Pharmacotherapeutics for Veterinary Dispensing

Edited by
Katrina L. Mealey

WILEY Blackwell
Pharmacotherapeutics for Veterinary Dispensing
This book is dedicated to the two loves of my life: My husband, Bob, who shares my love of veterinary medicine and my son, Stephen, who shares my love of pharmacology.
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Preface

*The greatness of a nation and its moral progress can be judged by the way its animals are treated.*

Mahatma Gandhi

A number of in-depth veterinary pharmacology resources have been written that are aimed at the veterinary profession (veterinarians, veterinary students, and veterinary researchers). Similarly, there are a multitude of clinical pharmacology and pharmacotherapeutics resources available on the human side aimed at physicians and pharmacists. To our knowledge, this book represents the first effort to “marry” the disciplines of veterinary medicine and pharmacy.

Veterinary medicine, and veterinary pharmacotherapeutics in particular, are undergoing immense changes. No longer is veterinary pharmacology an inexact extension of human pharmacology. Veterinary pharmaceutical products are no longer discarded human drug candidates that are subsequently developed for animals. Targeted enzyme pathway inhibitors (tyrosine kinase and JAK kinase) and even species-specific monoclonal antibody therapies have been developed by the veterinary pharmaceutical industry and are currently marketed for veterinary patients. The companion animal pharmaceutical market is a multibillion dollar per year industry. In an effort to gain part of this market share, corporate (traditionally “human”) pharmacies have actively lobbied to introduce legislation at both state and federal levels that requires veterinarians to provide prescriptions to pet owners rather than dispense drugs directly to pet owners. Veterinarians have independently started writing more outpatient prescriptions rather than dispensing drugs from their own formulary because (i) carrying a large drug inventory is expensive, and (ii) a number of human-approved formulations are used off-label for companion animal disorders.

Consequently, pharmacists are increasingly encountering pet owners in their pharmacies, dispensing drugs for veterinary patients, and being asked to provide counseling on veterinary pharmacotherapeutics. Unfortunately, most pharmacists are not adequately trained to provide these services for veterinary patients. The wealth of information pharmacists acquire in pharmacy school regarding “human” medicine, pharmacology, therapeutics, and so on is often not applicable to other species. Because the pharmacy oath is not limited to one species (i.e. human patients), all pharmacists have an obligation to gain the knowledge and skills necessary to assure optimal outcomes for *all* patients (human and animal).

The primary goal of this book, therefore, is to improve safety and efficacy of pharmacotherapeutics in veterinary patients – to minimize mistakes based on the presumption that human pharmacology applies to all species, and to maximize therapeutic efficacy by enabling pharmacists to be an integral member of the veterinary healthcare team. The book is not intended (nor is it possible) to include every drug and indication for each veterinary species. The book is not intended
to rehash information that pharmacists and pharmacy students have already mastered (i.e. mechanisms of action of drugs used in humans). To emphasize important points, text boxes are used throughout the book. Yellow boxes indicate “Practiced but Not Proven” use of medications by veterinarians (common use of a particular drug without strong evidence supporting that use). Gray boxes indicate when there is a “Dramatic Difference” between species with respect to drug disposition, particularly between humans and animals. Pink boxes indicate “Mandatory Monitoring” for a particular drug, providing the reader with information that can be used to counsel pet owners.

Each contributor, whether a veterinarian, pharmacist, or both, is a recognized expert in his or her field, having received advanced training, achieving certification in their discipline, and most importantly having acquired extensive clinical experience. Collectively, we hope this text will enable more Schools of Pharmacy to provide courses in veterinary (or comparative) pharmacology and/or veterinary pharmacotherapeutics because it isn’t enough to know that a dog is not a small person and a cat is not a small dog.
1

Introduction to Veterinary Pharmacy

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Key Points

- Several organizations exist that support veterinary pharmacy practice, including a training and credentialing process that culminates in the designation of Diplomate, International College of Veterinary Pharmacy (ICVP).
- Veterinary pharmacists are uniquely trained specialists that provide competent care and drug products to nonhuman species and can be resources for community pharmacists dispensing drugs to animals.
- Veterinary pharmacotherapy is rapidly entering the mainstream of pharmacy practice, despite the fact that most pharmacists are not adequately trained in the field.
- Veterinary drug law is significantly different from human drug law. For example, there is not currently a legal avenue for pharmacists to recommend human over-the-counter (OTC) drug products for veterinary patients.
- Veterinary pharmacy residency training programs have grown substantially since 1989.
- Core competencies for veterinary pharmacy education must be standardized and uniformly implemented across pharmacy school curricula.

1.1 Introduction

Although the practice of providing medicinal therapy to animals dates back to the Mesopotamian healer Urlugaledinna in 3000 BCE (Royal College of Veterinary Surgeons 2017), it took society nearly 5000 years to realize that pharmacists were well-placed medical professionals that could provide safe and effective pharmacotherapy and monitoring to animal patients as well as to humans. In 1761, the first college of veterinary medicine was established in Lyon, France (Larkin 2010); and from that time until the mid-twentieth century, the preparation, dispensing, and monitoring of medicinal agents for animals were almost exclusively performed by veterinarians. In the late twentieth century, the practice of clinical pharmacy for human medicine was established, and veterinary professionals began to recognize the unique therapeutic contributions made by clinically trained Doctors of Pharmacy. Veterinary pharmacy, which is practiced by pharmacists, is unique from the field of veterinary pharmacology, which is practiced by veterinarians, because it encompasses a three-pronged approach that utilizes medicinal chemistry, pharmacology, and species-specific pharmacotherapeutics to evaluate the best action plan for a specific patient.
Beginning with a handful of pharmacists interested in veterinary medicine, veterinary pharmacy has now evolved into a globally impactful specialty area of pharmacy practice and residency training programs and encompasses a broad spectrum of practice settings, including veterinary teaching hospitals, veterinary medical practices, community pharmacies, governmental agencies, and the pharmaceutical industry.

While most pharmacists are not trained as veterinary pharmacy specialists, most community pharmacists will encounter prescriptions for nonhuman patients in their practice. A survey of more than 13,000 licensed pharmacists in North Carolina revealed that 77% of respondents filled prescriptions for animal patients in their practice (Sorah et al. 2015). A similar survey of pharmacists in Oregon also revealed that 77% of respondents filled prescriptions for veterinary patients (Mingura 2017). Pharmacists are the only healthcare professionals expected by society – and legally permitted by regulatory authorities – to provide pharmaceutical care and drug products for all species. Yet despite this unique position, only 4% of pharmacy students who graduated in 2015 reported receiving any training in veterinary pharmacy (Arnish et al. 2015). In fact, the pharmacy oath (Figure 1.1) does not distinguish between human patients and veterinary patients. Despite the lack of standardized education in veterinary pharmacy, a US Food and Drug Administration (FDA) guidance document released in 2015 estimated that 75,000 pharmacies fill 6,350,000 compounded prescriptions for animal patients annually (FDA 2015). It is important to note that this estimate was only for compounded veterinary prescriptions and did not account for the number of all prescriptions dispensed from pharmacies to animals. Because most pharmacists have not received adequate training in comparative pharmacology and veterinary pharmacotherapeutics, one would have to question whether pharmacists are fulfilling the oath’s obligations when it comes to dispensing drugs to veterinary patients.

Drugs that achieve desired therapeutic effects in humans do not always produce the same effects in nonhuman patients, and vice versa. Using the wrong drug or the wrong dose of medications in animals can result in therapeutic failure or serious adverse events. In addition, statutes, regulations, rules, and guidance for drug use in animals are significantly different from those for humans, particularly with respect to animal species whose tissues or milk may be consumed by humans. Consequently, there is a critical need for community pharmacists to understand basic comparative pharmacology principles, laws surrounding drug use in food animal species, and pharmacotherapy of common veterinary diseases in order to serve

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Figure 1.1 The pharmacist’s oath.

"I promise to devote myself to a lifetime of service to others through the profession of pharmacy. In fulfilling this vow:

- I will consider the welfare of humanity and relief of suffering my primary concerns.
- I will apply my knowledge, experience, and skills to the best of my ability to assure optimal outcomes for my patients.
- I will respect and protect all personal and health information entrusted to me.
- I will accept the lifelong obligation to improve my professional knowledge and competence.
- I will hold myself and my colleagues to the highest principles of our profession’s moral, ethical, and legal conduct.
- I will embrace and advocate changes that improve patient care.
- I will utilize my knowledge, skills, experiences, and values to prepare the next generation of pharmacists.

I take these vows voluntarily with the full realization of the responsibility with which I am entrusted by the public."
the needs of the pet‐owning public. There is an additional need for a designated veterinary pharmacy specialty to meet the unique needs of providing legally compliant pharmaceutical products, compounds, counseling, and monitoring of veterinary patients on an in‐patient basis, as well as serving as a resource for community pharmacists outside of the veterinary practice setting.

1.1. History

Historically, the role of pharmacists in veterinary medicine was limited to incidental compounding of medications and dispensing human‐approved prescription drugs for pets within the community pharmacy practice. Veterinary pharmacy, as an exclusive practice, originated in colleges of veterinary medicine in North America. In 1965, Laurence Reed Enos, PharmD, became the first veterinary pharmacist when he was hired by the University of California (UC) Davis School of Veterinary Medicine (Laurence Reed Enos, personal communication, May 9, 2011; Jeanne Enos, personal communication, June 13, 2016). Clinical pharmacy was just beginning in human medicine at that time, and Dr. Enos was hired to serve a clinical role providing pharmaceutical care for veterinary patients and to provide education in pharmacotherapeutic principles to veterinary students. He held administrative, teaching, and service roles within both the School of Veterinary Medicine and the College of Pharmacy during his 37 years of practice there. His philosophy was to develop a strong clinical program in veterinary pharmacy that emphasized teaching, research, and therapeutics. In 1968, Faye Kernan, BSP, MTS, became Canada’s first veterinary pharmacist, hired by the Western College of Veterinary Medicine at the University of Saskatchewan (Faye Kernan, personal communication, May 9, 2011). Like her US counterpart at UC Davis, Ms. Kernan established a model for veterinary pharmacy practice and earned tremendous respect from her veterinarian and pharmacist peers. Fifty years later, Kernan remains an active and vital contributor to veterinary pharmacy practice. Several other veterinary schools followed suit in hiring pharmacists in the late 1970s and early 1980s, and today all but one of the veterinary schools in the USA and Canada employ at least one pharmacist in a faculty, administrative, or professional staff position. In 1982, a group of veterinary pharmacists, including Kernan, met in Lincoln, Nebraska, to establish the Society of Veterinary Hospital Pharmacists (SVHP), the first professional organization representing veterinary pharmacists. The organization has steadily grown and now hosts more than 165 veterinary pharmacist members practicing throughout the world. In 1989, the Auburn University College of Veterinary Medicine and College of Pharmacy collaborated to create the first veterinary pharmacy residency program, and selected Dr. Bobbi Anglin as the first veterinary pharmacy resident (Dr. Sue Duran, personal communication, Auburn University College of Veterinary Medicine, March 19, 2017). Since then, UC Davis, North Carolina State University, Purdue University, and the University of Wisconsin have all established veterinary pharmacy residency training programs, producing many residency‐trained veterinary pharmacists. Compared to their humble beginnings in 1965, today’s veterinary pharmacists provide a significant and positive impact on animal healthcare.

1.2 Veterinary Pharmacy Professional Organizations

1.2.1 Society of Veterinary Hospital Pharmacists

The SVHP is an organization of pharmacists who work exclusively in the veterinary field, primarily at veterinary teaching hospitals in colleges of veterinary medicine (see www.svhp.org). Membership is international; the USA, Canada, the Netherlands, Denmark, South Africa, Australia, Spain, Austria, and New Zealand are currently represented.
The SVHP membership meets annually to participate in the Accreditation Council for Pharmacy Education (ACPE) and accredited continuing education activities, and to exchange ideas and information about veterinary pharmacy practice. While membership as an SVHP Fellow is restricted to licensed pharmacists who practice in nonprofit veterinary institutional settings providing professional service, teaching, or research (or some combination thereof), associate membership is open to pharmacists, veterinarians, and other animal health professionals who have an interest in veterinary pharmacy. The number of practicing veterinary hospital pharmacists continues to grow steadily.

1.2.2 International College of Veterinary Pharmacy

In 2000, the International College of Veterinary Pharmacy (ICVP) was established by the SVHP to develop a recognized specialty college and certification for veterinary hospital pharmacy. Appropriately trained SVHP Fellows would qualify for specialty certification through an arduous credentialing process and would then be eligible to sit for a rigorous certification examination. In 2001, the first 13 diplomates of the ICVP were awarded the credentials of Diplomate, ICVP. Today, there are 31 diplomates of ICVP, with approximately 10 additional candidates undergoing the certification process.

1.2.3 American College of Veterinary Pharmacists

The American College of Veterinary Pharmacists (ACVP) is affiliated with the American College of Apothecaries and was established to support the efforts of independent pharmacists in developing and strengthening the services they provide for animals and strengthening the support services they provide for veterinarians. Pharmacist membership is open to any licensed pharmacist meeting ACVP Practice Standards. ACVP develops and disseminates ACPE-accredited educational materials, sponsors programs (including compounding and disease state management courses), serves as an information resource, and works closely with allied organizations to enhance the veterinary pharmacy care offered by pharmacy practitioners.

1.3 Veterinary Organizations with Pharmacological Expertise

1.3.1 The American Academy of Veterinary Pharmacology and Therapeutics (AAVPT)

The AAVPT was founded in 1977 and consists of approximately 300 veterinary pharmacology trained professionals from over 20 countries. Members of AAVPT share a common interest in research and teaching in veterinary pharmacology. The Academy’s stated objectives are to support and promote education and research in comparative pharmacology, clinical veterinary pharmacology, and other aspects of pharmacology of interest to the veterinary profession; to sponsor a journal publishing related pharmacology manuscripts; to provide educational meetings and symposia in veterinary pharmacology and therapeutics; to enhance the exchange of educational materials and ideas among veterinary pharmacologists; and to organize advisory committees of experts to address problems in veterinary therapeutics. The AAVPT has been very supportive to veterinary pharmacists since its inception and has welcomed many of them into its membership.

1.3.2 The American College of Veterinary Clinical Pharmacology (ACVCP)

Similar to the relationship between the SVHP and ICVP, the ACVCP originated from the AAVPT in 1990 as an AVMA-recognized board specialty in veterinary clinical pharmacology. Veterinarians must complete a residency, board examinations, and graduate training in veterinary clinical pharmacology to
achieve diplomate status. The logo of ACVCP demonstrates the college’s commitment to advancing the practice of clinical pharmacology in veterinary medicine: “To cure with compassion, knowledge, and diligence.” More than 60 veterinary pharmacologists have achieved diplomate status in ACVCP, with many more pursuing certification. ACVCP-boarded veterinary pharmacologists often work collaboratively with veterinary pharmacists in veterinary teaching hospitals, and many routinely provide clinical pharmacology support to community veterinarians and pharmacists seeking their expert knowledge of clinical veterinary therapeutic strategies.

1.4 Impact of Veterinary Pharmacy Practice

Veterinary drug sales approximated $76.4 billion in 2010 (Animal Health Institute 2017). In 2010, approximately 31% of all dog owners and 18% of cat owners received prescriptions for medication from their pet’s veterinarian (American Veterinary Medical Association 2010). It is unknown how many of these prescriptions were dispensed by pharmacists adequately trained in veterinary pharmacotherapy. Several recent reports describe serious errors made by pharmacists when dispensing drugs to veterinary patients, some of which resulted in patient fatalities. The author is aware of legal action directed at pharmacists because of dispensing errors. Adequate training of pharmacists in veterinary pharmacotherapy as part of a core pharmacy curriculum would prevent many dispensing errors. The pet-owning public demands and deserves high-quality medical care for their animals that does not stop abruptly at the pharmacy when they encounter a pharmacist not adequately trained in veterinary pharmacotherapy.

Although the impact of the human–animal bond cannot be measured quantitatively, the benefit animals provide to human life is great. A Mintel Market Report on America’s pet owners (America’s Pet Owners US 2016) determined that 87% of US pet owners surveyed consider their pets as family members. Animals provide service, entertainment, protection, food, and companionship, and even answer medical research questions for humans in ways that greatly improve the quality and length of human life. Pharmacists can play a major role in maintaining animal health, and by doing so also contributing to the health and well-being of humans, whether by strengthening the human–animal bond, preventing the spread of zoonotic disease, or preventing drug residues in human food. Veterinary pharmacists (those whose practice is limited to veterinary patients) may play a larger role in these efforts, but the role of community pharmacists in maintaining animal health continues to grow.

The benefits that veterinary pharmacists provide to veterinary teaching hospitals have been measured (Jinks and Paulsen 1982), demonstrating that in addition to positive effects on patient care, veterinary pharmacists add value in areas of drug distribution, academic development, and clinical research. The impact of pharmacists adequately trained in veterinary pharmacy that are practicing in the community, industrial, and governmental sectors has not been measured, but predictably would reveal equally valuable contributions. The scope of veterinary pharmacy practice by veterinary pharmacists (those individuals who have deliberately chosen to limit their practice to veterinary patients) also continues to expand as pet owners and veterinarians recognize the valuable contributions that veterinary pharmacists make as part of the veterinary healthcare team.

The role of community and even hospital pharmacists in veterinary medicine continues to expand regardless of whether or not an individual pharmacist intended to dispense medications to veterinary patients. This is the result of both state and federal legislation (proposed and passed) that encourages or mandates veterinarians to provide prescriptions to pet owners instead of dispensing medication directly from the veterinary hospital.
1.5 Scope of Pharmacist Involvement in Veterinary Medicine

The current scope of veterinary pharmacy practice includes, but is not limited to, veterinary academia, veterinary specialty referral centers, community and online (Internet) pharmacies that serve veterinary patients only, the pharmaceutical and agricultural industry, and governmental public health and regulatory sectors. The scope of pharmacy practice that incorporates both human and veterinary patients includes community pharmacies (chain and independent) and sometimes hospital pharmacies. This section of the chapter describes the various levels of involvement pharmacists may have in veterinary medicine, from roles that require postgraduate training and documentation that a certain level of expertise has been acquired (Diplomates, ICVP) to those that only occasionally fill prescriptions for veterinary patients. It is important to note that even the latter role requires a basic level of understanding of comparative pharmacology and veterinary drug law in order to fulfill the profession’s responsibility to patient care.

The desire, by veterinarians, to proactively involve pharmacists in veterinary medicine was well documented over four decades ago. In 1977, a survey of veterinarians in Wyoming demonstrated the need for pharmacist involvement in veterinary medicine and recommended the establishment of a veterinary pharmacy specialty that should require specialized education and examination for licensure (Nelson 1977). Unfortunately, the Board of Pharmaceutical Specialties (BPS) still does not include veterinary pharmacy as a pharmacy specialty practice. However, veterinary pharmacy certainly qualifies for consideration in light of BPS’s overriding mission “to ensure that the public receives the level of pharmacy services that will improve a patient’s quality of life (Board of Pharmaceutical Specialties 2017). BPS’s stated mission does not characterize patients as being limited to the human species, nor does the pharmacist’s oath. The public expects competency from pharmacists when providing pharmaceutical care for all family members, human or otherwise. As human reliance on animals increases (e.g. companionship, service, research, food, agribusiness, and entertainment), most pharmacists will eventually find themselves providing some degree of pharmaceutical care and drugs to a nonhuman patient. Many pharmacists have devoted a large portion, if not all, of their professional practice to providing pharmaceutical expertise and specialized skills to care for animals. Pharmacists desiring to effectively participate in animal care have many career options, some of which are described throughout the remainder of this section, starting with venues that require greater veterinary pharmacy expertise and then discussing those that may require less veterinary pharmacy expertise.

1.5.1 Veterinary Teaching Hospitals

The most well-established practice of veterinary pharmacy resides in veterinary academic teaching hospitals (Figure 1.2) associated with Colleges of Veterinary Medicine (Appendix A). Pharmacists in these roles provide expertise in areas of service (drug selection, distribution, and control), teaching (didactic, incidental exchanges, client counseling, in-service education, and continuing education programs for pharmacists and veterinarians), and research (clinical trial development and administration, compounded preparation quality assurance, adverse drug reaction and medication error reporting, publication of articles in scientific and professional journals, and responding to drug information queries).
1.5 Scope of Pharmacist Involvement in Veterinary Medicine

A typical day for a veterinary teaching hospital pharmacist involves attending service rounds with clinical veterinary faculty, house officers, and students; preparing and delivering lectures for veterinary, pharmacy, and veterinary technology students; providing drug utilization reviews and therapeutic interventions; maintaining hospital pharmacy operations (inpatient and outpatient drug distribution, preparing sterile and nonsterile compounds, and admixture of intravenous and chemotherapeutic therapies); and engaging in a variety of incidental teaching and consultative activities with students, veterinary practitioners, and animal owners. Veterinary pharmacists at teaching hospitals, and their staff, are valuable resources for community pharmacists.

1.5.2 Veterinary Specialty Referral Centers

Many pharmacists are not aware that veterinary specialization exists. Specialty training programs (generally three years) and certification examinations exist in veterinary ophthalmology, oncology, anesthesiology, cardiology, neurology, surgery, dentistry, and so on. While veterinary teaching hospitals often employ many of these specialists, there are an increasing number of large, private veterinary hospitals that limit their practice to specialized veterinary medicine. These are called referral hospitals or referral centers because the primary care veterinarian “refers” patients to these hospitals. Small-animal (canine and feline) oncology, internal medicine, cardiology, neurology, and ophthalmology are among the most common specialties at these private veterinary hospitals. Recently, veterinary specialty referral centers are employing veterinary pharmacists. Interventions by these pharmacists have a direct and positive impact on patient care, patient well-being, and practice revenue (Dorsey n.d.). Some veterinary pharmacists in these settings are species specialists and are noted for their expertise and skills in providing pharmaceutical care for a single species, such as pharmacists caring for horses in exclusively equine veterinary practices.

A typical day for a veterinary pharmacist practicing in a specialty referral center involves many of the distributive and consultative duties that are performed by pharmacists at veterinary teaching hospitals but with less emphasis on teaching and research.

1.5.3 “Community” Veterinary Pharmacies

One of the most rapidly growing areas of veterinary pharmacy practice is in the community pharmacy setting. When the Animal Medicinal Drug Use Clarification Act (AMDUCA) of 1996 codified the extra-label use of human drugs in animals, veterinarians began prescribing more and more human drugs for use in animal patients. As a result, pharmacists in chain and independent pharmacies were presented with an unprecedented number of prescriptions for animals. The professional rewards of helping animals combined with the financial rewards of cash-paying customers (third-party payment for veterinary patients is rare in the USA) caused retail pharmacy market analysts to set their sights on the veterinary prescription market. Independent pharmacies also began actively collaborating with veterinarians to provide compounded preparations for animal patients, and large retail chains began allowing pets into the discounted generics plans traditionally offered for human prescriptions. The result has been the emergence of several veterinary-only pharmacies catering solely to animal patients, and most recently, veterinary-only online pharmacies are becoming more prevalent. In 2011, the Fairness to Pet Owners Act was debated by the US Congress, proposing legislation that would force veterinarians to provide written prescriptions to all pet owners, giving them the option to purchase prescription drugs outside of the veterinary clinic. Failing to get out of committee in 2011, the bill was reintroduced in 2014 as HR4203. While the fate of the bill is not yet determined, discussion did prompt the Federal Trade Commission to examine the portability of
pet medications. This is anticipated to further increase the flow of veterinary prescriptions into retail pharmacies. A critical point that has not been part of the debate around the Fairness to Pet Owners Act is the lack of competence of most pharmacists in veterinary pharmacology. Instead, the debate has been centered on potential cost savings for pet owners if drugs are purchased at chain pharmacies rather than veterinary hospitals. For community pharmacists to provide the same level of expertise for veterinary patients as they do for human patients, additional education is necessary. Optimally, veterinary pharmacotherapeutics would become a core curricular requirement in accredited US colleges of pharmacy.

1.5.4 Industry (Pharmaceutical and Agricultural)

Pharmacists with veterinary expertise are valuable to the animal health industry. Because of their unique training that combines pharmacological expertise, clinical decision making, and marketing skills, pharmacists with specialized veterinary training make excellent professional representatives for the veterinary pharmaceutical industry. They can easily explain the pharmacodynamics and clinical advantages of new drugs to veterinarians and can serve as consultants for adverse event monitoring and reporting. Veterinary pharmacists also serve in research and development roles in the veterinary pharmaceutical industry by designing and overseeing pre- and postmarketing clinical trials for veterinary drugs. Veterinary pharmacists with expertise in the livestock or poultry industry are contracted by producers to consult in areas of medication management, specialized compounding, and avoidance of drug residues in the tissues of food-producing animals. As pharmacists are well trained in pharmacokinetic principles, they are able to collaborate with producers to predict drug depletion profiles for therapeutic agents used in food-producing animals.

1.5.5 Government Sectors (FDA, CDC, NIH, and Disaster Relief)

Veterinary pharmacists provide valuable services to governmental and regulatory sectors. The Center for Veterinary Medicine of the US Food and Drug Administration (FDA CVM) employs many veterinary pharmacists in areas of compliance, surveillance, adverse event reporting, and medication error prevention. The Centers for Disease Control and Prevention (CDC) also employ veterinary pharmacists who are charged with overseeing the distribution and use of biological agents and drugs used to prevent or treat rare diseases that are zoonotic. The National Institutes of Health (NIH) employ a veterinary pharmacist responsible for providing conventionally manufactured drugs, compounds, and consultation for research animals in NIH-funded protocols. Among other responsibilities, pharmacists in this role may focus their efforts on minimizing the stress that drug administration can cause to research animals, which involves developing combination drug dosage forms (to avoid multiple administrations) and transmucosally absorbed drugs for nasal and buccal administration.

Veterinary pharmacists may also serve on disaster relief teams. These specially trained pharmacists are parts of multidisciplinary teams that also may include veterinarians and veterinary technicians that are ready to be deployed regionally. When called upon, these teams of veterinary professionals are deployed to stricken areas to provide triage, medical care, and treatment for displaced and injured animals. One of the largest deployments of a Veterinary Medical Assistance Team (VMAT) was during the Hurricane Katrina recovery in 2005. Many veterinary pharmacists were involved in these efforts.

1.5.6 Animal Poison Prevention and Consultation

Veterinary pharmacists may also serve as poison control specialists at animal poison control centers such as the Pet Poison
Pharmacists often are the last line of defense in recognizing and preventing potential animal poisoning. Unfortunately, pharmacists traditionally are trained only in human toxicology, which can be vastly different from veterinary toxicology. In fact, canine toxicology can be vastly different from feline toxicology, which can be vastly different from equine toxicology. Factors that affect the risk of toxicity vary greatly among species; they include (but are not limited to) differences in absorption, distribution, metabolism, and elimination; anatomical characteristics, such as the inability to vomit; the age and size of the animal; and seasonal and environmental influences. Veterinary pharmacists possess a working knowledge of species-specific susceptibilities to toxins and can work with boarded veterinary toxicologists (DVMs with specialty training in veterinary toxicology) for more unusual toxic exposures. The American Society for the Prevention of Cruelty to Animals reported that 16% of pet poisonings in 2015 were attributable to human drugs (American Society for the Prevention of Cruelty to Animals 2017). Lack of knowledge on the part of pet owners can result in inadvertent poisonings when pets are accidentally or intentionally exposed to drugs. In some instances, pet owners attempt to treat animals with human OTC products or their own prescription drugs; pharmacists who are adequate trained in veterinary pharmacology are ideally positioned to intervene and provide valuable post-ingestion consultation.

**Dramatic difference**

It is important for community pharmacists to understand that emetics that are effective for inducing vomiting in one species may not be effective for another species (Chapter 6).

### 1.6 Veterinary Pharmacy Practice Considerations

#### 1.6.1 Basic Considerations

The two most profound differences between human and animal patients are that animal patients do not communicate using spoken words, and animals and their byproducts are consumed as food by humans. These two differences drive many of the rules and regulations regarding drug use in animals. A complete discussion on drug therapy in food-producing animals is provided in Chapter 22.

To fully appreciate the differences in veterinary pharmacy practice as compared to human pharmacy practice, it is also important to consider the unintended impact of human healthcare systems and human behaviors on veterinary medicine. The complex systems of private, and state or federally mandated, third-party payor programs are mostly unique to human medicine, and although private third-party insurance is available to animal owners, it is rarely encountered by pharmacists. Because most payment for veterinary healthcare is out of pocket, animal owners must carefully consider the expense of purchasing medications for their animals. This consideration often drives them out of the veterinary practice to large discount outlets or the Internet to find the least expensive options for therapy. The lack of veterinary pharmacology knowledge and risk of poor-quality drugs in some of these outlets can result in disastrous consequences for pet owners who are trying to save money. For example, purchasing a cheap or compounded version of the immunomodulating therapy cyclosporine instead of the FDA-approved version for a dog with life-threatening immune-mediated disease can result in subtherapeutic blood concentrations or often therapeutic failure. As a result, the pet owner is forced to spend considerably more money back at the veterinary clinic trying to re-stabilize the animal or is forced to opt for humane euthanasia. Unlike human
1 Introduction to Veterinary Pharmacy

medicine, veterinary practitioners and animal owners have the option of humane euthanasia to end suffering when circumstances (financial or medical) necessitate.

State and federal third-party payor systems for Medicare and Medicaid (Center for Medicare and Medicaid Services [CMS]) also strongly influence the human medical system through approved reimbursement formularies and a mandate for pharmacists to substitute generic drugs when filling prescriptions for CMS patients. As a result, human pharmacy software programs require a national prescriber identification number (NPI) that verifies that prescriber in the CMS database before new prescriptions can be processed. Community pharmacists often request NPI numbers from veterinarians and find it difficult to proceed in the software without this verification number. The alternative verification is through the prescriber’s DEA [Drug Enforcement Administration] number, but DEA has stated that it “strongly opposes the use of a DEA registration number for any purpose other than the one for which it was intended, to provide certification of DEA registration in transactions involving controlled substances. The use of DEA registration numbers as an NPI is not an appropriate use and could lead to a weakening of the registration system” (DEA n.d.). Veterinarians express significant frustration when asked for NPI or DEA numbers or when pharmacists automatically substitute generic medications even when the veterinarian has indicated that therapeutic substitution is not permitted. Community pharmacists should be prepared for a different approach when filling prescriptions for animals: (i) Instead of NPI or DEA numbers, identify an alternate prescriber verification number (e.g. the state veterinary license number), (ii) do not substitute generically without the veterinarian’s authorization, and (iii) only require DEA numbers for prescriptions for controlled substances.

As mentioned in this chapter, opioid shortages may occur due to manufacturing shortages or interruption of the supply chain during and after natural disasters. However, human behavior also strongly influences the availability of opioids. Because of the rampant rise of human addiction to opioids, all 51 states and territories in the USA have Prescription Drug Monitoring Programs (PDMPs) that closely monitor and often severely restrict the quantity of opioids that a prescriber can give to a human for use outside of a hospital admission. To decrease supplies of opioids, federal mandates have also been issued to reduce manufacturing of opioids. The unintended consequence for veterinarians and animal patients is an increasing difficulty in obtaining opioids to meet patient needs. In 16 of the states with PDMPs, veterinarians have been specifically excluded from these restrictions, but community pharmacists often do not realize that opioid prescriptions for animals may be exempt from their state PDMP rules. It is critical that community pharmacists remain current and informed of all state and federal rules and regulations that may affect animal patients.

The third-party payor system also heavily influences the drug approval and marketing process. The human pharmaceutical industry (Pharmaceutical Researchers and Manufacturers of America [PhRMA]) consistently ranks as the most profitable industry in the USA, and was relatively resistant to the economic crisis that affected the USA in 2009. The insurance industry also remains relatively lucrative (Kaiser Health News 2009). Because third-party payors almost always cover the costs of human drug therapy
for their constituents, there is little incentive to reduce the astronomical prices that are charged for new human drug therapies. Profits by the pharmaceutical industry are used to subsidize drug approval fees for new submissions, and the approval system is largely subsidized by these profits. In 2017, there were more than 35,000 drugs approved for humans, while only 1,564 were approved for use in animals. The FDA approved 45 new human drugs in 2015 and consistently averages about 28 new drug approvals annually. In comparison, FDA CVM approved five new animal drugs in 2015 and was praised in the 2017 budget for “exceeding all performance goals” in 2015 (FDA 2017). Comparing the 2015 FDA budgets for human and animal new drug approval, the human drug approval budget was almost eight times larger than that for animal drugs. Considering the vast number of species and diseases requiring new drug therapy in veterinary medicine, the ratio of expenditure and drug availability for humans versus animals seems upside down.

The priority of human need over animal need is also evident during shortages of human drug supplies. Manufacturing problems, mergers, and natural disasters all contribute to significant drug shortages, which grow steadily every year. When drug supplies are short, many drug manufacturers and wholesalers operate in a distribution mode known as “allocation,” whereby human providers get top priority for receiving drugs, and amounts are based on the provider’s purchasing history of the shorted item. During shortages of intravenous fluids, electrolytes, chemotherapy drugs, and opioids, many veterinary providers are denied access to drugs because their patients are not human. Because community pharmacists are well positioned to serve all species of patients, they serve a valuable role in helping veterinarians and pet owners identify affordable and available drug therapy for their patients.

Postmarketing adverse drug events are also more likely in animal patients, since cohorts of only 50–300 animals are required for animal drug approval. Human drug approval is based on cohorts of several thousand humans. Occasionally, a drug intended to be marketed for humans is successful in Phase I (animal) testing but is determined to be toxic to humans in Phase II or III (human) premarketing studies. To attempt to recoup some of the research and development investment for these drugs, they are sometimes taken up by the animal pharmaceutical industry (Animal Health Institute [AHI]) for development for animal use. Some examples of these drugs include flunixin meglumine, enrofloxacin, and tilmicosin for which the FDA CVM approved labeling bears a strong warning that these products are not for use in humans. It is important to note that these warnings or potential drug interactions with other drugs will not be included in any drug interaction/pharmacy alert software. The vast number of species, breeds, and genetic polymorphisms encountered in veterinary pharmacotherapy have thus far prevented the development of any intelligent drug interaction software for animal patients. As mentioned further in this chapter, community pharmacists must become familiar with the pharmacology and toxicity of veterinary-only drugs and employ methods that will prevent them from being erroneously dispensed to humans.

Finally, there are many sound-alike drugs that can be problematic for community pharmacists accepting verbal prescriptions from veterinarians. For example, Soloxine® (oral levothyroxine tablets) sounds identical to Ciloxan® (ciprofloxacin ophthalmic ointment or solution). Usually, the instructions would prompt a pharmacist to request clarification, but if the veterinarian states “use as directed” without distinction to route of administration, then dispensing errors may occur. Another common and more consequential mistake is when veterinarians are phoning in prescriptions for Hycodan® for cough suppression in dogs, to be followed by a written or faxed prescription. Instead of Hycodan, the pharmacist thinks he hears the more commonly prescribed drug for humans, Vicodin®. Vicodin contains a fatal dose of
acetaminophen for cats and a potentially fatal dose of acetaminophen for small dogs. Although the paper prescription would eventually alert the pharmacist to this error, severe morbidity or death could have likely ensured in the few days between verbal and written orders. Community pharmacists are well advised to have veterinarians spell out drug names if there is any doubt at all as to what the veterinarian is prescribing.

1.6.2 Veterinary Drug Law

It is important for pharmacists to understand that regulations for veterinary drug use are different from those that apply to human drug use, but it is even more complicated than that. There are a specific set of regulations that apply to only some animals (food animal species) but not others. Detailed information about drug use in food animals is presented in Chapter 22, but a summary is in this chapter. All other veterinary drug regulations apply to both food animals and companion animals.

Veterinary pharmacists must work within the boundaries for drug use established by a number of agencies at both the federal and state levels. These agencies include the FDA, DEA, US Department of Agriculture (USDA), and Environmental Protection Agency (EPA) (see Table 1.1, “Classes of Veterinary Products Approved by Agency”), in addition to the state boards of pharmacy and veterinary medicine. In the USA, regulations governing veterinary drugs have much in common with the regulations that govern human drugs. For example, both human and animal drugs are regulated by the FDA under the Federal Food, Drug, and Cosmetic (FDC) Act. New animal drugs must have an approved New Animal Drug Application (NADA), similar to the New Drug Application (NDA) for human drugs. Animal drugs, like human drugs, must be shown to be safe and effective for their intended uses. Generic copies of new animal drug products can be approved pursuant to submission of an Abbreviated New Animal Drug Application (ANADA).

1.6.3 Regulations for Drugs Intended for Food-Producing Animals

Regulations for human and “food-producing” animal drugs differ in important ways because humans may consume animal tissues and byproducts. The administration of drugs to food-producing animals (see Chapter 22 for additional information), including drugs in animal feed or water, has the potential to generate residues of the parent drug or its metabolites that could be consumed by (and pose health hazards to) humans. It is necessary to determine when it is safe for the public to consume tissues from an animal that has been treated with a drug. This information is part of the FDA-mandated approval process for drugs labeled for use in food animals. That is why there are major differences in regulations related to extra-label use of drugs (i.e. use for an indication that has not received FDA approval) in food animals compared to humans. After a drug is approved for human use, the FDA does not limit or control how physicians prescribe medications. In contrast, extra-label use of drugs in food animals is permitted only under limited conditions to ensure public safety. For some drugs, extra-label use is expressly prohibited (see Chapter 22).

1.6.4 Regulations for Drug Use in Companion Animals

In 1996, a milestone veterinary drug law, AMDUCA, was enacted, permitting extra-label
use of many approved animal and human drugs by or on the lawful order of a veterinarian within the context of an established set of conditions known as a “veterinarian–client–patient relationship” (VCPR; see Figure 1.3, “Elements of the Veterinarian–Client–Patient Relationship”). Prior to AMDUCA, the law required veterinarians to use drugs exactly as labeled for the approved indication, at the approved dose, by the approved route, for the approved duration, and only in the approved species. This effectively rendered any other drug use, including use of any human-labeled drug, illegal. Because AMDUCA grants veterinarians the ability to prescribe human-labeled drugs for use in animals, the need for pharmacists trained in veterinary pharmacotherapy has emerged as a needed discipline. The quality of medical care for companion animals is substantially enhanced with access to human-approved drugs because there are so few approved veterinary drugs in comparison.

1.6.4.1 Prescription Drugs

Prescription animal drugs (also known as legend drugs) are restricted by federal law to use by or on the order of a licensed veterinarian, according to Section 503(f) of the FDC Act. The law requires that such drugs be labeled with the statement “Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian” (see Figure 1.4) within the confines of a VCPR (see Figure 1.3). The VCPR primarily evolved because animal patients cannot communicate verbally with their healthcare providers. While a human patient can phone a prescriber and describe symptoms that can lead to a reasonable diagnosis, animal patients cannot. For this reason, veterinarians must have either physically examined the animal or visited the site where the animal is housed.

<table>
<thead>
<tr>
<th>Elements of the Veterinarian–Client–Patient Relationship</th>
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<tr>
<td>A Veterinarian–Client–Patient relationship. A VCPR means that all of the following are required:</td>
</tr>
<tr>
<td>a. The veterinarian has assumed the responsibility for making medical judgments regarding the health of the patient, and the client has agreed to follow the veterinarian’s instructions.</td>
</tr>
<tr>
<td>b. The veterinarian has sufficient knowledge of the patient to initiate at least a general or preliminary diagnosis of the medical condition of the patient. This means that the veterinarian is personally acquainted with the keeping and care of the patient by virtue of:</td>
</tr>
<tr>
<td>i. a timely examination of the patient by the veterinarian, or</td>
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<tr>
<td>ii. medically appropriate and timely visits by the veterinarian to the operation where the patient is managed.</td>
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<tr>
<td>c. The veterinarian is readily available for follow-up evaluation or has arranged for the following:</td>
</tr>
<tr>
<td>i. veterinary emergency coverage, and</td>
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<tr>
<td>ii. continuing care and treatment.</td>
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<tr>
<td>d. The veterinarian provides oversight of treatment, compliance, and outcome.</td>
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<tr>
<td>e. Patient records are maintained.</td>
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1.6.4.2 Over-the-Counter Drugs

Unlike human OTC drugs, veterinary OTC drugs undergo full approval by the FDA. The FDA is responsible for determining whether an animal drug product will be available by prescription only or sold directly to laypersons. OTC status hinges on whether it is possible to prepare “adequate directions for use” under which a layperson can use the drug safely and effectively. Safe use includes safety to the animal, safety of food products derived from the animal, safety to persons administering the drug or otherwise associated with the animal, and safety in terms of the drug’s impact on the environment.

**Dramatic difference**

It is important for the pharmacist to understand that human OTC drugs are not labeled for use in any species other than humans. Consequently, federal law prohibits the use

of a human OTC drug in an animal unless such use is specifically pursuant to a prescription order by a licensed veterinarian within the context of a valid VCPR. This means that there is not currently a legal avenue for pharmacists to recommend human OTC drug products for veterinary patients. Hopefully, this can change as the pharmacy profession adopts veterinary pharmaco-therapeutics as a core competency.

1.6.5 Veterinary Drug Compounding

Drug compounding is the process by which a veterinarian or pharmacist prepares a medication in a manner not stipulated in the product labeling to create a compound specifically tailored to the needs of an individual patient. Compared with the number of drugs approved by the FDA for use in humans, the number of drugs approved for use in veterinary species is low, so the need for compounded therapies to treat animals is consequently high. Even though current federal law permits veterinarians to use and prescribe drugs that are FDA approved for human use in an extra-label fashion, many human medications are only available in formulations impractical or unsafe for use in pets (e.g. the use of xylitol as an artificial sweetener). Compounding also allows access to medications that are not currently commercially available, such as drugs discontinued by pharmaceutical companies for economic reasons or as a result of voluntarily or federally mandated withdrawals (e.g. cisapride, potassium bromide, and diethylstilbestrol), and drugs unavailable for use due to temporary shortages (e.g. electrolytes and fluids, and opioid injections). A comprehensive discussion on compounding is provided in Chapter 3.

1.6.6 Veterinary Adverse Drug Event Reporting

Recognizing and reporting adverse drug events (ADEs) in animal patients comprise an integral role for the veterinary pharmacist.