



October 8, 2020

Mr. Eric Nelson  
Division of Compliance (HFV-230)  
Center for Veterinary Medicine  
c/o Dockets Management Staff (HFA-305)  
Food and Drug Administration  
5630 Fishers Lane, Rm 1061  
Rockville, MD 20852

**Re: Docket #:** [FDA-2018-D-4533](#) CVM GFI #256 - Compounding Animal Drugs from Bulk Drug Substances

Dear Mr. Nelson:

On behalf of the American Veterinary Medical Association (AVMA) and our more than 95,000 member veterinarians, we thank you for the opportunity to provide comments on [Draft Guidance for Industry \(GFI\) #256, Compounding Animal Drugs from Bulk Substances](#)<sup>1</sup>, as the Food and Drug Administration (FDA) works to clarify its regulatory approach. The AVMA sincerely appreciates that many of our comments provided in response to previous Draft GFI # 230 have been considered while drafting GFI # 256.

Our overarching comments are provided immediately below. Next, we share more specific comments on Section III, followed by a request for additional clarity around some definitions and concepts.

***Overarching comments***

Veterinarians treat a myriad of species with an even greater number of diseases and conditions. The AVMA strongly supports the FDA drug approval process as we desire access to FDA-approved products that have been demonstrated to be safe, effective, properly manufactured following cGMP requirements, accurately labelled, and subject to post-market approval requirements. However, compounding from bulk drug substances (BDS) is a necessary practice because there will never be an FDA-approved, conditionally approved, or indexed drug product available for treating every species and condition that we see. Intermittent drug shortages and commercial unavailability of FDA-approved drug products also drive the need for compounded preparations within veterinary practice. While FDA has not identified cost as an appropriate reason for compounding from BDS, the AVMA acknowledges that cost can be a reason that veterinarians may seek to use compounded preparations, because that may be the only way a client can afford to treat their animal.

The AVMA believes compounding from BDS is medically necessary in three situations: the approved product is not commercially available; the needed compounded preparation cannot be made from the approved product; or there is no approved product from which to compound the needed preparation. AVMA also supports the veterinarian's ability to maintain sufficient quantities of compounded preparations in their office ("office stock") for urgent administration or dispensing in emergency situations. In some cases, a compounded animal drug is needed immediately, and the time needed to compound a drug in response to an individual patient prescription may result in animal suffering or death.

To use these medications, we believe the prescribing veterinarian must be acting within a veterinarian-client-patient relationship (VCPR) as defined in 21 CFR Section 530.3(i)<sup>2</sup>; that compounding should occur under the direct supervision of the veterinarian or pharmacist; and that, in the case of a pharmacist, such compounding should occur in a state-licensed pharmacy or federal facility (as proposed in III.A.1, III.B.1, and III.C.1).

We strongly support GFI #256 being finalized by FDA as long as the final product addresses the concerns we describe below.

#### ***Compounding in compliance with USP chapters***

With conditions, the AVMA supports provisions (III.A.2, III.B.3) that require a drug be compounded in accordance with current USP chapters applicable to compounding, presently proposed to include USP Chapters <795> "Pharmaceutical Compounding – Nonsterile Preparations" and <797> "Pharmaceutical Compounding – Sterile Preparations". However, the AVMA notes there are provisions within USP's current and proposed Chapters <795> and <797> that are not relevant, appropriate, applicable, or practical for veterinarians compounding medications for animal patients. The AVMA continues to work closely with the USP to create a veterinary-specific compounding chapter. We ask that the USP provisions in Chapters <795> and <797> be applicable to compounding from BDS that is performed within state-licensed pharmacies and federal facilities, but that they not be applied to veterinary practitioners compounding from BDS within the scope of their professional practice, and within a VCPR, until there is a veterinary-specific chapter that more appropriately addresses the compounding activities of veterinary practitioners.

Many of FDA's enforcement actions<sup>3</sup> identified lack of sterility assurance<sup>4</sup> or actual lack of sterility,<sup>5</sup> which supports meeting standards for sterility like those provided within the USP chapters when compounding preparations. However, observations of subpotent<sup>6</sup> preparations were also reported. Additionally, and perhaps more importantly, adverse events reported by FDA Center for Veterinary Medicine (FDA CVM) associated with compounded selenium<sup>7</sup> and pyrimethamine<sup>8</sup> in 2014<sup>9</sup> and 2019<sup>10</sup> involved superpotent compounded preparations. Quality requirements in current and proposed USP chapters do not appear to require potency testing prior to release of the medication, so may not mitigate the risk of superpotent compounded preparations, such as those associated with the reported selenium or pyrimethamine equine deaths. Consequently, AVMA supports

stakeholder discussion of how laboratory testing to confirm the identity and strength<sup>11</sup> of preparations compounded for major non-food animal species prior to distribution may impact the compounding of preparations used for office stock to reduce the risk of further animal deaths associated with superpotent compounded preparations.

### ***Adverse event reporting***

The AVMA continues to believe there is a need for ongoing development and strengthening of adverse event reporting (AER) systems for all adverse events associated with compounded preparations, including lack of efficacy.<sup>12</sup> We believe there must be a strong, science-based, transparent, and systematic surveillance system, especially considering the wide scope of species and disease conditions that veterinarians treat. The AVMA supports development of a user-friendly, easy to access form for all adverse events related to compounding. A user-friendly electronic system would be anticipated to promote both reporting by those compounding and ease of review by FDA. Ideally, a database of recently reported adverse events could be maintained for veterinarians and pharmacists to use as a resource. Sufficient and meaningful data inputs (adverse event reports) are imperative for a strong reporting system. We are concerned that the FDA's current 1932a form and the accompanying reporting system currently in place do not provide an appropriate means of capturing adverse events nor do they provide the robustness FDA needs to detect and act on potential quality problems.

Our recent experience with querying the current FDA system, openFDA, supports the need for stakeholder discussion regarding AER that most effectively informs veterinarians of any risk distinctions between compounded and FDA-approved, conditionally approved, and indexed new animal drugs. We are aware that openFDA has posted animal drug adverse event reports since 1987.<sup>13</sup> Relevant to this example, we note that the FDA CVM has recorded a webinar explaining the [proposed guidance on bulk compounding](#) and published reports of horse deaths associated with compounded [selenium](#)<sup>7</sup> and [pyrimethamine](#)<sup>8</sup> in 2014<sup>9</sup> and 2019.<sup>10</sup>

On September 10, 2020 we entered "compounded" at the openFDA animal drug adverse event report site and retrieved 53 records. Entering "pyrimethamine" resulted in retrieval of 34 records and entering "selenium" provided access to 501 records. Unfortunately, the site does not appear to distinguish between adverse events associated with compounded and FDA-approved drugs. Given these results, it is difficult to see how filing form 1932a helps make veterinarians aware of the greater safety risks associated with compounded preparations when compared to FDA-approved drugs, despite the reported horse deaths resulting from use of the compounded formulations. In addition, the AVMA understands that compounding pharmacies and boards of pharmacy are involved in investigating adverse events; those groups appear to be missing from the proposed system.

Having had this experience with form 1932a and openFDA, and recognizing the related reporting responsibilities of compounding pharmacies at the state level, we request FDA engage in further discussion with stakeholders to identify and agree upon an efficient and effective method of filing and managing reports of adverse drug experiences at the state

and federal levels so that veterinarians are appropriately informed of the different risks associated with compounded and FDA-approved, conditionally approved, or indexed new animal drugs.

***Comments on specific provisions within Draft GFI #256***

**Section III.A. Compounding pursuant to patient-specific prescriptions for nonfood-producing animals**

Item 3: The AVMA supports the requirement that the drug be dispensed directly from the pharmacy to the prescribing veterinarian or to the patient's owner or caretaker, or by the veterinarian to the owner or caretaker of an animal patient or to another veterinarian in the same practice in the same physical location, and that it is not otherwise dispensed or transferred by the pharmacy, pharmacist, or veterinarian to a third party (e.g., distributor, retailer, veterinarian in another practice).

Items 4 and 5: Please see the AVMA's comments regarding the definitions of "copy" and "marketed" in the section on definitions and concepts below.

The AVMA strongly opposes the requirement that the compounded drug produce a "clinical difference" in the identified patient and that the medical rationale be documented on the prescription. As shared in our feedback on draft GFI #230, the AVMA believes documenting the medical rationale in the patient's record is sufficient to make and use a compounded preparation. Unfortunately, the phrase "clinical difference" does not capture other considerations that might create a need for a compounded preparation, such as certain worker and client safety needs, client compliance, and the potential for creating unnecessary animal stress (e.g., cats that cannot be safely and compliantly pillled). These needs are not related to "clinical difference," *per se*, but rather, the ability to successfully and safely medicate patients. We ask that FDA strike references to "clinical difference" as they appear in III.A.4 and III.A.5.

We agree that documenting why the compounded preparation was chosen is appropriate for the medical record and believe that such documentation should align with that required for extralabel drug use by 21 CFR Sec. 530.5.<sup>14</sup> FDA should not require any additional documentation in medical records, which are otherwise under the oversight of state boards of veterinary medicine. The AVMA does not believe it is appropriate to include that medical rationale on the prescription. Requiring the medical rationale on the prescription intrudes too far into the practice of veterinary medicine and is not required for other prescribers. It appears that FDA is assuming veterinarians routinely act inappropriately when prescribing compounded preparations made from BDS, or the agency is inappropriately imposing this requirement to make its own inspection and enforcement easier. We believe FDA is fully capable of investigating suspected improper compounding without imposing this requirement. We request that FDA strike language in III.A.4 and III.A.5 that requires the veterinarian to document the medical rationale on the prescription.

Item 6: The AVMA supports the requirement that the entity or person compounding the drug determine and document why an FDA-approved, conditionally approved, or indexed animal

drug(s) or an FDA-approved human drug(s) cannot be used as the source of the active ingredient(s).

Item 7: See our comments above regarding the need for stakeholder dialogue regarding AER.

Item 8: AVMA supports proper labeling of prescription products and agrees with the guidance included in this item, except for reporting adverse events to FDA using online Form FDA 1932a. Please see our comments above regarding AER.

Section III.B. Compounding without patient-specific prescriptions (“office stock”) for nonfood-producing animals

We reiterate that AVMA supports the veterinarian’s ability to maintain sufficient quantities of compounded preparations (“office stock”) in their office for urgent administration or dispensing in emergency situations. We believe it is within the veterinarians’ professional judgement to determine what formulations and for which conditions these preparations are needed.

Item 2: As proposed, the AVMA strongly opposes language in the guidance suggesting that a preparation may only be compounded from a BDS for use as office stock in nonfood-producing species if it appears on the [List of Bulk Drug Substances for Compounding Office Stock Drugs for Use in Nonfood-Producing Animals or Antidotes for Food- Producing Animals](#). Veterinary medicine is unique in that we treat a multitude of nonfood-producing species with a variety of diseases and conditions, many of which need to be treated expediently.

We do not believe creating a positive list, as currently conceived, is practicable because:

- (1) The supporting information that CVM/FDA requires to consider adding a substance to the list is not generally available to veterinarians so will be next to impossible to provide for all of the BDS needed to prepare office stock to treat urgent needs of nonfood-producing animals (discussed more fully below);
- (2) We respectfully do not observe that FDA has created and maintained such a comprehensive positive list for the compounding of drugs under Sections 503A and 503B, so we are concerned that an analogous positive list for animal patients will not be created and maintained in a manner that meets the clinical needs of veterinary practice relative to nonfood-producing animals;
- (3) There are no provisions addressing needs during times when FDA-approved, conditionally approved, or indexed drugs are not commercially available; and
- (4) There are no provisions that allow special consideration for BDS needed to prepare drugs for nonfood minor species or for BDS that are not found as active ingredients in FDA-approved, conditionally approved, or indexed drugs.

As currently proposed, the level of detail required in the Appendix to GFI # 256 would severely restrict the number of BDS available for use in office stock and prevents veterinarians from meeting the urgent and emergent needs of our patients, and will undoubtedly result in animal suffering and, potentially, death.

Despite not supporting a “positive list” in our response to GFI # 230, the AVMA, and many allied veterinary groups, invested considerable effort in submitting dozens of nominations to FDA CVM, virtually all of which were deemed to be without sufficient supporting evidence.<sup>15</sup> Neither the AVMA, nor the allied veterinary groups, know what the deficiencies are in each of these nominations, nor do we know whether CVM had the resources to review them, and thus are prevented from responding with specificity to any deficiencies in our prior nominations. Nevertheless, our general concerns are as follows.

The nomination requirements appear to ask for information required of a drug sponsor pursuing a new animal drug application<sup>16</sup> much of which is beyond the reach of practicing veterinarians.

With respect to item 2 of the requirements in the Appendix, while veterinarians may certainly provide chemical and, perhaps, common names, determination of the chemical grade (e.g., USP-NF, ACS), strength, stability, and purity of the BDS requires knowledge of the method(s) of manufacture and purification of the BDS that are not normally available to veterinarians, and in many instances may be proprietary.

Because the method of manufacture and purification of the BDS often cannot be determined from the publicly available scientific literature, including for FDA-approved, conditionally approved, or indexed drugs, determining the degree to which the scientific literature supports safety and effectiveness data for a particular BDS appears to present an impossible standard to consistently meet.

Item 4(a) within the Appendix similarly presents challenges. As an example, FDA CVM has approved applications for the control of mortality in freshwater-reared warmwater finfish.<sup>17</sup> For many conditions in major species of animals, the request for the species and condition is reasonable, however very few conditions have been identified in minor species beyond the syndrome stage and separate nominations for each genus and species of minor species in which the same or a similar syndrome has been identified seems overly burdensome. To illustrate, is a separate nomination required for every species of bat for which white-nose syndrome has been reported?

And, regarding Appendix item 4(e), if no FDA-approved human or animal drug exists may conditionally approved and indexed drugs be used in an extralabel manner in minor species? If not, is saying that sufficient to satisfy 4 (e)?

In lieu of a list, we request that FDA amend provisions in III.B.2. to strike the reference to a list and insert language derived from the Appendix as follows:

2. The drug is intended for use in a nonfood-producing species and is compounded from a bulk drug substance when—
  - a. There is no commercially available FDA-approved, conditionally approved, or indexed animal drug that can be used as labeled to treat the condition;

- b. There is no commercially available FDA-approved animal or human drug that could be used in an extralabel manner under section 512(a)(4) or (a)(5) of the FD&C Act and 21 CFR part 530 to treat the condition;
- c. The drug cannot be compounded from a commercially available FDA-approved animal or human drug consistent with 21 CFR part 530;
- d. Immediate treatment with the compounded drug is necessary to avoid animal suffering or death; and
- e. FDA has not identified a significant safety concern specific to use of the bulk drug substance in animals.

Item 4: The AVMA supports the provision that office stock medications not be dispensed or transferred to a third party. However, we request confirmation that this does not preclude a client from transferring the compounded drug to other premises owned by the same person<sup>18</sup> as long as those premises are in the same state (e.g., zoos, animal rehabilitation centers, University, research, state or federally owned facilities with more than one state premise) and the compounded drug does not incorporate a DEA scheduled substance.

Item 5: Please see our comments regarding AER above.

Item 6: AVMA supports proper labeling of prescription products and agrees with the guidance provided, except the statement to report adverse events to FDA using online Form FDA 1932a. Please see our comments regarding AER above.

### Section III.C. Compounding drugs for use as antidotes for food-producing animals

Although AVMA does not support a list for nonfood-producing animals for the reasons provided above, the AVMA does support a list for food-producing animals.

Item 2: The AVMA continues to believe that a publicly available, current list of BDS that can be used to compound drugs for euthanasia, depopulation, and as poison antidotes for food animal species within a VCPR<sup>19</sup> should be published. The AVMA contends that compounding from BDS in food-producing animals is medically necessary for these purposes when use of an FDA-approved product per label or in an extralabel fashion is not feasible. Veterinarians must also be able to legally maintain sufficient quantities of these compounded preparations in their office for urgent administration needs or emergency situations. Without access, animals may die before the medication could be delivered (e.g., use of methylene blue to treat nitrate toxicosis in cattle). We recognize veterinarians' need to ensure food safety, maintain required records, and label drugs appropriately, as required under FDA's extralabel drug use rules. We support the use of a positive list in this context because the necessary BDS are few in number, easily identified, and create a bright line for food-producing animals. These circumstances are in stark contrast to the nonfood-producing animal situation.

We request FDA amend this provision as follows:

2. The drug is compounded from a bulk drug substance on the "List of Bulk Drug Substances for

Compounding ~~Office Stock Drugs for Use in Nonfood-Producing Animals or Antidotes, Depopulation, and Euthanasia Drugs for Food-Producing Animals~~".

Additionally, AVMA asks that the BDS used to compound drugs referenced in AVMA's euthanasia<sup>20</sup> or depopulation<sup>21</sup> guidelines where a corresponding FDA-approved, conditionally approved, or indexed drug is not available or not "commercially available", be added or incorporated by reference into the list for food-producing animals. The AVMA believes that if adequate scientific information is not available to determine a withdrawal time, the compound cannot and should not be used in a food animal or the treated animal cannot enter the food supply.

Item 3: The AVMA supports this provision if "specifies" replaces "establishes" to read, "The veterinarian specifies and documents a scientifically based withdrawal time that ensures residues of the antidote and the underlying toxin are not present in the animal at the time of slaughter or the veterinarian ensures the animal does not enter the food supply." The AVMA supports the use of scientific literature, the Food Animal Residue Avoidance Databank (FARAD), textbooks, and peer-reviewed journals to support withdrawal, withholding, or discard times, and the FARAD's ability to advise veterinarians on appropriate withdrawal times for compounded poison antidotes in food-producing animals.

Item 4: See our comments above regarding the need for stakeholder dialogue regarding AER.

Item 5: The AVMA supports proper labeling of prescription products and agrees with all but the statement to report adverse events to FDA using online Form FDA 1932a. Please see our comments above regarding AER.

***Comments regarding Past Approvals and Denials to the [Nominated Bulk Drug Substances That May NOT Be Used to Compound Office Stock Drugs or Antidotes for Use in Animals \(No List\)](#) and the current [List of Bulk Drug Substances for Compounding Office Stock Drugs for Use in Nonfood-Producing Animals or Antidotes for Food-Producing Animals \(Yes List\)](#)***

The AVMA requests clarification as below regarding the [Nominated Bulk Drug Substances That May NOT Be Used to Compound Office Stock Drugs or Antidotes for Use in Animals \(No List\)](#) and opposes the [List of Bulk Drug Substances for Compounding Office Stock Drugs for Use in Nonfood-Producing Animals or Antidotes for Food-Producing Animals](#) as it pertains to nonfood-producing animals(Yes List).

The AVMA opposes a requirement that all alternative drug Active Pharmaceutical Ingredients (API) with potential efficacy be evaluated by a licensed veterinarian prior to writing a prescription for an unmarketed API that is required to compound a drug for a patient, and we have not understood 21 CFR part 530.5 to require that such an analysis be provided in the veterinarian's records. Such an additional requirement makes the prescription writing analysis extraordinarily burdensome and the licensed veterinarian does not have access to quantity

marketed and other data for an extensive Medically Necessary Veterinary Product (MNVP)<sup>22</sup> analysis.

No List: The FDA states it reviewed nominated BDS and determined idoxuridine does not meet the criteria for inclusion on the Yes List because, “There are FDA-approved human drugs that can be used extralabel to treat feline herpesvirus keratoconjunctivitis in cats.” DrugsatFDA lists NDAs #014169, #013935, #013934, #015868 as discontinued. If an NDA is discontinued, can CVM confirm that it is not “marketed” or as discussed below “commercially available.”

FDA also indicated that itraconazole with DMSO does not meet the criteria for inclusion on the Yes List, in part, because of “...the availability of an alternative compounded ophthalmic drug for keratomycosis in horses that can be compounded using the FDA-approved drug product Vfend.®” The AVMA notes that Vfend® (New Drug Approvals [NDAs] #021266, #021267, #021464, #021466, and #021630) contains voriconazole as the API, not itraconazole.

The AVMA has interpreted GFI # 256 to indicate that only marketing of FDA-approved, conditionally approved, or indexed new animal drugs or FDA-approved human drugs with the same API be considered when compounding preparations under GFI # 256. If that is the case, then idoxuridine and itraconazole, as previously discussed, should not have been placed on the No list as the reasons for their denial are due to discontinued NDAs or the availability of drugs that do not have the same API.

Yes List: AVMA agrees that animal suffering and death will occur without compounded apomorphine hydrochloride, cisapride, guaifenesin, metronidazole benzoate, miconazole nitrate, potassium bromide, and tacrolimus. See AVMA’s alternative recommendation to the Yes List in our comments pertaining to “office stock”. The amount of animal suffering and death that will occur due to lack of availability of needed compounded new animals drugs not currently on the Yes List and the burden required to resubmit nominations that were already provided in conjunction with our comments regarding GFI #230 for which no feedback has been given have led AVMA to continue to oppose such a Yes List for nonfood-producing animals.

### ***Definitions and Concepts***

Food-producing animals<sup>23</sup>: The AVMA asks that species that are sometimes eaten, but also kept under conditions that preclude their routine use as food, or animals that belong to the early non-food life stage of a food-producing minor species where that life stage is not eaten, be defined as nonfood-producing animals<sup>24</sup> for purposes of GFI # 256. Examples include, but are not limited to, bear and antelope in zoos, fish eggs that are not eaten, and oyster larvae.

The AVMA asks whether (1) minor species in wildlife rehabilitation clinics that are held for 45 days or until the slaughter withdrawal time has lapsed, (2) minor species on tribal, state, or national lands from which harvest is illegal and enforced outside fishing or hunting seasons, (3) minor species with a state agency-inserted “call before consume” ear tag, and (4) any near threatened, vulnerable, endangered, critically endangered, or extinct in the wild minor species listed in the International Union for Conservation of Nature’s Red List of Threatened Species<sup>25</sup>

or in Appendix I or II of the Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES)<sup>26</sup> list will be considered as species that are sometimes eaten but kept under conditions that preclude their use as food for purposes of GFI # 256.

Patient: The AVMA agrees a patient is an animal or group of animals examined or treated by a licensed veterinarian.<sup>27</sup>

Copy: Within the guidance, the FDA defines a copy as having the same, similar, or an easily substitutable strength as an approved product where a same or similar dosage can be achieved by administration of fractional or multiple doses of a drug product. Parameters describing what would be considered a reasonable fractional dose or a reasonable number of multiple doses that would be required to achieve the desirable dosage are not provided. The AVMA strongly believes that determining whether the same or similar dosage can be achieved by administration of fractional or multiple doses of a drug product rests within the prescribing veterinarian's professional judgement.

Marketed: Guidance around copies of marketed drugs is introduced with two different definitions of "marketed."

AVMA requests the term "commercially available" be used in lieu of "marketed." The fact that a drug is marketed does not necessarily mean it is available for use by a veterinarian or pharmacist during drug shortages, and commercial unavailability is often one reason veterinarians need preparations compounded from BDS. For example, in 2020, some drugs in short supply have preferentially been distributed for use in humans. So, although they were "marketed" through distribution channels for human use, they were not "commercially available" to veterinarians or pharmacists compounding preparations.

Footnote 5 of GFI #256 also states, "In addition, an FDA- approved human drug is not "marketed" if it is on the drug shortage list in effect under section 506E of the [Food, Drug, and Cosmetic Act] FD&C Act."

The AVMA requests that FDA clarify whether preparations may be compounded from BDS for any API listed on FDA's [Drug Shortages](#) webpage? If yes, is the quality standard for that compounding, cGMP or USP when the compounded drug is intended for use in animals other than humans? If no, how does the definition of not "marketed" in Section 506E of the FD&C Act or listing on FDA's Drug Shortages webpage impact compounding of preparations for non-human animals?

As an illustration, in the appendix to this letter, the AVMA notes in Tables 1 and 2 those drugs listed as currently in shortage on the [FDA Drug Shortages](#) webpage, but not on FDA CVM's [Current Drug Shortages](#) webpage on June 20, 2020 and September 21, 2020, for which FDA CVM-approved applications exist. Reference to FDA's Drug Shortage list in GFI #256 implies that for all APIs on FDA's Drug Shortage list BDS may be used to compound preparations, despite the presence of FDA CVM-approved applications that are not listed on FDA CVM's Current Drug Shortage webpage, giving the appearance of eroding FDA CVM's drug approval process.

Conditionally approved and indexed drugs: The AVMA supports allowing flexibility to use conditionally approved or indexed new animal drugs as starting material for compounding. However, in support of animal health, animal welfare, and public health, particularly with respect to minor species, the AVMA suggests stakeholder discussion and further guidance regarding appropriate extralabel use of conditionally approved or indexed drugs without the need to compound them first if the veterinarian's medical rationale, under a VCPR, is recorded in the patient's medical record. Such flexibility, analogous to that in CPG 615.115,<sup>28</sup> may increase use of conditionally approved or indexed new animal drugs reviewed by FDA CVM and mitigate any erosion of safety, efficacy, or quality that compounding may introduce.

**Conclusion**

In closing, we remain supportive of guidance for veterinarians that will allow access to needed medications and create structure around the use of drugs compounded from BDS. For questions regarding the AVMA's comments, please contact Dr. Dharati Szymanski, Assistant Director, Division of Animal and Public Health at 847-285-6742 or [dszymanski@avma.org](mailto:dszymanski@avma.org).

Sincerely,

A handwritten signature in black ink that reads "Janet D. Donlin DVM, CAE". The signature is written in a cursive style with a large, looped initial "J".

Janet D. Donlin, DVM, CAE  
Executive Vice President and Chief Executive Officer

MM/DS/AM/GCG

**Appendix**

**Table 1:** Injectable drugs listed as being in shortage on the [FDA Drug Shortage webpage](#) on June 26, 2020, but not listed as in shortage on FDA CVM's [webpage](#), with FDA CVM-approved applications posted at [Animal Drugs@FDA](#).

|   | <u>Also listed as in Shortage on Sept 21, 2020</u> |
|---|--|
| Atropine sulfate injection  | Yes  |
| Bupivacaine hydrochloride and epinephrine Injection, USP                        | Yes  |
| Bupivacaine hydrochloride injection, USP  | Yes  |
| Dexamethasone sodium phosphate injection  | Yes  |
| Dexmedetomidine injection   | Yes  |
| Dextrose 25% injection  | Yes  |
| Dextrose 50% injection  | Yes  |
| Enalaprilat injection, USP  | Yes  |
| Epinephrine injection, 0.1 mg/mL  | Yes  |
| Epinephrine injection, Auto-Injector  | Yes  |
| Erythromycin lactobionate for injection, USP                                    | Yes  |
| Fentanyl Citrate (Sublimaze) injection  | Yes  |
| Furosemide injection, USP   | Yes  |
| Ketamine injection  | Yes  |
| Lidocaine hydrochloride (xylocaine) and dextrose injection solution-premix bags | Yes  |
| Lidocaine hydrochloride (xylocaine) injection                                   | Yes  |
| Lidocaine hydrochloride (xylocaine) injection with epinephrine                  | Yes  |
| Oxytocin injection, USP synthetic   | Yes  |
| Propofol injectable emulsion  | Yes  |
| Sodium chloride 23.4% injection   | Yes  |
| Sodium chloride injection USP, 0.9% vials and syringes                          | Yes  |
| Triamcinolone acetonide (trienesence) injection, suspension                     | Yes  |

**Table 2:** Capsule, Tablet, or Ophthalmic drugs listed as being in Shortage on the [FDA Drug Shortage webpage](#) on June 26, 2020, but not listed as in shortage on FDA CVM's [webpage](#), with FDA CVM-approved applications posted at [Animal Drugs@FDA](#).

|                                      | <u>Also listed as in Shortage on Sept 21, 2020</u> |
|--------------------------------------|--|
| Atropine sulfate ophthalmic ointment | Yes  |
| Erythromycin ophthalmic ointment     | Yes  |
| Hydrocortisone tablets, USP          | Yes  |
| Ketoprofen capsules                  | Yes  |

<sup>1</sup> CVM GFI # 256 – [Compounding Animal Drugs from Bulk Drug Substances](#).

<sup>2</sup> [21 CFR Section 530.3\(i\)](#)

<sup>3</sup> [Inspections, Recalls, and Other Actions with Respect to Firms that Engage in Animal Drug Compounding](#)

---

<sup>4</sup> Event ID: 82555, 72405, 83772, 70669, 72501, 77937, 80962, 83790, 69442, 77910, 71802, 66857, 65020, 82720, 81368, 83172, 81911, 82290, 80792, 83708, 66636, 72180

483 19 July 2013 , 483, 483, 483,

Recall

Warning letters; FLA-14-22, FL-14-04, 423162, 2014 DAL-WL-02, 14-ATL-03,

<sup>5</sup> Recall request; Event ID: 62111, 73764

<sup>6</sup> Event ID: 65185, 65481

<sup>7</sup> Compounding issues resurface in wake of ponies' deaths

<sup>8</sup> 4 Horses die after receiving compounded EPM drug

<sup>9</sup> FDA Alerts Horse Owners and Veterinarians About Adverse Events Associated with Certain Unapproved Compounded Drugs in Horses

<sup>10</sup> Compounded Unapproved Animal Drugs from Rapid Equine Solutions Linked to Three Horse Deaths

<sup>11</sup> Analogous to that required in 21 CFR Sec. 211.165

<sup>12</sup> Adverse event reporting policy

<sup>13</sup> Animal drug adverse event reports since 1987

<sup>14</sup> 21 CFR Section 530.5 Veterinary records.

<sup>15</sup> Bulk Drug Substances Nominated Without Sufficient Supporting Evidence

<sup>16</sup> New Animal Drug Application Guidances

<sup>17</sup> Approved Aquaculture Drugs

<sup>18</sup> 21 U.S. Code § 321(e ) The term "person" includes individual, partnership, corporation, and association.

<sup>19</sup> Compounding from unapproved (bulk) substances in food animals

<sup>20</sup> AVMA Guidelines for the Euthanasia of Animals: 2020 Edition

<sup>21</sup> AVMA Guidelines for the Depopulation of Animals: 2019 Edition

<sup>22</sup> What Is a Medically Necessary Veterinary Product ?

<sup>23</sup> See GFI # 256 footnote 4.

<sup>24</sup> See beginning of page 10 in GFI # 210: The Index of Legally Marketed Unapproved New Animal Drugs for Minor Species.

<sup>25</sup> The International Union for Conservation of Nature's Red List of Threatened Species

<sup>26</sup> Convention on International Trade in Endangered Species of Wild Fauna and Flora

<sup>27</sup> See paragraph 15, page 8 in AVMA's Model Veterinary Practice Act.

<sup>28</sup> CPG Sec 615.115 Extralabel Use of Medicated Feeds for Minor Species