

# Maintaining Academic Creativity in Industry - Related Research

**Jim E. Riviere, D.V.M., Ph.D.**

*Burroughs Wellcome Fund Distinguished Professor of Veterinary Pharmacology and  
Director, Cutaneous Pharmacology and Toxicology Center, College of Veterinary Medicine  
North Carolina State University, Raleigh, North Carolina 27606*

---

## Introduction

The purpose of this presentation is to overview how an industry-supported academic research program would ideally be structured to optimize intellectual creativity in a university environment. I will take the approach of Plato (Jowett, 1871) by considering what I would define as the "ultimate form" of a "perfect" research program. Such a program would meet all conceivable goals thereby keeping all involved parties fully satisfied. Of course in such an ephemeral world, financial constraints would never exist.

In order to accomplish this goal, one must first define what all parties in this endeavor actually want out of a research relationship. Although there are only two primary players, the industrial and university partners, each of these in turn are internally divided into groups with potentially conflicting needs. When financial and temporal constraints are applied, these turn into potentially conflicting priorities.

## Industrial Goals Through the Eyes of an Academician

The needs of industry have been well reviewed by the other speakers in this symposium. They primarily relate to drug development with the end product being a new or improved pharmaceutical which is safe, efficacious, and approvable by FDA. This product should generate a profit for the company's stockholders when it reaches the marketplace and successfully compete against existing therapeutic modalities.

Each of these goals can be expanded into another hierarchy of needs. For example, FDA approvability brings up concerns of formulation stability, rigid study designs which will meet regulations, and of course quality assurance. Similarly, marketing will demand that studies demonstrate the efficacy of the product being studied and if possible, its superiority over those of competitors.

The above criteria primarily are determined by development and marketing needs. What this author would consider more closely aligned with academic concerns would be early research in drug discovery and preclinical studies. These types of research projects are less constrained and have open experimental designs. Often, research collaboration with academia is supported so that the industrial researchers can keep a "pulse" on what is happening in university research laboratories.

## Goals of Academia

In contrast, the needs of academia are different. The mission of a modern research university falls into the convenient categories of teaching, research and service. The programs discussed in this presentation relate primarily to graduate education and research, not the professional DVM curriculum. This author has previously touched upon some of these concerns in the Sixth and Seventh AAVPT Symposiums (Riviere, 1988; 1992).

Most veterinary colleges would become involved with industrial funded pharmaceutical research in order to

support the research needs of faculty and to provide the mechanism for training graduate students or more recently, clinical pharmacology residents.

In order to exist in a modern university environment, faculty must show evidence of scholarly activity which generally is reflected in publications. Depending on the type of research, such primary evidence of intellectual productivity may also take the form of patents or registered copyrights for new computer software development.

Any other evidence of peer-reviewed research productivity will count toward evidence of a successful academic career. This includes success in getting extramural funding from *competitive* sources. Whether intentional or not, this tends to be biased toward federal support. In order for such funds to support graduate student training, it generally has to be for multiple years. Sometime small, "one shot" industrial contracts often can be helpful to the academician to obtain support for pilot studies; however their utility pales in comparison to multi-year grants from agencies such as NIH or USDA. To some in academia, the latter sources of funding are also considered more "prestigious."

The needs of an academician are also directly related to the type of appointment the individual holds and to the nature of the department to which he or she is appointed. Thus, a person in a "basic science" department such as pharmacology or physiology, who has a large time assigned to research, would tend to feel the large grant pressure more so than an individual in a "clinical" department with a smaller effort assigned to research. In the latter case, smaller grants may leverage clinical research activity and provide material to train residents in research techniques. Because resident training usually is associated with the teaching hospital, there is not the requirement for all grants to get full cost recovery as is discussed below for basic research grants. These costs are often covered by the hospital and thus ultimately the client. For the new breed of ACVCP

certified clinical pharmacologists, this type of funding may be very useful.

Graduate student education is a primary mission. In order to train graduate students in the "art" of research, it is the opinion of this author that there should be minimal constraints on the experimental design or scope of a research question. The student should become familiar with the field of study and with the help of an advisor, select an important and exciting topic to address. Pilot studies are then conducted and the "art" of experimental design learned. By staging research into successive studies, questions are progressively answered, new hypotheses developed, and the investigative abilities of the student honed. Finally, there should be no publication restrictions which would impede the student from getting "public credit and review" of their research results. Viewed from another perspective, the student should be able to demonstrate to prospective employers evidence of peer-acceptance of a research project. Confidential reports often required by industry do not serve this purpose.

### **The Ideal Academic-Industrial Collaboration.**

With the goals of both parties in hand, what is the ideal collaboration? First, the research topic should be broadly defined so as to leave sufficient latitude of experimental design for the student to be able to exercise some creativity. Second, the academic advisor and the industrial scientist should be able to meet openly with the student and serve as a sounding board for experimental ideas. They *should not* dictate experimental design! This distinguishes the investigative scientist from the technician. Third, the topic of study should be exciting, important and *not* be bound by confidentiality restrictions. In this way the student can openly discuss the work with other faculty and present "research in progress" at local seminars. This work would involve a topic that the pharmaceutical company would be

interested in promoting, possibly with portions of it restricted because of the needs for regulatory approval.

Fourth, the project should be of sufficient duration that the "trial and error" concept discussed earlier can be fully implemented throughout the student's doctoral program. This must be viewed in the context of other responsibilities of the student (e.g. classes, teaching duties, clinical cases for a resident, examinations). Fifth, the project must provide sufficient capital to insure that the proper equipment is available and that funds are sufficient to cover the inevitable mistakes that may occur in the early process of student learning. In many cases, funds are also needed to cover the student's stipend, additional technical support, supply and animal costs, services, hazardous material and radiation safety surcharges, faculty salary cost-sharing and institutional indirect costs, all items which are included on the typical federally-supported research grant. Also, these costs must be uniformly charged on all extramural grants and contracts and justified in the event of audit. This has become especially true in 90's when federal agencies must prove that universities charge equally for all of their services.

### **The Realities of Modern Economics**

Now that we have discussed the ideal situation, let us get realistic! First, the profit potential and market size of veterinary pharmaceuticals pale in relation to human drugs, especially where small animal and exotic species are concerned. Thus, the R&D budgets of animal health products are likewise a small fraction of that available to human R&D expenditures. However, the costs of running a university research laboratory are essentially identical whether it is investigating animal or human drugs. Secondly, the regulatory climate for veterinary pharmaceuticals is not slackening, nor should it. However, "extra"

development funds are not pouring into industrial research budgets.

The third economic fact is that state government budgets, which once subsidized graduate education, have contracted to the point that minimal funds are available to directly subsidize veterinary pharmacology research. There is also the impression that such drug-related research should be supported by industry funds. Lets face it, both industrial and state budgets have uniformly undergone contraction, not expansion! Finally, federal funds available specifically to fund veterinary pharmacology research *do not exist* as there once was with the FDA Minor Species Consortium. IR4 funds are available, but again these are development and *not* basic research funds. They are probably appropriate for training clinical pharmacology residents. NIH funds are available, but only if the research can be shown to be relevant to human health.

### **Personal Perspective**

As any astute reader can appreciate, this is not good news for the future of veterinary pharmacology. I can best illustrate what I see as a crisis in veterinary pharmacology research by illustrating my experiences over the past decade or so. I take my perspective from four vantage points. The first, is as the recipient of federal (NIH, USDA, DoD) and both human and veterinary pharmaceutical industry funding. The second, is through monitoring of veterinary pharmacology research productivity as a former editor of the *Journal of Veterinary Pharmacology and Therapeutics* and as a co-founder and participant in FARAD. The third is as an advisor to pharmacology graduate students and the fourth is as a consultant to all the actors in this play.

As far as I can ascertain, the primary support of veterinary research is directed toward clinical trials and pre-clinical pharmacokinetic studies. All of these studies appear very directed toward specific drug approval endpoints. This is

expected since this is the primary goal of industrial R&D programs. Secondly the size of these grants is generally in the \$10,000-30,000 per year range, and in some cases, they are significantly smaller. There is little flexibility in experimental design since if the protocols are significantly varied, the data will not serve the regulatory requirements. These studies are the primary generators of pharmacokinetic data in the veterinary literature. They also support a lot of analytical methods development. However, are they the primary support for generating new ways to do pharmacokinetics?

Our research group has been the recipient of a significant amount of human pharmaceutical research funding which can be divided into two distinct categories. The first is very similar to that described above for veterinary firms, both in intent and dollar size. Although these studies generated some interesting results, they did not support any thesis research or contribute to infrastructure costs. Both these smaller grants and my veterinary support also were worked on by graduate students whose stipends were supported by veterinary school funds.

In contrast, the average size of the larger industrial grants was about \$250,000 per year and most ran for a minimal period of three years. These grants were essentially indistinguishable from my federally-supported work and fully supported the costs of a post-DVM graduate student. These grants generally consisted of two parts: a basic research component which was totally controlled by the graduate student's research needs and a restricted, GLP development program which served the needs of the industrial sponsor. All of these programs generated significant publications and even resulted in some patents. Although they all utilized pigs as the primary species, none had a direct veterinary endpoint.

The typical federal grant was approximately \$250,000 per year and usually ran for three year periods. These grants covered full costs of doing research including paying for graduate student

stipends and salary recovery for faculty salaries. The majority of my graduate students were supported from these funds. If it were not for these larger types of grants, I doubt that our laboratory could ever have afforded to even be involved in the smaller veterinary oriented projects. Typical for all of these grants was complete freedom in experimental design and publication.

## Discussion

If one looks at the structure of pharmacology nationwide, one sees a decrease in the number of pure veterinary-oriented research programs. One also sees a greater number of non-DVM PhDs in the most productive departments, which are primarily supported by NIH type funding. Most of veterinary pharmacology is being directed at analytical methods development and clinical pharmacology and applied pharmacokinetics. This may be good for the ACVCP, however, it is not a healthy direction for basic veterinary pharmacology.

A great deal of excellent pharmacology is also being conducted in oncology programs nationwide, much of this supported by NCI funding. However, who is supporting and or studying basic veterinary pharmacology?

Lest we forget, there are some major problems in veterinary pharmacology that need studying. Much of human pharmacokinetics is moving toward physiological modeling. This has not occurred in veterinary species where it would be very useful for interspecies extrapolation. The whole area of interspecies extrapolation is conducted for toxicology or oncology endpoints. Tissue residues are ignored in cutting-edge pharmacokinetic research as are covalent residues. Drug metabolism is exploding, yet novel techniques have not been widely applied to veterinary species for the purpose of animal health. Novel methods of drug delivery research may occur within some industrial labs; however, they are not being studied in academic labs. Is there a

critical nucleus of biochemical pharmacology labs in veterinary schools studying veterinary problems? It is probable that a focused research effort in some of these areas (e.g. interspecies extrapolations, residues) could decrease regulatory requirements and thus drug development costs.

I trust most agree that the reason behind this lack of veterinary pharmacological prowess is funding. As state budgets have contracted and as faculty search for research topics, it is easy to see why the above situation has developed. I have even seen the situation with new post-DVM students in my lab when selecting a research project. They go where the support and unrestricted funds are which allows them the most potential to be creative and offers them the most security for actually getting the research done! If this trend continues, who will support the training of veterinary pharmacologists interested in veterinary pharmacological endpoints?

In fact, this is the crux of my answer to the question posed in the title of this presentation. The way to maintain academic creativity in industry-related research is to provide an atmosphere that has the least restrictions and most freedom in experimental design. This requires stable funding sources. If this is to benefit veterinary pharmacology, then the overall direction of the projects must be in this field. I thus challenge those responsible for funding veterinary pharmacological research to realize the long term implications of the current strategies to the production of basic veterinary researchers in the future. Additionally, who will provide the funds for supporting ACVCP training programs? These issues must be addressed if there is to be any future for veterinary pharmacology!

### Acknowledgment

The author thanks Drs. Art Aronson and Mark Papich of NCSU for their comments on this manuscript.

### References

Jowett, B. (1871) *The Dialogue of Plato*, Jefferson Press, Boston.

Riviere, J.E. (1988) Integration of pharmacology research and graduate training. *Proc. 6th Biennial A.A.V.P.T. Symposium*, 66-69.

Riviere, J.E. (1992) Role of veterinary pharmacologists in academia in the 1990's. *Proc. 6th Biennial A.A.V.P.T. Symposium*, 39-42.