The goal of this article is to help practitioners understand the regulatory framework and basis for the approval of new animal drugs, the terminology and specific meaning of terms related to drug approval, and the marketing and use of veterinary drugs in companion animal practice. Understanding the differences between approved versus unapproved drugs and their use helps practitioners make the appropriate clinical decisions on their patients’ treatment. Only when buying approved animal drugs can clinicians be assured of product safety, effectiveness, and manufacturing to the strict standards for quality, purity, and potency, as well as truthful and complete labeling.

This article describes clinical examples in which pharmacokinetic parameters can be used to optimize veterinary patient care. Specific applications include extrapolating drug dosages, optimizing therapy with therapeutic drug monitoring, interpreting pharmacokinetic information provided by drug labels and pharmaceutical companies, and adjusting drug dosages in patients with hepatic or renal failure.

The cytochrome P-450 (CYP) drug metabolizing enzymes are essential for the efficient elimination of many clinically used drugs. These enzymes typically display high interindividua variability in expression and function resulting from enzyme induction, inhibition, and genetic polymorphism thereby predisposing patients to adverse drug reactions or therapeutic failure. There are also substantial species differences in CYP substrate specificity and expression that complicate direct extrapolation of information from humans to veterinary species. This article reviews the available published data regarding the presence and impact of genetic polymorphisms on CYP-dependent drug metabolism in dogs in the context of known human-dog CYP differences.

Although it is widely appreciated that cats respond differently to certain drugs compared with other companion animal species, the causes of
these differences are poorly understood. This article evaluates published
evidence for altered drug effects in cats, focusing on pharmacokinetic
differences between cats, dogs, and humans, and the molecular mecha-
nisms underlying these differences. More work is needed to better un-
derstand drug metabolism and disposition differences in cats, thereby
enabling more rational prescribing of existing medications, and the devel-
opment of safer drugs for this species.

Idiosyncratic Drug Toxicity Affecting the Liver, Skin, and Bone Marrow in
Dogs and Cats 1055
Lauren A. Trepanier

Idiosyncratic drug toxicity reactions are, by definition, uncommon, but can
lead to serious or even fatal organ toxicity. The liver, skin, and peripheral
blood cells/bone marrow are common targets. Most of these reactions
are the result of reactive metabolites, which may cause local cell or organ-
elle damage, or may be amplified by a systemic immune response. Individ-
ual risk may depend on differences in drug biotransformation, levels of
oxidative stress, or antigen presentation.

Adverse Drug Reactions in Veterinary Patients Associated with Drug Transporters 1067
Katrina L. Mealey

For many drugs used in veterinary practice, plasma and tissue concentra-
tions are highly dependent on the activity of drug transporters. This article
describes how functional changes in drug transporters, whether mediated
by genetic variability or drug-drug interactions, affect drug disposition and,
ultimately, drug safety and efficacy in veterinary patients. A greater under-
standing of species, breed, and individual (genetic) differences in drug
transporter function, as well as drug-drug interactions involving drug trans-
porters, will result in improved strategies for drug design and will enable
veterinarians to incorporate individualized medicine in their practices.

Antimicrobials, Susceptibility Testing, and Minimum Inhibitory Concentrations
(MIC) in Veterinary Infection Treatment 1079
Mark G. Papich

Veterinarians are quick to attribute an unsuccessful antimicrobial treat-
ment to a failure of the culture and susceptibility test. There are many rea-
sons why antimicrobial treatment fails. When evaluating a patient that has
failed to respond to therapy, one must consider any of the many factors
that contribute to antibiotic failure.

Antibiotic Treatment of Resistant Infections in Small Animals 1091
Mark G. Papich

There are few veterinary clinical studies to support a recommended use
and dose for treating resistant bacterial infections in small animals. Resis-
tance against many common antibiotics is possible and a susceptibility
test is advised. Infections caused by Pseudomonas aeruginosa presents
a special problem. Staphylococcus isolated from small animals is most
likely to be Staphylococcus pseudintermedius. The most important
resistance mechanism for *Staphylococcus* is methicillin resistance. The only antimicrobials to which some gram-negative bacilli are sensitive may be extended-spectrum cephalosporins, carbapenems (penems), selected penicillin derivatives, amikacin, or tobramycin. A susceptibility test is needed to identify the appropriate drug for these infections.

**Outpatient Oral Analgesics in Dogs and Cats Beyond Nonsteroidal Antiinflammatory Drugs: An Evidence-based Approach** 1109

Butch KuKanich

This article evaluates the current literature on oral analgesics and analgesic adjuncts in dogs and cats. An overview of how dosing recommendations are made covering controlled clinical trials, experimental study design, and pharmacokinetic studies is included. The weight of evidence for each drug is reviewed and compared with the gold standard, controlled clinical trials. Other evidence such as experimental studies, extrapolation of pharmacokinetic studies, and case reports/series is also considered. It is important to know from what data dosing recommendations are derived and how much evidence supports the use of oral analgesics and analgesic adjuncts in dogs and cats.

**Update: Seizure Management in Small Animal Practice** 1127

Karen R. Muñana

Seizures are the most common neurologic condition encountered in small animal practice and arise from an imbalance of excitatory and inhibitory mechanisms in the brain. Epilepsy refers to recurrent seizures of any cause. Successful management of epilepsy requires knowledge of the pharmacologic properties of available antiepileptic medications, regular patient evaluations to assess response to therapy and monitor for adverse effects, and thorough client education to ensure that goals and expectations of therapy are understood. Recommendations for emergency care of seizures at home should be provided for patients with seizures that are not controlled with maintenance antiepileptic therapy.

**Update on Immununosuppressive Therapies for Dogs and Cats** 1149

Katrina R. Viviano

Treatment of immune-mediated disease in dogs and cats continues to evolve as new therapies are introduced or adapted from human medicine. Glucocorticoids remain the first-line therapy for many of the immune-mediated or inflammatory diseases of cats and dogs. The focus of this article is to provide an update on some of the common immunosuppressive therapies used in small animal veterinary medicine. The goals of therapy are to induce disease remission through the inhibition of inflammation and the modulation of lymphocyte function.

**Nutraceuticals for Canine Liver Disease: Assessing the Evidence** 1171

Jean-Michel Vandeweerd, Carole Cambier, and Pascal Gustin

Nutraceuticals, or nutritional supplements, have been promoted for the ancillary treatment of liver disease in dogs. However, minimal information
is available in the scientific literature about commonly used nutraceuticals, such as S-adenosylmethionine, silymarin, and vitamin E. No strong clinical evidence exists regarding the efficacy of these compounds as hepatoprotectants in canine liver disease. Until this evidence exists, individual veterinarians must assume responsibility for their decision to use nutritional supplements in their canine patients with liver disease.