

# Veterinary Drug Standards and Information

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## What is USP and Why is it Unique?

If I was to ask a group of veterinarians to describe USP, most of them could not do it. In fact, if the same question was posed to veterinary pharmacists, we would in all probability get the same result. There may be a general recognition of what USP is and does, but the exact workings of the organization and its potential for impact on veterinary practice largely remain unrecognized and a mystery to most health care professionals.

So, for those of you who need it, here is a quick, basic primer on USP:

- USP is not part of the federal government; it is a private, not-for-profit organization. At the same time, however, the work USP does in establishing official drug standards of strength, quality, purity, packaging, and labeling is enforceable by the Food and Drug Administration and all manufacturers must meet the standards USP sets.
- USP does not represent medicine, pharmacy, or any of the other professions. It is essentially a public interest organization. Although the governing body that elects members of the Board of Trustees and Committee of Revision is comprised of delegates from the medical professions and other interested groups, the decisions made relating to drug standards and information are intended to protect the public's health.
- USP is not controlled by the U.S. government, by the pharmaceutical industry, or by any special interest group. Although the views of all interested parties are considered in the decision-making process, the decisions are made by elected experts serving on the Committee of Revision and are based on scientific and medical fact.
- USP gets no money for its ongoing standards and information development programs from government, industry, or the organized professions. All income for these programs is self-generated, allowing

decisions to be made on scientific/medical merit and not on who is paying the bills.

- The decisions made by USP are made by the experts elected to the Committee of Revision and its associated advisory panels. Staff has no vote and serves only to facilitate the work of the Committee. Thus, decisions relating to drug standards and information remain under the control of the professions, who are ultimately responsible for patient care.

## How and Why did USP Start?

USP predates organized medicine and pharmacy in the U.S. by several decades. In 1820, physicians concerned with standardization of the medicinals they were using in their practices, established USP to develop common standards (or at that time, recipes) for the preparations considered to be the best available. Their work, which took place in the old Senate chamber of the U.S. Capitol, resulted in the publication of the 1st U.S. Pharmacopeia, and allowed practitioners and patients to have confidence in what was prescribed and dispensed, whether the transaction took place in Massachusetts or North Carolina.

Several decades later, the profession of pharmacy became a participant in the revision process; and several decades after that, the U.S. Congress recognized the standards of strength, quality, and purity as set by the USP Convention (along with those set by the National Formulary and the Homeopathic Pharmacopeia) as being the enforceable standards for drugs in the United States.

Thus, USP was started to meet the needs of the public in relation to the quality of drugs prescribed and dispensed. The professions saw a need that transcended their individual practices and took steps to rectify it. And the U.S. Congress, in recognizing the importance of those same needs, institutionalized the work of USP rather than establishing another center within government to react to those needs.

## What Has Happened Since?

USP continues to set the official drug standards of strength, quality, purity, packaging, and labeling for the United States (and in fact for a sizeable percentage of the world). But there are new activities as well. Just as physicians reacted to a specific need in 1820, other needs have surfaced and have been responded to. Of particular relevance to the veterinary community are the following:

Need #1: Drug information--In 1970, delegates to the USP Convention indicated that programs should be established to develop clinically relevant information for prescribers, dispensers, and patients. The consensus was that the drug information needs of practitioners were not being met by manufacturer-developed, FDA-approved product labeling as published in the *Physicians Desk Reference*. And drug information materials for the patient were practically nonexistent.

The result--*USP DI*, a clinically-relevant, consensus-based, continuously-revised data base directed at both the health care provider and the patient was developed. And just as the drug standards initially established in 1820 were eventually recognized by state and federal governments over time, we are now seeing the same thing with the *USP DI* data base. For example, *USP DI* was specified (along with AMA-DE and AHFS-DI) in the Medicare Catastrophic Health Coverage Act of 1988 as being the base for determining the acceptability of using FDA-approved drugs for unlabeled ("unapproved") indications; third party payers across the country, including Medicaid carriers, are using *USP DI* in the same way; and, over a dozen states in their pharmacy practice acts now recognize *USP DI* as a primary source of information necessary for the practice of pharmacy.

Need #2: Veterinary drug standards and information--In 1990, delegates to the Quinquennial meeting of the USP Convention passed the following resolution: "The United States Pharmacopeial Convention is encouraged to develop USP standards and information for additional veterinary drugs."

Although there are few words in this resolution, it is power packed. Delegates to the Convention have told us that the veterinary area is an important one to focus on during the upcoming 5-year revision period.

The work and recommendations of the Veterinary Medicine Advisory Panel over the past 10 years, coupled with the speech Dr. Art Aronson

made to the delegates to the USP Convention at their March meeting, had a very significant impact on the actions taken.

## What Has USP Done to Date in the Veterinary Area?

It is important to recognize that the 1990 veterinary resolution does not open a new area of work for USP; rather, it emphasizes the fact that more work needs to be done in relation to veterinary drugs and resources should be allocated accordingly.

On the drug standards side of USP, standards of strength, quality, purity, packaging, and labeling for human drugs and dosage forms apply to veterinary products as well. Thus, a large number of drugs and dosage forms that are used both in human and animal populations are already covered. In addition, USP drug standards monographs for a number of veterinary-specific drugs and dosage forms (3 for amprolium and 29 for antibiotics) already have been developed.

On the drug information side, the Expert Advisory Panel on Veterinary Medicine under the leadership of Dr. Lloyd Davis (who has chaired the Panel since its inception in 1980, and has just been re-elected to another 5-year term), has developed 29 veterinary drug information monographs that cover 32 drug substances and 85 dosage forms. In addition, a "Veterinary precautions" subsection has been added to human drug monographs to alert health care professionals to potential dangers with certain drugs in various animal species.

For those of you unfamiliar with the work of our Veterinary Medicine Panel, in a typical veterinary monograph you will find the following types of information:

- Indications for use (including both FDA-labeled and medically accepted but unlabeled uses; of the 83 indications listed in the current 29 USP DI veterinary monographs, 44 are not included in the FDA-approved product labeling; for the 6 veterinary only monographs, the breakdown is 7 approved and 10 unlabeled indications; for the 6 monographs covering drugs approved for humans but not animals, there are 16 unlabeled indications; and for the 17 monographs covering drugs approved for both veterinary and human use, there are 32 labeled and 18 unlabeled indications)
- Chemistry

- Pharmacology/pharmacokinetics
- Precautions to consider, including:
  - species sensitivity
  - pregnancy/reproduction
  - lactation
  - pediatrics
  - geriatrics
  - drug interactions
  - medical problems/contraindications
  - diagnostic interference
  - patient monitoring
  - regulatory considerations
- Side/adverse effects
- Client consultation guidelines
- Veterinary dosing information (doses, treatment of overdose)
- Withdrawal times
- Dosage forms/strengths available
- Incompatibilities
- Packaging and storage
- USP requirements

### What's Next?

In response to the 1990 veterinary resolution, staff submitted to the Board of Trustees the following plan for meeting the intent of the resolution:

#### Objectives for FY '91

- Identify all drug substances and dosage forms used exclusively in animals and assign priorities for standards development.
- Identify all drug substances used in animals and assign priorities for information development.
- Publish not fewer than two monograph proposals for animal drugs in *Pharmacoepial Forum*.
- Develop 25 new veterinary monographs for inclusion in the USP DI data base.

#### Goals for 1995

- Establish standards (at least through *Pharmacoepial Forum*) for all drugs and unique dosage forms used exclusively in animals.
- Develop USP Official Reference Standards for at least 75% of all drugs used in animals.
- Create information monographs through the

USP DI process for each animal drug and for the major human drugs used in animals, and publish in the *USP DI*, or in a new product, animal drug information for veterinarians and animal owners.

This plan was accepted by our Board of Trustees, and staff is in the process of planning specific steps for implementation. There is much work to be done.

### Developing Information on Veterinary Drugs.

The information development process for veterinary drugs follows the same process that we have been using since 1977 in the development of human use drugs. Essentially the process is a two-tiered consensus generating system that encompasses both Delphi and group processes. Specifically, the steps involved are as follows:

#### Phase One (Internal)

- Parameters are established by the Drug Information Division Executive Committee on an annual basis, utilizing user input.
- Drafts of information are developed by USP staff, utilizing U.S. and Canadian product labeling, labeling from other countries, the literature, and comments received.
- Drafts are reviewed by USP expert advisory panels, by ad hoc reviewers who are expert in the use of the particular agent, and by manufacturers.
- Re-iterative feedback cycle(s) allow the advisory panel reviewers to see proposed changes based on the previous round(s) of review.
- Initial consensus of USP advisory panels is established.

#### Phase Two (External)

- Initial consensus drafts are published in *USP DI Review*.
- This second level of review allows any interested party to review and comment on the proposed text.
- Comments received from the public review are fed back to the panels for consideration.
- Republication of revised text in *USP DI Review* allows for additional public comment.

- Final consensus by the expert advisory panels is determined and the text is released for inclusion in the *USP DI* data base.

This information development process is labor intensive and expensive but maintaining the integrity of the process is critical to the work that USP does. Whether its developing public standards or establishing drug use guidelines, the processes used must be beyond reproach. They must be as unbiased as they possibly can be; they must be open; they must be responsive to change; and the decisions made must rest with the experts, not the bureaucrats.

### Participating in USP Activities.

As more work is done on veterinary drug standards and information, and as the impact of USP's activities on veterinary practice becomes more significant, greater involvement of the veterinary community is essential. USP does not dictate to the veterinary community; USP is the veterinary community.

### What are the Possibilities?

- Reviewing draft text--The more veterinary reviewers that participate in the information development process, the better. Just as we have a stable of hundreds of ad hoc experts who review human use drug monographs, we need a stable of veterinary reviewers providing a similar type of review, feeding comments to the Veterinary Medicine Advisory Panel for consideration. This review can occur on the initial drafts considered in the phase one process or it can occur during phase two, with review of text published in *USP DI Review*. Input can come from teachers, researchers, practitioners, students, consumers, regulators, or manufacturers.
- Serving on the USP Committee of Revision

or the Veterinary Medicine Advisory Panel--Although participation is more limited at this level because of a defined number of positions, the individuals serving in these positions are key to USP's work in the veterinary area. There is one position on the Committee of Revision for Veterinary Medicine that is filled by election every 5 years. And to support this position, and Expert Advisory Panel on Veterinary Medicine is appointed. All individuals serve in a voluntary capacity.

- Participating in the USP Convention--The USP Convention is comprised of delegates from schools and state associations of medicine and pharmacy, and national associations and Federal agencies with an interest in drugs. The only representation from veterinary medicine is the American Veterinary Medical Association. Should there be other representation? Although easier said than done since all new members to USPC must be voted on by members of the Convention, additional veterinary representation may be appropriate for consideration in light of USP's new efforts in the veterinary area. Should AAVPT seek membership? Should all veterinary schools have the opportunity to appoint a delegate just as all medical and pharmacy schools do now? These are issues you have to discuss. But the time is appropriate since one of the resolutions passed at our Convention this year directed us to look at expanded representation.

### In Summary.

USP is doing much in the veterinary area. We are trying to react to the needs of the public and the practitioners involved in veterinary practice. And we need your help.

