

Current Issues and Viewpoints in Veterinary Pharmacology: An Industrial Perspective

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The decade of the 1990's is about to unfold for all the societies of the world. Notice I said *about* to unfold because, as you scholars of the Julian/Gregorian calendar know, the 90's will officially begin on New Years Day, 1991 as there was no Year "0" A.D. (Caesar 46 BC). This bit of detail does illustrate the value of accuracy but I think you will also agree that understanding what's behind numerical and social values is much more important.

My principal theme today is that we, in industrial pharmacology, cannot serve the global society very well without a clarity of agreed upon definitions; practicing a brand of understandable science in both the halls of the laboratory and legislature; and most importantly a large increase in the dosage of trust and confidence from the consuming public in we, the technocrats. During this symposium you have heard about the voice of the public-at-large and how much say they should have. I suggest they are the *ultimate clients* of all those assembled here and we must 1) listen to them, 2) learn from them, and 3) act on their behalf (and subsequently our own) to improve the quality of global life.

Never before has the freedom to conduct business responsibly under the competitive system of capitalism been more challenged at its very reasons for existing. The fall of communism from an economic perspective validates in a great humanistic way our means of free enterprise. As it is a business imperative to produce positive cash flows to finance progress, we must also measure what we do in terms of public acceptance. The rewards of the 21st century clearly belong to those who successfully balance input costs and risks with socially acceptable gains such as a believable, safe food supply and clean air and water.

What does all this moral philosophy have to do with today's discussions? Hopefully, it serves as a guiding light for achieving applied technical results. Let me show you what I mean. We will share today some thoughts and solutions from the industrial viewpoint on contemporary issues in pharmacology. As I have worked in our industry for the past six years, my colleagues have made me a "limited",

card-carrying spokesperson for the industrial community - an honor that beats most others!

I have chosen to approach the subject of current industrial implications of pharmacologic issues from three points of the high ground. They are: 1) communications, both product and public, 2) generic animal drugs, and 3) specifics for action.

Communications-Products and Public

Product Communications The word "communication" is the greatest buzzer of our times and has multiple meanings. But in this context I will apply it to the subject of product labeling. Hold on! This topic will not put you to sleep (I hope). The purpose of labeling is to inform, balance risks, and get desired results for the user and/or prescriber. The appearance of some of today's labeling results from the pursuit of legalistic product liability prevention (aka "C.Y.A." an anatomical reference) and quite frankly is often very confusing. For example, 20-30 page leaflets that still remain in place for some OTC products is an oxymoron serving little but the gods of protectionism and history. How often have you heard the comment that the law or regulations require this or that here or there -- all to the detriment of communications of the real need to know information?

What we need is user friendly and public valued labeling, with flexibility for the *licensed graduate veterinarian* and greater simplicity for the lay direct purchaser. The balance here from the industrial perspective lies in relaxing the data and labeling extremes required for supervised drug approvals and use and simplifying the directions for unsupervised use products now.

By flexible labeling I mean recognition by FDA that clinical veterinary medicine is both art and science. FDA's requirements for Rx drug approval should take on the characteristics and scientific fashion of human Rx drug approvals with the inherent trust built in of a learned profession, the practicing veterinarian, who will oversee utilization. Before my FDA colleagues labeled me as totally turn-coated,

I'm not suggesting less data substance in approvals, merely more judgement by FDA on what a professional needs for safe and effective use of animal drugs in the practice of medicine. For example, pharmacokinetic data is badly needed for many new and existing products. Let's consider it a trade-off for lesser amounts of clinical cases required to approve the product. A little trust goes a long way and lets not be dismayed by the few bad actors; on the contrary, lets support the lawful majority!

I think we should all stop whaling about the fog from the past on product decisions and cease bashing the institutions and professionals that **MUST** be relied upon for proper drug usage. Let's consider doing away with the gremlins of tradition that don't work, keep the productive things that do like net contents and hazard information, and re-evaluate the information needs for the contemporary pharmaceutical user. I will offer more later on the tactics of how to greatly improve the means of product communications for the buyer, the FDA, and the sponsor. The core of an action in this area is holding a Public Summit Conference on Product Communications that leads to **CHANGE**. CVM/FDA is the obvious institution to lead such revolution of product communication. Again let me be so bold to remind you that the public will not permit our industry, nor our regulators to do as we have! But, they will give us their permission to advance the quality of living.

Two controversial subjects that deserve attention under product communication are 1) the categorization of animal drugs as prescription (Rx) or over-the-counter (OTC) and 2) extra label product uses under tight or flexible labeling schemes. Much has been said about these topics independently but I suggest it is worthwhile for us to consider them in unison.

Legal conditions that prohibit extra label use should not exist! A key public purpose for the practicing veterinarian to use drugs as he determines medically necessary is driven by the relief of animal pain and suffering coupled with the protection of the food supply. Can we do less for the welfare of animals that provide us food and companionship that we do for ourselves? I think *not*! What the licensed veterinarian needs is pharmacokinetic data prominently displayed in labeling to assure that a "Good Clinical Withdrawal Time" (GCWT) occurs with each case. Such data should be available for all legend drugs whether or not there is a discard and/or

a withdrawal time. Now with the coming of generic animal drug approvals in 1991 based on pharmacological studies, such data will become widely available. Most importantly, these data must be on all legend drug labeling. Medicine is not an exact science and the art demands utmost flexibility in the labeling of legend animal drugs consistent with patient welfare. Studies will show that professionally supervised drug use is *not* a major case of food contamination. I suggest that FDA expand trust in the practicing veterinarian with the same vigor as that applied to the physician in human medicine. For you lawyers in the audience who might say the laws prevent trusting licensed individuals, I say, if that be so, the laws are unacceptable, so change them! To not do so, risks our life quality needlessly. I, for one, trust society at large to do things right including the placement of *earned trust* in positive groups like veterinarians and regulators.

Public Communications Let me say that those disciples of the refrain that the public is ill trained to understand what we scientists say, are living in another time warp. As suggested by the National Research Council Report (1989) on *Improving Risk Communications*, it is our obligation to make our ever increasing complex discovery processes more comprehensible, not for everyone, but for those who wish to listen. The public is asking, even demanding, the right to choose whom to trust and instill confidence in for health and safety decisions. I suggest we come off our ivory towers and pedestals of pontification and join in the discussion with the "average" citizens. I am musically illiterate in most ways, but I can still choose the music that plays on my compact disc player. The public just wants to know that we are driven as a business by quality and not quantity alone.

Coming out into the limelight and sharing wider participation in product decisions is fraught with doing many things the right way, and it does not mean passing the buck on making the major commercial decisions of what to develop - for that right remains with the businessmen.

A recent illustration of the social situation we are now faced with in animal health and nutrition is the worldwide debates about biotechnology based products for agriculture such as BST. Great efforts have been spent by four sponsors to communicate both the many benefits and perceived risks of this scientific application from those interested in improving the quality of life for the majority. The

underlying challenge, however, is not scientific but pivots around understanding the public's values concerning the development of this and related products.

A special congratulations for communications excellence is due the Food and Drug Administration and the Animal Health Institute for their collective openness, then early voluntary release of BST facts not fiction, and then willingness to invest in clarifying attacks against the social apparatus in which we manage today's animal drugs. I think we should hear the BST messages loudly being sent to us, and change the way we do things in conversing with the public and their elected representatives. In the past decade no other new animal health product has changed the social dimensions of development that will need attention. While BST is a production enhancing agent for direct use by dairy farmers, can a similar revolution for the conditions for development and use of veterinary therapeutics be far behind? I think not.

Generic Animal Drugs

The creation by the 100th Congress of the Generic Animal Drug and Patent Term Restoration Act (PL No. 100-670, 1988) combined drug "me-to" animal drug approvals with patent term restoration. This law will be commercially effective in 1991 through product introductions and it is a factor in the overall approach of pioneer product development and related financial parameters. For biotechnology-derived drugs it will be venturing our capital as usual, but for traditional agents, marketing forecasts and total profitability will include a discount for a loss of revenue over the total product lifespan due to "me-toos" commercialization. Most economic data suggest a flat or slow grow profile for animal and other agricultural products in the 90's global market, so the economic impact of generic drugs may simply be percentage shifting in terms of market share among competitors with little purchaser direct pricing shifts.

For veterinary pharmacologists, the advent of the Generic Animal Drugs Program is a veritable god-send for progress. At last, there will be a recognition of the value and usefulness of the pharmacologic expertise and principles available through the Academy (AAVPT) and its membership. But along with this long overdue recognition goes a social and scientific responsibility that the public will trust. Those in the animal health business cannot afford to repeat the mistakes that occurred in the

management of human generic drugs and the resultant great collapse of confidence in both public health officials and industrial activities.

We should never be overcome with negativism, but rather consider how we can better respond to the generic animal drug challenge by establishing a "technically sound and trustworthy" better program. The first principle must be *open, open, open up* the process and allow meaningful participation on the part of less biased referees from the academic and public community.

I suggest that CVM, FDA contract promptly with the AAVPT to serve as the progenitor of the fundamental building blocks of contemporary pharmacology and their direct application to product comparability decisions under this new law. This would include advising CVM on the scientific credibility of, say, the first dozen or so approvals (and exceptionally thereafter) under the legislation. AAVPT's contribution should include the *policy* aspects as well as the technical data elements on specific products.

This suggestion is not intended to denigrate the role of CVM for they are the ultimate deciders of approvability of applications. FDA has already recognized the desirability of having such direct advice in this arena by having Dr. Gary Koritz, one of our pharmacologist colleagues, complete a sabbatical from the University of Illinois at FDA. Utilizing the AAVPT on a more permanent basis through its non-industrial members as expert panel evaluators would assure that the best available pharmacological advice is right at hand during the decision making process.

The advantages of this scheme to the public and our implementing institution, CVM/FDA, are tremendous through gaining instant credibility through openness; ensuring ready access to competent outside technical opinions; seeing that only proper flexibility in medical judgements occur; creating a legacy of contemporary procedures and logistics that will remain with the Agency at a time when much of the CVM staff is changing; and executing the mandates of Congress quickly and effectively with a sunshine approach in operations.

The greatest positive for industry is the creation and maintenance of a level playing field in which to do business through generic animal drugs. Yes, my friends, I did say "business" because without the free market capitalism we so vastly depend upon, all is lost in the pursuit of technical fulfillment of good

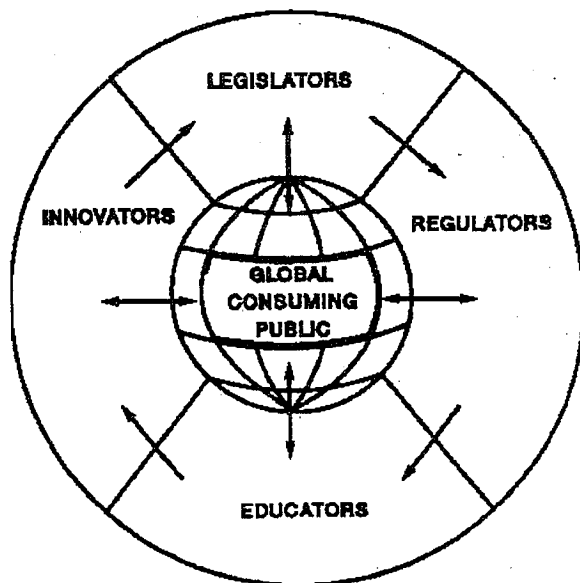
science for the world - a pursuit I took on almost 30 years ago and my technical forefathers long before that. The perceived as nasty five letter word "profit" describes the only fuel for creativity and our employment. Profit drives the engines of prosperity and sustenance for all life forms as we now know them. The strongest testament for the worthiness of honest gains in profitability is the economic revolution in Eastern Europe and the USSR which has turned to our way of doing things. All should be cheered on to loftier works.

In general, I do not feel that the means of drug comparability testing through pharmacology constitutes commercially advantageous territory. Product comparability demonstration by classical blood level techniques are well known and easy to replicate at relatively low costs.

Protocols, designs, and techniques for such work are widely available in the published literature and from the technical experience over the last two decades with human pharmaceuticals. Interpretations of the biological and medical significance of these data are much more artistic and policy setting, and in need of expert guidance and advice.

Areas of unique and commercial advantages are more prone to occur in the production drug field and with products requiring clinical comparisons for demonstrations of similarity. These contrasts are more challenging both financially and scientifically and could result in greater risk, innovation, and follow-on rewards.

1990 Business Empowerment Curve



Specifics for Action

Following are some recommendations for action for all of us to consider and discuss at this symposium and thereafter.

For the Food and Drug Administration

- Become more public "need" focused and flexible without abnegation of responsibility.
- Continue to do well the critical job of communications with the general public, who have a right to know about technology, products and regulation. Include the "activists" and heed the public lessons from BST.
- Open up your doors to available and willing talent in all you do, such as that which exists in the American Academy of Veterinary Pharmacology and Therapeutics (AAVPT).
- Engage formally with the AAVPT to assist you with startup and implementation of the Generic Animal Drug Program to include both *product* and *policy* decisions.
- Call a Products Communications Summit Conference to hear *all* points of view on labeling, flexible and traditional, and Rx versus OTC classification and then *act* for change.

For Industry

- Join in with the FDA to serve the public "need" along with obtaining necessary profit as these two objectives are not incompatible and cannot be so for the 1990's.
- Accept that the public-at-large has changed the permissible ways of doing business and are setting a new agenda for us all.
- Stop fighting the use of the Rx legend as a marketing style when FDA offers you product flexibility in either data types or generalized claims.
- Assure that all therapeutic drugs benefit from pharmacokinetic data and *make it available* for professional use regardless of a products marketing classification.
- Continue pioneer research with vigor for new technologies as therein lies social value, technical satisfaction, and true profitability as an industry.

Conclusions

On several occasions speaking before an AAVPT sponsored session, I have tried to be a catalyst for change. My great desire is to recruit you all, here today, as *change agents* par excellence for the animal

health industry and veterinary pharmacology. It is our ethical challenge to show the world that we can be trusted with the well being of our environment, animals other than ourselves, and the global food supply. It will take the combined and committed leadership within FDA, industry, and academia to take action to regain recognition from the public of our social value as technocrats, officials of institutions, and stewards of the welfare of the animal kingdom. Failing to capture the public trust, I sense we are doomed to re-enter a Second Medieval Dark Ages blocking improvements in the global quality of life for mankind and our special charge for all living things.

The 21st century is nearly upon us (it literally is only a heart beat away) and what we do today will become the world's scenario in the year 2001. I am proud to have done what I have and so *you* should be too. You have the freedom as the U.S. Army advertises to "be all you can be". You have little and more likely nothing to apologize for from the past (for what can you do about it anyway?) but you have *much* to do for the future of this planet...and we must do it *right the first time*.

Acknowledgement

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References

Caesar, Gains Julius (46 BC) Ed., Pope Gregory XIII (1582 AD).

"CYA" (1989), *Anonymous Personal Communication*.

Generic Animal Drug and Patent Term Restoration Act (1988), Public Law No. 100-670, Washington, D.C., 21CFR Part 500, Subchapter E, Animal Drugs inclusive.

Price, R. (eds.), Improving Risk Communication, National Research Council, pp. 2-11. National Academy Press, Washington, D.C.