence of antibiotic residues in market fluid milk. In 1954, 94 samples were collected and examined: 3.2% contained penicillin. In 1955, the work was expanded by the collection of 474 samples of milk collected from all parts of the country; 11.8% contained antibiotics. The 1955 samples contained up to approximately 80 units of penicillin per quart. One sample in the first survey appeared to contain bacitracin and a single sample in the second survey appeared to contain one of the tetracyclines. However, there are no identity tests for small quantities of these antibiotics except penicillin, and the inhibitory activity shown by the two samples could not be attributed to these drugs with complete certainty.

The results of the 1955 survey were sent to a number of nationally recognized experts in the field of antibiotic therapy, pediatrics and allergy to obtain their opinion as to a possible public health significance of these quantities of penicillin in market milk. Little evidence was available on which to base an opinion and it was necessary for these authorities to arrive at their conclusions through their experience in their respective fields, plus their knowledge of the sensitizing potential of penicillin. The majority of these experts concluded that these amounts of antibiotics in milk were not dangerous for the consumer to ingest on the basis of his daily consumption. The majority expressed the opinion that these amounts would not sensitize the nonsensitive individual, would not cause emergence of resistant micro-organisms, would not change the normal intestinal flora, and would not change the normal oral flora. However, the great majority were of the opinion that the ingestion of the amounts of penicillin found in milk conceivably could cause a reaction in the extremely sensitive individual. With the consensus of these 31 nationally recognized medical experts on the results of our 1955 survey, the Food and Drug Administration initiated a third and considerably more extensive survey, completed in February, 1958, to obtain more accurate information as to the true incidence of antibiotic residues in the nation's milk supply. Each of the Administration's sixteen Districts participated in the survey and 1640 samples of pasteurized and 66 samples of raw milk were collected for a total of 1706. All states and the District of Columbia were included in the survey. After collection, the samples were frozen, packed in dry ice and shipped via air to the Division of Antibiotics in Washington, where they remained frozen until thawed for assay. Each sample was tested quantitatively for penicillin, streptomycin, bacitracin, and the tetracyclines. Of the 1706 samples tested in the survey, 101 or 5% contained residues of penicillin as confirmed by the penicillinase identity test. One sample contained both penicillin and streptomycin. The concentrations of penicillin found ranged from 0.003 to 0.550 units per milliliter. In the 1955 survey, you will recall, 11.6% of the 474 samples contained penicillin in concentrations ranging from 0.003 to 0.080 units per ml. Although the percent of samples with antibiotic residues collected in the 1956 survey is less than that for the 1955 survey, that is, 6.9% as contrasted with 11.8%, the average concentration of penicillin found in the positive samples of the 1956 survey is higher than that found in the 1955 survey. Furthermore, the highest concentration of penicillin found in individual samples collected in the 1956 survey was 0.550 units per ml as contrasted to 0.08 units per ml found in the 1955 survey. These higher concentrations may give us cause for concern. Although the medical experts which were consulted are concerned about the situation they are not sure that an imminent public health hazard has been demonstrated. Nevertheless the Food and Drug Administration is seeking means of getting penicillin out of milk. We have asked the U.S. Department of Agriculture to cooperate with us in a very broad educational campaign designed to acquaint dairymen with the steps they must follow to produce clean milk free of antibiotics. In February we published a proposed change in the Regulations to limit the amount of penicillin in a mastitis preparation to 100,000 units per dose. The Federal Register of May 14 published the final order, establishing 100,000 as the maximum single dose to be recommended in the labeling. This notice states:

"The principal adverse comments were: (1) that penicillin could be kept out of milk without reducing the unit dosage, by incorporating a nontoxic dye in the drugs, which will color milk from treated animals as long as penicillin is being excreted in the milk; and (2) that the public health would be adequately protected by restricting use of the drugs to or on prescription of licensed veterinarians."
"Consideration has been given all views and comments submitted, together with other available relevant information, including the fact that no non-toxic dye suitable for the intended purpose, has been found; that restricting such drugs to use by licensed veterinarians would involve added expense and possible hardship to the farmer, due to the inaccessibility to veterinarians in some geographical locations; and that adequate directions for lay use can be written for these drugs.

"On the basis of these facts, it is concluded that such amendments are necessary for the protection of the public health."

The possibility that the use of intramammary preparations might one day become a public health problem was recognized early in the use of these drugs. It was at this time in 1951 that a notice was published in the Federal Register. This notice to manufacturers and labelers of antibiotic drugs for veterinary use stated:

"Unless a proper interval of time is allowed following the use of antibiotic drugs for the treatment of mastitis in milk-producing animals, the antibiotic drugs may get into the general milk supply. Because of the specific action of antibiotic drugs on cheese starters, milk containing such drugs is of no value to cheese manufacturers. The direct or inadvertent addition of antibiotic drugs to milk to be sold for human consumption or for the manufacture of dairy products may constitute an adulteration within the meaning of Sec. 402 of the Federal Food, Drug, and Cosmetic Act. The labeling of antibiotic drugs intended for intramammary use in the treatment of mastitis in milk-producing animals should bear a prominent statement designed to prevent milk from treated portions of the udder from entering the general milk supply. The following statement is recommended for this purpose: Important: Milk from treated segment of udders should be discarded or used for purposes other than human consumption for at least 72 hours after the last treatment."

On April 22, 1957, the Commissioner of Food and Drugs, after careful consideration of the views and comments from interested parties and other relevant information available to him, amended the general regulations for the certification of antibiotic drugs intended for intramammary infusion in the treatment or prevention of mastitis in dairy animals. The amended regulation states that whenever the labeling of an antibiotic drug suggests or recommends its use in the prevention or treatment of mastitis in dairy animals by intramammary infusion the label of such immediate container shall bear the statement "Warning—Milk taken from dairy animals within ....... hours after the latest treatment for mastitis must not be used for human consumption," the blank being filled in with the number "72" unless the person who requests certification has submitted to the Commissioner information adequate to prove that milk from dairy animals treated with the drug as prepared by him contains no antibiotic after a time period that is shorter than 72 hours after the latest treatment. In such cases the blank shall be filled in with the number "60," "48," "36," or "24" as authorized by the Commissioner. This regulation will become effective on July 29 unless it is stayed in whole or in part by the filing of objections from persons who on reasonable grounds may be adversely affected.

Consumers, law-enforcement officials, and the dairy industry are concerned about any chemical which may be found in the nation's milk supply. Through cooperation of all interested parties and widening our joint educational efforts we believe that antibiotic residues in dairy products can be and will be eliminated.