FOOD DRUG & COSMETIC ACT (FDCA) PROHIBITS COMPOUNDING FROM BULK DRUG SUBSTANCES FOR USE IN ANIMALS

Compounder Claims

In an email circulated to veterinarians, a large seller of bulk drug substances boldly proclaims there is no law prohibiting the compounding of drugs from bulk drug substances for use in animals.

- "[T]he AHI and AVMA currently claim that all compounding from bulk ingredients for animal use is illegal. In fact, there is no such law!" – Jim Smith, President, Professional Compounding Centers of America, email circulated March 11, 2013.

- This bold statement is erroneous. ALL compounding from bulk drug substances for use in animals is prohibited by the FDCA. The Professional Compounding Centers of America has even been notified of this by FDA in an official Warning Letter:

  "Most animal drugs compounded by a pharmacist are in violation of section 501(a)(5) of the Act because they are new animal drugs, which are not approved, when they bear directions for use in animals. Unlike human drugs, animal drugs are not covered by section 503A, Pharmacy Compounding, of the Food and Drug Administration Modernization Act. Therefore, animal drugs compounded from active pharmaceutical ingredients are subject to the same approval requirements as manufactured animal drugs. The exception to this is found in the Animal Medicinal Drug Use and Clarification Act (AMDUCA) codified at 21 CFR part 530.13, which legalized the compounding of animal drugs from already approved products." http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2001/ucm178377.htm.

FDA's Statement of the Law

According to the FDA, ALL preparations compounded from bulk drug substances are New Animal Drugs within the meaning of the FDCA, are unsafe unless approved and subject to the adulteration and misbranding provisions of the FDCA.

> "FDA's longstanding position is that drugs produced by compounding fall squarely within the FDCA's definitions of "new drug" and "new animal drug" and are therefore subject to the agency's jurisdiction and oversight. Compounded drugs lack FDA approval and, thus, have not been subjected to the rigorous safety and effectiveness pre-marketing review required by the FDCA. As a consequence, such drugs have the potential to pose serious harm to public and animal health."
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> FDA's Brief, at page 3, *US v. Franck's Lab, Inc.*, , (11th Cir. 2012)(No. 11-15350-BB)(dismissed as moot when Franck's lab represented it was no longer doing business, relinquished it state pharmacy license, and the principal filed an affidavit that he has no intent to compound animal medications in the anticipated future.).

Federal Courts of Appeal

Every Federal Court of Appeals that has considered the issue has held that under the FDCA, preparations compounded from bulk drug substances for use in animals are New Animal Drugs and therefore subject to the unsafe, adulterated and misbranding provisions of the FDCA. Their introduction into interstate commerce is prohibited.

- United States Court of Appeals for the 5th Circuit. "We therefore conclude, in agreement with the two other circuits that have considered the issue, that compounded drugs are "new animal drugs" within the meaning of § 321(v)(1) of the FDCA. And unless the compounded drugs are exempt under the FDCA's AMDUCA provisions, § 360b(a)(4) and (5), compounded animal drugs are subject to the FDCA's unsafe, adulteration, and misbranding requirements." *Med. Ctr. Pharmacy v. Mukasey*, 536 F.3d 383, 408 (5th Cir. 2008).

- United States Court of Appeals for the 7th Circuit. In a case involving FDA's seizure of bulk drug substances that were to be used for compounding preparations for use in animals, the 7th Circuit stated that FDA could have "prosecuted thousands of individual veterinarians for administering unsafe drugs (any new animal drug is deemed unsafe unless approved by FDA" and found that the FDCA "essentially forbids the sale, in any form, of drugs formulated or put to new uses ... without the approval of the FDA." 9/1Kg. *Containers, More or Less, of an Article of Drug for Veterinarian Use*, 854 F.2d 173, 174-175 and 179 (7th Cir. 1988), *cert. denied*, 489 U.S. 1010, 109 S. Ct. 1118, 103 L. Ed. 2d 181 (1989).

- United States Court of Appeals for the 3rd Circuit. The 3rd Circuit specifically agreed with the 7th Circuit and held that the FDCA definition of a new animal drug "[d]oes not exempt drugs that are compounded by veterinarians." *United States v. Algon Chem. Inc.*, 879 F.2d 1154, 1158 (3d Cir. 1989)

- The decisions of these Federal Courts of Appeal are binding upon the lower federal district courts in their jurisdictions. It is interesting to note that in each of these instances the Court of Appeals reversed the lower federal district court. Compounders often reargue or quote from the very same trial court opinions that have been overruled or vacated by Courts of Appeal.

Statutory Analysis under the Federal Food, Drug & Cosmetic Act

The following provisions of the Federal Food, Drug & Cosmetic Act (FDCA) and implementing Federal Regulation prohibit the compounding of drugs for use in animals from bulk substances –

- Preparations compounded from bulk drug substances for use in animals are **Drugs** under the FDCA
    - The FDCA definition for "drug", found in section 201(g) [21 USC §321(g)] includes material "intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals" and material "intended to affect the structure or any function of the body of man or other animals"
    - Preparations compounded from bulk drug substances for use in animals are prescribed in order to (1) diagnose, cure, mitigate, treat, or prevent disease in animals, or (2) affect the structure or function of the animal's body. If not, for what other purpose are they compounded?
- Preparations compounded from bulk drug substances for use in animals are **New Animal Drugs** under the FDCA

- The FDCA definition for "new animal drug", found in section 201(v) [21 USC §321(v)], includes "any drug intended for use for animals other than man" that is "not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of animal drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof…". Federal courts have consistently interpreted the "not generally recognized . . . as safe and effective" provision as invoking the statutory standard that must be met to gain FDA approval. Hence, any drug for use in animals that has not already been approved by the FDA constitutes a new animal drug within the meaning of the statute.

    - Preparations compounded from bulk drug substances for use in animals are drugs intended for use in animals other than man and are not generally recognized as safe and effective. Indeed, one prominent compounder specifically disclaims any efficacy for their products – "Wedgewood Pharmacy does not make claims for the efficacy of our compounded preparations." http://www.wedgewoodpetrx.com/ (last accessed on March 13, 2013).

- Because they are unapproved new animal drugs, preparations compounded from bulk drug substances for use in animals are deemed **unsafe** by Section 512(a)(1) of the FDCA [21 USC § 360b(a)(1)], and therefore **adulterated** under Section 501(a)(5) [21 USC § 351(a)(5)]. Because they are adulterated new animal drugs, the FDCA prohibits the introduction into interstate commerce of preparations compounded from bulk drug substances for use in animals under Section 301(a) [21 USC § 331(a)].

- The provisions of the Animal Medicinal Drug Use Clarification Act (AMDUCA) provided for legal compounding using approved human or animal drugs.

    - In 1994 Congress passed the Animal Medicinal Drug Use Clarification Act (AMDUCA). AMDUCA drew policy lines relative to "off-label" or "extra-label" uses and encompassed compounding from approved drugs. The line is draw such that compounding from approved human or animal products can be part of legal extra-label use, but compounding from bulk drug substances remains illegal. Nevertheless, FDA stated it would also exercise enforcement discretion relative to compounding from bulk drug substances per its Compliance Policy Guide (CPG). In 1996 when FDA implemented Federal Regulations under AMDUCA, it again set forth these policy lines.

    - In the Federal Register in 1996, when proposing Federal Regulations under AMDUCA, FDA stated:

      "FDA considers compounding from an approved drug to be an extralabel use. Thus, the agency views the language of the AMDUCA as giving statutory authorization to the compounding of finished drug products from approved human or approved animal drugs, within limits, under the same conditions as for any other extralabel use. FDA has certain concerns relative to compounding and the use of compounded drugs that can be distinguished from those issues associated with simple extralabel use of an approved finished drug product. In view of the above, the proposed rule includes several major factors in addition to the general criteria set forth elsewhere in this proposed rule applicable to the extralabel use by compounding from approved drugs. The proposal provides that such extralabel use is permissible if: (1) All relevant portions of proposed part 530 have been complied with; (2) there is no marketed or approved human or new animal drug that, when used as labeled or in conformity with criteria established in this part, will, in the available dosage form and concentration, appropriately treat the condition diagnosed; (3) compounding is performed by a licensed pharmacist or veterinarian within the scope of a professional practice; (4) adequate processes and procedures are followed that ensure the safety and effectiveness of the compounded products; (5) the scale of the compounding operation is commensurate with the established need for compounded products (e.g., similar to that of comparable practices); and (6) all relevant State laws relating to the

compounding of drugs for use in animals are followed. The AMDUCA does not authorize compounding from bulk drugs or unapproved drugs. **Compounding by or for veterinarians from bulk drugs or unapproved drugs results in the production of an unapproved NAD that may be subject to regulatory action. Accordingly, proposed § 530.13 provides that allowable extralabel use by compounding applies only to compounding of a product from approved drugs by a veterinarian or a pharmacist on the order of a veterinarian within the practice of veterinary medicine, and that nothing in proposed part 530 is to be construed as permitting compounding from bulk drugs or unapproved drugs.** Additional guidance on the subject of compounding may be provided in guidance documents to be issued by FDA."

AMDUCA Proposed Regulations, 61 Fed Reg 25106, 25108 (May 17, 1996)(emphasis added)

- Later that same year, FDA finalized the proposed AMDUCA regulations and responded to comments about compounding submitted to the proposed regulations. In the Federal Register in 1996, when finalizing federal regulations under AMDUCA, FDA stated:

  "Compounding (§ 530.13)

  (36) One comment suggested that rules implementing the AMDUCA should not include regulations regarding compounding. The comment suggested that the regulation merely state that the AMDUCA does not authorize compounding from bulk drugs or unapproved drugs, and refer to separate guidance on compounding. Compounding for use in food animals raises unique concerns with respect to drug residues. The detailed regulations for extralabel use of finished products, while generally applicable to compounding, do not fully address these unique concerns. Therefore, the agency believes that regulations specific to compounding allowed as a result of the AMDUCA are necessary.

  (37) In contrast, several comments requested that CPG 608.400, ''Compounding of Drugs for use in Animals,'' be issued under notice and comment procedures so that the entire content of CPG would be made part of the regulations. CPG's, which set out FDA's regulatory priorities are intended to provide information and guidance. Because such policies are discretionary, they are not binding either on the agency or the public and can be changed from time to time. Notice and comment rulemaking and resulting regulations, on the other hand, establish policies which have the force and effect of law. Therefore, the use of such procedures is not appropriate for CPG's. The agency notes that it followed its usual practice and published a Federal Register notice that announced the availability of the CPG (61 FR 34849, July 3, 1996) which included the entire text of the CPG and specifically provided opportunity for comment.

  (38) One comment suggested that all cutaneously administered compounds (e.g., foot bath preparations) be exempted from the compounding restrictions. The agency believes that the comment may refer to the use for compounding of drug products that have not been approved. Because the AMDUCA applies only to approved drugs, the agency does not have authority in its implementing regulations to exempt extralabel use, including compounding, of unapproved drugs. If the comment intended to address compounding from approved drugs for a specific use (i.e., cutaneous administration), such compounding must be consistent with these final rules. As stated above, further detailed guidance for compounding is provided in its compounding CPG.

  (39) One comment recommended that § 530.13 be modified to be consistent with § 530.20 to state that, if available, an approved animal drug must be utilized for compounding before using a human drug for compounding. The agency agrees, and it has made the appropriate modification of § 530.13. To be consistent with § 530.30, however, the restriction will apply only to drugs compounded for use in food animals.

(40) One comment suggested that the recently issued CPG on compounding contradicts the second sentence in § 530.13(a), and that this sentence should be deleted. The sentence states that the regulations shall not be construed as permitting compounding from bulk drugs. On the other hand, the CPG states that the agency will generally exercise enforcement discretion in very limited circumstances with regard to compounding from bulk substances. The comment suggests a misunderstanding of the difference in scope and purpose between the AMDUCA and its implementing regulations, and the compounding CPG. The AMDUCA applies only to approved products, therefore, compounding from bulk drugs could not be permitted under the AMDUCA regulations. However, limited compounding from bulk substances may be subject to FDA's enforcement discretion as expressed in the CPG. Thus, the second sentence in § 530.13(a) is not in conflict with the CPG."

AMDUCA Final Regulations, 96 Fed Reg 57732, 57739 – 57740 (November 7, 1996)

- The final AMDUCA Federal Regulation provides the parameters for legal compounding from approved human and animal drugs.

"Sec. 530.13 Extralabel use from compounding of approved new animal and approved human drugs.

(a) **This part applies to compounding of a product from approved animal or human drugs by a veterinarian or a pharmacist on the order of a veterinarian within the practice of veterinary medicine. Nothing in this part shall be construed as permitting compounding from bulk drugs.**

(b) **Extralabel use from compounding of approved new animal or human drugs is permitted if**:

(1) All relevant portions of this part have been complied with;

(2) There is no approved new animal or approved new human drug that, when used as labeled or in conformity with criteria established in this part, will, in the available dosage form and concentration, appropriately treat the condition diagnosed. Compounding from a human drug for use in food-producing animals will not be permitted if an approved animal drug can be used for the compounding;

(3) The compounding is performed by a licensed pharmacist or veterinarian within the scope of a professional practice;

(4) Adequate procedures and processes are followed that ensure the safety and effectiveness of the compounded product;

(5) The scale of the compounding operation is commensurate with the established need for compounded products (e.g., similar to that of comparable practices); and

(6) All relevant State laws relating to the compounding of drugs for use in animals are followed.

(c) Guidance on the subject of compounding may be found in guidance documents issued by FDA."

21 CFR § 530.13 (emphasis added)