

Transcript of FDA Webinar

Draft Guidance for Industry #256, Compounding Animal Drugs from Bulk Drug Substances

November 21, 2019

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Amber McCoig, DVM, MPH: Thank you for joining us today. We appreciate the opportunity to share information on the *Draft Guidance for Industry, Compounding Drugs from Bulk Drug Substances*. My name is Amber McCoig. I am the Deputy Director for Compliance here at the Center for Veterinary Medicine, or CVM. And I am also a veterinarian. I am very familiar with the complexities of compounding from both my veterinary background and practice and regulatory experiences that I've had over the last 15 years.

Today I will be joined by Janice Steinschneider, our Senior Regulatory Counsel for CVM's OS&C, Office of Surveillance and Compliance. We will be presenting together, and Janice is a lawyer who has been with FDA since 2003. She has worked on drug regulatory issues for both the Center for Veterinary Medicine and the Center for Drug Evaluation and Research, which evaluates drugs intended for human use.

Before Janice and I get started, let me turn the microphone over to our Director, Dr. Solomon.

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Steven M. Solomon, DVM, MPH: Hello, everybody. We're very pleased you could join us today for our public webinar that address Guidance for Industry Compounding Animal Drugs from Bulk Drug Substances. As Amber said, I'm Steve Solomon. I'm the Director of FDA Center for Veterinary Medicine, or CVM as you'll hear folks throughout the presentation today.

The mission of the Center for Veterinary Medicine is protecting human and animal health. Meeting this mission is what motivates the staff at CVM, who are deeply committed to public health and passionate about animals. I want to take a moment to thank everyone in CVM and in the Food and Drug Administration who helped develop this draft Guidance and prepare this webinar.

In November 2017, CVM withdrew our previous draft Guidance on Compounding Animal Drugs as we heard from people – as we heard from more than 150 stakeholders through the public comment process that we just didn't quite get it right. One specific concern was that we were applying authorities granted by Congress under the Drug Quality and Security Act, or DQSA, to animal drug compounding while DQSA only applies to compounding of drugs for human use.

We thoroughly reviewed your comments to the previous Draft Guidance and made significant revisions and are now publishing this new Draft Guidance. We think it strikes the right balance between our current understanding about the safety, effectiveness, and quality of animal drugs compounded from bulk drug substances and the need for veterinarians to meet the legitimate medical needs of their animal patients where no FDA approved, conditionally approved, or indexed drug can be used to treat the animal. FDA approval means an animal drug is safe, effective, quality manufactured, and truthfully labeled. It also means that the drug becomes part of our post-approval pharmacovigilance where we monitor adverse events, product defects, advertising, and manufacturing and labeling changes.

Animal drugs compounded from bulk drug substances do not have these benefits. We recognize, however, that sometimes there are circumstances where veterinarians must turn to compounded drugs because no FDA approved, conditionally approved, or indexed product can be used, on label or off label, to treat a specific animal condition. My colleagues are going to go into all the details of this draft guidance, describing when FDA would choose not to take action against animal drugs compounded from bulk drug substances. For now, let me reiterate that our objective is to strike the right balance between

the gold standard of FDA review and drug availability. We think we've done that in this Guidance, but we welcome your opinions and observations.

Today's webinar is only the start of us reaching out to engage stakeholders in our thinking and to gain input on the Draft Guidance. Please participate in the public process by submitting your comments on the Draft Guidance to the docket. You can also submit nominations to be added to the list of bulk drug substances approved for compounding for office stock or for antidotes. There will be details on how to do this later in the webinar and they're also in the Guidance itself.

So now let me turn it back over to Dr. Amber McCoig and Janice Steinschneider. Dr. McCoig will go over the agenda. Once again, thank you all for joining today.

McCoig: Thank you, Dr. Solomon.

First, I'd like to provide a little bit of background. FDA's thinking about the risks of animal drugs compounded from bulk drug substances has evolved and been expressed in various Agency policy statements called Guidances. In May, 2015, FDA withdrew the Compliance Policy Guide Section 608.400, *Compounding of Drugs for Use in Animals*, that had been in effect since 2003. And we published the Draft GFI 230, *Compounding Animal Drugs from Bulk Drug Substances*.

FDA withdrew the Draft GFI 230 in November 2017 based on public comments from approximately 150 stakeholders, as Dr. Solomon discussed. We reviewed public comments, recrafted our policies, and focused on specific stakeholder concerns in this current Draft GFI 256, *Compounding Animal Drugs from Bulk Drug Substances*. This presentation covers the legal status of compounded animal drugs, the human and health considerations on which the policy guidance is based, an overview of the policies in Draft Guidance GFI 256, *Compounding Animal Drugs from Bulk Drug Substances*. Please note: this presentation is not intended to be a forum for addressing comments that you may have on the Guidance. Comments should be submitted in writing, and we will discuss how to do that before the end of the presentation. We encourage you to provide comments.

We also note that the guidance we are discussing today is a draft Guidance. The proposals it contains will not be enforced until after the public comment period and after we finalize the Guidance.

We ask that you hold your questions and comments on the presentation until the end. We have allowed time to respond to written questions at that time.

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Veterinarians face a daily challenge of treating a wide variety of species for unique diseases with a limited amount of approved animal drugs. Before 1994, a veterinarian could only use an animal drug approved by FDA for use in animals as directed by the approved labeling. Congress passed the Animal Medicinal Drug Use Clarification Act, or AMDUCA, in 1994 to allow veterinarians with a valid veterinary-client-patient relationship to prescribe approved human and animal drugs for extra-label uses in animals under their care, including compounding from approved products.

It is important to understand that when FDA approves a drug, what we are approving is the finished dosage form, which includes the active pharmaceutical ingredient and inactive ingredients, manufactured and labeled in a particular way. AMDUCA does not permit animal drug compounding directly from an active pharmaceutical ingredient, or API, even if the API is an ingredient in an approved drug. APIs are also referred to as Bulk Drug Substances.

AMDUCA has provided vets with more treatment options to address the unique needs of their diverse population of patients, as you can see here on the slide. Even with AMDUCA, there are still times when veterinarians do not have access to necessary treatments in the proper dosage or formulation to meet the unique needs of their patients. In these instances, vets have sometimes turned to drugs compounded from bulk drug substances. As we – as we discussed, compounding from bulk drug substances is not authorized under the Food, Drug, and Cosmetics Act, and may expose humans and animals that are

unsafe or ineffective because drugs compounded from bulk drug substances lack assurances of safety and effectiveness that are provided by the approval process.

FDA also recognizes that drugs compounded from bulk drug substances may be the only treatment option for an animal, so we issued Draft GFI 256, Compounding Animal Drugs from Bulk Drug Substances, to describe our policy to reconcile and strike a balance between those concerns. The Guidance addresses only prescribing and compounding animal drugs from bulk drug substances by veterinarians and pharmacists. The Draft Guidance does not apply to compounding for humans or compounding animal drugs from a finished, FDA-approved drug. This is addressed in extra-label use under AMDUCA.

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FDA recognizes that there may not be an FDA-approved product to treat the variety of illnesses and conditions that occur in many different species of animals treated by veterinarians. FDA Draft GFI 256 focuses on veterinary medical needs of the multiple animal species within a vet-client-patient relationship. Animal drug compounding is a priority for the Center of Veterinary Medicine. We want compounding to continue to be a tool for veterinarians to use when necessary. However, we also want to make sure that approved drugs are used when there is one available, since the safety and effectiveness of that approved drug has been established under the approved conditions of use.

Draft GFI 256 attempts to strike a balance between FDA's current understanding about the risks of animal drugs compounded from BDS and the need for those drugs when no FDA-approved or indexed drug can be used to treat the animal.

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New animal drugs cannot be legally marketed unless they have been reviewed and approved, conditionally approved, or index listed by FDA. New animal drug approvals are required for both original FDA-approved animal drugs and their generic counterparts. Another pathway to marketing a new animal drug is to have a drug conditionally approved, which allows a sponsor to market an animal drug shown to be safe, and reasonably expected to be effective, for up to five years while completing studies showing that it is effective. In the past, conditional approval was only for minor species or minor uses in major species. A minor species is a non-human species that is not a major species. Major species are cattle, horses, swine, chickens, turkeys, dogs, and cats. Some examples of minor species include sheep, salmon, guinea pigs, and parrots. A minor use is an intended use of a drug that occurs in a small number of animals annually.

Now, conditional approval has been expanded to certain new animal drugs for major species intended to treat serious or life-threatening diseases or to treat diseases that are particularly difficult to study.

Lastly, it is possible to have an animal drug listed on the Index of Legally Marketed Unapproved Drugs for Minor Species in order for it to be legally marketed. This Index limited – is limited to non-food minor species and the non-edible early life stages of some edible species.

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At the Center for Veterinary Medicine, our mission is to protect human and animal health and prevent human and animal suffering. The Food, Drug and Cosmetic Act approval process serves those goals by providing assurances that an approved animal drug is safe and effective for its labeled usage.

In the preapproval stage, FDA reviews data demonstrating safety, efficacy, and labeling adequacy. Safe means safe for the targeted animal. And when a drug is for a food-producing animal, that it is safe for people to eat the animal's meat, milk, and eggs.

During the preapproval process, FDA also reviews the drug's manufacturing methods and facilities used to process and package the drug to be sure they are adequate to ensure the drug's strength, quality, and purity.

After a new animal drug is approved, FDA monitors adverse events, product defects, advertising, and changes in manufacturing and labeling, post-approval monitoring of adverse events, and signaling systems for safety concerns detected during premarketing testing of FDA-approved animal drugs. Sometimes post-approval adverse events indicate that when used in a wider population than tested in preapproval, for example, wider ranges of ages, breeds, or body weight, and the like, the drug has an unexpected or unintended consequence.

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FDA acknowledges that there are circumstances in which no FDA-approved or indexed product can be used on label or in an extra-label manner to treat a specific animal's condition. In some of these cases, vets may turn to compounded drugs.

Compounding an animal drug using finished approved drugs as a source of the active ingredient, instead of bulk drug substances, can be legal extra-label use, as we discussed earlier, if the extra use regulations in 21CFR Part 530 are followed. All of the regulations that generally apply to extra-label use apply for this kind of compounding.

In addition, among other things, the regulations limit such compounding to situations in which no approved animal or human drug should be used in an extra-label manner without compounding from it and require that adequate procedures and processes are followed to ensure the safety and effectiveness of the compounded product.

How is compounding from a bulk drug substance different than compounding from an approved drug? The first choice is always the approved product because FDA's review of the approval process includes evaluating the quality of ingredients in the approved product. Bulk drug substances used to compound animal drugs may not have been evaluated for their quality, among other factors.

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For animal drugs, the Food, Drug, and Cosmetic Act does not distinguish between compounding animal drugs from bulk drug substances and other methods of animal drug manufacturing. Therefore, all requirements for approval, labeling, and manufacturing apply to animal drugs compounded from bulk drug substances, as they do with other new animal drugs.

Compounding animal drugs from bulk drug substances creates a product that requires FDA approval or index listing under the federal Food, Drug, and Cosmetics Act. Animal drugs compounded from bulk drug substances are new animal drugs and do not have a legal marketing status. However, in certain circumstances, a veterinarian may conclude that a drug compounded from bulk drug substances is the only appropriate, and available, treatment for their patients.

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FDA approves and indexes finished products. Bulk drug substances are only evaluated by FDA when they are part of a new animal drug approval package. Animal drugs compounded from bulk drug substances are not FDA approved, brand name, or pioneer drugs, even if they contain the same bulk drug substance as the approved drug.

It is also important to understand that animal drugs compounded from bulk drug substances are not FDA-approved generic drugs, even if they contain the same bulk drug substance as an approved animal drug. This is a common misconception.

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Drugs compounded from bulk drug substances have not been evaluated by FDA. Drugs compounded from bulk drug substances do not have the same assurances of safety, efficacy, manufacturing quality, and labeling adequacy as FDA-approved drugs. The Center for Veterinary Medicine has received reports of illnesses, and in some cases death, in animals administered compounded drugs containing too much of an active ingredient, or super potent, or the wrong active ingredient. Some compounded drugs have been recalled due to sterility, stability, and potency assurance. A few compounded drugs that were super potent due to compounding error have led to multiple animal illnesses and death. While we sometimes receive reports of adverse events and product defects associated with drugs compounded from bulk drug substances, there are no regulatory requirements for reporting them like there are for approved or indexed drugs.

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Based on our current understanding of the risk of drugs compounded from bulk drug substances, at this time we are prioritizing our efforts on drugs compounded from bulk drug substances that present a human or animal safety concern, are for use in food-producing animals, are copies of approved, conditionally approved, or index marketed animal drugs, are compounded without a patient-specific prescription, and sold to veterinarians as office stock. Drugs that present a particular animal safety concern include, for example, drugs that contain more or less than their labeled amount of active ingredient or have bacterial or fungal contamination.

Here are some examples. In 2009, compounded vitamin and mineral injectable solutions with 100 times the intended selenium led to the death of 21 polo ponies. In 2014, compounded toltrazuril/pyrimethamine oral suspension containing 20 times the labeled pyrimethamine led to the death of two horses and illnesses of six others. In 2019, compounded toltrazuril/pyrimethamine oral paste containing 18 to 21 times the labeled pyrimethamine led to the death of three horses in two states.

Drugs that present particular human safety concerns are drugs that may present a risk to a person administering the drug or to people in contact with the treated animal. Drugs compounded from bulk drug substances for food-producing animals are of special concern because the potential for drug residues in edible tissue of food-producing animals is a human health issue. As part of approval process, the Agency reviews data on human food safety issues, and the approved labeling contains data-based conditions to use to prevent violative residue such as withdrawal and discard times.

As we describe below, we will focus on drugs compounded from these bulk drug substances for food-producing animals unless they are on a list of antidotes developed by the FDA.

Compounding copies of FDA-approved or index drugs is a special concern because it discourages firms from investing in the animal drug development. This undermines animal health because there will be fewer approved and proven animal drugs available.

Office stock is of particular concern because it potentially exposes larger numbers of animals to drugs of unproven quality. It also has a greater potential to undermine the integrity of the approval process because large quantities of unapproved drugs are made as office stock without the rationale of a patient presenting with a particular treatment need that could be met with an approved product.

However, we are aware that there are some drugs compounded from bulk drug substances that veterinarians may need to have on hand for immediate treatment because the animal cannot wait for a prescription to be compounded. We are developing a list of those drugs and will prioritize action against office stock compounded from bulk drug substances that are not on that list. We will discuss how to nominate bulk drug substances for the list of bulk drug substances for office use or office stock and antidotes later in this presentation.

Janice will now provide more detail on our Draft GFI.

Janice Steinschneider, JD: So, the first thing to know, as we've discussed, compounding from bulk drug substances violates the Food, Drug, and Cosmetic Act, and nothing we say in this Guidance makes that

legal. Rather, the Draft Guidance describes our current thinking about the circumstances under which FDA does not intend to take action against animal drugs compounded from bulk drug substances, and that's based on our current understanding of the risks.

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So, what the Guidance does, is it outlines circumstances that define compounding from bulk drug substances that is of less concern from the perspective of the regulatory priorities that Amber described. And you will see these reflected as we discuss the circumstances, so I'm going to just review them again. We're concerned about drugs with human or animal safety concerns. We are concerned about drugs compounded for use in food-producing animals. We're concerned about drugs compounded from bulk drug substances that are copies of approved, conditionally approved, or indexed marketed animal drugs. And we are concerned about drugs compounded from bulk drug substances without a patient prescription and sold to veterinarians as office stock.

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So, pardon me. So, one of the first principles that applies throughout any type of compounding under this Guidance is that only veterinarians and pharmacists can compound from bulk drug substances under GFI 256. FDA expects that pharmacists and veterinarians who choose to compound drugs, whether from bulk drug substances or finished products, will have adequate training in compounding practices to produce as safe of a compounded product as possible.

Another important principle in the Guidance, if finalized, is that drugs compounded from bulk drug substances should only be prescribed and dispensed when a veterinarian is acting within a valid client-patient relationship and there is no medically-appropriate FDA approved drug that can be used on or extra-label to treat the patient. And, of course, the reason a valid veterinarian client-patient relationship is essential is because that's necessary for a reliable determination by the veterinarian that no other option than a drug compounded from bulk drug substances will do for the patient.

Lastly, we ask that veterinarians and pharmacists who compound from bulk drug substances under the Guidance should report adverse events and product defects to the FDA. Reporting adverse drug events helps everyone - FDA, veterinarians, pharmacists, and animal owners - learn more about the risks of specific products and risks in general of using compounded products. And you can report adverse events at the link shown on this slide by following the following the instructions to report on FDA Form 1932A.

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So now what we're going to talk about is three categories or scenarios of compounding from bulk drug substances. In addition to those circumstances I just described, each of these has its own particular set of circumstances, and you have to meet all of the circumstances to be compounding within the Guidance.

So, just as a preview, the three categories are compounding with a patient specific prescription for a nonfood-producing animal, compounding office stock for nonfood-producing animals, and antidotes for food-producing animals. And we're going to talk about the circumstances for each of these categories in turn.

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So first, turning to compounding with a patient-specific prescription for nonfood-producing animals. We do not intend to take action if all of the following circumstances are met. And I emphasize *all* of them.

First, the drug is not a copy of a marketed FDA approved or indexed human or animal drug. For purposes of this Guidance, a compounded product with minor variations from an approved drug is considered a copy of that product. Specifically, if the compounded animal drug compared to an approved drug has the same active ingredient, *and* is in the same route of administration, *and* is in the same, similar, or easily-substitutable strength, it is considered a copy under this Guidance. So, for example, if the approved

product is a tablet, a product compounded from bulk drug substances of the same strength in an oral liquid form would be a copy because they are the same strength and they are the same route of administration. Tablet versus oral liquid. However, a product compounded from bulk drug substances in the same strength in injectable form would not be considered a copy because it's a different route of administration.

Now, FDA recognizes that there may be some cases where there is a medical need for a minor variation from an approved product, or from indexed products, and where a minor variation would, in fact, make a clinical difference for the particular patient. So under those circumstances, we do not intend to take action against the compounding of a copy from bulk drug substances if the medical rationale is documented in the prescription or if a veterinarian is compounding the drug and the medical rationale is noted in the patient's medical records. So, you either need to have a brief explanation on the prescription if the drug is being compounded at a pharmacy, or if it's actually being compounded by the veterinarian, the medical rationale should be in the – the need for the copy should be in the patient's medical record.

So, an example of this situation would be if there was an approved product that could be used except that it contained an active ingredient – I'm sorry, an *inactive* ingredient that a particular patient was allergic to. In that case, that would be a copy if you made the same strength, same route of administration but didn't have the inactive ingredient that the patient was allergic to.

Second set of circumstances - again, this is an "and" - the compounded drug cannot be made using an approved drug as the source of the active ingredient. So, the preference is if you need a compounded drug, just compound it from using an approved product as the source of the active ingredient. But if you can't, you can account for that, but you have to determine that the compounded drug cannot be made using the approved drug as the source of the active ingredient.

And, here we need to talk about active moieties because if the active moiety is in an approved product, the compounder should document the reason an improved product cannot be used to compound the drug. Now what do we mean by active moiety? Active ingredient is probably the more familiar term, and the best way to describe what an active moiety is by way of an example. For example, if you take the active ingredients erythromycin stearate, erythromycin ethylsuccinate, and erythromycin lactobionate, the active moiety in all of them is erythromycin. So, if you have an approved product that has the same even active moiety, so it might be a different salt form, you need to see if you can use that – there is some reason that you can't use that to compound the drug that you need.

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Third, and, again, this is an and, so we've got it can't be a copy and you can't make it from the approved product, the third thing is that the compounded drug is dispensed to the patient's owner or caretaker, or to the prescribing veterinarian if it's coming from a pharmacy, could go to the veterinarian; and *not* to a distributor, retailer, or other third party. Compounding animal drugs is to meet the needs of specific patients that cannot be met with legally-marketed products, not to fill a pharmaceutical pipeline with unapproved drugs. So, there's no transfer to another distributor or retailer. It's really for the particular patient.

Lastly, the drug should be compounded according to the standards in the U.S. Pharmacopeia and National Formulary, or the USP. USP standards include general chapters on compounding nonsterile and sterile drugs, sometimes referred to as chapters 795 and 797, respectively. And monographs – it also includes monographs on active ingredients in finished products. Depending on the products being compounded, there may be additional USP general chapters that – that apply as well.

Now some of you who follow USP matters closely may be aware that on June first of this year, USP published revisions to general chapter 797 and 795. But because these revisions were repealed and are currently under review, they never went into effect. So, what you need to look at is the official versions that are in effect at the time you're compounding the drug.

The thing to understand about the USP and National Formula standards is that they are minimum standards. Some states have standards that exceed these national standards, and the pharmacist or veterinarian compounding the drug should follow the state standards as they exceed USP standards.

And the reason we're talking about the USP is this is consistent with our concern that in order to protect human and animal safety, we need to have some standards of – to assure some standards of quality in the product.

So, that was a lot. I'm just going to review briefly the circumstances for compounding drugs for bulk drug substances with a patient-specific prescription.

First of all, it's got to be the – the drug has to be for a nonfood-producing animal. Nonfood producing. That it's not a copy except for a minor variation that produces a clinical difference for the patient and that's documented in the record or the – on the prescription. Third, that you can't use an approved product to compound the drug that you need, and that's documented. That it's dispensed only to the patient's owner, caretaker, or to the prescribing vet and not sold further on. And that in the compounding of that drug, the USP and the standards are followed at a minimum.

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So now we're going to turn to office stock. FDA does not – and office stock, just to be clear, is the drug compounded from bulk drug substances that you have on hand to administer or dispense when the patient needing the drug is in the clinic.

FDA does not intend to take action against drugs for nonfood-producing animals compounded from bulk drug substances as office stock when *all* of the following circumstances are met.

First, the drug has to be compounded from a bulk drug substances on FDA's "[List of Bulk Drug Substances for Compounding Office Stock Drugs for Use in Nonfood-Producing Animals or Antidotes for Food-Producing Animals](#)," which we may just call the list for the rest of this presentation.

Now what FDA intends to put on this list, only bulk drug substances needed for drugs that a veterinarian must have on hand for immediate treatment in an emergency, because waiting for a pharmacy to fill a patient-specific prescription would cause animal suffering or drug. And we will only include drugs on that list when there is no approved product that can treat the condition or species that the drug is intended to treat.

These conditions limit the use of office stock compounded from a bulk drug substance when that is the absolute only treatment option and it must be available on hand right away at the clinic. And, again, it's for nonfood-producing animals. These would be for nonfood-producing animals only.

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Another circumstance is that the drug is not dispensed or transferred to the third party except in the case of office stock for a veterinarian dispensing to an animal's owner.

And three, when the drug is compounded according to the standards in the USP and National Formulary.

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Lastly, we're going to discuss antidotes. And this is, because of the human food safety concerns associated with drug residues, the FDA will generally prioritize action against any drug compounded from bulk drug substances for food-producing animals. The only exception is the compounding of antidotes to counteract a poison in a food-producing animal. And the rationale for this exception is that these are needed in extreme emergencies to prevent animal suffering or death.

Again, one of the circumstances is that the antidote has to be on the list.

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And secondly, the veterinarian prescribing or compounding the antidote either establishes and documents a scientifically-based withdrawal, withholding, or discard time for the meat, milk, and eggs that will be derived from the treated animal. So you'd have to have a withdrawal time. Or that you – the veterinarian ensures that the animal does not enter the food supply.

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So, we invite the public to submit nominations to the list of bulk drug substances for office stock or antidotes. These nominations may be submitted electronically or in writing. Among other information, for office stock the submission must document and explain why a veterinarian must have the drug on hand for immediate treatment and why waiting for a pharmacy to fill a prescription would cause animal suffering or death. And for antidotes, among other information, submission must include scientific information the veterinarian can use to determine withdrawal, withholding, and discard times.

So, for a complete list of the required information and directions on how to submit nominations, you would look at the appendix in the Draft or the Federal Register notice inviting nominations. If all required information is submitted in the nomination, FDA will review the nomination to determine whether the bulk drug substance meets the criteria to be on the list, but if all the information isn't included, we may not be able to review the nomination.

And now I'm going to turn this over back to Amber to go through, summarize, the key points for different stakeholder – the perspectives of different stakeholders.

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McCoig: Okay. Thank you for hanging in with us so far. And we just wanted to go over a few key points that we think different groups may be interested in.

First of all, we have some key points that are of particular interest to veterinarians. Compounded drugs are not FDA approved, and FDA has not evaluated their safety, efficacy, and manufacturing methods. However, we recognize that vets may need other options to treat specific patients when no FDA-approved or indexed product exists. Veterinarians are responsible for determining whether an approved or indexed product can be used for a specific patient. Veterinarians are also required to comply with their state's veterinary practice laws. In the absence of a legal treatment option, vets will be able to compound or prescribe drugs for specific nonfood-producing patients. Veterinarians will also be able to compound or prescribe drugs for office stock for nonfood-producing patients, and for antidotes for food-producing animals, if those bulk drug substances have been nominated, approved, and included on our bulk drug substance list. Otherwise, there is no compounding for bulk drug substances for food-producing animals.

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We received thoughtful comments from veterinarians on our last Draft Guidance, and we hope that you're going to take the time to familiarize yourself with this Guidance and provide us with your input. Vets should also submit nominations for office stock and antidotes. The current draft bulk drug substance list is available online. Please take a look at the list and submit additional nominations if you have them. Currently there are no antidotes on the BDS list, and we would like to know what antidotes veterinarians think are critical in practice.

And as a reminder, GFI 256 is still a draft Guidance until we publish the final Guidance on this issue. FDA intends to look at the totality of circumstances in determining whether to take enforcement action for unlawful animal drug compounding activity.

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There are also several key points that may be of particular interest to pharmacists. Licensed pharmacists will be able to compound drugs from bulk drug substances when prescribed by a veterinarian under circumstances described in Draft GFI 256 if finalized.

If there is an approved product with the same active moiety, as Janice discussed earlier, pharmacists should only use bulk drug substances if the approved drug cannot be used as a source of the active ingredient.

We will focus enforcement efforts on compounded copies of approved drugs except in cases where a prescribing veterinarian has documented and there is a clinical difference for a specific patient.

Under Draft GFI 256, if pharmacists – if a pharmacist receives a patient-specific prescription for a copy of an approved drug, as the Guidance defines copy, the pharmacist should confirm that the prescribing veterinarian has identified a clinical difference for a specific patient.

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GFI 256 limits the bulk drug substances that can be used for office stock compounding to the bulk drug substances on the bulk drug substances list. We will prioritize action for – against drugs compounded from bulk drug substances for food-producing animals except for antidotes compounded from bulk drug substances on the bulk drug substances list.

We are interested in your input and suggestions. Please submit comments by February 18, 2020.

And the same reminder we offered to veterinarians, GFI 256 is a Draft Guidance. Until we publish the Final Guidance on this issue, FDA intends to look at the totality of circumstances when determining whether to take enforcement action for unlawful animal drug compounding activity.

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And finally, there are several key points that may be of interest to the pharmaceutical industry.

FDA is prioritizing action against compounding copies of approved or indexed drugs, particularly compounding and selling copies in large quantities as office stock. We recognize that this type of compounding undermines the approval process, competes with approved products, and may even contribute to shortages of approved products.

Draft GFI 256, if finalized, will limit compounding copies of approved drugs to situations where the veterinarian documents a clinical difference for a specific patient. Draft GFI 256, if finalized, expects the compounder will consider using an FDA-approved drug or drugs for the source of – sorry, I just realized – sorry about that.

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Draft GFI, if finalized, expects that the compounder will use the approved drug or drugs as the source of an active ingredient and will document the reason they cannot be used when compounding for bulk drug substances.

We are interested in your input and suggestions. Please submit comments by February 18, 2020. And we'll repeat the same reminder that we offered to veterinarians and pharmacists. Draft GFI 256 is the Guidance. Until we publish Final Guidances on this issue, FDA intends to look at the totality of circumstances when determining whether to take enforcement action for unlawful animal drug compounding activity.

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And we want to thank you. We do – we did receive a few questions in writing that we would like to address.

Steinschneider: And the way we're going to do this is Amber is going to read the question and I will read the answer.

McCoig: Okay. The first question is, currently under New Jersey state law, veterinary hospitals can only stock a small supply of compounded medications to be dispensed to patients in emergent situations. Will this new Guidance policy change this in any way? Will it allow veterinary hospitals to stock a larger supply of certain compounded drugs?

Steinschneider: And the answer is no, the Guidance only addresses circumstances under which FDA does not intend to take action for certain violations of the federal Food, Drug, and Cosmetic Act. It does not affect state law or the obligation of veterinarians and pharmacists to meet the requirements and limitations of state law.

McCoig: Okay, question number two. Under Section b, number three, who will be enforcing these standards, USP, on veterinarians compounding? Will FDA start doing inspections? If so, when will they start?

Steinschneider: We really can't comment on any future enforcement activities. But as a general matter, FDA does not conduct routine inspections in veterinarians' offices.

McCoig: Question number three. Under Section b, number four appears to allow a veterinarian to dispense for transfer compounded office stock. This would mean a pharmacy is acting as an outsourcing facility without the requirements of VGMP practice. Is this what is intended? What is the limit on veterinarians dispensing of a pharmacy compounded preparation?

Steinschneider: The Drug Quality and Security Act, DQSA, recognized a type of facility called an outsourcing facility. But the DQSA applies only to human drug compounding. And so when a state-licensed pharmacy compounds animal drugs as office stock under the Guidance, that does not transform them into an outsourcer. What is intended is that in the limited circumstances described in the Guidance, state-licensed pharmacies, acting under state pharmacy law, would be able to compound office stock for veterinarians to have on hand for use in emergency situations. When compounding office stock under the Guidance, pharmacists must comply with their state's limitations as well. Under the Guidance, veterinarians can only dispense compounded office stock to a patient under their care or transfer it to another veterinarian at the same location in the same practice.

McCoig: Question number four. Under Section b, number six, if number four allows a veterinarian to dispense office stock compounded by a pharmacy, who is responsible for meeting the labeling requirements in number six?

Steinschneider: So, the Guidance does describe what the labeling on these products should look like. And in this scenario, when a veterinarian dispenses office stock compounded by a pharmacy, there are two responsible parties. First, the pharmacist is responsible for providing labeling as described in the Guidance when sending the drug to the veterinarian. Second, the veterinarian is responsible for providing labeling as described in the Guidance when dispensing the drug to the patient.

McCoig: Question number five. The Guidance only addressed the use of bulk drug substances for vet compounding. Are there any Guidances planned to address vet extra-label compounding? 21 CFR Part 530, 21 USC 360, does not clearly define allowable practices and appear only to allow compounding after the receipt of a patient-specific prescription.

Steinschneider: We cannot discuss any plans for any potential future Guidances. But we do appreciate the questioner's suggestions for aspects of the extra-label use regulation that stakeholders would like clarified.

McCoig: And those are the questions we received to this point. Please submit any other questions that you have to AskCVM, and the address is on your screen right now. And we realize there was a little bit of a delay at the end with the slides. Those slides are going to be publicly available, and they can also be –

they will be posted online on our website – online on our website. And you can also request them again through the AskCVM website.

And we thank you all for hanging in there with us and for your interest in compounding animal drugs from bulk drug substances. We encourage you all to make comments prior to the comment period in February 2020. And reach out to us if you have any specific questions.

Thank you very much.

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