An anesthetic plan should include all drugs used for a particular patient, including dosages, routes, and order of administration. In addition, the protocol should include oxygen flow rates, monitoring equipment, and anticipated plan for recovery from anesthesia. Use of protocols that utilized neuroleptanalgesia (sedative/tranquilizer plus opioid) may be helpful as it can reduce the deleterious effects of high doses of induction and maintenance drugs.

**Sedatives/Tranquilizers**

**Acepromazine**
Acepromazine is a phenothiazine tranquilizer. The sedation effects are due to dopamine blockade. Depending on the source, acepromazine is classified as an anxiolytic, though this is controversial. Onset of sedation following acepromazine administration is variable, but typically sedation occurs in 3 to 5 minutes following IV administration, and 15 to 30 minutes following IM administration. Duration of action is 2 to 4 hours. Used clinically as a premedicant prior to general anesthesia to produce a cooperative patient. Acepromazine typically produces mild sedation in small animal patients. The sedative effects of acepromazine can be enhanced through co-administration of an opioid.

Acepromazine causes vasodilation and hypotension, due to alpha-1 blockade. Heart rate usually increases after acepromazine administration. The effects of acepromazine on the respiratory system are minimal. Acepromazine may lower the seizure threshold in dogs, though this is controversial; many retrospective studies do not support this assertion. Acepromazine may cause a decrease in platelet aggregation. Acepromazine has anti-emetic and anti-histaminic properties. Acepromazine undergoes hepatic metabolism. Acepromazine is not reversible. Acepromazine does not have analgesic properties though it can enhance the effects of opioid analgesics.

**Alpha-2 agonists**
Dexmedetomidine, xylazine, and romifidine are alpha-2 agonists. The sedation effects are due to Alpha-2 receptor agonism of the supraspinal autoreceptors. Onset of sedation following alpha-2 agonist administration is variable, but typically sedation occurs in 3 to 5 minutes following IV administration, and 15 minutes following IM administration. Duration of action is dependent on the drug administered. Used clinically as a premedicant prior to general anesthesia to produce a cooperative patient. Alpha-2 agonists typically produce moderate to profound sedation in small animal patients, depending on the dose and route of administration. The effects of alpha-2 agonists can be enhanced through co-administration of an opioid.

Alpha-2 agonists can cause profound vasoconstriction in small animal patients. Heart rate often decreased due to a reflex bradycardia as well as a centrally-mediated mechanism. Alpha-2 agonists can cause profound respiratory depression, depending on dose and route of administration. CNS depression is quite marked in patients following alpha-2 agonist administration. Alpha-2 agonists may stimulate emesis, then cause decreased gastrointestinal motility, cause insulin suppression, and increase urination. The sedative effects of the alpha-2 agonists are reversible by administered an alpha-2 antagonist.

**Benzodiazepines**
Midazolam and diazepam are the most commonly used benzodiazepines in veterinary anesthesia. These drugs enhance the binding of GABA to the GABA receptor. The drugs are often used for muscle relaxation, and may cause sedation in some patients. Onset of sedation following benzodiazepine administration is variable, but typically sedation occurs in 1 to 3 minutes following IV administration, and 15 to 20 minutes following IM administration (midazolam). Duration of action is 1 to 2 hours. Used clinically as a premedicant prior to general anesthesia to produce a cooperative patient, benzodiazepines can also result in excitement or decreased inhibition. The sedative effects of benzodiazepines can be enhanced through co-administration of an opioid.
The effects of benzodiazepines on the cardiovascular and respiratory systems are minimal. Benzodiazepines may be used to treat seizures. Benzodiazepines may stimulate appetite. Benzodiazepines undergo hepatic metabolism and are reversible using a benzodiazepine antagonist.

**Opioids**

**µ agonists**

**Morphine:** provides analgesia for mild to severe pain. Typical doses range from 0.1 to 0.4 mg/kg IV, IM, or SQ. Duration of action is 4 to 6 hours. Morphine may also cause a release of histamine and should be avoided in patients with mast cell disease. Vomiting may occur and mild to moderate sedation is common following morphine administration.

**Fentanyl:** provides analgesia for mild to severe pain. The duration of fentanyl from a single IV bolus is approximately 15 minutes, and as a result, fentanyl is often administered as a constant rate infusion. Fentanyl is administered as a single bolus of 2 µg/kg IV, as a CRI in awake patients at 2 to 5 µg/kg/hr, and as a CRI in anesthetized patients at 5 to 10 µg/kg/hr. Vomiting and salivation may occur, and mild to moderate sedation is common following fentanyl administration, though dysphoria may also occur with fentanyl.

**Hydromorphone:** provides analgesia for mild to severe pain. Doses range from 0.05 to 0.2 mg/kg IV, IM, or SQ. Duration of action is 2 to 4 hours. Vomiting and salivation may occur, and mild to moderate sedation is common following hydromorphone administration.

**Methadone:** Methadone is a µ opioid receptor agonist and NMDA antagonist and provides analgesia for mild to severe pain. Typical doses range from 0.1 to 0.4 mg/kg IV, IM, or SQ. Duration of action is 4 to 6 hours. Methadone has been associated with bradycardia in some patients. Vomiting and sedation are uncommon following methadone administration.

**Oxymorphone:** provides analgesia for mild to severe pain. Doses range from 0.05 to 0.1 mg/kg IV, IM, or SQ. Duration of action is 2 to 4 hours. Vomiting and salivation may occur, and mild to moderate sedation is common following oxymorphone administration.

**Partial µ agonist**

**Buprenorphine:** provides analgesia for mild to moderate pain. The dose range of buprenorphine is 0.005 to 0.02 mg/kg IV or IM. Subcutaneous administration may be associated with variable uptake in most patients. Duration of action is 8 to 12 hours. Buprenorphine does not typically result in vomiting or excessive sedation.

**µ antagonist, κ agonist**

**Butorphanol:** provides analgesia for the mildest of pain. The dose of butorphanol ranges from 0.1 to 0.2 mg/kg, and can be administered IV, IM, or SQ. Duration of action is up to 1 hour.

**Anesthetic Induction Drugs**

**Propofol**

Propofol is an alkyl phenol-derivative that is chemically unrelated to other anesthetic drugs. The drug is solubilized in an emulsion of soybean oil, glycerol, and egg lecithin. This base can support microbial growth and it is important to maintain strict aseptic technique when handling this drug. Contents of unused drug should be discarded within 6 to 7 hours. Propofol is not currently controlled.

Propofol is an extremely lipid soluble intravenous drug that produces immediate unconsciousness. Induction and recovery are rapid and smooth. Duration of action is 5 to 15 minutes after a single bolus dose; dogs and cats are typically able to stand between 20 and 30 minutes post injection. The duration of action is dependent upon rapid redistribution, and hepatic and extra-hepatic metabolism. Used clinically as an anesthetic induction drug due to its rapid onset and rapid recovery even in animals with organ system dysfunction. Propofol can also be used to provide long term restraint when administered as a continuous rate infusion or when combined with other drugs for total intravenous anesthesia.

Propofol causes potent vasodilation and hypotension. Usually, this is short-lived. Caution should be used when administering propofol to hypotensive or volume-depleted patients. Heart rate usually increases after propofol administration. Propofol causes a dose dependent decrease in myocardial contractility. Propofol is a potent respiratory depressant. It is not unusual for patients to become apneic or have severe hypoventilation after
propofol administration. This can be a function of dose and how fast the drug is administered: very slow IV injection results in less respiratory depression. Inject propofol over a span of 30 seconds to avoid apnea. Propofol enhances the effects of GABA (an inhibitory neurotransmitter). Chloride conduction is increased which result in hyperpolarization of postsynaptic neurons. Propofol can induce pain or discomfort on injection; people report a burning sensation travelling up the vein. Discomfort on injection can be decreased by prior administration of an opioid, sedative or tranquilizer, or lidocaine. Perivascular administration is not associated with tissue damage. Propofol is an appetite stimulant (Contemp Top Lab Anim Sci 2000;39:43-46). Propofol has been associated with Heinz body formation in cats after multiple day dosing or multi-day infusions. Propofol is a phenolic compound, and phenols are eliminated through glucuronidation (phase II hepatic metabolism). Cats are deficient in glucuronyl transferase enzyme activity. The phenols oxidize red blood cell hemoglobin resulting in Heinz body formation. However, propofol-associated Heinz body formation may not be clinically significant (J Am Vet Med Assoc 2007;231:1347-1353). Propofol is associated with relatively poor analgesia and should not be used as a sole anesthetic for painful procedures.

Ketamine

Ketamine acts at the thalamo-neocortical projection system, which limits the ability to interpret sensory input. There is also some activity at the spinal cord dorsal laminae and reticular formation. The analgesic action is attributed to NMDA receptor antagonism. Analgesia occurs even at sub-anesthetic concentrations of ketamine, and the analgesic effects outlast the anesthetic effect.

The duration of action of ketamine is related to redistribution to lean body tissues and fat, and the duration of the anesthetic action is shorter than elimination half-life. Ketamine is metabolized to norketamine in the liver (which is an active metabolite). Norketamine is then hydroxylated to an inactive metabolite, which is then excreted in urine in dogs and horses. In the cat, ketamine is metabolized to norketamine, which is then excreted unchanged in urine. Ketamine is used in more species than any other anesthetic drug other than the inhalation anesthetics (humans, large and small domestic species, avian, wildlife, pocket pets, and reptiles). In high doses, ketamine can be used as a sole anesthetic, but this is not recommended, due to increased muscle tone, tremors, occasional seizures, and rough recoveries. In lower doses, ketamine can be combined with sedatives, tranquilizers, and opioids. Anesthetic induction and short-term immobilization can be accomplished with ketamine-diazepam or ketamine-midazolam combinations, guaifenesin-ketamine or guaifenesin-ketamine-xyazine, or as a general anesthetic with dexmedetomidine-ketamine-opiods.

Ketamine causes indirect cardiovascular stimulation via the sympathetic nervous system, which results in increased mean arterial blood pressure, heart rate, and cardiac output. Ketamine also results in direct myocardial depression, which manifests during hemodynamic shock and related conditions. Finally, ketamine increases myocardial oxygen consumption. Ketamine causes transient, mild respiratory depression, which manifests itself as a decrease in minute ventilation and an apneustic breathing pattern (at higher doses). Laryngeal reflexes (swallowing) are maintained but are depressed; it is important to not rely on this for maintaining a patent airway. Ketamine causes dose-related unconsciousness and analgesia, but is not a “complete” anesthetic even at high doses. Ketamine administration results in a cataleptoid state with patients that have open eyes, palpebral reflex, and dilated pupils. Patients maintain a swallow reflex and typically have increased salivation. People report amnesia associated with ketamine use, and emergence reactions that are described by people include vivid dreams, extracorporeal experiences (floating outside of one’s body), and illusions with fear, excitement, and dysphoria. Ketamine increases cerebral metabolic rate, cerebral blood flow, intracranial pressure, and intraocular pressure. Ketamine is contraindicated following head trauma or patients with intracranial masses, seizure disorders, and in patients with intraocular foreign bodies or descemetoceles. Ketamine produces good analgesia due to its effects as an NMDA antagonist. Typically, when used as an analgesic it is used in relatively low dosages and often in combination with other analgesic drugs. Ketamine alone does not provide any muscle relaxation. Ketamine has a pH of 3.5 – this is one reason for stinging on IM injection.

Telazol™

Telazol is a 1 to 1 (mg to mg) combination of tiletamine (a dissociative drug more potent than ketamine) and zolazepam (a benzodiazepine tranquilizer more potent than diazepam). It is available as a crystalline powder, which is reconstituted with sterile water, which has implications and usefulness as an immobilization and “capture” drug.

The duration of action of telazol is related to redistribution to lean body tissues and fat, and the duration of the anesthetic action is shorter than elimination half-life. The effects of tiletamine and zolazepam last for different
lengths of time, and is species dependent; in cats, zolazepam has a longer elimination half life than tiletamine, but in dogs, tiletamine lasts longer than the zolazepam. Telazol is metabolized in the liver. In high doses, Telazol can be used as a sole anesthetic, but this is not recommended due to the different rates of metabolism of zolazepam and tiletamine, and the increased risk of rough recoveries. In lower doses, Telazol can be combined with sedatives, tranquilizers, and opioids. Anesthetic induction and short term immobilization with Telazol and Telazol combinations have been utilized in horses, pigs, dogs, and cats. In zoo and wildlife capture, telazol can be reconstituted with other drugs in place of sterile water.

Similar to ketamine, tiletamine causes indirect cardiovascular stimulation via the sympathetic nervous system (endogenous catecholamine release). However, due to the inclusion of zolazepam, cardiac output often remains unchanged, blood pressure transiently decreases then increases, and heart rate increases. Telazol has not been associated with increased myocardial oxygen consumption, but research on the use of Telazol in cardiac compromised patients is limited and so should be used with caution in cardiac patients. The respiratory effects of telazol are similar to ketamine. Telazol causes a dose-related anesthetic effect. Because of the different rates of metabolism of tiletamine and zolazepam, in some species, the tiletamine effects can predominate in the later anesthetic period. In general, Telazol administration results in open eyes, palpebral reflex, and dilated pupils. Patients maintain a swallow reflex and typically have increased salivation. Telazol has not been associated with the increased cerebral metabolic rate, cerebral blood flow, intracranial pressure, and intraocular pressure seen with ketamine, but research on Telazol in compromised patients is limited. There is good muscle relaxation associated with Telazol administration due to the zolazepam.

**Etomidate**

Etomidate is an imidazole derivative, which is chemically unrelated to any other anesthetic drug. It is supplied as single isomer (R(+)). It is solubilized in 35% propylene glycol (4600 mOsmol/L), and is associated with pain on injection. It is classified as a hypnotic drug.

Etomidate penetrates the brain rapidly, reaching peak levels within approximately 1 minutes of IV injection. Induction can be rough, resulting in involuntary myoclonus, gagging, and retching. Recovery is rapid and smooth. Duration of action is 5 to 10 minutes after a single bolus dose. The duration of action is dependent upon rapid redistribution, and the drug is metabolized in the liver. Used clinically as an anesthetic induction drug due to its rapid onset and rapid recovery even in animals with organ system dysfunction. Like propofol, etomidate can also be used to provide long-term restraint when administered as a continuous rate infusion.

Cardiovascular stability is characteristic of induction of anesthesia with etomidate. Etomidate is associated with minimal changes in cardiac output, arterial blood pressure, and heart rate. Etomidate causes minimal respiratory depression. Occasionally etomidate administration may induce decreases in tidal volume, which are offset by increases in respiratory rate. Etomidate is relatively selective as a modulator of GABA\_A receptors, and exerts its effect by binding to a specific site on the GABA\_A receptor and enhancing the affinity of GABA for the GABA receptor. Etomidate can induce pain or discomfort on injection; people report a burning sensation travelling up the vein. Discomfort on injection can be decreased by prior administration of an opioid, sedative or tranquilizer, or lidocaine. Myoclonus and retching often accompany etomidate inductions; appropriate sedation/premedication can help to prevent these effects. The most significant side effect of etomidate is that it causes adrenocortical suppression by producing a dose-dependent inhibition of the conversion of cholesterol to cortisol, which can last for 4 to 8 hours after an induction dose of etomidate. Etomidate is associated with no analgesia and should not be used as a sole anesthetic for painful procedures.

**Alfaxalone**

Alfaxalone is a neuroactive steroid used as a general anesthetic in dogs and cats. It is not currently approved for use in the US. The drug has been studied for IV or IM administration. Alfaxalone (Alfaxan®) is currently formulated in a cyclodextrin solution, which increases its solubility. Induction and recovery are rapid and smooth. Used clinically as an anesthetic induction drug due to its rapid onset and rapid recovery (Vet Anesth Analg 2008;35:451-462). Alfaxalone can also be used to provide long term restraint when administered as a continuous rate infusion or when combined with other drugs for total intravenous anesthesia.

Alfaxalone can cause vasodilation at doses used for anesthetic induction. Respiratory effects are minimal at lower doses. Hypoventilation and apnea are associated with higher doses. Alfaxalone modulates neuronal cell membrane chloride ion transport, induced by binding of alfaxalone to GABA\_A cell surface receptors. Alfaxalone provides good muscle relaxation.