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FOOD SAFETY:
RESIDUES IN ANIMAL-DERIVED FOODS
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1986 Food Marketing Institute survey revealed that consumers are more concerned about residues in their diets than about color additives, irradiation, fat, cholesterol, sugar or salt.1 While Americans enjoy the safest food supply of any people in the world, people think that problems with food safety exist.2,3, This gap between perception and reality may have developed partly because of efforts to keep the US food supply above reproach.

Why the Concern about Residues?

About 80% of all food animals are administered drugs during their lifetime. Some 750 drug products, containing about 100 basic drugs, are used in food animal production. Most are needed to ensure a continuing safe, wholesome, affordable food supply for the populace. About 30% of chickens, 80% of veal calves and pigs, and 60% of beef cattle are routinely fed medicated rations. Livestock are also routinely treated with dewormers and insecticides.

Putting the Concern about Residues in Perspective

Risk

The purpose of scientific risk calculation is to get the best estimate of the true risk using available information. However, the concept of risk used in regulatory agencies is quite different. To assure the public safety, regulatory agencies go beyond scientific risk. To calculate regulatory risk, agencies first start with the scientific risk level. Then, they do the following calculations:

They figure what the maximum consumption would be if that item were consumed every single day for a person's entire lifetime.

They multiply that risk by a factor of 100 or 1,000. 10

Before being approved, an animal drug must be extensively tested. The drug sponsor (usually the manufacturer) must establish scientifically that the substance is safe and effective. The sponsor must also demonstrate that any drug residues remaining in a food-producing animal at slaughter pose no threat to human health.

As science progresses and scientists are able to detect extremely tiny amounts of a substance, regulatory agencies are beginning to have problems enforcing rules about residues. In fact, tests can now detect one in one quadrillion (1/1,000,000,000,000,000). Yet Section 409 of the Federal Food, Drug, and Cosmetic Act contains the Delaney Clause (1958) which states that, "no additive shall be deemed safe if it is found to induce cancer when ingested by man or animal...". Development of sensitive tests since 1958 have made the Delaney Clause unworkable.

If toxicological studies raise the suspicion that a drug may cause cancer, the FDA now requires the sponsor to conduct chronic feeding studies in rats and mice. If the results show that the chemical causes cancer, the FDA uses a conservative risk assessment procedure to determine how much residue presents the consumer with no significant risk of cancer. Under this procedure the FDA allows the upper limit of lifetime risk of cancer to be one in one million (that is, if one million consumers ingested the residue for their entire lifetime of 70 years, one of them might get cancer from the drug residue).

This risk is approximately 10 times less than the risk of being struck by lightning.

Tolerances

As part of the drug approval process, the FDA establishes what levels of each drug's residues are acceptable in edible animal tissues. These levels are called tolerance levels and are based on regulatory risks; that is, the tolerance includes a built-in safety factor or margin to assure that the drug has no harmful effects on consumers.

To come up with that extra safety factor, the sponsor must first determine the highest dose at which the drug does not produce any measurable physiological effect in laboratory animals. Tolerances are then set at 1,000 or 100 times below the "no-effect" level. If no safe threshold has been established, the tolerance is zero. 10 The tolerance is legally zero for any substance known to be carcinogenic.

Who Monitors Residues?

Several US government agencies and their subsidiaries, along with state agencies, share the responsibility to keep our food supply safe. They do a remarkably good job.

The Food and Drug Administration (FDA) is a branch of the US Department of Health and Human Services. FDA is responsible for assuring the safety and wholesomeness of foods. All food ingredients are subject to the requirements of the Federal Food, Drug and Cosmetic (FD&C) Act.4,5

The Center for Veterinary Medicine (CVM), a branch of FDA, is responsible for assuring the safety and effectiveness of animal drugs and feed additives. Drugs and feed additives intended for use in food-producing animals are also evaluated for any effects they may have on human health. Scientists investigate what would happen if residues from these substances remained in meat, milk, or eggs. In cases where residues occur in amounts that violate the law, FDA has the responsibility to investigate, determine the cause of the violation and take appropriate regulatory action.6

The Environmental Protection Agency (EPA), an independent federal agency created in 1970, approves pesticides and their methods of use. The EPA sets tolerances for residues of pesticides and products that result when these pesticides degrade in foods and feeds of plant origin.

The EPA also determines tolerances or action levels for toxicants that occur naturally in the environment, such as aflatoxins and fluorides. A "tolerance level" is a threshold. Below it, the amount of toxicant is legal, and above, illegal. An "action level" is a threshold above which EPA or FDA may prosecute for allegedly disregarding the health or safety of people or animals.

The EPA establishes residue tolerances for pesticides which will be applied to anything that food-producing animals later eat as part of their feed. However, the FDA follows up if violative residues are detected in meat, milk, or eggs.

The Food Safety and Inspection Service (FSIS) is a branch of the US Department of Agriculture (USDA). FSIS monitors and investigates conditions in slaughter plants. It takes tissue samples from slaughter plants and analyzes them for chemical residues. Carcasses or products found in violation are condemned and destroyed. Results of violative samples are sent to FDA for investigation and possible prosecution. FSIS then requires that at least five subsequent animals sent to slaughter from the offending source be tested until the offenders are in compliance.

FSIS conducts both random sampling (monitoring) and sampling for cause (surveillance).7,8

Monitoring provides a 95% assurance that a residue of any targeted substance is detected if it occurs in more than 1% of product lots.7,8

Surveillance is used to investigate and control the movement of potentially adulterated products. Slaughter animals may be targeted for surveillance testing if they appear diseased, have injection marks, or come from questionable sources. Residues above legal limits are found in about 1% of slaughtered livestock.

Major segments of the industry such as fed cattle and poultry, have extremely low incidences of illegal residues (much lower than 1%). However, small segments of the industry continue to have a higher rate of violation, notably veal calves and cull dairy cows.8 Sulfamethazine residues in hogs have been at unacceptable levels.7,9

When possible violations are dealt with, FDA has responsibility for the animal while it is on the farm; FSIS has responsibility during processing; and FDA again assumes responsibility when the products are in the grocery store.

The Cooperative Extension Service (CES), another branch of USDA, shares responsibilities with other USDA agencies. CES provides educational materials and information to everyone from producer to consumer. CES continues to be vitally involved in assuring the safety of our nation's food supply.8

Sulfamethazine (SMZ), a drug given to most hogs, provides an example of how tolerances work. Extremely large doses of SMZ, when administered to rats and mice daily over their lifetime, cause some to have thyroid tumors.11 If the Delaney Clause were applied to SMZ, and the present tolerance of 0.1 ppm SMZ in pork were reduced to zero, pork producers could no longer use SMZ. Even if that happened, SMZ would cause residues in pork for years after its use was discontinued, because it persists in swine housing and feeding facilities.

Other Regulations

Withdrawal Time -- A withdrawal period is a time allowed for residues to deplete to safe levels (tolerances) between the last treatment and slaughter or milking.

Labeling -- The label accompanying a drug for animal use must contain all necessary information, including: species in which it may be used, conditions for which it may be used, dosage for each application, and withdrawal periods.5,12

Any use or dosage not specified on the label is termed "extra-label" and must be administered only with a veterinarian's order and supervision. The veterinarian is responsible for determining and ordering a withdrawal period (usually extended) to assure no residues in edible product, when a drug is prescribed for extra-label use.

A drug can still be approved with liberal tolerances when a sponsor proves to the FDA that it does not threaten human health.a Some drugs are not granted approval for use in food animals because of proven or potential toxicity. Some are banned after having been approved or used in an "extra-label" manner. Formerly used drugs decreed illegal for use in food animals now include chloramphenicol, diethylstilbestrol (DES), dimatridazole, and ipronidazole.b

"Accidental" Exposure

Food-producing animals may accidentally consume feedstuffs contaminated with pesticides, industrial chemicals or natural toxicants.13 They can absorb, metabolize and retain those substances in muscle tissue, organ meats, fat, milk, and eggs. Livestock may be fed waste by-products from many and varied

sources. There is hardly any form of agricultural or industrial processing from which someone doesn't try to salvage livestock feed. Some waste products have nutritional value, some provide bulk and some just need disposing of. Examples include: paper, grain dust, ethanol distillers byproducts, poultry litter, waste fat and oil 14, grain and oilseed hulls, citrus pulp, packing plant offal and meat and bone meal.15 Products fed illegally that have resulted in contaminated animal-derived foods include pesticide-treated seed and PCB-contaminated industrial oils.16,17 Some recent incidents of human food becoming contaminated with chemicals occurred because people ate contaminated animal products.
Discontinued and restricted-use pesticides are a potential source of poisoning and contamination. Persistent and dangerous chlorinated hydrocarbons include DDT, heptachlor, endrin, aldrin, and chlordane. Heptachlor residues in dairy cattle and poultry have recently drawn national attention to Arkansas and surrounding states.7,8 Both the cattle and the poultry incidents resulted from heptachlor-treated seed being routed into the animal feed supply. Chlorinated hydrocarbons have mostly been replaced by organophosphates and carbamates. If not less toxic, they are at least less persistent in the environment and in animal tissues.7
Livestock exposed to substances like PCBs and chlorinated hydrocarbons continue to have residues in body fat for several months. Incidents of accidental exposure of livestock to hazardous chemicals are usually publicized in the press. This results in increased public concern about the wholesomeness of meat and other livestock products. Some positive results of the publicity are increased awareness by other livestock producers of the problem, and continued vigilance by the agencies and persons responsible for assuring the safety of our food supply.

a Ceftiofur, an antibiotic marketed since 1988 and structurally similar to penicillin, is presently labeled only to treat respiratory infections in cattle. It was developed by Upjohn specifically for use only in animals, not in humans. Upjohn proved to FDA that people allergic to penicillin should not have adverse reactions if exposed to ceftiofur. They also proved that it had an extremely low toxicity. Consequently, ceftiofur has no withdrawal period. An animal can be slaughtered immediately after the last injection of a 5-day treatment. The tissue tolerance level is 3 ppm in muscle, 12 ppm in fat, and 30 ppm at the injection site, very high compared to most drugs.
b Chloramphenicol is a very toxic antibiotic. It is used to treat people with life-threatening infections that are unresponsive to other antibiotics. However, a few people's lives are jeopardized by contact with a minute quantity of chloramphenicol. Chloramphenicol was never approved for use in food animals. However, veterinarians found that it worked well to treat stubborn cases of diarrhea and pneumonia in calves and pigs, so they prescribed it extra-label. Because of the extraordinary risks associated with exposure of hypersensitive people to chloramphenicoL FDA has made it illegal to use in food animals, even by veterinarians.

Conclusion

Even though the FDA applies safety factors of 1,000X, and one-in-a-million people over a lifetime cancer risk, consumers still perceive significant health risks in animal-derived foods. While continuing to expect every reasonable effort to protect life and health, consumers also need to better understand risk analysis and the importance of having an adequate supply of high quality food at reasonable cost. Livestock producers and processors need to be continually more aware of residue problems and concerns. They need to institute everbetter, formal quality assurance programs to further increase the

safety of animal-derived foods.

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Notes

2. "Three out of five (consumers) view antibiotics in poultry and livestock as a serious health hazard." "Nearly one-half of consumers feel they have some responsibility to assure the food they purchase is safe." "Less than one-third feel the government does a good job of protecting their interest in food safety."
Residues from pesticides and herbicides were a concern of 96% of respondents to a survey. Antibiotics and hormones ranked as a problem by 94% of those surveyed.
5. FDA regulations grounded in the FD&C Act have the effect of law; they are just as binding as the statute.
Proper animal drug use is defined by Federal law not only in the FD&C Act but also in regulations

promulgated by the FDA.
"Labeling" includes not only the label on the immediate or outside container but also "other written, printed, or graphic material accompanying such article".
A new drug application for a drug to be used in food-producing animals must contain data showing the safety of residues of the drug or its metabolites, and acceptable methods for recovery and measurement of such residues from tissue of any food-producing animal for which it is intended.6 An animal drug is approved for a particular specie or species, for a specific indication or indications, at a stated dosage, and, where appropriate, with use restrictions such as a withdrawal period.
7. The 1989 National Residue Program (NRP) includes 49,000 monitoring sample unit analyses and approximately 30,000 surveillance sample unit analyses. The 1989 NRP includes assays for 120 compounds.
The focus of monitoring is on violations. Only compounds with established safe limits are considered. In addition to profile information, monitoring provides a basis for further action (surveillance).
Surveillance sampling is often purposely biased. It is directed at particular carcasses or products in response to information from monitoring or other sources, or from observations during inspection.
9. Cows, veal calves, and market hogs were the market classes most often associated with drug residues in both the FDA/CVM and VDACS reports.
10. In early 1986, the FDA discovered the pesticide heptachlor in animal feed during routine testing for aflatoxin. Local state and federal officials responded to contain the problem, protect the public health and aid the producers who had fed their animals stillage (mash, by product of gasohol production) and had unknowingly fed heptachlor residues.
Animals on about 140 dairy farms in Arkansas, Oklahoma, Missouri and other states were affected, including quarantines on nearly 50 farms. Thousands of gallons of milk were dumped or withheld from market.
14. "FDA's concern over the use of industrial by-product oils in feeds is that, because of the nature of the oils, any number of contaminants may be present. It is, therefore, impractical if not impossible, to analyze such material for all potential contaminants. The use of such materials in feeds creates the risk of injury to animals and creates the potential for unsafe residues in human food derived from the animals."
15. "Sulfamethazine has been identified by scientists in FDA and USDA as a problem drug which cannot be used in food-producing animals safely as long as illegal drug residues in tissue result from such use."
Many ingredients used in animal feeds are waste by-products from food processing, where pesticide residues concentrate in excess of the permitted tolerance for the raw agricultural commodity from which the by-products were derived. And, chaff and fines, common waste products from agricultural and ornamental commodity harvesting, are pelleted for feed use. These products often contain residues of pesticides for which no tolerance has been established and for which no analytical method has been developed to detect residues in meat, milk, and eggs.
There are no waste products from industrial or agricultural processing that some entrepreneur does not try to salvage. Competition in the marketplace puts economic pressure on both dealers and producers for inexpensive feed ingredients. Some waste products have nutritional value, some provide bulk. Lacking either, some are blended with other ingredients in a deliberate effort to lose their unacceptable identity as feed grade materials. Whatever the situation, all lack exposure and safety data to support an EPA tolerance for pesticide residues. The task frequently falls to CVM to define these products,

determine their regulatory status, and to encourage EPA to establish tolerances or action levels which the FDA can use for enforcement purposes and the industry can use to legitimize waste by-products for feed use.

16.Unprincipled brokers buy and sell nonfeed oils, such as waste industrial by-products, and label them for animal feed use. One case evolved from the findings of polychlorinated biphenyl (PCB) residue in turkeys marketed for human food. FDA field investigators traced the PCBs to waste oils from a chemical plant's scum pond, labeled "industrial waste not for animal feed use." Further investigation showed that brokers buy and sell railcars and tankers of oils and invoice the products to feed manufacturers as feed grade regardless of source. The manufacturer may be aware that the product is suspect but, since the price is right, blends it with other fats and oils so its original identity and any contaminants are greatly diluted.

18. More than two million pounds of raw chicken has been held by USDA/FSIS at several locations in Arkansas after initial quality assurance testing, on January 4, 1989 by Campbell Soup Co., detected the presence of heptachlor in boneless chicken meat supplied to Campbell's by Townsend's of Arkansas, and subsequent investigations indicated a problem. FSIS confirmed heptachlor residues in the 0.05 to 2.4 parts per million (ppm) range in the chicken. The permitted level established by EPA is 0.3 ppm in fat. Laboratory tests by FDA indicate that feed may have been contaminated with heptachlor since December 16, 1988. FDA is testing milo from three of Townsend's suppliers since high levels of heptachlor have been found in milo used in the feed supplied to the birds slaughtered on January 4 and 9. Since early January, the search for contaminated chickens has spread into more Arkansas slaughter plants and plants in southern Missouri. A series of recalls and continuing pretesting are being used to keep the contaminated chicken off the market. EPA has started the process to completely ban the use of heptachlor as a seed treatment because it is considered to be carcinogenic. Originally, the treatment was approved for grain seeds to be planted, not for grain seeds to be used in feed. The exact cause of the contamination has not been established conclusively; however, there is strong indication that heptachlor treated seed may have been included in the poultry feed.