The Bovine Practitioner and the Licensing of Veterinary Biologics

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It's a pleasure to be here today to discuss the licensing of veterinary biologics, an issue that I know has been on your minds for some time. . .and on the minds of the folks at the U.S. Department of Agriculture. I think what I say today will clarify this agency's position on new legislation . . .and the benefit to you . . .the practitioner.

But before I discuss licensing, let me just say a few words about my long personal relationship with the American Association of Bovine Practitioners.

For some 30 years, before I ever contemplated joining the federal service, I was a cattle rancher in Oregon. I owned 250 head of cattle then, and I remember all too well working sun up to sun down to save my herd from an outbreak of foothill abortion (Epizootic Bovine Abortion).

I wasn't alone during that trying time. My local bovine practitioner was there with me. We worked so hard trying to save the sick animals that we forgot about protecting the yet unborn, until we finally lost 125 head. High levels of chlortetracycline would have prevented that large death loss.

Both you and I know the importance of being able to depend on quality biologics. These products are our first line of defense. Often it is only that USDA license on the label that tells you the product has been screened for safety and effectiveness.

And in those rare cases where problems arise in field use, livestock producers and veterinarians know they will get prompt and responsible attention from both the industry and the regulating agency.

APHIS regulations cover quality control, testing, surveillance, and the monitoring of biologics. But our rules only apply to interstate producers. And although the Food and Drug Administration has responsibility for **intrastate** producers, they have not exercised their authority. These producers also fall under state regulations...where enforced.

Data gathered from 30 states show that most do not actively regulate the manufacture or marketing of veterinary biological products. About 200 or so unlicensed manufacturers of veterinary biologics are clustered in these states with no regulatory controls whatsoever.

Of the 19 states that **do** have laws administering veterinary biologics, most cover only the distribution of those products. They do not require monitoring for safety and effectiveness. And, ony two states report any testing of their approved products.

What does this mean to you—the practitioner?

It means that you and the user have a choice of purchasing your biologics from either a USDA-licensed producer or from someone who may be making concoctions at a rest stop . . .in the back of his van along Interstate I-40.

But, you're thinking, "These products have been around for years. Any first year microbiology student can put the ingredients together."

If you're thinking this way, I have to say: "Don't kid yourself."

Not too long ago the Department of Agriculture sampled 36 lots of unlicensed animal biologics from 14 producers. Our scientests tested them for sterility, safety, and potency. The overall failure rate of these unlicensed biologics was 56 percent. In contrast, the failure rate for USDA-licensed biologics during this same period was only 4-to-5 percent.

Our mandate is clear: We need to protect the industry and the livestock population of this country from unlicensed, untested, and unsafe biologics. Generally speaking, the states have not been successful thus far. And although the Department of Agriculture and the Food and Drug Administration have agreed on who should be at the helm, legislation to formally establish that authority has not been enacted.

In my hand is a proposed bill...drafted by a coalition of livestock industries and interstate and intrastate biologics manufacturers...called the Virus-Serum-Toxin Act Amendments. I am pleased to announce that this bill has the full support of the USDA, the FDA, the livestock industry, the licensed and unlicensed biologics industry, and several members of Congress back in Washington, D.C.

There are several key points in here that I would like to share with you.

FIRST, veterinarians may continue to prepare autogenous and other biologics for use in animals they are treating...as long as this is done within the framework of a veterinarian-client-patient relationship. Criteria necessary for such a relationship as:

1. The veterinarian has assumed the responsibility for making medical judgments regarding the health of the animal(s) and the need for medical treatment, and the client (owner or other caretaker) has agreed to follow the instruction of the veterinarian; and when
2. There is sufficient knowledge of the animal(s) by the veterinarian to initiate at least a general or preliminary diagnosis of the medical condition of the animal(s). This

means that the veterinarian has recently seen and is personally acquainted with the keeping and care of the animal(s) by virtue of an examination of the animal(s), and/or by medically appropriate and timely visits to the premises where the animal(s) are kept; and when

3. The practicing veterinarian is readily available for follow-up in case of adverse reactions or failure of the regimen of therapy.

SECOND, in the past the USDA said that autogenous products had to be used in the same diseased herd or flock, when made from organisms isolated from diseased animals and grown in culture. Recent versions of the regulations allow veterinarians to use autogenous products in other herds or flocks. This will continue under the new proposal.

THIRD, licensing exemptions are encouraged when a disease breaks out locally and a specific biologic is called for. Under this scenario, testing data normally required for long-term use biologics could be substantially reduced.

To meet emergency conditions, such as minor species diseases or low incidence diseases or to meet special local needs and other special circumstances...the USDA may issue a product license under a shortened procedure. Many of you may remember that a vaccine for Vesicular Stomatitis was made available on short notice under these procedures. Others are being handled on an everyday basis. At present 61 manfacturers are licensed to market over 1,200 products.

I might add that the USDA recognizes the contribution that many intrastate manufacturers have made to the health of the U.S. livestock population...especially in times of emergency, limited markets, and other circumstances.

This bill will allow unlicensed establishments 4 years to phase-in the licensing of their products. Establishments in states that have licensing programs that meet the criteria set out in the proposed amendments will be exempt from federal regulations.

This is a quick summary of the Virus-Serum-Toxin Act Amendments. I will be happy to respond to questions on all phases of APHIS operations. But before I open up the floor, I'd like to say a few words as this centennial year of animal health draws to an end.

In 1884...when Congress established the Bureau of Animal Industry...animal diseases threatened our livestock industry at home and our export markets abroad. Foreign governments had no confidence in the quality of our livestock, and our own producers could not trust each other.

But, cooperative arrangements with all the industries, the states, and veterinary associations allowed the pendulum to swing to the plus side. Twelve major diseases and pests of livestock and poultry were soon eradicated.

We needed each other in 1884; we needed each other 30 years ago when you helped save my herd; and we needed each other all the years in between.

In this same spirit, let us move forward together, confident in our resolve to protect this nation's livestock from disease and devastation.

Thank you.

Abstracts

Advances in antiviral chemotherapy

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The small number of licensed antiviral compounds indicates the difficulties encountered in treatment of infections caused by obligate intracellular parasites. For most antiviral agents, proof of efficacy and safety have been confounded by the narrow margin between the dose that is just tolerated by human beings and the minimum effective dose. This ratio (therapeutic index) has been close to 1:1 in the case of most chemotherapeutic agents leaving only a small number of safe and effective drugs for a limited number of viral diseases and a great variety of proported therapies, as ineffective as they are numerous.

The last 3 decades have seen only 5 antiviral agents advance from the limited exposure of clinical investigation to broader availibilty in routine clinical practice. Amantadine hydrochloride is effective only against influenzae A virus and 4 other compounds are restricted to herpesvirus group infections. Three of these 4 antiviral compounds have great limitations and the most recently approved agent, acyclovir, has potential for wide-spread clinical use.

Although the virus must be admired as one of the ultimate parasitic forms, the simplicity of its replicative process belied the difficulty in developing effective agents against the virus. Nature has defined biological efficiency in the virus-host cell interaction. Because viruses generally commandeer host cell molecular and macromolecular processes to make new virus particles, the task of identifying unique targets for chemotherapy is difficult. The field of antiviral drug development has matured slowly. Successful drug mechanisms must match the efficiency and sophistication of the virus replicative process if safe and effective therapies are to emerge. Such a mechanism is associated only with the most recently developed agent, acyclovir. The broader spectrum of activity and wide therapeutic index of acyclovir have identified it as a new generation of agents with great potential. A variety of agents have been unsuccessful after substantial preclinical and clinical evaluation. However, important lessons have been learned from evaluation of these agents and have advanced the antiviral field for the more efficient development of newer agents to come.