Honey bee medicine for veterinarians and guidance for avoiding violative chemical residues in honey

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Honey bees (*Apis mellifera*) face a number of health and survival challenges owing to infectious diseases. Given that honey bee colonies are comprised of a high density of closely related individuals living in close proximity, they are particularly vulnerable to viral and microbial infections. Hives are maintained at a constant temperature of 35 °C, which is an ideal temperature for pathogen proliferation and mold growth. Furthermore, pests and predators are attracted to hives because the colony represents a rich source of year-round carbohydrates (honey) and proteins (pollen, bees, and brood). People have long recognized and appreciated honey bees for their important role in pollinating commercial crops while also providing natural products for use in the food, cosmetic, and pharmaceutical industries. Owing to their susceptibility to infection and usefulness to people, medications are often used to prevent honey bee death and colony decline.

Veterinarians are excellent candidates to be strong advocates for the care and treatment of honey bees. They are expected to be able to perform physical examinations, make diagnoses, identify treatment strategies, and prescribe medications for all sorts of vertebrates and invertebrates. However, veterinarians typically receive little to no exposure to clinical honey bee medicine during routine formal education. Consequently, they often need additional training to best serve their beekeeper clients.[1]

One of the challenges associated with treatment of honey bees is the dispensing of medication. In the US, drugs approved by the FDA for medicating honey bee colonies are not packaged as unit-of-use containers. Therefore, to use those drugs, veterinarians, and sometimes pharmacists, must repackage medications into the exact doses to be administered to the colony by the beekeeper. Given that pharmacists do not receive any mandatory education on veterinary species and neither pharmacists nor veterinarians receive much, if any, education specific to honey bee pharmacology, both professions are vulnerable to lack of knowledge regarding treatment of disease in honey bees.

The information provided in this FARAD Digest is not intended to educate veterinary professionals in every aspect of apiary management. It is, however, intended as an introductory primer on the annual cycle of honey bees and common diseases, pests, and drugs used to treat those diseases and pests in honey bees. This information is critical for guiding treatment and prevention strategies and for avoiding violative chemical residues in honey and hive products. Because some honey bee treatment strategies involve ELDU (eg, the use of lincomycin soluble powders labeled for species other than honey bees owing to the discontinuation of the lincomycin product labeled for use in honey bees by the manufacturer), this digest will also address medication use and recommendations for ensuring that honey intended for human consumption meets US regulatory requirements for entering the human food chain.

ABBREVIATIONS

AFB	American foulbrood
EFB	European foulbrood
ELDU	Extralabel drug use
EPA	Environmental Protection Agency
FARAD	Food Animal Residue Avoidance and Depletion Program
MRL	Maximum residue limit
OTC	Over the counter
VCPR	Veterinarian-client-patient relationship
VFD	Veterinary Feed Directive

FDA-Approved Medications Labeled for Use in Honey bees

In the US, 11 medications, each with 1 of 3 active ingredients (lincomycin hydrochloride, oxytetracycline hydrochloride, and tylosin tartrate), have been approved by the FDA for use in controlling infections in honey bees. Of those 11 medications, 10 require a prescription and 1 is subject to the VFD.

Antimicrobials approved by the FDA for use in honey bees, sorted on the basis of VFD and prescription status, have been summarized **(Table 1)**. Package inserts describe the strength of the approved product or medicated feed as provided by the sponsor, with specific instructions for further dilution to administer to bee colonies and describe associated withholding periods to avoid violative drug residues in honey. Instructions for medication administration may include the preparation of a dust (medication mixed with powdered sugar), sugar syrup (medication mixed in a sugar and water solution), or extender patty (medication mixed with vegetable shortening and sugar, also known as a grease patty), the choice of which is generally dependent on the scale of the beekeeping operation and the number of colonies affected. As part of the FDA-approval process, sponsors of medications intended for administration in feed (VFD drugs) must provide instructions describing how the medicated feed is to be prepared by the beekeeper for application to the hive. Those instructions are called Blue Bird labels and are available on the FDA animal drugs website.[2] A medication that is labeled for administration in powdered sugar may have a different stability or drug-residue profile when it is administered in sugar syrup or extender patties; therefore, the product label may not include instructions for mixing that medication in sugar syrup or extender patties.

Label instructions for antimicrobial use must be followed exactly to avoid violative drug residues in honey. Currently, antimicrobial labels only list the withholding period on the basis of treatment completion, so users must take care to remove honey supers (the removable frames of the hive that beekeepers place in shallow boxes on top of the hive for harvesting honey) for the entire period during which the medication is being administered as well as the labeled withholding period; that collective duration can be thought of as the honey super withholding period. It is worth mentioning that the prescription antimicrobials approved by the FDA for use in honey bees are the same products that are approved for mixing into the drinking water of other food-producing species, so if those products are left with the beekeeper, care must be taken to ensure that the appropriate directions and withholding periods are followed for administration of the product to honey bees. For example, there are currently no commercially available lincomycin prescription products labeled for use in honey bees. If a veterinarian dispenses a generic lincomycin power that is not labeled for use in honey bees, that represents ELDU, and the veterinarian must inform the beekeeper of an extended honey super withholding period.

In the US, the AMDUCA allows ELDU of FDA-approved medications only under the direction of a veterinarian. For example, a veterinarian may prescribe the use of a tylosin soluble powder that is not labeled for use in honey bees to control foulbrood if the labeled tylosin product is not available. Although the list of FDA-approved medications for use in honey bees is fairly limited (Table 1), AMDUCA permits

Table 1—Antimicrobials approved by the FDA for use in honey bees as of September 22, 2020.

Active ingredient	Formulation	Brand names	NADA No.	Indication	Dosage	Honey super withholding period (d)*	Comments
Antimicrobials available by VFD order							
Oxytetracycline	Medicated feed(9 g/kg). Concentrate to make 200 mg/oz when mixed in feed as directed by veterinarian.	Pennox 100 Hi-Flo Pennox 100-MR Pennox 200 Hi-Flo Pennox 50 Terramycin 10 Terramycin 100 Terramycin 100MR Terramycin 200 Terramycin 200 granular Terramycin 30 Terramycin 50 TM-100 TM-100D TM-50 TM-50D	095–143, 008–804, 138–938	AFB or EFB	200 mg/colony; applied every 4–5 days for 3 treatments (treatment duration, 12–15 days)	54–57	Must be obtained from a licensed authorized VFD distributor. Can be formulated in various ways and sold either in a ready-to-use form or with instructions for the beekeeper to make the final mixture. Often mixed with powdered sugar, sugar syrup. or extender patties. ELDU not permitted.
Antimicrobials available by prescription from a veterinarian or pharmacy							
Oxytetracycline hydrochloride	Soluble powder	Terramycin-343 Terramycin Terramycin soluble powder concentrate Tetroxy 25 Pennox 343 Tetroxy 343	008–622, 200–146, 200–026, 200–247	AFB or EFB	200 mg/colony as a direct dusting or mixed in sugar syrup and applied every 4–5 days for 3 3 treatments (treatment duration, 12–15 days)	54–57	P-glycoprotein pump inhibitor. Avoid concurrent use with azole fungicides, and prochloraz.
Lincomycin hydrochloride	Soluble powder	Lincomix soluble powder	111–636	AFB	100 mg in 20 g of powdered sugar dusted over the top bars of the brood chamber once weekly for 3 wk (treatment duration, 21 days)	49	CYP 450 substrate. Avoid concurrent use with other CYP substrates, inducers, or inhibitors.
Tylosin tartrate	Soluble powder	Tylan soluble	013–076, 200–455, 200–473	AFB	200 mg in 20 g of powdered sugar dusted over the top bars of the brood chamber once weekly for 3 wk (treatment duration, 21 days)	49	CYP 450 substrate. Avoid concurrent use with other CYP substrates, inducers, or inhibitors.

*Honey super withholding period = treatment period + label withdrawal time.
NADA = New animal drug application.

ELDU of FDA-approved medications in food-producing animals provided certain stipulations, which are outlined in 21 CRF 530.20,[3] are met. However, the FDA prohibits ELDU of some medications (eg, chloramphenicol, clenbuterol, diethylstilbesterol, fluoroquinolones, glycopeptides, nitroimidazoles, and nitrofurans) in all food-producing species. It is important for veterinarians to remember that regulations regarding drug use in food-producing species vary widely from country to country. Many of the online beekeeping communities and discussion forums have members from throughout the world, and some of the drug use in honey bees suggested on those sites might be prohibited in the US.

FDA Classifications of Drugs and Medicated Feeds

Before specific antimicrobial use in honey bees is described, it is important for readers to understand the organization of FDA drug and feed classifications. Prescription drugs have special safety concerns related to the animal, administrator, or food safety. In the US, prescription drugs have the following warning statement on the label: "Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian."

Veterinary Feed Directive drugs are medicated feeds intended for administration to food-producing animals and can only be used under the direction and order of a licensed veterinarian within the confines of a valid VCPR. Extralabel use of VFD drugs is prohibited in the US. Currently, oxytetracycline is the only VFD drug approved for use in honey bees (Table 1). Drugs requiring a VFD order are divided into a complex classification system outlined in 21 CFR 558.[4] This system includes 2 major categories (I and II). Category I medicated articles require no withholding period when used in food-producing animals that are considered major species (cattle, swine, chickens, and turkeys); however, the FDA makes some exceptions for VFD drug use in minor food-producing species, such as honey bees. For example, oxytetracycline is classified as a category I drug, and although it does not have a withholding period when administered to major food-producing animals, the VFD product label does include a withholding period for honey. Category II medicated articles require a withdrawal period when used in major food-producing species or are known carcinogens in humans and have more restrictions regarding distribution. As previously mentioned, oxytetracycline is currently the only VFD drug approved for use in honey bees and is classified as a category I medicated article. Category I and II medicated articles are further classified as type A (ie, drugs that are intended for use in feed or are used to manufacture medicated feeds), B (ie, drugs that must be diluted prior to feeding), and C (ie, ready-to-feed medicated feeds) articles. Among those 3 types of articles, type C articles are the VFD drugs practicing veterinarians will generally dispense for honey bees because they are ready to feed. The FDA Center for Veterinary Medicine has developed a document entitled *Guidance for Industry #120: Veterinary Feed Directive Regulation Questions and Answers*[5] that addresses questions commonly posed about the manufacture and distribution of VFD drugs and a brochure entitled *Requirements for Distributors Who Do Not Manufacture VFD Feed*[6] that provides helpful definitions and outlines responsibilities for the writing of VFD orders and distribution of VFD drugs. In general, veterinarians who choose to dispense a VFD drug for the treatment of honey bees will write a VFD order for a type C medicated article, and an FDA-authorized or notified VFD distributor will provide that article to the beekeeper on receipt of the veterinarian-signed VFD order.

Distribution of Antimicrobials for Use in Apiaries

Prescription drugs labeled for use in honey bees are not provided in unit-of-use packaging, and the containers those drugs come in often provide far more treatments than are required for the affected colonies, which leads to drug hoarding, sharing of prescription drugs among beekeepers outside a valid VCPR, and use of expired leftover medications. Veterinarians can repackage prescription medications into units of use (eg, 200-mg doses of oxytetracycline or tylosin, and 100-mg doses of lincomycin) and dispense to beekeepers the exact number of packaged doses required for the prescribed treatment period to avoid leftover medications. Prescription drug repackaging also minimizes the need for medication manipulation and provides for greater accuracy and ease of administration for beekeepers. However, for veterinarians who do not provide care for multiple apiaries, this may result in large quantities of unused drug inventory that expire before the repackaged units are used. For veterinarians who serve apiaries with small numbers of colonies, writing a VFD order for a small quantity of a type C medicated feed from a VFD distributor may be the best option to avoid drug leftovers and waste.

The requirements and procedures for writing VFD orders are similar to those for writing prescriptions for other food-producing species. The veterinarian must have a valid VCPR with the beekeeper and honey bee colony to be treated to write a prescription or VFD order for that colony. Information required for both prescriptions and VFD orders includes the client name, address, contact information, species (honey bees), date, drug, dosage (ie, dose, route, frequency, and duration) and other pertinent instructions for administration, FDA-approved medication honey super withholding period, number of refills allowed, and the veterinarian's signature and contact information. Prescriptions can be filled by the veterinarian or a retail pharmacy. Veterinary Feed Directive orders

can be filled by the veterinarian or FDA-authorized or notified VFD distributor. All medications dispensed to beekeepers must be accompanied by the manufacturer's original lot number, expiration date, approved labeling, and instructions for storage, handling, administration, and disposal.

More on the VFD

Since the implementation of the VFD[7] and FDA's *Guidance for Industry #213*[8] in January 2017, antimicrobial agents deemed medically important for human medicine can only be administered to food-producing species on a veterinarian's order by means of a prescription for medications that are administered parenterally, orally, or via water or a VFD order for medications administered via the feed.[9] Prior to the implementation of the VFD, many of the medications used to treat diseases in bees were available OTC, so the changes in regulations resulted in an expanded role for veterinarians in the diagnosis and treatment of diseases in honey bees. Again, a veterinarian must have a valid VCPR with an apiary before issuing a VFD order regardless of whether that apiary has only a few bee colonies or is a large commercial operation with hundreds of colonies. Also, it is important for veterinarians to remember that ELDU of VFD drugs is prohibited. Therefore, medicated feed articles must be fed to the treated bee colony and the honey super withholding period must be adhered to exactly as described on the VFD order to avoid violative drug residues in honey.

Veterinarians can use either paper or electronic forms for VFD orders. Regardless of the type of form, VFD orders are valid for only 6 months from the initial issuance date, and each party involved (veterinarian, VFD distributor, and animal owner [beekeeper]) must keep a copy of the VFD order on file for at least 2 years. Electronic VFDs are provided by various software companies, and an example of the paper form that contains all required elements can be found through various veterinary medical associations.[10–12] A VFD order in a fillable PDF, which prompts users to provide the required information, is available through the Honey Bee Veterinary Consortium.[13] Veterinarians can ask beekeepers whether they prefer a paper or electronic form to take to a VFD distributor. Many VFD distributors (eg, honey bee supply companies) have systems that allow submission of electronic VFD orders.

Veterinarians are encouraged to routinely consult the FDA animal drugs website[2] and search The Green Book, Blue Bird labels, and medicated feed sections to review the current listings of all FDA-approved prescription and VFD medications. The FARAD website[14] also has a list of FDA-approved medications for honey bees (www.farad.org/vetgram/min_bees.asp) as well as lists of FDA-approved VFD drug combinations for groups of animals (www.farad.org/vfd-drug-combinations.html), although no VFD drug combinations are approved for use in honey bees at the present time. Beekeepers will generally be familiar with sources for acquiring VFD drugs; however, it they are not, any beekeeper supplier can be contacted to determine the availability of VFD drugs.

Pesticide Use in Honey Bees

Besides antimicrobials, pesticides are a common drug class used for the treatment of disease in honey bees. Because most pesticides are available OTC, veterinarians should encourage beekeepers to keep meticulous records of all treatments applied. Additionally, if a honey bee colony is struggling for unknown reasons, the veterinarian should consider all pesticides and products applied to the colony and the surrounding forage for up to a 3-mile radius as well as pesticides applied to pets, livestock, and humans (eg, flea and tick products applied to outdoor pets, insecticides and fly repellents applied to horses and other livestock, insecticides and repellents used by humans, and long-acting insecticides applied to the ground to prevent termite infestation) because those products may persist in the environment and be accessible to foraging bees that take them back to the hive. In the US, veterinarians are encouraged to contact FARAD or the EPA for advice if honey bees have been mistakenly or inadvertently exposed to pesticides (eg, drift from pesticides applied to crops or for mosquito control). Chemical drift and pesticides brought back to the hive by foraging bees can cause toxicosis in the bees and unintended residues in honey.

Drug Residues, Tolerances, and Testing

Drug use or pesticide exposure in honey bees is associated with a risk for violative drug residues in honey. We were unable to find any published reports regarding violative drug residues in honey in the US, but drug residue testing of honey is probably not as widespread as it is for other food products such as milk. Drug and pesticide residues have been found in honey outside the US,[15] and thiacloprid and amitraz are the most commonly detected residues in honey in the European Union.[16]

In the US, the FDA is the agency responsible for approving antimicrobials for the control of disease in honey bee colonies and has established tolerances for those drugs in honey. The tolerance is the highest concentration of a drug or chemical substance allowed in food products intended for human consumption. Established tolerances for FDA-approved drugs in honey are available in US Code of Federal Regulations (21 CFR 556).[17] Canada,[18] China,[19] the European Union,[20] India,[21] Japan,[22] and New Zealand[23] likewise have established recommended maximum concentrations or MRLs for drugs in honey. Other bee- and hive-derived products, such as pollen, bees-

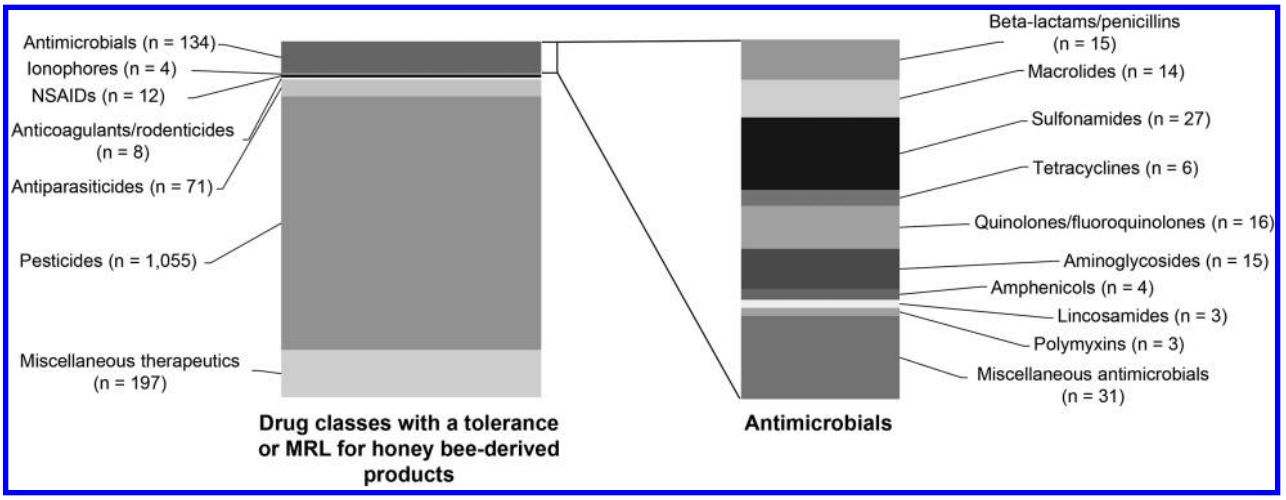

Figure 1—Bar charts that depict the categorization of chemicals for which MRLs or tolerances have been established for bee-derived food products as derived from the gFARAD-1DATA Consortium Project database.[24] The left bar chart represents a broad categorization of all chemicals (n = 1,481) with an MRL for any bee-derived food product. The right bar chart separates the antimicrobials (n = 134) into specific antimicrobial classes. A broad overview of MRLs and withdrawal times can be accessed through the online portal for the gFARAD-1DATA Consortium Project database, but a more complete investigation will require assistance from the gFARAD-1DATA Consortium Project.

wax, propolis, and royal jelly, are also used or consumed by humans. Although Japan has established guidance regarding MRLs in royal jelly, guidance on avoiding drug and chemical residues in those products is generally lacking in other countries.

For honey produced and processed in the US, the tolerance is 500 ppb for tylosin and 750 ppb for oxytetracycline and lincomycin.[17] A global MRL and withdrawal period database[24] indicates that 81 countries have established MRLs for > 1,400 chemicals, 74% of which are pesticides or other products applied to plants to stimulate growth or prevent pest activity. Approximately 10% of the established MRLs are for antimicrobials, with sulfonamides and quinolones being the most represented, whereas parasiticides, NSAIDs, anticoagulants or rodenticides, and ionophores account for 5%, 0.8%, 0.6%, and 0.3% of the established MRLs, respectively. The remaining established MRLs (approx 14%) are for miscellaneous therapeutic classes of drugs and herbal medicines **(Figure 1)**. The most common global MRLs for chemicals in honey are 0.01, 0.05, and 0.1 ppm. Products that are approved by the FDA (drugs) or registered by the EPA (pesticides) and their associated tolerances are discussed in detail elsewhere in this digest.

In the US, pesticides in honey are monitored by the USDA.[25] The FARAD has recently published a listing of commercial drug residue screening tests for honey.[26] These tests allow honey producers to rapidly test honey for residues of the drugs listed.

Honey Super Withholding Period

If a beekeeper wishes to treat a bee colony, US and European Union regulations require that the honey supers be removed from the colony before, throughout the duration, and for a prescribed period after drug treatment is discontinued. The intended purpose for keeping the bees (eg, to increase bee populations or maximize honey harvest) will determine the best time to administer treatments because the treatment process can be lengthy and potentially affect honey harvest.

In the US, medication withholding periods for animal-derived food products are usually documented on the packaging of FDA-approved or EPA-registered products. Although the time honey must be discarded or not used for human consumption following treatment may be equated to the withdrawal time for other animal-derived food products, it is not practical for honey to be removed from the hive on a daily basis. Therefore, it is more appropriate to consider a honey super withholding period that includes the duration during and following treatment that honey supers must not be placed on the hive. The reasoning behind such regulations is due to the lack of metabolism of drugs or other substances stored within a wax comb. Most chemicals present in honey at the time of its production will persist after it is deposited and capped in the super. The exceptions are drugs such as tylosin and oxytetracycline, which degrade in honey owing to the high temperature, 35 °C, of the hive interior; however, the degradation products of those drugs will persist in the honey.

The following scenario is an illustrative example for avoiding drug residues in honey. The package instructions[27] for the miticide amitraz 3.33% direct users to remove honey supers from the hive, place the amitraz 3.33% strips in the hive for minimum of 42 days but no longer than 56 days, remove the strips, and not replace the honey supers in the hive until 14 days after the strips are removed from the hive. So, although the EPA-registered label for amitraz states that the honey super withholding period

is 14 days after the treatment is removed from the hive, in an operational sense, the actual time that honey from amitraz-treated hives must be discarded, or not used for human consumption, ranges from 56 to 70 days (duration of treatment [42 to 56 days] + the 14-day withholding period following discontinuation of treatment). In-depth honey super withholding period information has been summarized for FDA-approved antimicrobials (Table 1) and EPA-registered miticides **(Table 2)** commonly administered to honey bees.

Annual Beekeeping Cycle

It is important for US veterinarians who treat honey bees to understand the annual cycle of hive growth in North America and the annual schedule of beekeeping when considering medication use.

Table 2—List of EPA-registered miticides approved for use in honey bees.

Chemical (brand name)	Mechanism	Dosage	Restrictions	Efficacy (%)	Pros	Cons	EPA honey tolerance (ppm)	EPA wax tolerance (ppm)	Honey super withholding period (d)*
Synthetic chemicals									
Amitraz 3.33% strips (Apivar)	MAO inhibitor	2 strips/brood chamber for 6 wk	Do not use more than twice a year	95	Easy, effective	Potential for resistance; potential residues in wax and honey	0.2	9	56–70
Fluvalinate 10.3% strips (Apistan)	Pyrethrin	2 strips/ brood chamber for 6–8 wk	Best results at temperatures > 10° C	95–99	Highly effective, easy to use	Resistance emerging, potential for additive and synergistic toxic effects with pesticides in landscape, potential residues in wax and honey	0.02	—	56–70
Coumaphos 10% strips (CheckMite)	Organo-phosphate	2 strips/brood chamber for 6 wk	Do not use in queen-rearing colonies	85–99	Easy to use, effective, and also effective against small hive beetles	Organophosphate residues in hive products, toxic to queens and drones, potential for additive and synergistic toxic effects with other pesticides in landscape	0.15	45	56
Essential oils									
Thymol 25% bags (Apiguard), 15-g crystals (Thymovar)	Essential oil fumigant	Spread gel or place crystals in mesh bag on top of frames twice at 2-wk intervals	Cannot use when honey supers are on. Must be used between 15 and 40.6° C.	74–95 (efficacy improves with warmer temperatures)	Easy to use, naturally derived	MAO inducer, may counteract amitraz; may reduce queen laying, skin irritant; may cause bees to beard in hot weather	Exempt†	Exempt†	30
Thymol 74.09%, eucalyptol 16%, menthol 3.73%, camphor 3.73% tablets (ApiLifeVar)	Essential oil fumigant	3 tablets/brood chamber placed on top of frames at corners for 7–10 days for 2–3 treatments	Do not use more than twice a year; do not use with honey supers in place; must be used between 18.3 and 29.4° C	70–90 (efficacy improves with warmer temperatures)	Natural product, easy to use	Must only be used in warmer weather, menthol will drive bees out of hive, oils may taint the taste of honey, bees become irritable during treatment	Eucalyptus exempt at < 2 g/hive at concentrations > 80%; menthol exempt*	Eucalyptus exempt at < 2 g/hive at concentrations > 80%; menthol exempt*	Eucalyptus, N/A; Menthol, 51–60
Organic acids									
Formic acid 46.7% strips (Mite Away Quick Strips)	Organic acid fumigant	2 strips/brood chamber for 6 wk. Strips may be left in hive after treatment.	Can use with honey supers on hive. Use acid-resistant gloves when applying; keep screened bottom board open and use spacer above brood chamber to increase ventilation. Use when temperature between 10 and 33.3° C.	61–98 (less effective at temperatures > 33.3° C		Can cause brood and queen mortality and absconding if used > 33.3° C. Skin, eye, and lung irritant to humans.	Exempt*	Exempt*	N/A
Oxalic acid (wood bleach)	Contact miticide	Follow fumigation label if fumigating. For topical application, dilute solution 1:1 with sugar syrup and apply 5 mL/frame (not > 50 mL/colony) between frames of brood chamber. Some beekeepers recommend using glycerin as vehicle to keep bees from ingesting.	Do not use more than twice a year. Use only during broodless periods.	82–99 when brood not present	Effective for removal of mites from adult bees	Corrosive, may chill cluster if applied during cold temperatures	Exempt*	Exempt*	N/A
Hops beta acids 16% strips (HopGuard II)	Contact miticide	2 strips/brood chamber for 4 wk. Do not use more than 3 times/y. Do not use when brood are present.	Not legal in all states. May be used with honey supers in place. Do not collect honey from brood combs; collect honey only from honey supers.	Unclear	Natural product	Not approved in all states; check with state apiary inspector prior to use. Strips are messy to use. Wear disposable gloves.	Exempt*	Exempt*	N/A
Hops beta acids 16% strips (HopGuard III)	Contact miticide	2 strips/brood chamber for 2–4 wk. Do not use more than 4 times/y. Do not use when brood are present.	Not legal in all states. May be used with honey supers in place. Do not collect honey from brood combs; collect honey only from honey supers.	Unclear	Natural product	Not approved in all states; check with state apiary inspector prior to use. Strips are messy to use. Wear disposable gloves.	Exempt*	Exempt*	N/A

Nonchemical methods

Screened bottom board—Mites drop through open screen onto ground. Minimally effective. Should not be used as a sole treatment.

Drone brood culling—Remove and cull all drone brood, which contains the highest number of mite eggs. Not as effective as chemical treatments. Constant removal of drones has unknown consequences to the colony, although removal of ≥ 5 frames at once does have a negative impact on the colony.

Brood interruption—Divide colony (split) or cage queen for 1–2 wk to prevent egg laying. Decreases the amount of brood available for mites to lay eggs in. Risks damage to queen and requires either purchase of an artificial queen or time for the split colony to make a new queen. Risky and minimally effective, compared with chemical treatments.

Requeening with hygienic queen—Introducing a queen with known hygienic (mite-removing) properties. Long-term solution to reduce the need for chemical treatments. Risk of new queen being killed by the colony.

Powdered sugar dusting—Dusting adults with powdered sugar 1–2 times/wk. Theoretically, mites are removed from bees by grooming from other bees. Not a stand-alone treatment and very labor intensive. Potential contaminants in powdered sugar may lead to toxicosis (eg, glyphosate and pesticides in corn starch anticaking additives).

*Exempt indicates that the EPA has not established a maximum tolerance for this substance in this hive product.
MAO = Monoamine oxidase. N/A = Not applicable.

Knowing when the colony is dormant, brood (the developmental stages of honey bees) are increasing, swarming is going to occur, brood are dwindling, and bees are forming the winter cluster to stay warm is critical to understanding when and when not to apply treatments to the colony. It is also important to know when the beekeeper plans to apply annual miticides and other nonprescription treatments relative to the honey flow to mitigate the risk for chemical residues in honey. Veterinarians should familiarize themselves with the annual cycle of beekeeping in their area because it can vary widely and will impact treatment decisions.

At temperatures less than approximately 10 °C, bees decrease foraging and will form into a cluster inside the hive to maintain the brood in the center of the cluster at a constant 35 °C. During the winter months when the mean ambient temperature is substantially < 10 °C and nectar in the landscape is scarce, bees do not forage and produce only minimal brood, keeping the population fairly static. As the ambient temperature increases to > 14 °C and nectar sources begin to increase, the colony ramps up brood rearing and nectar foraging. In early spring when brood and bee populations are increasing, beekeepers open the hive to inspect it and administer any required treatments. This ensures that adequate honey super withholding periods can be observed prior to the main honey flow, which begins later in the spring.

During the honey-making season, beekeepers add boxes of specialized frames (honey supers) to the tops of the hives, which are likely to be filled with honey and no brood owing to their shorter dimensions. As bees forage nectar, they place it into their honey stomach (crop) where it is mixed with enzymes produced in the hypopharyngeal glands that can later convert it into honey. On returning to the hive, the bees regurgitate the nectar mixture and pass it to younger food-handling bees that repeat the nectar storage and mixing process before regurgitating it into drawn-out wax combs, which are produced by wax-secreting glands of young adult bees and shaped into honeycomb cells in either the brood frames (to be used sooner by the bees) or the honey supers (to be consumed later by the bees or by humans if harvested). Bees fan their wings over the honey until the water content is evaporated to < 18% to prevent bacterial growth and fermentation. The honeycomb cells are then capped with wax to store the honey for when nectar sources become scarce. The colony population and food stores increase steadily as the summer solstice approaches.

After the summer solstice, the number of daylight hours decreases, the spring nectar flow stops, and food supplies become scarcer, so the bees begin preparing for winter by tapering off brood rearing. If no nectar is available, the bees will start consuming honey stores. Beekeepers typically harvest the honey supers at this time. Because bees store a little honey in the brood-making frames, they usually have enough to provision them through the summer when fewer food supplies are available. However, some beekeepers may opt to feed their bees additional sugar syrup during this time. When the fall nectar flow starts, usually in late summer or early fall, the bees begin foraging again and will show little interest in any offered sugar syrup. At this time, the beekeepers will place the honey supers back on the hive so the bees have plenty of space to store foraged nectar. Many beekeepers leave the honey supers in place to provision the bees through winter, but some beekeepers will harvest the supers and resume feeding sugar syrup so that the bees can store the sugar syrup for use in winter.

As the nights get colder, < 10 °C, the colony will only make as much brood as its adults can effectively cover and keep warm in the cluster at the center of the colony. At some point during the late fall and early winter, the queen stops laying eggs, and the population slowly declines to its lowest number. Understanding where the bees are in the nectar flow and honey producing cycle is a critical factor for prescribing drug treatments to honey bees. If honey bee colonies are in the peak of honey production during nectar flows, beekeepers are unlikely to apply treatments that would cause them to remove honey supers and lose honey production. Additionally, some diseases and pests are seasonal and may become self-limiting without drug treatments, so it is important for veterinarians to understand this cycle and avoid prescribing drug use whenever possible during nectar flows. Because temperature and nectar flow vary widely across temperate climates, veterinarians are encouraged to be familiar with the phenology of their local landscapes and to consult with local beekeeping associations to gain an understanding of the annual beekeeping cycle in a given area.

Bee Husbandry

Honey bee management differs substantially from the management of other food-animal species with which most veterinarians are familiar; therefore, more detail about apiary husbandry is provided to ensure medicant applications do not result in violative chemical residues in honey destined for human consumption. Unlike other animal-sourced foods, such as eggs and milk that are produced by individual animals, honey stores accumulated by tens of thousands of bees in a colony cannot be discarded on a daily basis. Consequently, care must be taken to remove the honey supers both during and after treating a colony to ensure the honey is free of violative residues. Additional information regarding honey bee biology, nutrition, and husbandry can be found on the honey bee species page of the FARAD website.[14]

Beekeepers use a wide variety of hive body styles to house bees, and the only requirement for honey production is that the hive body has frames that can

be easily removed for inspection. For the sake of simplicity, information in this digest will primarily refer to use of the Langstroth hive body, which is one of the most commonly used hive types. The husbandry information provided in this digest has been oversimplified and is not intended to convey a complete understanding of beekeeping. Readers are encouraged to seek additional resources and supplemental references **(Appendix)** for a more comprehensive understanding of apiculture, hive body types, and awareness of factors contributing to the rapid and worldwide decline of honey bee colonies.

Infectious Diseases of Honey bees

American foulbrood

American foulbrood is caused by the bacterium *Paenibacillus larvae*, which infects older, sealed larvae or pupae causing them to decay, which results in a foul odor, hence the name of the disease. American foulbrood usually leads to the death of infected colonies. Thus, state apiary inspectors closely monitor for evidence of this disease. Hives affected by or lost to AFB should be destroyed to prevent stronger bee colonies from robbing leftover honey stores and transmitting the bacterial spores to healthy colonies. American foulbrood can be detected in suspect cells (discolored, sunken, perforated, or partially capped cells) by use of the ropiness test, which consists of inserting a toothpick or tweezers and twisting out the cell contents. The disease is confirmed if the cell contents twist and rope out of the cell then spring back into the cell when the strand breaks. The USDA Bee Research Laboratory (www.ars.usda.gov/northeast-area/beltsville-md-barc/beltsville-agricultural-research-center/bee-research-laboratory/) in Beltsville, Md, can perform diagnostic testing for AFB and test *P larvae* isolates for antimicrobial resistance. In many states, AFB is a reportable communicable disease, and the state apiary inspector must be contacted whenever AFB is diagnosed. All tools used to diagnose AFB should be safely disposed of or carefully sanitized with bleach and heat before subsequent use. Many state inspectors recommend sealing the used tools in a plastic bag immediately after completion of the test and thorough hand hygiene before inspecting another hive to prevent contamination between hives. When AFB is diagnosed, state apiary inspectors will likely inspect surrounding apiaries to determine whether the disease has spread to other colonies. In some instances, veterinarians may be asked to prescribe antimicrobials to neighboring apiaries in an effort to control the spread of AFB by bees foraging from the infected colonies. In Europe, AFB is not treated, and AFB-infected colonies and contaminated equipment must be destroyed.

In the US, treatment of AFB is controversial because it does not eliminate *P larvae* spores and may mask signs of the disease in infected hives making detection more difficult. Regulations regarding the treatment of AFB vary among states; therefore, veterinarians are advised to consult with the local apiary inspector for guidance regarding the management of AFB-infected hives. Some states, such as Florida, mandate that bees from *P larvae*–infected hives be euthanized and contaminated equipment burned,[28] whereas other states allow AFV-infected hives to be treated with an appropriate antimicrobial and do not require destruction of contaminated equipment. In states that allow treatment of AFB-infected hives, antimicrobials approved by the FDA to control AFB in bees include oxytetracycline (200 mg/colony, applied every 4 to 5 days for 3 treatments), lincomycin (100 mg/colony, applied every 7 days for 3 weeks), or tylosin (200 mg/colony, applied every 7 days for 3 weeks). All 3 antimicrobials are available as prescription drugs, and oxytetracycline is also available as a VFD drug. Although oxytetracycline-resistant *P larvae* isolates have been reported, oxytetracycline is the antimicrobial most commonly used to treat AFB because it is available in several formulations allowing flexibility in prescribing.

European foulbrood

European Foulbrood is more common and less severe than AFB. It is caused by the nonspore-producing bacterium *Melissococcus* (formerly *Streptococcus*) *pluton*. Similar to AFB, EFB infects larvae, but unlike AFB, it infects only younger unsealed larvae. Although AFB-infected larvae are elastic and ropy, EFB-infected larvae appear rubbery and granular and fail the ropiness test, thereby ruling out AFB. The odor associated with EFB can be sour but is not foul and sulfurous like the odor associated with AFB. European foulbrood is seasonal, often occurring in the early spring before initiation of nectar flow, disappearing during nectar flow and summer, and reappearing in fall. European foulbrood is generally preventable by maintaining large healthy unstressed colonies.

European foulbrood is associated with a dearth of nectar, high Varroa mite populations, and other colony stressors. Typically, EFB-infected colonies can rid themselves of the disease once a steady nectar flow begins in the spring. Many beekeepers avoid the use of antimicrobials, replace infected brood nests with a clean foundation, and watch the colony to see if it can resolve EFB without treatment. However, antimicrobials may be used if the colony is unable to stop the spread of disease. At the present time, oxytetracycline is the only antimicrobial approved by the FDA for control of EFB; there are no antimicrobials approved by the FDA for prophylaxis of EFB. Heavily infected colonies can be treated with oxytetracycline (200 mg/colony) mixed in powdered sugar and spread on top of the bars on the frames of the brood nest every 4 to 5 days for 3 treatments. Prophylactic use of oxytetracycline for prevention of EFB is not recommended owing to the risk for the development of antimicrobial resistance and the numerous drug and chemical interactions involving oxytetracycline

(eg, oxytetracycline disrupts the specific ABC transporter pump for the miticide fluvalinate in honey bees).[29]

In areas where EFB is endemic, oxytetracycline may be used prophylactically, in which case the honey super withholding period is the same as that indicated on the label for treatment of EFB (ie, a total of 54 to 57 days, based on a 12- to 15-day treatment period and a 42-day posttreatment withholding period). Ideally, all woodenware in EFB-infected hives should be destroyed. Some sources may recommend scorching wooden frames with a blowtorch and then disinfecting them with 1.5% sodium hypochlorite (bleach); however, that may not completely eradicate all *M pluton* bacteria and likely represents more effort than it is worth. Any nonwooden tools used in EFB-affected colonies should be thoroughly disinfected with bleach before being reused.

Nosema

Nosema is caused by the protozoa *Nosema apis* and *Nosema ceranae,* with the latter being the most prevalent and causing more serious problems in bees.[30] *Nosema apis* infection, also known as bee dysentery, occurs most commonly in fall and early spring, causes distended abdomens and diarrhea, and is distinguished by bees crawling around the front entrance of the hive with wings held at odd angles.[30] Nosema is suspected when diarrhea splatters are visualized on the bottom board or front of the hive body; however, it is important to note that Nosema is not the only cause of diarrhea in bees. *Nosema ceranae* infection can occur during any time of the year and may cause large population losses but is not associated with dysentery, diarrhea, or the crawling behavior associated with bees infected with *N apis*. Both forms of Nosema are strongly linked to stress and are best prevented by maintaining strong healthy colonies. Diagnosis of Nosema is confirmed by microscopic examination of bee hindgut contents and identification of spores characteristic of *Nosema* spp.[30]

Historically, fumagilin-B was used for both prevention and control of Nosema. Fumagilin-B is toxic to mammals and is not used in human medicine. Consequently, it is not considered medically important for humans, is not covered under the VFD, and is available without a prescription. Although fumagilin-B has no recognized legal status in the US, it is available from retailers as a dry powder (fumagilin-B concentration, 20 mg/g) for dilution with a 2:1 sugar-water syrup (heavy sugar syrup) at a rate of 4.5 g of powder (90 g of fumagillin-B)/3.8 L (1 gallon) of heavy sugar syrup. The mixture is fed to bees at a rate of 7.6 L (2 gallons [180 mg of fumagillin])/2 chambers of bees (approx 30,000 bees). Feeding the fumagilin-B mixture to bees for 4 weeks is believed to be sufficient to clear Nosema infection, even though the label instructs that the mixture should be fed for a period of several weeks. It is often administered in the fall after the honey flow has stopped. Heavy sugar syrup is used as the delivery vehicle for fumagilin-B because the low water content of the syrup is believed to encourage bees to store it for later use, and they will consume it over a longer period (ie, > 4 weeks) than they would if it was delivered in lighter syrup, powder, or extender patties. Some beekeepers prefer to dilute the fumagillin-B powder in a 1:1 sugar-water syrup and place 1.9 L (0.5 gallons) of the freshly made mixture in the hive once weekly for 4 weeks to ensure consistent consumption. The labels of available fumagillin-B products indicate that it should not be fed to bees immediately before or during honey flow, but they do not provide honey super withholding period.

Other treatment options for Nosema include the feeding of plant phytochemicals and probiotics to strengthen the honey bee gut microbiome. It is important to note that drugs such as metronidazole or tinidazole, which are used to treat honey bees for *N ceranae* in other countries, are prohibited from use in honey bees in the US.

Mites

As early as 1921, 2 different mites (Varroa mites and tracheal mites) were recognized as parasites of honey bees. However, because of efforts by the US government to restrict importation of affected bees, those 2 species of mites were not detected in US honey bees until the late 1980s. Unfortunately, migratory beekeeping (the practice of maintaining bees for crop pollination purposes, which requires transportation of bees to various crop locations) and the shipment of bees for apiculture purposes have resulted in the widespread dissemination of both types of mites, although Varroa mites are the more serious threat to honey bee health.

Varroa mites—Varroa mites (*Varroa destructor*) represent a serious health threat to honey bees and are prevalent in all countries except Australia where strict biosecurity measures at ports of entry and vigilant surveying by beekeepers have been effective in keeping varroa out. Varroa mites were first discovered in US honey bees in 1987 and rapidly spread to all states.[31] Unlike tracheal mites, fluctuations in Varroa mite populations mirror those in honey bee colonies (ie, increasing in the summer, peaking in the fall, and then dropping off over winter and remaining low during spring). Varroa mites that are not eliminated in late summer and early fall will most certainly become more problematic in winter and spring. In the spring and summer, the mites mostly infest drone (male bee) brood, with some mature mites infesting adult male and female bees. In the fall and winter, the mites primarily infest adult bees as the brood population declines. Reproduction of Varroa occurs entirely within a brood cell. A female mite enters a brood cell before it is capped, begins to feed on the pupal fat body,[32] then lays eggs after the brood cell is capped. Newly hatched mites mate, and the mated females

Table 3—Summary of common methods used to assess honey bees for mites.

Method	Directions	Treatment threshold	Pros	Cons
Sticky board or natural drop	Cover removable bottom board with vegetable oil or petroleum jelly. Count mites that have dropped onto the board after 3–5 days. Divide the total number of mites counted by the number of days sampled.	Seasonal. Spring, 5–10 mites/d; fall, 50–60 mites/d.	Noninvasive and does not require sacrificing bees (nonsacrificial).	Inaccurate because dropped mites can be scavenged by ants before they are counted, brood-encased mites do not drop, and mites may crawl back up into the colony.
Sugar shake jar	Collect 0.5 cup (approx 300) of live bees from frames over the brood nest and place in a pint jar covered with 1/8-inch hardware mesh lid. Add 2 tablespoonfuls of powdered sugar through the mesh lid and shake the jar until the bee sare covered with sugar. Allow the jar to sit for 3–5 min, then invert it and shake the sugar and mites into white container full of water. Add another tablespoonful of powdered sugar into jar, shake, and wait at least 30 s, then shake sugar and mites into the white container. Mites should be easy to see against the white backround. Count the mites. Divide the number of mites by the approximate number of bees (300), then multiply by 100 to calculate the mite load percentage (eg, 6 mites/300 bees X 100 = 2%). Release the bees in front of the hive where they were collected.	See Table 4.	Accurate and nonsacrificial.	Invasive.
Alcohol or soap wash jar	This method results in the unnecessary euthanasia of healthy honey bees and is strongly discouraged by these authors.			Invasive and sacrificial.

Table 4—Summary of the mite load percentage thresholds used to determine whether miticide treatment is necessary for honey bee colonies on the basis of colony phase.

	Treatment indication based on percentage of mites counted in relationship to the number of bees sampled		
Colony phase	No treatment needed	Treatment indicated	Immediate treatment required
Dormant with brood (late winter, early spring)	< 1%	1%–2%	> 2%
Dormant without brood (late fall, winter)	< 1%	< 2%–3%	> 3%
Population increasing (spring)	< 1%	< 2%–3%	> 3%
Peak population (spring, summer)	< 2%	< 2%–3%	> 5%
Population decreasing (early fall)	< 2%	< 2%–3%	> 3%

emerge to migrate and infect other brood cells. Varroa mites cause morbidity and death in bees by 2 primary mechanisms. The first mechanism is the loss of fat body stores leading to the death of infected brood. The second mechanism is the transmission of viral disease. Varroa mites have been identified as the vector for 8 viruses.[33] The most commonly recognized Varroa mite–vectored virus of bees in North America is the deformed-wing virus. Bees infected with the deformed-wing virus are easily recognized because they are observed crawling with deformed wings, legs, and abdomens, which makes them unable to fly. If left untreated, honey bee colonies infected with Varroa mites typically die within months to a few years, depending on the climate.

Beekeepers use various methods to check for the presence of mites **(Table 3)**, and it is recommended that mite counts be performed at least 4 times a year. The least invasive, and least accurate, method of counting mites is called the natural drop or sticky board method, whereby the removable bottom board of the hive is covered with vegetable oil or petroleum jelly to capture mites that fall out of the hive.[34] This method is often inaccurate for several reasons. Two-thirds of the mite load may be in brood in the spring and therefore not dropping out of the hive, scavengers such as ants may eat the dropped mites before they can be counted, and live mites may crawl back up into the colony and reattach themselves to bees before the count is performed. Jar sampling methods are more accurate for counting mites, and the mite thresholds for treatment are summarized **(Table 4)**.

Numerous miticides are available for the treatment of Varroa mites in honey bees. These miticides vary in terms of complexity of use, seasonal restrictions, and toxic effects (Table 2). All miticides are sold OTC; however, some require a special license for use by beekeepers or are banned from use in certain states (eg, 10% coumaphos and hops β acids). Before advising the use of OTC miticides, veterinarians should check with the appropriate state apiary inspector's office (apiary-inspectors.org/us-inspection-services/) to determine whether the state restricts the use of certain miticides. Some miticides are EPA-registered products, which means that the EPA has established tolerances for residues of those products in honey and wax comb and extralabel use is not permitted. Updates on EPA tolerances for chemicals in honey and wax can be found in the US Code of Federal Regulations (40 CFR 180).[35] It is important to note that miticides may have additive or synergistic toxic effects with other miticides or chemicals used for agricultural purposes.[36] Veterinarians should remind beekeepers to not use more than one miticide at a time and to consult a veterinarian before any hive treatments or agricultural chemicals are used in combination with a miticidal agent because some chemical combinations can result in violative residues in honey as well as toxicosis and death of the bees or brood.

Tracheal mites—As their name implies, tracheal mites (*Acarapis woodi*) reside within the trachea of honey bees. Tracheal mite populations are cyclical, increasing in the fall, peaking in the winter, and rapidly declining in the summer, which is opposite of the

population cycle for Varroa mites. The mechanism by which tracheal mites cause the death of honey bees is unclear. Bees infested with tracheal mites do not die from asphyxiation; however, the mites do compromise respiration, which impairs the ability of affected bees to fly and forage. Tracheal mite–infested bees also have a characteristic disjointed appearance to their wings, known as K-wing, which may contribute to their inability to fly.[31]

Tracheal mites are rarely a problem for honey bees in North America, although almost all US state entomology services provide recommended treatment schedules and many beekeepers prophylactically treat their hives against tracheal mites. Menthol is the only EPA-registered product approved for the treatment and control of tracheal mites in honey bees. Menthol crystals work through volatilization and must be applied (dose, 50 g/colony) to the hives when ambient temperatures are consistently warm (eg, 15.6 to 26.7 °C). Menthol crystals should not be applied to hives on days when the temperature is > 26.7 °C because the increased rate of crystal volatilization may result in menthol concentrations that are lethal to bees. The only EPA-registered menthol product[a] currently available in the US contains 99.94% menthol crystals in a 25-kg package. Thus, beekeepers need to accurately measure the volume of menthol crystals necessary to achieve the recommended dose (50 g/colony). Veterinarians should be aware that the EPA-registered label for this product is confusing, and violative menthol residues in honey may result if the instructions are misunderstood by the beekeeper.[37]

Bees find menthol unpleasant and may be driven from the hive and stop all brood rearing while menthol is present. Because beekeepers do not wish to drive bees from the hive and the label instructions on menthol crystals are confusing, some beekeepers opt to remove the honey supers, place 50 g of menthol crystals wrapped in cheesecloth on top of the brood frames as soon as the daily ambient temperature exceeds 15.6 °C, remove the menthol packet from the brood frames after 14 days, and replace the honey supers 30 days later to avoid menthol residues and taste in the harvested honey. Most beekeepers consider menthol to be a natural substance and prefer to use it even if an illegal extralabel manner.

Small hive beetles

Small hive beetles (*Aethina tumida*) were first observed in the US in the mid-1990s and are currently present in all states.[38] Small hive beetles are small (length, 0.6 cm [0.25 inches]) black beetles that are generally observed on the inside of the inner cover of the colony hive box when it is opened. They are usually considered more of a nuisance than a pathogen and are particularly troublesome for smaller colonies that cannot keep up with sequestering the beetles at the periphery of the colony. Small hive beetles lay eggs in honey bee colonies, and the secretions (slime) from the hatched larvae contaminate the honey causing it to ferment, thereby ruining the honey harvest.

Once a hive becomes contaminated with small hive beetle slime and the honey ferments, the frames within the hive should be removed for thorough cleaning because the bees will not be able to clean them. Most beekeepers will place oil-filled beetle traps inside the hive to catch and drown small hive beetles. Outside the hive, small hive beetle larvae can be prevented from pulpating by drenching the ground underneath the hive with ground treatments such as permethrin. Neither the oil used in the beetle traps nor treating the ground underneath the hive with permethrin has been associated with violative chemical residues in honey.

Wax moths

Greater wax moths (*Galleria mellonella*) and lesser wax moths (*Achroia grisella*) do not cause direct harm to adult bees or larvae but can be particularly destructive to comb, honey, and hive woodenware. Wax moths are generally not a problem in strong honey bee colonies but can be easily identified by evidence of silken tunnels and black fecal droppings on the honeycomb.

Wax moths prefer to rear their brood on stored frames of comb, so many beekeepers store comb in freezers to kill any wax moth eggs and larvae present, melt all used comb into beeswax, or use a chemical agent on combs stored outside the hive. There are no FDA-approved products for the treatment of wax moth infestation inside a colony where bees are present, but there are EPA-registered products that can be used to protect empty combs against wax moth predation outside the hive. Those products include paradichlorobenzene and the biologic larvicide *Bacillus thuringiensis aizawai* B402 and must not be used inside hives where bees are present. Although EPA-registered naphthalene products (moth balls) are used to protect stored clothes from moth predation, they should not be used to protect beehives from wax moth predation because their lipophilic nature may permanently contaminate the wax comb.

Case Examples

The following scenarios are provided as examples of common apiary-related challenges veterinarians may encounter to further illustrate how veterinarians can prescribe medications for honey bees.

Scenario 1

American foulbrood was recently diagnosed at local apiary (A). A nearby apiary (B) with 5 honey bee colonies would like to control any AFB that may be transmitted to their colonies by foraging bees entering colonies at the infected apiary A. A veterinarian examines the colonies in apiary B, does not find evidence of active AFB, and determines that administration of a VFD oxytetracycline product will

be the best method to control AFB in apiary B. The veterinarian pulls out their laptop computer and uses a fillable PDF to complete a VFD order that includes the following information: veterinarian's name and contact information, beekeeper's name and contact information, drug name (oxytetracycline), drug concentration (6,400 g/ton), duration of treatment (15 days), animal species (honey bees), number of refills (none), indications for treatment (control of AFB), cautions (do not apply to uncapped open brood, use exactly as directed), number of honey bee colonies to be treated (5), address where the treatment will be applied (apiary address if different from the beekeeper's address), special instructions (Remove honey supers. Place 1 oz [2 tablespoonfuls] of this feed on the outer ends of the top bars of the brood frames every 5 days for a total of 3 times. Do not get any of the dust in the open brood cells.), honey super withholding period (total of 57 days from the first day of treatment. Any honey that was in the hive during the 57 days following the first day of treatment should not be consumed by humans.), date of issuance, VFD expiration date (maximum of 6 months after date of issuance), and veterinarian's signature.

The veterinarian submits the VFD order electronically to a beekeeping supplier that is authorized to dispense medicated type C feeds, emails a copy of the VFD order to the beekeeper and tells them to maintain a copy for 2 years, and saves a copy of the order in the electronic medical record that documents the details of their visit to the apiary. The veterinarian asks the beekeeper if they have any questions and tells the beekeeper to call the veterinarian if the beekeeper has any additional questions or concerns.

Scenario 2

American foulbrood has been diagnosed in an apiary where 10 of 25 colonies were infected. The infecting strain of *P larvae* was confirmed to be resistant to oxytetracycline by the USDA Honey Bee Research Laboratory. The state apiary inspector has recommended euthanasia of the bees in the 10 infected hives and destruction of the contaminated equipment and has called a veterinarian to institute control methods to prevent the spread of AFB to the remaining 15 colonies. Because the infecting organism is resistant to oxytetracycline and the lincomycin product labeled for honey bees has been discontinued, the veterinarian decides to prescribe and dispense tylosin tartrate to control AFB in the remaining 15 colonies. The tylosin product approved for use in honey bees is commercially packaged as 100 g of soluble tylosin tartrate powder in a jar. The label dosage of control of AFB is 200 mg of tylosin tartrate/colony once weekly for 3 weeks. The molecular weight of tylosin tartrate is approximately 1.2 times that of tylosin base, so the veterinarian has worked with a compounding pharmacist to repackage the commercial tylosin powder as follows: 240 mg tylosin tartrate powder into a gelatin capsule containing 200 mg of tylosin base. Because that is the dose of tylosin tartrate that the veterinarian uses for small animal patients, it is a convenient size for them to stock in their ambulatory practice. The veterinarian dispenses 45 of the compounded capsules to the beekeeper with the following instructions for each colony: Remove the honey supers. Mix the contents of 1 capsule (tylosin base, 200 mg) with 20 g (approx 5 teaspoonfuls) of powdered sugar and spread the mixture on the top of the brood chamber frames of the colony. Repeat the dosing procedure once weekly for a total of 3 treatments for each colony. Honey supers may not be replaced on the treated colony until at least 49 days after the first dose of tylosin is applied.

Scenario 3

During the initial spring inspection of their hives, a hobbyist beekeeper suspects that 2 colonies are infected with EFB. The preceding weeks have been rainy and cold. and the nectar flow has not yet started. A veterinarian visits the apiary and confirms that some larvae have been infected with EFB. Because EFB is seasonal and may disappear after the spring nectar flow, the veterinarian suggests that the beekeeper replace the frames with infected larvae with new frames and foundation and wait until the nectar flow is in full swing before deciding whether to apply an antimicrobial. The veterinarian returns in 6 weeks to reinspect the hives. There are no infected larvae, and all brood appear to be healthy. As a precautionary measure, the veterinarian advises the beekeeper to rotate out and destroy the frames in the existing colonies because *M pluton* may persist in the comb.

Summary

Veterinarians have a crucial role in honey bee medicine, especially with the passing of the VFD legislation in 2017. Combined with an understanding of honey bees and honey bee husbandry, veterinarians can use their unique knowledge about physical examination, diagnostic techniques, and pharmacology to provide care for honey bees while avoiding violative drug residues in honey and other hive products. Veterinarians can anticipate and mitigate the effects of honey bee exposure to intended treatments and unintended exposures by careful evaluation of diet, environment, and concomitant chemical exposures. Partnering with apiary inspectors and beekeepers, veterinarians help maximize honey bee vitality by ensuring rational chemical use in a manner that minimizes the risk of violative chemical residues in honey and other hive products intended for human consumption.

Acknowledgments

The FARAD Program is funded by a USDA National Institute of Food and Agriculture grant.

Footnotes

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Appendix

Additional resources and supplementary readings regarding the treatment and care of honey bees.

Websites

AVMA. Honey bees: a guide for veterinarians. Available at: www.avma.org/sites/default/files/resources/honey bees-veterinary-medicine-guide-for-veterinarians.pdf
FARAD. Honey Bees. Available at: www.usfarad.org/honey-bees.html
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USDA-APHIS National Veterinary Accreditation Program. Module 30: the role of veterinarians in honey bee health. Available at: nvap.aphis.usda.gov/BEE/bee0001.php

Supplemental reading

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