The Role of the CVM/FDA Advisory Committee*

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Background

Over the past several years, the CVM/FDA* has made a significant attempt at controlling illegal use of drugs in animals. Much of the effort has centered on the veterinary profession where, in various ways, drugs have been used or distributed illegally. The effort has also involved distributors engaged in illegal drug sales. This activity is altogether proper for the CVM/FDA since it is one of their major functions mandated by law. Frustrated by attempts at regulating illegal activities through the various state regulating bodies and the courts, the CVM/FDA has resorted to a series of policy changes to accomplish the goals they see as necessary. Some of these policy changes have met with great resistance by the veterinary profession and the various producer groups.

The disagreements are understandable in the context of the different perspectives of the FDA, practicing veterinarians, and producers on how they each get their jobs accomplished. Yet in a larger sense, the overall goal of the CVM, practicing veterinarians, and producers is the same. It is to assure that the public has proper assurances that animal food products are free of drug residues or adverse drug effects, that the animals are produced in a wholesome, safe manner, and that animal products are produced as efficiently as possible. It is therefore essential that all parties involved, including the CVM/FDA, work in unison toward this objective. The idea of adversarial roles does not fit in this larger context.

For some time the CVM/FDA has considered instituting an advisory commitee. These considerations escalated when the extra label use of drugs policy was resisted by segments of the veterinary profession. It was felt that one function of such a committee would be to advise the CVM on policy so that major deficiencies could be identified and adjustments made before policy is announced. Dr. Crawford has stated that most major policies will be directed to the committee before being promulgated.

Early in 1984, the plans for an advisory committee were finalized and nominations for membership were opened. The precise function of the advisory committee can be best abstracted from the charter.

Veterinary Medicine Advisory Committee Charter

The **purpose** of the committee is to "advise the commissioner (of FDA) in discharging his responsibilities as they relate to assuring safe and effective drugs, feeds and feed additives, and devices for animals use."

It is noteworthy that the committee actually answers to the commissioner rather than the director of CVM, although I expect to work almost exclusively with the director.

The **function** of the committee is to "review and evaluate available data concerning the safety and effectiveness of marketed and investigational new animal drugs, feeds, and devices for use in the treatment and prevention of animal diseases and increases animal production and make appropriate recommendations to the commissioner of food and drugs."

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**CVM/FDA: Center of Veterinary Medicine/Federal Drug Administration.*

This statement would seem to indicate that the committee will actively be participating in the drug approval process. On the contrary, indications so far are that we will only be acting on matters of policy and direction rather than specific drug applications.

The charter also specifies that the committee will consist of eleven members and will be appointed by the Secretary of Health and Human Services from the candidates nominated. Further, the members will be selected one each from the following categories:

Committee Members

Companion Animal Medicine—Barbara Stein
Food Animal Medicine—Glen Hoffsis—Chairman
Avian Medicine—David Anderson
Microbiology—Frederic Scott
Biometrics—James Williamson—Vice Chairman
Toxicology—Fred Oehme
Pathology—Robert Phemister
Pharmacology—Williams Jenkins
Animal Science—John Megown
Chemistry—Elwyn Schall
Consumer—Technically Qualified—Charles Lassiter

The members are appointed to overlapping terms of 4 years.

We met for the first time for two days in mid December in Washington at FDA. The meeting was devoted to orientation, organization, and briefing by CVM/FDA. The committee was divided into study panels, each focusing on a specific issue which was identified from the briefings as major concerns of CVM. These panels are:

1. Low Level Antibiotics in Animal Feed
2. Prescription/Bulk Drugs
3. Sulfa Residues

As the committee becomes more mature, other issues and policies will be examined. The committee agenda will arise from requests by CVM/FDA as well as initiatives from within the committee. We will meet at least twice annually with study panels meeting more often. The next meeting will be May 22, 23, 24 in Washington. All meetings are open to the public and the minutes are available upon request.

Since the committee has just started, it would be premature for me to predict what our advice to CVM/FDA will be on any specific question. However, I would like to make some general comments on some of the issues.

Extra Label Use of Drugs (ELUD)

In July, 1983 the CVM/FDA announced a policy which would have made extra label use of drugs illegal. This threatened to seriously disrupt food animal practitioners in their efforts to deliver medically sound therapy to food producing animals. The policy allowed no latitude by the practitioner regarding species indications or dosages of products. The veterinary specialty organizations including AABP and the Academy of Veterinary Consultants joined AVMA in negotiating with the CVM/FDA to bring about revision which would both aid the CVM/FDA in achieving tighter controls on usage of drugs as well as allowing practicing veterinarians the ability to deliver medically and legally sound health care to livestock. The revised policy allows veterinarians the prerogative of using drugs in an extra label manner so long as the usage is medically justified and prudent. However, the policy gives this prerogative only to veterinarians and only to those who

have established a veterinarian/client/patient relationship. Although this policy gives veterinarians a better defined position on drug usage than they had prior to ELUD policy, it also puts more responsibility on practitioners to justify their use on a medical basis.

Although the controversy over the ELUD policy has subsided, there still remains some questions which beg for better solutions. The CVM/FDA has only two categories of drugs: Approved and Unapproved. However, in recent times we have seen a new category of drugs immerge which are immune to usage under the ELUD policy. These are D.E.S. and chloramphenicol. This category could be called strictly forbidden or banned products. Whether other products are currently in the banned category and immune to ELUD in the opinion of the CVM/FDA, is open to speculation. Products such as butazoladin have a label "Treated animals should not be slaughtered for food purposes." Use of this kind of drug still gives pause to practitioners in light of the recent experience with chloramphenicol.

Practitioners have a continuing problem in determining logical and safe withdrawal times of most drugs when used in an extra label manner. The problem stems from the fact that there are only approved and unapproved categories of drugs. The CVM/FDA will not furnish withdrawal times on unapproved products even if known because to do so would give tacit approval for their use. However, it should be recognized that withdrawal times given for approved products are merely recommended times. These times are derived in normal animals and since practitioners usually treat sick animals, withdrawal times may vary considerably due to the diseases of organs of elimination or state of hydration. It may also vary with the age of the animal, route of administration, duration of treatment, and dosage.

I believe most practitioners would welcome additional label information which would allow extrapolation of more accurate dosages, indications, and withdrawal times. This type of label information was recently recommended by the American Academy of Veterinary Pharmacology and Therapeutics. Futhermore, practitioners have a difficult time obtaining sound information on the proper withdrawal time on any extra label product. There is an urgent need for a compilation of drug residue information on commonly used extra label products and dosages which would allow practitioners the ability to make more accurate estimations of proper withdrawal times on various products. Certainly such a list would never be official but it would be a vast improvement over the "Seat-of-the-pants" estimations being given in practice today. This information would not obviate the need for pre sale meat and milk residue testing.

The continuing efforts to avoid drug residues in meat and milk puts more emphasis on the utilization of on-site residue testing in live animals prior to use of the products for food. Use of the Delvo Test-P and penzyme test for milk testing and the L.A.S.T. and C.A.S.T. for testing urine in slaughter cattle are major steps in the right direction. With the use of emerging technology which should lead to *Cow-side* residue testing, practitioners will have increased confidence that residues are being avoided from both approved and extra label drugs.

Low Level Antibiotics in Feed

One recent development which has consumed the attention of the FDA and the advisory committee is the heightened controversy over the use of penicillin and tetracycline in animal feeds. Some contend that low level antibiotics in animal feeds causes the selection of resistant organisms which then gain access to the human population where they are more virulent and less responsive to treatment. This premise has been proposed for decades but never substantiated.

In 1984 Holmberg *et al* published reports which allegedly established the link between use of antibiotics in animal feed and human disease. Although these reports are very controversial, they have sent shock waves through the scientific community and have caught the attention of various groups seeking to ban penicillin and tetracycline.

The culmination of this new publicity was an imminent hazard petition filed by the National Resources Defense Council which resulted in a hearing with FDA on January 25, 1985. The hearing brought into sharper focus the issues faced by the FDA in trying to establish whether low level antibiotic feeding is dangerous or not. In 1977 the FDA requested the National Academy of Sciences to study the issue. They concluded that a scientific judgment could not be rendered with available data and suggested more large scale epidemiologic based studies on plasmid borne resistance be completed. These studies conducted at several universities and hospitals are completed or near completion. Specifically, the Seattle King County Study, is just completed and is under review by a scientific panel to review this new data in 1984.

The process which will lead to the decision regarding this issue will begin with the decision by FDA on whether or not to grant the imminent hazard petition. This decision must be made next month. If they grant the petition, a ban will be instituted. If the FDA denies the petition, the orderly process of review of the studies just completed will proceed with no set time as to when the decision must be reached.

The FDA advisory committee will have no role to play in the decision regarding the petition. However, if the petition is denied, the advisory committee will enter into the process of evaluating the available information and advising the CVM on its courses of action. In this regard I have appointed a study panel from the committee members and chaired by Dr. William Jenkins of Texas A & M University to specifically assemble information on this issue for the benefit of the committee at large. So far, the panel has just become organized and this issue has not been discussed with the full committee. Without pre-empting this panel and speaking for myself rather than the committee, I would make some observations.

Anyone involved in the livestock industry must seek to maintain the confidence of consumers that animal food products are safe and wholesome. Once the various factions with special interests enter the discussions of issues such as this, it becomes more difficult to distinguish the facts. We should all therefore implore the FDA to decide this question strictly on scientific evidence. I believe the FDA is proceeding in this manner and will not yield to any special interest concerns. Once the decision is rendered based on scientific evidence, we should all support it regardless of the outcome.

The scrutiny of the scientific review panel is the key ingredient. If the ban is not granted even though the evidence is convincing, the loss of confidence in animal products by consumers and the health of some people is at stake. On the other hand, if a ban is imposed in the absence of compelling scientific evidence, the confidence of livestock producers, veterinarians, and the pharmaceutical industry is at stake.

The concerns of the drug companies are particularly noteworthy. We live in an age where we rely on the use of various drug products in order to maintain health and improve performance of our livestock. Without most of these products, animal production would be much less efficient and result in higher food costs. It is unrealistic to think that animal production in our modern age can exist at present levels in the absence of some drug products under "back to nature" management.

Producers and veterinarians continually search for more products which will reduce disease and increase production. The drug companies spend millions of dollars per product to meet the criteria of safety and efficacy before such products can be approved by FDA for use.

Because these standards for safety testing are so rigid and extensive during the approval process, the removal of drugs from the market should not be taken lightly. It would seem logical that the same degree of testing and scrutiny for removal should be applied as was necessary for approval. If companies see products easily removed at the demand of speical groups or for less than sound scientific reasons, they will become timid in attempting to approve new products.

In the same light, I feel it is potentially counterproductive for producer groups to voluntarily boycott from use of certain products. Although it is compelling to voluntarily ban a product for the sake of yielding to demands to appear concilliatory, there is a danger of sending wrong signals to the special interest groups involved. Caving in to the desires of a group who attacks a particular product or practice,

gives encouragement to take the next step and attack a new and different product. On the other hand, it emphasizes to drug companies the extreme instability of product use and discourages initiatives for new product development.

Prescription and Bulk Drugs

The CVM/FDA has become increasingly alarmed over the sale of prescription drugs to producers by laymen or by veterinarians who have not established a veterinarian/client/patient relationship. Recently they attacked the problem by publishing a proposed prescription guideline for veterinarians which was designed to tighten the control of these drugs. The proposal met with resistance from producer groups and the AVMA as being an invasion into the practice of veterinary medicine and a needless addition to record keeping and expense. Dr. Crawford announced at the Cornell Conference in January 1985 that he was concealing the proposed guidelines.

He went on to say, though, that the problems persist and he challenged the audience to formulate solutions. In suggesting possible avenues for attacking the problem, he called for the profession to develop standards to guide practitioners in use of prescription products. He called for improved state-federal enforcement and changing of some state laws. Finally he suggested the creation of a new class of drugs. This last point especially intrigued me. It seems the veterinary profession generally mimics the medical profession. Yet our problems, and therefore solutions are often very different. The veterinary profession very likely has a class of prescription drugs because the medical profession has them. The nature of a new classification of drugs is open for discussion but the concept is certainly worthy of more thought. The CVM/FDA and the advisory committee would welcome input from any interested person or group on this concept.

Some time ago the CVM/FDA instituted a program called "Import Alert" to curb the importation of chemical grade drugs in large bulk quantities. Not only were these drugs being illegally imported, but some confiscated shipments were found to not contain the drug labelled and others were in mislabeled concentrations. There is concern about these products over purity, contamination, correct salts, and quality. The concerns and illegal imports still exist and better solutions to the problem have yet to be found. The advisory committee is studying the issue and will work closely with the AVMA-COBTA in making recommendations. We would welcome all innovative thinking on this topic.

In conclusion, I have faith in food animal practitioners and in livestock producers, that we all want to assure to ourselves and the consumers of our country that our animal food is pure, safe, and free of drug residues. Practitioners and producers want the ability to use products responsibly, legally, and in a medically sound manner to maintain health, and effectively treat disease. At the same time, the CVM/FDA is obligated to responsibly regulate drugs as mandated by law. The advisory committee provides an added avenue by which the CMV/FDA can be aided in accomplishing what in reality is our common goal.

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