The Rule

This amendment to 14 CFR part 97 is effective upon publication of each separate SIAP as amended in the transmittal. For safety and timeliness of change considerations, this amendment incorporates only specific changes contained for each SIAP as modified by FDC/P–NOTAMs.

The SIAPs, as modified by FDC P–NOTAM, and contained in this amendment are based on the criteria contained in the U.S. Standard for Terminal Instrument Procedures (TERPS). In developing these chart changes to SIAPs, the TERPS criteria were applied to only these specific conditions existing at the affected airports. All SIAP amendments in this rule have been previously issued by the FAA in a FDC NOTAM as an emergency action of immediate flight safety relating directly to published aeronautical charts. The circumstances which created the need for all these SIAP amendments requires making them effective in less than 30 days.

Further, the SIAPs contained in this amendment are based on the criteria contained in TERPS. Because of the close and immediate relationship between these SIAPs and safety in air commerce, I find that notice and public procedure before adopting these SIAPs are impracticable and contrary to the public interest and, where applicable, that good cause exists for making these SIAPs effective in less than 30 days.

Conclusion

The FAA has determined that this regulation only involves an established body of technical regulations for which frequent and routine amendments are necessary to keep them operationally current. It, therefore—(1) Is not a ''significant regulatory action'' under Executive Order 12866; (2) is not a ''significant rule'' under DOT Regulatory Policies and Procedures (44 FR 11034; February 26, 1979); and (3) does not warrant preparation of a regulatory evaluation as the anticipated impact is so minimal. For the same reason, the FAA certifies that this amendment will not have a significant economic impact on a substantial number of small entities under the criteria of the Regulatory Flexibility Act.

List of Subjects in 14 CFR Part 97

Air Traffic Control, Airports, Incorporation by reference, and Navigation (Air).

Issued in Washington, DC on July 13, 2007.

James J. Ballough,

Director, Flight Standards Service.

Adoption of the Amendment

■ Accordingly, pursuant to the authority delegated to me, Title 14, Code of Federal Regulations, Part 97, 14 CFR part 97, is amended by amending Standard Instrument Approach Procedures, effective at 0901 UTC on the dates specified, as follows:

PART 97—STANDARD INSTRUMENT APPROACH PROCEDURES

■ 1. The authority citation for part 97 continues to read as follows:

Authority: 49 U.S.C. 106(g), 40103, 40106, 40113, 40114, 40120, 44502, 44514, 44701, 44719, 44721–44722.

■ 2. Part 97 is amended to read as follows:

§§ 97.23, 97.25, 97.27, 97.29, 97.31, 97.33, 97.35, and 97.37 [Amended]

By amending: § 97.23 VOR, VOR/DME, VOR or TACAN, and VOR/DME or TACAN; § 97.25 LOC, LOC/DME, LDA, LDA/DME, LDA w/GS, SDF, SDF/DME; § 97.27 NDB, NDB/DME; § 97.29 ILS, MLS, TLS, GLS, WAAS PA, MLS/RNAV; § 97.31 RADAR SIAPs; § 97.33 RNAV SIAPs; § 97.35 COPTER SIAPs, § 97.37 Takeoff Minima and Obstacle Departure Procedures. Identified as follows:

Effective Upon Publication

FDC date	State	City	Airport	FDC No.	Subject
07/05/07	IN	NEW CASTLE	NEW CASTLE—HENRY CO MUNI	7/7352	NDB OR GPS RWY 9, AMDT 5.
07/11/07	AR	FORT SMITH	FORT SMITH REGIONAL	7/7963	ILS RWY 25, AMDT 21A.

[FR Doc. E7–14079 Filed 7–25–07; 8:45 am]

BILLING CODE 4910–13–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 20, 510, 514, and 516

[Docket No. 2005N–0329]

RIN 0910–AF60

Designation of New Animal Drugs for Minor Uses or Minor Species

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Minor Use and Minor Species Animal Health Act of 2004 (MUMS act) amended the Federal Food, Drug, and Cosmetic Act (the act) to establish new regulatory procedures that provide incentives intended to make more drugs legally available to veterinarians and animal owners for the treatment of minor animal species and uncommon diseases in major animal species. At this time, FDA is issuing final regulations to implement the act. These regulations describe the procedures for designating a new animal drug as a minor use or minor species drug. Such designation establishes eligibility for the incentives provided by the MUMS act.

DATES: This rule is effective October 9, 2007.

FOR FURTHER INFORMATION CONTACT: Bernadette Dunham, Center for Veterinary Medicine (HFV–50), Food and Drug Administration, 7519 Standish Pl., Rockville, MD 20855, 240–276–9090, e-mail: *Bernadette.Dunham@fda.hhs.gov*.

SUPPLEMENTARY INFORMATION:

I. Background

In enacting the MUMS act (Public Law 108–282), Congress sought to encourage the development of animal drugs that are currently unavailable to minor species (species other than cattle, horses, swine, chickens, turkeys, dogs, and cats) in the United States or to major species afflicted with uncommon diseases or conditions (minor uses). Congress recognized that the markets for drugs intended to treat these species, diseases, or conditions are often so small that there are insufficient economic incentives to motivate sponsors to develop data to support approvals. Further, Congress recognized that some minor species populations are too small or their management systems too diverse to make it practical to conduct traditional studies to demonstrate safety and effectiveness of these animal drugs. As a result of these limitations, sponsors have generally not been willing or able to collect data to

support legal marketing of drugs for these species, diseases, or conditions. Consequently, Congress enacted the MUMS act, which amended the Federal Food, Drug, and Cosmetic Act (the act) to provide incentives to develop new animal drugs for minor species and minor uses, while still ensuring appropriate safeguards for animal and human health.

In the **Federal Register** of September 27, 2005 (70 FR 56394), FDA issued proposed regulations to implement section 573 of the act (21 U.S.C. 360ccc-2). These regulations proposed procedures for designating a new animal drug as a minor use or minor species drug. Such designation provides eligibility for certain incentives established by the MUMS act, including exclusive marketing rights associated with the conditional approval or approval of designated new animal drugs and for grants to support designated new animal drug development. The proposed rule initially provided for a 75-day public comment period during which the agency received several comments asserting that 75 days was not an adequate amount of time to prepare and submit meaningful comments. In response to this, in the **Federal Register** of December 28, 2005 (70 FR 76732), FDA reopened the comment period allowing an additional 30 days of public comment.

II. Changes to the Proposed Rule

In response to public comment, or in two places to provide added clarity, FDA has made the following changes to the proposed rule:

§ 516.3 *Definitions*. The definition of ''*Infrequently*'' was changed by adding the words ''on an annualized basis'' to the end of the proposed definition. The definition now reads: ''*Infrequently*, as used in the minor use definition, means a disease or condition that is uncommon or that occurs only sporadically on an annualized basis.''

§ 516.21 *Documentation of minor use status*. The language in § 516.21(b) was revised for clarity.

§ 516.28 *Publication of MUMS-drug designations*. In § 516.28(b), the term ''generic name'' was changed to ''established name'' to avoid confusion with abbreviated applications approved under section 512(b)(2) of the act.

§ 516.31 *Scope of MUMS-drug exclusive marketing rights*. In § 516.31(a)(2), the words ''or proposes to withdraw'' were removed.

III. Comments

The agency received comments from 9 organizations or individuals on the September 27, 2005, proposal. Comments were received from a trade organization representing new animal drug manufacturers, a trade organization representing pet product manufacturers, an animal feed manufacturer, a professional association representing veterinarians, an association representing zoos and aquariums, a consumer advocacy organization, and 3 consumers.

A. Comments on the Proposed Rule

(Comment 1) In § 516.3(b) one comment stated that for added clarity and consistency we should add the words ''on an annualized basis'' to the end of the definition for infrequently.

(Response) We agree. We explained in the preamble to the proposed rule why we thought that it was appropriate to annualize the data on the number of animals in which the indication occurs (see 70 FR at 56395 to 56396). Therefore, we have revised the codified section accordingly.

(Comment 2) Two comments stated that the requirement for a specific product development plan as part of a request for MUMS-drug designation in § 516.20(b)(6) is unnecessarily arduous and premature in the designation process. Commentors also stated that frivolous requests for designation should not be burdensome to the agency; and, therefore, that the requirement for a specific product development plan is unnecessary.

(Response) We do not agree that the requirement for submission of a description of the product development plan is arduous or premature. Also, the basis for this requirement is not primarily to reduce burden on the agency due to frivolous requests for designation. The primary reasons for requiring a specific product development plan as part of a request for MUMS-drug designation are as follows. As we explained in the preamble to the proposed rule (70 FR 56394 at 56399), for new animal drugs, unlike for human orphan drugs, each designation must be unique with respect to drug, dosage form, and intended use. In this way, the MUMS act, which was enacted to address the critical shortage of approved animal drugs for minor species/minor uses, facilitates the development of a broad range of animal drugs in part by discouraging multiple sponsors from pursuing identical uses. Because each MUMS designation is unique, it is important to the effective implementation of section 573 of the act that initial designation of a drug be based on evidence that requesting sponsors clearly understand their responsibilities in terms of drug research and development and are prepared to accept those responsibilities.

Submission of a description of the product development plan helps to ensure that timely development of the drug, consistent with the requirement of section 573(a)(2)(B) to actively pursue approval with due diligence, is feasible. Designation of a drug that could not feasibly be approved under the sponsor's current drug development plan would inappropriately delay development and marketing of a needed drug by the same or a different sponsor and undermine the goals of the MUMS act. Submitting the description of the product development plan also facilitates meaningful communication between the sponsor and the agency to help ensure that safety and effectiveness testing, which for designated drugs may be supported by grants or contracts under section 573(b) of the act, is efficiently designed and conducted. Efficient and effective use of sponsor and agency resources, which is enabled by this and other requirements of final § 516.20, is critically important to alleviating the shortage of new animal drugs addressed by the MUMS act.

(Comment 3) Two comments stated that the documentation requirements for minor use status in § 516.21 are too burdensome. They believe there is a lack of balance between the documentation required for a minor use designation versus a minor species designation. More specifically, both commentors believe that § 516.21(b) is asking sponsors to prove a negative concerning the lack of medical justification and one of these commentors stated that the financial information requested in § 516.21(c) is, for the most part, confidential. As an alternative approach, these two commentors submitted similar two-part working definitions for minor use that could be used in place of the proposed provisions for § 516.21 as follows:

Either:

1. The drug is not currently approved, it is unlikely the ''minor use'' designation for the drug will be applicable to a majority of the major species population, and the need for the drug for a specific disease or condition has been clearly identified by animal health professionals or an animal industry. One commentor also added a fourth provision that if the drug has the same active ingredient as other approved drugs, the environmental safety assessment of the combined active ingredient of all such drugs is shown to be adequate.

Or;

2. The annualized commercial return on investment for the product is not reasonably expected to exceed the development and maintenance costs of the product.

(Response) We do not agree that the requirements for documentation of minor use status in § 516.21 are too burdensome. FDA agrees that these implementing regulations should not be overly burdensome to drug sponsors in order to achieve the objectives set forth in the MUMS Act. However, it is unavoidable that a certain amount of additional information will be required in a request for minor use designation that will not be required in a request for minor species designation. Section 516.21 describes this additional information and comprises three paragraphs.

Section 516.21(a) asks for an estimate of the total number of animals to which a drug could potentially be administered on an annual basis. Whether compared to a predetermined small number of animals or as part of a case-by-case determination, this number will be essential to any request for minor use designation. Simply put, this estimated number of animals serves as documentation that the intended use of a proposed MUMS drug is limited to a ''small number of animals'', as required by the MUMS Act.

Section 516.21(b) describes how to define a minor use population if the proposed MUMS drug is under development for only a subset of the estimated total number of animals to which the drug could potentially be administered on an annual basis. In this situation, a sponsor may utilize the provisions of this paragraph to argue that administration of a proposed MUMS drug is only justified for a small subset of a larger major species population potentially affected by a particular disease or condition and that administration to the remaining larger affected population is medically inappropriate. If the number of animals in this medically justified subset is a small number of animals, then such a use is a minor use.

The provisions in this paragraph were apparently misinterpreted by two of the commentors. Its purpose is not to require medical justification to the effect that a drug approved for disease A could not be used for disease B or C or D. Its purpose is to allow drug sponsors to restrict the intended use of a drug to a subset of the animals affected by disease A, thereby reducing their estimate of the total number of animals eligible to be treated as required in § 516.21(a), by providing medical justification that only a subset of animals afflicted with disease A are amenable to treatment. For improved clarity, we have revised the language of § 516.21(b).

Section 516.21(c) requires drug sponsors to provide economic information relevant to why their MUMS drug should be considered a minor use drug. In the preamble to the proposed MUMS designation rule (70 FR 56394) we cited the Senate report (S. Rept. 108–226) concerning the bill before the Senate (S. 741), which discusses the minor use definition and how minor use should be determined: ''This definition incorporates the existing definition in the Code of Federal Regulations (21 CFR 514.1(d)(1)) with a further limitation to ''small numbers'' to assure that such intended uses will not be extended to a wider use. The Secretary is expected to further clarify this definition in regulations implementing this section. FDA is given broad latitude in determining what constitutes a minor use in a major species. The Congress intends for FDA to make the determination of minor use by evaluating, in the context of the drug development process, whether the incidence of the disease or condition occurs so infrequently that the sponsor of a drug intended for such use has no reasonable expectation of its sales generating sufficient revenues to offset the costs of development. The Congress does not intend for FDA to establish a test of commercial value, but rather directs FDA to determine whether the expected low use of a drug would discourage its development.'' (S. Rept. 108–226 at 12–13.)

In evaluating whether the incidence of the disease or condition is so infrequent that the sales are not reasonably expected to offset development costs, we might take two different approaches. First, we could consider each request on a case-by-case basis utilizing the information provided in § 516.21(c). Alternatively, we could establish, by regulation based on industry-wide economic data, a specific small number of animals for each of the seven major species to be used as a yardstick against which we would measure the estimated total number of animals to which a drug could potentially be administered on an annual basis, as documented under § 516.21(a). If such ''small number'' for each major species is established by regulation at some point in the future, there would no longer be a need for requiring the information requested in § 516.21(c).

(Comment 4) With respect to § 516.24, two comments stated that FDA should respond to requests for designation within 60 days from the time the request was submitted.

(Response) FDA agrees that timely processing of requests for designation is important. However, because of limitations on agency resources, the agency does not believe that it is feasible to commit to responding to all requests for designation within 60 days. We intend to issue guidance in the future to describe target timelines for the designation process consistent with current resources.

(Comment 5) Two comments stated that FDA should update the publicly available list of MUMS-designated drugs within 60 days of granting a new MUMS designation.

(Response) We agree that timely updating of the list of MUMS-designated drugs is appropriate. However, the agency does not believe it is feasible to commit to definite timelines in these regulations because of uncertain resource limitations. As discussed above, we intend to describe target timelines for our actions related to the designation process in future guidance.

(Comment 6) Two comments stated that a 1-year advance notification for discontinuing the manufacture of a drug, as specified in § 516.29(b), is excessive and a 30–60 day timeframe would be more appropriate.

(Response) A 1-year advance notification for discontinuing the manufacture of a MUMS-designated drug is required by section 573(a)(2)(C) of the act and, therefore, is not subject to alteration by regulation.

(Comment 7) One commentor requested clarification on the hypothetical situation in which FDA has withdrawn designation status after notification by a sponsor (sponsor A) of its intent to discontinue production, but the drug is still being sold, as permitted in accordance with the lengthy pre-notification required by the statute. The commentor asked if another sponsor (sponsor B) could potentially achieve designation and conditional approval, and thus block any further sale by sponsor A, even if sponsor A still has time left on their notification and still has drug to be sold.

(Response) In this situation, FDA has only withdrawn sponsor A's designation and, therefore, its exclusivity. The approval or conditional approval remains intact. Therefore, while approval or conditional approval may be possible for sponsor B, designation cannot be granted for sponsor B because the MUMS Act only allows designation when a specific drug, dosage form, and intended use is not already approved or conditionally approved.

(Comment 8) In § 516.31(a)(2) one comment stated that the words § or proposes to withdraw'' should be removed because this appears to negate the right of the sponsor to due process.

(Response) We agree that the exclusivity of an approved or conditionally approved MUMS-designated drug should not be abrogated by a proposal to withdraw the approval or conditional approval. We have revised the codified section accordingly.

(Comment 9) One comment stated that oral dosage form new animal drugs and new animal drugs for use in animal feeds should not be considered two different dosage forms for the purpose of MUMS designation. It argues, for example, that if an oral dosage form new animal drug is designated and approved subsequent to the designation and approval of a medicated feed containing the same drug and for the same intended use, it will negatively impact the business case and success of the medicated feed.

(Response) The agency believes that this same argument could apply to any drug that is available in more than one dosage form. For example, an approved injectable product could be negatively impacted by approval of an oral form of the drug.

As stated in the preamble to the proposed rule (70 FR 56394 at 56398), current federal regulations recognize the following dosage forms: Oral dosage forms (21 CFR part 520), implantation or injectable dosage forms (21 CFR part 522), ophthalmic and topical dosage forms (21 CFR part 524), intramammary dosage forms (21 CFR part 526), miscellaneous dosage forms (21 CFR part 529), and drugs in animal feeds (21 CFR part 558). The preamble also notes that medicated feeds are subject to different limitations from those for other oral dosage forms (70 FR 56394 at 56398), which also supports treating medicated feeds as a different dosage form for the purpose of MUMS designation.

In addition, the markets for medicated feeds and other oral dosage forms may be different. An oral dosage in the form of a drench or a water treatment may be appropriate in different settings than those requiring treatment through the use of medicated feeds. For example, pheasants in a hatchery setting can be treated with medicated water while those in large outdoor pens are more efficiently treated with medicated feeds. Because the populations served by medicated feeds and by other oral dosage forms can be different enough to represent separate markets and because, as already noted, the same potential overlap can occur between any two dosage forms, we believe it is appropriate to treat medicated feeds and other oral dosage forms as different for MUMS designation purposes.

(Comment 10) In the definition section under § 516.13, under *Intended Use*, one comment asked if treatment, control, and prevention are the same thing (i.e., one designation) or are they three different things (i.e., three possible designations).

(Response) Given that requirements for approval may differ significantly for these three categories, they are considered to be different for purposes of designation.

(Comment 11) One comment disagreed with the third principle of sameness discussed in the preamble to the proposed rule, under which an intended use for a disease or condition caused by one organism is considered different from an intended use for the same disease or condition caused by a different organism. The comment perceived this approach to determining sameness to be a disincentive to seeking MUMS designation.

(Response) This comment raises the general issue of how different intended uses must be to be considered separate intended uses. If the uses are clearly separable and have different data requirements for approval, we believe it is appropriate to permit separate MUMS-drug designations. Intended uses for diseases or conditions caused by different organisms are clearly separable and would need to be supported by different data for approval; therefore, we believe that allowing separate MUMS-drug designations for drugs for such uses would be appropriate.

(Comment 12) One comment was concerned that many zoo animals may be included in the broad major species categories. It stated that FDA should specifically identify the species and subspecies that are considered ''major species'' with the recognition that some species/subspecies may be appropriate only for public display or exhibition, and that these non-domestic animals should be identified separately for appropriate drug approval under MUMS regulations.

(Response) Zoo species will not be lumped with major species for the purposes of drug approval. The major species are the domesticated species only, not including hybrids or closely-related wild species. Whether an animal belongs to a major or minor species is not affected by its location or use; it is strictly a matter of the species.

Currently, FDA considers the major species to be:

Cattle—*Bos taurus taurus* / *Bos taurus indicus*
Horses—*Equus caballus*
Swine—*Sus domesticus*
Dogs—*Canis familiaris* (also called *Canis lupus familiaris*)
Cats—*Felis domesticus* (also called *Felis catus* or *Felis silvestris catus*)
Chickens—*Gallus gallus*
Turkeys—*Meleagris gallopavo gallopavo*

All other species are considered to be minor. Therefore, there should be no cause for concern regarding the status of zoo animals in terms of new animal drug approval. The agency intends to clarify this issue in guidance to be published in the future.

(Comment 13) One comment stated that a manufacturer of a drug that is already approved in countries with substantially the same approval requirements as the United States does not need incentives to develop data and should not be given a MUMS designation.

(Response) The MUMS incentives exist to encourage pharmaceutical companies to pursue approval of new animal drugs for minor uses and minor species. Even in cases where foreign approvals exist, sponsors generally need to provide considerable new data to meet the requirements for FDA approval. Therefore, the MUMS incentives remain appropriate when a drug has been approved in a foreign country.

(Comment 14) One comment stated that in order to monitor whether the MUMS rule is fulfilling its intended goal to increase the availability of drugs for minor uses, FDA should require annual reports on quantities sold of each designated and conditionally approved drug.

(Response) The agency agrees that knowledge of the quantity of designated drugs distributed on an annual basis would be useful information in terms of assessing the success of the MUMS act. The MUMS act itself requires the annual submission of information regarding quantities of conditionally approved products distributed (see 21 U.S.C. 360ccc(d)(2)(B)(ii)). All fully approved new animal drugs are required by regulation (21 CFR 514.80 (b)(4)(i)) to report the quantity of product distributed. The Office of Minor Use and Minor Species Animal Drug Development will have direct access to this information.

B. Comments on ''Small Number of Animals'' and Minor Use

(Comment 15) Three comments stated that companion animal ''small numbers'' should be considered separately from food animal ''small

numbers.'' Two comments asked FDA to consider the numbers of animals eligible to be designated under a minor species provision (e.g., sheep) as a benchmark against which to compare numbers of animals to benefit from minor use provisions.

(Response) The agency agrees that the ''small numbers'' for companion animals need to be considered separately from the ''small numbers'' for food animals. FDA also agrees that it is appropriate to consider the relationship between the number of animals of a minor species permitted to be designated under the MUMS act and the number of animals of a major species permitted to be designated in establishing ''small numbers'' of animals under the definition of minor use in the statute. However, the agency views the primary basis for establishing ''small numbers'' to be Congress' expression of intent in the report language accompanying the act that the agency further define minor use in a major species ''by evaluating, in the context of the drug development process, whether the incidence of the disease or condition occurs so infrequently that the sponsor of a drug intended for such use has no reasonable expectation of its sales generating sufficient revenues to offset the cost of development'' (S. Rept. 108–226 at 12–13).

Since Congress provided incentives in the MUMS act to stimulate drug development, the agency interprets the previous statement to mean that FDA should determine for each major species what the ''small number of animals'' eligible to be treated on an annual basis would need to be in order to represent a drug market value that (relative to drug development costs) would be considerably less likely to be pursued in the absence of the MUMS incentives, than in their presence.

(Comment 16) Two comments stated that ''small numbers'' should be based on epidemiological data and not on a percentage of the total major species population. Commentors stated that since such epidemiological data are not yet available, FDA should make minor use designations on a case-by-case basis rather than setting hard numbers.

(Response) In the preamble to the proposed rule for MUMS designation (70 FR 56394), the agency already rejected the idea of establishing ''small numbers'' based on a percentage of the major species population as overly simplistic. There the agency explained that using the human orphan drug prevalence limit of 200,000 cases (0.1% of the U.S. population in 1983) did not seem helpful for calculating ''small numbers'' in cattle, swine, chickens, and turkeys because the populations involved, the manner of drug use in those populations, and the drug development processes for those species are too dissimilar to the human drug scenario (70 FR 56394 at 56396). Further analysis made clear that these factors were not sufficiently comparable for this approach to be viable, even for dogs, cats, and horses (70 FR 56394 at 56396). On the other hand, as already noted, Congress directed the agency to define ''minor use'' and, by extension, ''small numbers,'' on the basis of determining whether a population of animals of a major species needing drug treatment would provide sufficient drug market value to offset the cost of drug development given the incentives provided by the MUMS act.

The use of epidemiological data comes into play at the point that the sponsor and the agency are trying to establish the population of animals eligible to be treated with a particular drug for a particular intended use. Such data need to be shared with the agency whether the determination of minor use is being made on a case-by-case basis or with respect to an established small number of animals.

(Comment 17) One comment stated that FDA should consider the potential of a drug to be used extralabel when making a minor use designation.

(Response) The agency understands the expressed concern regarding extra-label drug use, but extra-label drug use is an issue that clearly transcends the designation process. Extra-label use of approved new animal drugs is statutorily permissible under specified circumstances. (Extra-label use is not permitted for either conditionally approved or indexed drugs because such drugs have not met the full approval requirements of the statute.) There is no general prohibition regarding the extra-label use in minor species of products approved for use in major species or vice versa.

Therefore, under designation, a product designated and approved for a minor species can be legally used in an extra-label manner in a major species (subject to established statutory and regulatory conditions). The same is true for a product designated for a minor use in a major species. It is difficult enough to determine whether the population of animals associated with the disease or condition for which a drug is labeled for use fails to provide sufficient market value to offset the cost of drug development (or falls above or below an established small number of animals). It would be impossible to determine the population of all animals subject to all potential extra-label uses of a drug. In fact, it must be assumed that this population (which may include all potential uses of a drug in all animal species) would very often exceed a small number of animals. Therefore, consideration of potential extra-label use in the designation process would have the effect of essentially negating the designation provision of the statute and this would clearly be contrary to the intent of the legislation.

(Comment 18) One comment stated that long term use of a drug, even in a small number of animals, would constitute a much larger market than for shorter term use and that FDA should not consider animal numbers as ''small'' if food animals are to receive drugs for a long duration, perhaps for a period longer than 21 days, consistent with FDA's Guidance for Industry (GFI) #152.

(Response) As noted previously, the agency acknowledges the concern regarding the use of drugs in food animals and accepts that the concept of ''small numbers'' of animals included in the statutory definition of minor use is based, in part, on this concern. The agency will address the issue of establishing ''small numbers'' of animals for each major species in future rulemaking. However, a full assessment of the relative risks of individual drugs or drug uses is a matter that must be left to the comprehensive analysis associated with the review of individual new animal drug applications consistent with GFI #152 and other applicable policies and regulatory requirements.

IV. Legal Authority

FDA's authority for issuing this final rule is provided by the MUMS act (21 U.S.C. 360ccc *et seq.*). When Congress passed the MUMS act, it directed FDA to publish implementing regulations (see 21 U.S.C. 360ccc note). In the context of the MUMS act, the statutory requirements of section 573 of the act, along with section 701(a) of the act (21 U.S.C. 371(a)) provide authority for this final rule. Section 701(a) authorizes the agency to issue regulations for the efficient enforcement of the act.

V. Analysis of Economic Impacts

FDA has examined the impacts of the final rule under Executive Order 12866 and the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act of 1995 (Public Law 104–4). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic,

environmental, public health and safety, and other advantages; distributive impacts; and equity). The agency believes that this final rule is not a significant regulatory action under the Executive order.

FDA finds that the final rule does not constitute an economically significant regulatory action as defined in section 3(f)(1) of Executive Order 12866. We believe that the annual impacts will not exceed $100 million since by its very nature the rule applies to animal drugs that have a very small market. Similarly, the administrative costs are unlikely to have a significant economic impact on a substantial number of small entities.

Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that agencies prepare a written statement, which includes an assessment of anticipated costs and benefits, before proposing ''any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted annually for inflation) in any one year.'' The current threshold after adjustment for inflation is $122 million, using the most current (2005) Implicit Price Deflator for the Gross Domestic Product. FDA does not expect this final rule to result in any 1-year expenditure that would meet or exceed this amount.

FDA received nine comments to the proposed rule. Only two of these comments contained any remarks that addressed the impacts analysis of the proposed rule. Both stated that the requirement for a specific development plan before a designation is granted would be too burdensome. Neither of the comments provided any estimates on the size of the burden that would be imposed. FDA responded previously in this preamble to the burden issue in these comments. Further, FDA believes that the development of the plan would not be overly burdensome because, in most cases, it would be the same plan that a sponsor would establish with FDA under the regular animal drug review process, and because its cost, estimated at less than one thousand dollars each, would represent less than 0.1% of revenues of even the smallest establishments. Additionally, the MUMS act requires that FDA measure the diligence with which sponsors work towards final approval of a MUMS-designated drug, and a drug development plan is necessary for FDA to measure a sponsor's progress towards this goal. FDA has therefore not changed this provision in the final rule.

None of the changes made to the final rule would affect the expected impacts of the rule on the animal drug producers. Accordingly, lacking any other comments to its analysis of the proposed rule, FDA has reviewed its impacts analysis published in the proposed rule and retains it here for the final rule.

The intention of this rule, and therefore its benefit, is the creation of a system that would stimulate the development and marketing of animal drugs for rare diseases in major species and diseases found in minor species in the United States, which would otherwise not be economically viable under current market conditions. The countervailing cost, or risk of this final rule, would be the possibility of limited competition for approved drugs for a minor use drug indication or in a minor species drug due to the granting of the 7-year exclusive marketing right. In addition to the benefit-risk tradeoff mentioned previously, there would be additional administrative costs for those companies seeking the MUMS designation for a new animal drug application (NADA). We estimate that the designation request would require about 16 hours of preparation by a regulatory affairs official. At a benefit adjusted wage rate of almost $48 per hour for these employees, each request would have administrative costs of about $760.[1] We estimate that about 15 separate sponsors would each annually submit, on average, 5 MUMS designation requests. Administrative costs for these actions would total to about $57,300.

The agency is also requiring in § 516.22 that foreign sponsors requesting designation do so through a permanent resident U.S. agent. This is consistent with the current requirements of 21 CFR 514.1(a) since requests for MUMS designation will ultimately be submitted to an NADA file. The agency does not expect to receive many requests for designation from foreign sponsors, and estimates that number at less than one per year. As such, the agency has not quantified the cost of this provision but believes it would be negligible.

Amendments made to existing designations are expected to occur infrequently. We estimate that three amendments will be filed annually, requiring about two hours of preparation. At the same wage rate, this would cost an additional $300.

[1] 2000 National Industry-Specific Occupational Employment and Wage Estimates, U.S. Department of Labor, Bureau of Labor Statistics (*www.bls.gov/oes/2000/oesi3_283.htm*); Compliance officer wage rate adjusted to 2005 by 2000–20004 average annual wage inflator at BLS (*http://data.bls.gov/cgi-bin/surveymost*).

Sponsors may also transfer sponsorship of MUMS-designated drug or terminate the designation. We estimate that these activities would result in only 3 additional hours of administrative costs annually, totaling to $150. The preparation of the annual report that would be required for each MUMS-designated drug is estimated to take about 2 hours. In the first year, this would result in another 150 hours of administrative costs, or about $7,200 in total. FDA notifications to sponsors concerning insufficient quantities of approved MUMS-designated drugs are expected to be rare, about once each year. Sponsor responses are estimated to take 3 hours, at a cost of $150.

Assuming a sponsor chooses to seek the MUMS designation for its NADA, total administrative costs for this rule across all sponsors are estimated at about $65,000 in the first year, and to increase each year thereafter due to the annual reporting requirements.

Regulatory Flexibility Analysis

1. Small Business Impacts

The Regulatory Flexibility Act requires agencies to prepare a regulatory flexibility analysis if a rule is expected to have a significant economic impact on a substantial number of small entities. Although we believe it is unlikely that significant economic impacts would occur, the following along with other sections of this preamble constitute the regulatory flexibility analysis.

One requirement of the Regulatory Flexibility Act is a succinct statement of any objectives of the rule. As stated previously in this analysis, with this rule the agency intends to create a system, provided for by statute, that would stimulate the development and marketing of animal drugs for rare diseases in major species and diseases found in minor species in the United States, which would otherwise not be economically viable under current market conditions.

The Regulatory Flexibility Act also requires a description of the small entities that would be affected by the rule, and an estimate of the number of small entities to which the rule would apply. The Small Business Administration (SBA) defines the criteria for small businesses using the North American Industrial Classification System (NAICS). For pharmaceutical preparation manufacturers (NAICS number 325412), SBA defines small businesses as those with less than 750 employees. Census data shows that 723 companies with 901

establishments represent this category.[2] While about two-thirds of the establishments would be considered small using the SBA criteria, the agency acknowledges that many requests for MUMS designation would likely be received from multi-establishment companies that exceed the 750-employee limit on small businesses. Nonetheless, the cost of submitting a single request represents only about 0.1% of the revenues of the smallest set of establishments (those with 1–4 employees), and much smaller revenue percentages of all larger establishments. The agency believes that these costs would not represent a significant economic impact on these firms.

All of the costs described previously would be incurred by any small business that applies for MUMS designation. These include costs for request preparation, amendments to designations, preparing annual reports and responding to FDA notifications of insufficient quantities. The firms submitting requests for MUMS designation are expected to already have the necessary administrative personnel with the skills required to prepare the requests and fulfill reporting requirements as identified previously.

2. Analysis of Alternatives

The Regulatory Flexibility Act requires that the agency consider any alternatives to a rule that would accomplish the objective while minimizing significant impacts of the rule. As stated previously, the agency believes that the final rule, due to the relatively small costs, would not be likely to impose significant economic impacts on small businesses. As such, the agency believes the final rule achieves the objective with minimal costs to industry.

The statute that creates this system, Public Law 108–282, does not provide the agency a great deal of flexibility in the implementing regulations, such as in determining the length of the exclusivity period or granting an exclusivity to more than one animal drug without regard to sameness of drug, dosage form and intended use. The agency did consider, however, applying an explicit threshold number of animals of each major species as the upper bound of disease incidence in the definition of ''minor use'' of animal drugs. The agency determined that the data needed to develop these estimates would not be available in time for the publication date of the final rule as mandated by statute. The agency intends in the future to propose a separate rule defining the threshold numbers of animals of each major species. The agency will continue to consider the acceptability of each request for designation as a minor use animal drug on a case-by-case basis as provided for in the Senate report concerning the legislation, until it issues any final rule based on such a proposal.

VI. Paperwork Reduction Act of 1995

In the **Federal Register** of September 27, 2005, FDA published a proposed rule and invited comments on the proposed collection of information. Also in a **Federal Register** of December 28, 2005, FDA published a notice reopening the comment period for the proposed rule to allow interested persons additional time to comment. Concurrently, FDA submitted the information collection request to the Office of Management and Budget (OMB) for review and approval. OMB did not approve this collection of information, but as terms for clearance, filed comment. In filing comment on this collection of information, OMB requested that FDA examine public comment in response to the notice of proposed rulemaking and describe in the preamble of the final rule how the agency has maximized the practical utility of the collection and minimized the burden. Further, OMB requested for any future submissions of this information collection, FDA indicate the submission as ''new'' and reference OMB control number 0910–0590.

In response to these **Federal Register** notices, FDA did not receive any comments regarding the information collection requirements contained in the final rule. In response to OMB's request that the agency describe how it has maximized the practical utility of this collection and minimized the burden, an explanation has been provided elsewhere in the preamble of this final rule.

The information collection provisions of this final rule have been submitted to OMB for review. Prior to the effective date of this final rule, FDA will publish notice in the **Federal Register**, announcing OMB's decision to approve, modify, or disapprove the information collection provisions in this final rule. An agency may not conduct or sponsor, and a person is not required to respond to a collection of information, unless it displays a currently valid OMB control number.

Title: Designated New Animal Drugs for Minor Use and Minor Species—21 CFR Part 516, OMB Control No. 0910–0590.

Description: The MUMS act amended (the act) to authorize FDA to establish new regulatory procedures intended to make more medications legally available to veterinarians and animal owners for the treatment of minor animal species as well as uncommon diseases in major animal species. This legislation provides incentives designed to help pharmaceutical companies overcome the financial burdens they face in providing limited-demand animal drugs. These incentives are only available to sponsors whose drugs are ''MUMS-designated'' by FDA. Minor use drugs are drugs for use in major species (cattle, horses, swine, chickens, turkeys, dogs, and cats) that are needed for diseases that occur in only a small number of animals either because they occur infrequently or in limited geographic areas. Minor species are all animals other than the major species, for example, zoo animals, ornamental fish, parrots, ferrets, and guinea pigs. Some animals of agricultural importance are also minor species. These include animals such as sheep, goats, catfish, and honeybees. Participation in the MUMS program is completely optional for drug sponsors so the associated paperwork only applies to those sponsors who request and are subsequently granted ''MUMS designation.'' The proposed rule will specify the criteria and procedures for requesting MUMS designation as well as the annual reporting requirements for MUMS designees.

Under the new part 516, § 516.20 provides requirements on the content and format of a request for MUMS-drug designation, § 516.26 provides requirements for amending MUMS-drug designation, provisions for change in sponsorship of MUMS-drug designation can be found under § 516.27, under § 516.29 are provisions for termination of MUMS-drug designation, under § 516.30 are requirements for annual reports from sponsor(s) of MUMS designated drugs, and under § 516.36 are provisions for insufficient quantities of MUMS-designated drugs.

Description of Respondents: Pharmaceutical companies that sponsor new animal drugs.

FDA estimates the burden for this collection of information as follows:

[2] 2002 Economic Census, US Census Bureau, Manufacturing Industry Series, Pharmaceutical Preparation Manufacturing, Table 4.

TABLE 1.—ESTIMATED ANNUAL REPORTING BURDEN[1]

21 CFR Section	No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
516.20	15	5	75	16	1,200
516.26	3	1	3	2	6
516.27	1	1	1	1	1
516.29	2	1	2	1	2
516.30	15	5	75	2	150
516.36	1	1	1	3	3
Total					1,362

[1] There is no capital or operating and maintenance cost associated with this collection of information.

VII. Environmental Impact

We have carefully considered the potential environmental impacts of this final rule and determined under 21 CFR 25.30(h) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment, nor an environmental impact statement is required.

VIII. Federalism

FDA has analyzed this final rule in accordance with the principles set forth in Executive Order 13132. FDA has determined that the rule does not contain policies that have substantial direct effects on the States, on the relationship between the National Government and the States, or on the distribution of power and responsibilities among the various levels of government. Accordingly, the agency has concluded that the rule does not contain policies that have federalism implications as defined in the Executive order and, consequently, a federalism summary impact statement is not required.

List of Subjects

21 CFR Part 20

Confidential business information, Courts, Freedom of information, Government employees.

21 CFR Part 510

Administrative practice and procedure, Animal drugs, Labeling, Reporting and recordkeeping requirements.

21 CFR Parts 514 and 516

Administrative practice and procedure, Animal drugs, Confidential business information, Reporting and recordkeeping requirements.

■ Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR chapter I is amended as follows:

PART 20—PUBLIC INFORMATION

■ 1. The authority citation for 21 CFR part 20 continues to read as follows:

Authority: 5 U.S.C. 552; 18 U.S.C. 1905; 19 U.S.C. 2531–2582; 21 U.S.C. 321–393, 1401–1403; 42 U.S.C. 241, 242, 242a, 242l, 242n, 243, 262, 263, 263b–263n, 264, 265, 300u–300u–5, 300aa–1.

■ 2. Amend § 20.100 by adding paragraph (c)(43) to read as follows:

§ 20.100 Applicability; cross-reference to other regulations.

* * * * *

(c) * * *

(43) Minor-use or minor-species (MUMS) drug designations, in § 516.52 of this chapter.

PART 510—NEW ANIMAL DRUGS

■ 3. The authority citation for 21 CFR part 510 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 353, 360b, 371, 379e.

■ 4. Amend § 510.3 by revising paragraph (k) to read as follows:

§ 510.3 Definitions and interpretations.

* * * * *

(k) *Sponsor* means the person requesting designation for a minor-use or minor-species drug as defined in part 516 of this chapter, who must be the real party in interest of the development and the intended or actual production and sales of such drug (in this context, the sponsor may be an individual, partnership, organization, or association). Sponsor also means the person responsible for an investigation of a new animal drug. In this context, the sponsor may be an individual, partnership, corporation, or Government agency or may be a manufacturer, scientific institution, or an investigator regularly and lawfully engaged in the investigation of new animal drugs. Sponsor also means the person submitting or receiving approval for a new animal drug application (in this context, the sponsor may be an individual, partnership, organization, or association). In all contexts, the sponsor is responsible for compliance with applicable provisions of the act and regulations.

PART 514—NEW ANIMAL DRUG APPLICATIONS

■ 5. The authority citation for 21 CFR part 514 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 353, 360b, 371, 379e, 381.

§ 514.1 [Amended]

■ 6. Amend § 514.1 by removing paragraph (d).

■ 7. Add part 516 to read as follows:

PART 516—NEW ANIMAL DRUGS FOR MINOR USE AND MINOR SPECIES

Subpart A—General Provisions

Sec.
516.1 Scope.
516.2 Purpose.
516.3 Definitions.

Subpart B—Designation of a Minor Use or Minor Species New Animal Drug

516.11 Scope of this subpart.
516.12 Purpose.
516.13 Definitions.
516.14 Submission of requests for designation.
516.16 Eligibility to request designation.
516.20 Content and format of a request for MUMS-drug designation.
516.21 Documentation of minor use status.
516.22 Permanent-resident U.S. agent for foreign sponsor.
516.23 Timing of requests for MUMS-drug designation.

516.24 Granting MUMS-drug designation.
516.25 Refusal to grant MUMS-drug designation.
516.26 Amendment to MUMS-drug designation.
516.27 Change in sponsorship.
516.28 Publication of MUMS-drug designations.
516.29 Termination of MUMS-drug designation.
516.30 Annual reports for a MUMS-designated drug.
516.31 Scope of MUMS-drug exclusive marketing rights.
516.34 FDA recognition of exclusive marketing rights.
516.36 Insufficient quantities of MUMS-designated drugs.
516.52 Availability for public disclosure of data and information in requests.

Subpart C—[Reserved]

Subpart D—[Reserved]

Authority: 21 U.S.C. 360ccc–2, 371.

Subpart A—General Provisions

§ 516.1 Scope.

(a) This part implements section 573 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 360ccc–2) and contains the following subparts:

(1) Subpart A—General Provisions.

(2) Subpart B—Designation of a Minor Use or Minor Species New Animal Drug.

(3) Subpart C—[Reserved]

(4) Subpart D—[Reserved]

(b) References in this part to regulatory sections of the Code of Federal Regulations are to Chapter I of Title 21, unless otherwise noted.

§ 516.2 Purpose.

This part establishes standards and procedures for implementing section 573 of the act, including designation of minor use or minor species new animal drugs and associated exclusive marketing rights.

§ 516.3 Definitions.

(a) The definitions and interpretations contained in section 201 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 321) apply to those terms when used in this part.

(b) The following definitions of terms apply to all subparts of part 516:

Active moiety means the molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt (including a salt with hydrogen or coordination bonds), or other noncovalent derivative (such as a complex, chelate, or clathrate) of the molecule, responsible for the pharmacological action of the drug substance.

Functionally superior means that a drug has been shown to provide a significant therapeutic or physiologic advantage over that provided by a conditionally-approved or approved MUMS drug, that is otherwise the same drug, in one or more of the following ways:

(i) The drug has been shown to be more effective, as assessed by effect on a clinically meaningful endpoint in adequate and well-controlled clinical trials, than a conditionally approved or approved MUMS drug, that is otherwise the same drug. Generally, this would represent the same kind of evidence needed to support a comparative effectiveness claim for two different drugs; in most cases, direct comparative clinical trials will be necessary; or

(ii) The drug has been shown to be safer than a conditionally-approved or approved MUMS drug, that is otherwise the same drug, in a substantial portion of the target population, for example, by the elimination of an ingredient or contaminant that is associated with relatively frequent adverse effects. In some cases, direct comparative clinical trials will be necessary.

Infrequently, as used in the minor use definition, means a disease or condition that is uncommon or that occurs only sporadically on an annualized basis.

Limited geographical areas, as used in the minor use definition, means regions of the United States distinguished by physical, chemical, or biological factors that limit the distribution of a disease or condition.

Major species means cattle, horses, swine, chickens, turkeys, dogs, and cats.

Minor species means animals, other than humans, that are not major species.

Minor use means the intended use of a drug in a major species for an indication that occurs infrequently and in only a small number of animals or in limited geographical areas and in only a small number of animals annually.

MUMS drug means a new animal drug, as defined in section 201 of the act, intended for a minor use or for use in a minor species.

Same dosage form means the same as one of the dosage forms specified in the following parts of this chapter:

(i) Part 520: Oral dosage form new animal drugs (excluding use in animal feeds as specified in part 558 of this chapter).

(ii) Part 522: Implantation or injectable dosage form new animal drugs.

(iii) Part 524: Ophthalmic and topical dosage form new animal drugs.

(iv) Part 526: Intramammary dosage forms.

(v) Part 529: Certain other dosage form new animal drugs.

(vi) Part 558: New animal drugs for use in animal feeds.

Same drug means a MUMS drug for which designation, indexing, or conditional approval is sought that meets the following criteria:

(i) If it is a MUMS drug composed of small molecules and contains the same active moiety as a prior designated, conditionally-approved, or approved MUMS drug, even if the particular ester or salt (including a salt with hydrogen or coordination bonds) or other noncovalent derivative such as a complex, chelate or clathrate is not the same, it is considered the same drug; except that, if the prior MUMS drug is conditionally approved or approved and the second MUMS drug is shown to be functionally superior to the conditionally approved or approved MUMS drug for the same intended use, it is not considered the same drug.

(ii) If it is a MUMS drug composed of large molecules (macromolecules) and contains the same principal molecular structural features (but not necessarily all of the same structural features) as a prior designated, conditionally approved, or approved MUMS drug, it is considered the same drug; except that, if the prior MUMS drug is conditionally approved or approved and the second MUMS drug is shown to be functionally superior to the conditionally approved or approved MUMS drug for the same intended use, it is not considered the same drug. This criterion will be applied as follows to different kinds of macromolecules:

(A) Two protein drugs would be considered the same if the only differences in structure between them were due to post-translational events or infidelity of translation or transcription or were minor differences in amino acid sequence; other potentially important differences, such as different glycosylation patterns or different tertiary structures, would not cause the drugs to be considered different unless the subsequent drug is shown to be functionally superior.

(B) Two polysaccharide drugs would be considered the same if they had identical saccharide repeating units, even if the number of units were to vary and even if there were postpolymerization modifications, unless the subsequent drug is shown to be functionally superior.

(C) Two polynucleotide drugs consisting of two or more distinct nucleotides would be considered the same if they had an identical sequence of purine and pyrimidine bases (or their derivatives) bound to an identical sugar backbone (ribose, deoxyribose, or modifications of these sugars), unless

the subsequent drug is shown to be functionally superior.

(D) Closely related, complex partly definable drugs with similar pharmacologic intent would be considered the same unless the subsequent drug is shown to be functionally superior.

Same intended use means an intended use of a MUMS drug, for which designation, indexing, or conditional approval is sought, that is determined to be the same as (or not different from) a previously designated, conditionally approved, or approved intended use of a MUMS drug. Same intended use is established by comparing two intended uses and not by simply comparing the specific language by means of which the intent is established in labeling in accordance with the following criteria:

(i) Two intended uses are considered the same if one of the intended uses falls completely within the scope of the other.

(ii) For intended uses associated with diseases or conditions with multiple causative organisms, two intended uses are not considered the same when they involve different causative organisms or different subsets of causative organisms of that disease or condition when the causative organisms involved can reliably be shown to be clinically significant causes of the disease or condition.

(iii) Two intended uses of a drug are not considered the same if they involve different intended species or different definable subpopulations (including ''production classes'') of a species.

Sponsor means the person requesting designation for a MUMS drug who must be the real party in interest of the development and the intended or actual production and sales of such drug (in this context, the sponsor may be an individual, partnership, organization, or association). Sponsor also means the person responsible for an investigation of a new animal drug (in this context, the sponsor may be an individual, partnership, corporation, or Government agency or may be a manufacturer, scientific institution, or an investigator regularly and lawfully engaged in the investigation of new animal drugs). Sponsor also means the person submitting or receiving approval for a new animal drug application (in this context, the sponsor may be an individual, partnership, organization, or association). In all contexts, the sponsor is responsible for compliance with applicable provisions of the act and regulations.

Subpart B—Designation of a Minor Use or Minor Species New Animal Drug

§ 516.11 Scope of this subpart.

This subpart implements section 573 of the act. Specifically, this subpart sets forth the procedures and requirements for submissions to FDA of requests for designation of a new animal drug for a minor use or a minor species.

§ 516.12 Purpose.

This subpart establishes standards and procedures for determining eligibility for designation and the associated incentives and benefits described in section 573 of the act, including a 7-year period of exclusive marketing rights.

§ 516.13 Definitions.

The following definitions of terms apply only in the context of subpart B of this part:

Director means the Director of the Office of Minor Use and Minor Species Animal Drug Development of the FDA Center for Veterinary Medicine.

Intended use means the intended treatment, control or prevention of a disease or condition, or the intention to affect the structure or function of the body of animals within an identified species, subpopulation of a species, or collection of species.

MUMS-designated drug means a new animal drug, as defined in section 201 of the act, intended for a minor use or for use in a minor species that has been designated under section 573 of the act.

MUMS-drug exclusive marketing rights or *exclusive marketing rights* means that, effective on the date of FDA conditional approval or approval as stated in the approval letter of an application for a MUMS-designated drug, no conditional approval or approval will be given to a subsequent application for the same drug, in the same dosage form, for the same intended use for 7 years, except as otherwise provided by law or in this subpart.

§ 516.14 Submission of requests for designation.

All correspondence relating to a request for designation of a MUMS drug must be addressed to the Director of the Office of Minor Use and Minor Species Animal Drug Development. Submissions not including all elements specified in § 516.20 will be returned to the sponsor without review.

§ 516.16 Eligibility to request designation.

The person requesting designation must be the sponsor and the real party in interest of the development and the intended or actual production and sales of the drug or the permanent-resident U.S. agent for such a sponsor.

§ 516.20 Content and format of a request for MUMS-drug designation.

(a) A sponsor that submits a request for designation of a new animal drug intended for a minor use or minor species must submit each request in the form and containing the information required in paragraph (b) of this section. While a request for designation may involve multiple intended uses, each request for designation must constitute a separate submission. A sponsor may request MUMS-drug designation of a previously unapproved drug, or a new intended use or dosage form for an already conditionally approved or approved drug. Only one sponsor may receive MUMS-drug designation of the same drug, in the same dosage form, for the same intended use.

(b) A sponsor must submit two copies of a completed, dated, and signed request for designation that contains the following information:

(1) A request for designation of a new animal drug for a minor use or use in a minor species, which must be specific.

(2) The name and address of the sponsor; the name of the sponsor's primary contact person and/or permanent-resident U.S. agent including title, address, and telephone number; the generic and trade name, if any, of the drug; and the name and address of the source of the drug.

(3) A description of the proposed intended use for which the drug is being or will be investigated.

(4) A description of the drug and dosage form.

(5) A discussion of the scientific rationale for the intended use of the drug; specific reference, including date(s) of submission, to all data from nonclinical laboratory studies, clinical investigations, copies of pertinent unpublished and published papers, and other relevant data that are available to the sponsor, whether positive, negative, or inconclusive.

(6) A specific description of the product development plan for the drug, its dosage form, and its intended use.

(7) If the drug is intended for a minor use in a major species, documentation in accordance with § 516.21, with appended authoritative references, to demonstrate that such use is a minor use.

(8) A statement that the sponsor submitting the request is the real party in interest of the development and the intended or actual production and sales of the product.

(9) A statement that the sponsor acknowledges that, upon granting a

request for MUMS designation, FDA will make information regarding the designation publicly available as specified in § 516.28.

§ 516.21 Documentation of minor use status.

So that FDA can determine whether a drug qualifies for MUMS-drug designation as a minor use in a major species under section 573 of the act, the sponsor shall include in its request to FDA for MUMS-drug designation under § 516.20 documentation demonstrating that the use is limited to a small number of animals (annualized). This documentation must include the following information:

(a) The estimated total number of animals to which the drug could potentially be administered on an annual basis for the treatment, control, or prevention of the disease or condition for which the drug is being developed, including animals administered the drug as part of herd or flock treatment, together with a list of the sources (including dates of information provided and literature citations) for the estimate.

(b) The estimated total number of animals referred to in paragraph (a) of this section may be further reduced to only a subset of the estimated total number of animals if administration of the drug is only medically justified for this subset. To establish this, requestors must demonstrate that administration of the drug to animals subject to the disease or condition for which the drug is being developed other than the subset is not medically justified. The sponsor must also include a list of the sources (including dates of information provided and literature citations) for the justification that administration of the drug to animals other than the targeted subset is medically inappropriate.

(c) An estimate of the potential market associated with the total number of animals established in paragraph (a) of this section compared to an estimate of the development costs of the proposed drug, in the proposed dosage form, for the proposed intended use.

§ 516.22 Permanent-resident U.S. agent for foreign sponsor.

Every foreign sponsor that seeks MUMS-drug designation shall name a permanent resident of the United States as the sponsor's agent upon whom service of all processes, notices, orders, decisions, requirements, and other communications may be made on behalf of the sponsor. Notifications of changes in such agents or changes of address of agents should preferably be provided in advance, but not later than 60 days after the effective date of such changes. The permanent-resident U.S. agent may be an individual, firm, or domestic corporation and may represent any number of sponsors. The name and address of the permanent-resident U.S. agent shall be provided to the Director of the Office of Minor Use and Minor Species Animal Drug Development.

§ 516.23 Timing of requests for MUMS-drug designation.

A sponsor may request MUMS-drug designation at any time in the drug development process prior to the submission of an application for either conditional approval or approval of the MUMS drug for which designation is being requested.

§ 516.24 Granting MUMS-drug designation.

(a) FDA may grant the request for MUMS-drug designation if none of the reasons described in § 516.25 for refusal to grant such a request apply.

(b) When a request for MUMS-drug designation is granted, FDA will notify the sponsor in writing and will give public notice of the MUMS-drug designation in accordance with § 516.28.

§ 516.25 Refusal to grant MUMS-drug designation.

(a) FDA will refuse to grant a request for MUMS-drug designation if any of the following reasons apply:

(1) The drug is not intended for use in a minor species or FDA determines that there is insufficient evidence to demonstrate that the drug is intended for a minor use in a major species.

(2) The drug is the same drug in the same dosage form for the same intended use as one that already has a MUMS-drug designation but has not yet been conditionally approved or approved.

(3) The drug is the same drug in the same dosage form for the same intended use as one that is already conditionally approved or approved. A drug that FDA has found to be functionally superior is not considered the same drug as an already conditionally approved or approved drug even if it is otherwise the same drug in the same dosage form for the same intended use.

(4) The sponsor has failed to provide:

(i) A credible scientific rationale in support of the intended use,

(ii) Sufficient information about the product development plan for the drug, its dosage form, and its intended use to establish that adherence to the plan can lead to successful drug development in a timely manner, and

(iii) Any other information required under § 516.20.

(b) FDA may refuse to grant a request for MUMS-drug designation if the request for designation contains an untrue statement of material fact or omits material information.

§ 516.26 Amendment to MUMS-drug designation.

(a) At any time prior to conditional approval or approval of an application for a MUMS-designated drug, the sponsor may apply for an amendment to the designated intended use if the proposed change is due to new and unexpected findings in research on the drug, information arising from FDA recommendations, or other unforeseen developments.

(b) FDA will grant the amendment if it finds:

(1) That the initial designation request was made in good faith;

(2) That the amendment is intended to make the MUMS-drug designated intended use conform to the results of new and unexpected findings in research on the drug, information arising from FDA recommendations, or other unforeseen developments; and

(3) In the case of a minor use, that as of the date of the submission of the amendment request, the amendment would not result in the intended use of the drug no longer being considered a minor use.

§ 516.27 Change in sponsorship.

(a) A sponsor may transfer sponsorship of a MUMS-designated drug to another person. A change of sponsorship will also transfer the designation status of the drug which will remain in effect for the new sponsor subject to the same conditions applicable to the former sponsor provided that at the time of a potential transfer, the new and former sponsors submit the following information in writing and obtain permission from FDA:

(1) The former sponsor shall submit a letter to FDA that documents the transfer of sponsorship of the MUMS-designated drug. This letter shall specify the date of the transfer. The former sponsor shall also certify in writing to FDA that a complete copy of the request for MUMS-drug designation, including any amendments to the request, and correspondence relevant to the MUMS-drug designation, has been provided to the new sponsor.

(2) The new sponsor shall submit a letter or other document containing the following information:

(i) A statement accepting the MUMS-drug designated file or application;

(ii) The date that the change in sponsorship is intended to be effective;

(iii) A statement that the new sponsor has a complete copy of the request for

MUMS-drug designation, including any amendments to the request and any correspondence relevant to the MUMS-drug designation;

(iv) A statement that the new sponsor understands and accepts the responsibilities of a sponsor of a MUMS-designated drug established elsewhere in this subpart;

(v) The name and address of a new primary contact person or permanent resident U.S. agent; and

(vi) Evidence that the new sponsor is capable of actively pursuing approval with due diligence.

(b) No sponsor may relieve itself of responsibilities under the act or under this subpart by assigning rights to another person without:

(1) Assuring that the new sponsor will carry out such responsibilities; and

(2) Obtaining prior permission from FDA.

§ 516.28 Publication of MUMS-drug designations.

FDA will periodically update a publicly available list of MUMS-designated drugs. This list will be placed on file at the FDA Division of Dockets Management, and will contain the following information for each MUMS-designated drug:

(a) The name and address of the sponsor;

(b) The established name and trade name, if any, of the drug;

(c) The dosage form of the drug;

(d) The species and the proposed intended use for which MUMS-drug designation was granted; and

(e) The date designation was granted.

§ 516.29 Termination of MUMS-drug designation.

(a) The sponsor of a MUMS-designated drug must notify FDA of any decision to discontinue active pursuit of conditional approval or approval of such MUMS drug. FDA must terminate the designation upon such notification.

(b) A conditionally-approved or approved MUMS-designated drug sponsor must notify FDA at least 1 year before it intends to discontinue the manufacture of such MUMS drug. FDA must terminate designation upon such notification.

(c) MUMS designation shall terminate upon the expiration of any applicable period of exclusive marketing rights under this subpart.

(d) FDA may terminate designation if it independently determines that the sponsor is not actively pursuing conditional approval or approval with due diligence. At a minimum, due diligence must be demonstrated by:

(1) Submission of annual progress reports in a timely manner in accordance with § 516.30 that demonstrate that the sponsor is progressing in accordance with the drug development plan submitted to the agency under § 516.20 and

(2) Compliance with all applicable requirements of part 511 of this chapter.

(e) Designation of a conditionally approved or approved MUMS-designated drug and the associated exclusive marketing rights may be terminated if the sponsor is unable to provide sufficient quantities of the drug to meet the needs for which it is designated.

(f) FDA may also terminate MUMS-drug designation for any drug if the agency finds that:

(1) The request for designation contained an untrue statement of material fact; or

(2) The request for designation omitted material information required by this subpart; or

(3) FDA subsequently finds that the drug in fact had not been eligible for MUMS-drug designation at the time of submission of the request;

(4) The same drug, in the same dosage form, for the same intended use becomes conditionally approved or approved for another sponsor; or

(5) FDA withdraws the conditional approval or approval of the application for the new animal drug.

(g) For a conditionally approved or approved drug, termination of MUMS-drug designation also terminates the sponsor's exclusive marketing rights for the drug but does not withdraw the conditional approval or approval of the drug's application.

(h) Where a drug has been MUMS-designated for a minor use in a major species, its designation will not be terminated on the grounds that the number of animals to which the drug could potentially be administered on an annual basis for the treatment, control, or prevention of the disease or condition for which the drug is being developed, including animals administered the drug as part of herd or flock treatment, subsequently increases.

(i) When a MUMS-drug designation is terminated, FDA will notify the sponsor in writing and will give public notice of the termination of the MUMS-drug designation.

§ 516.30 Annual reports for a MUMS-designated drug.

Within 14 months after the date on which a MUMS drug is granted designation and annually thereafter until approval, the sponsor of a MUMS-designated drug shall submit a brief progress report on the drug to the investigational new animal drug file addressed to the Director of the Office of Minor Use and Minor Species Animal Drug Development that includes the following information:

(a) A short account of the progress of drug development including a description of studies initiated, ongoing, and completed, and a short summary of the status or results of such studies;

(b) A description of the investigational plan for the coming year, as well as any anticipated difficulties in development, testing, and marketing; and

(c) A brief discussion of any changes that may affect the MUMS-designated drug status of the product. For example, situations in which testing data demonstrate that the proposed intended use is inappropriate due to unexpected issues of safety or effectiveness.

§ 516.31 Scope of MUMS-drug exclusive marketing rights.

(a) After conditional approval or approval of an application for a MUMS-designated drug in the dosage form and for the intended use for which MUMS-drug designation has been granted, FDA will not conditionally approve or approve another application or abbreviated application for the same drug in the same dosage form for the same intended use before the expiration of 7 years after the date of conditional approval or approval as stated in the approval letter from FDA, except that such an application can be conditionally approved or approved sooner if, and at such time as, any of the following occurs:

(1) FDA terminates the MUMS-drug designation and associated exclusive marketing rights under § 516.29; or

(2) FDA withdraws the conditional approval or approval of the application for the drug for any reason; or

(3) The sponsor with exclusive marketing rights provides written consent to FDA to conditionally approve or approve another application before the expiration of 7 years; or

(4) The sponsor fails to assure a sufficient quantity of the drug in accordance with section 573 of the act and § 516.36.

(b) If an application for a MUMS drug cannot be approved until the expiration of the period of exclusive marketing of a MUMS-designated drug, FDA will so notify the sponsor in writing.

§ 516.34 FDA recognition of exclusive marketing rights.

(a) FDA will send the sponsor (or the permanent-resident U.S. agent, if applicable) timely written notice recognizing exclusive marketing rights when an application for a MUMS-

designated drug has been conditionally approved or approved. The written notice will inform the sponsor of the requirements for maintaining MUMS-designated drug exclusive marketing rights for the full 7-year term. This notice will generally be contained in the letter conditionally approving or approving the application.

(b) When an application is conditionally approved or approved for a MUMS-designated drug that qualifies for exclusive marketing rights, FDA will publish this information in the **Federal Register** at the time of the conditional approval or approval. This notice will generally be contained in the notice of conditional approval or approval of the application.

§ 516.36 Insufficient quantities of MUMS-designated drugs.

(a) Under section 573 of the act, whenever FDA has reason to believe that sufficient quantities of a conditionally-approved or approved, MUMS-designated drug to meet the needs for which the drug was designated cannot be assured by the sponsor, FDA will so notify the sponsor of this possible insufficiency and will offer the sponsor the following options, one of which must be exercised by a time that FDA specifies:

(1) Provide FDA information and data regarding how the sponsor can assure the availability of sufficient quantities of the MUMS-designated drug within a reasonable time to meet the needs for which the drug was designated; or

(2) Provide FDA in writing the sponsor's consent for the conditional approval or approval of other applications for the same drug before the expiration of the 7-year period of exclusive marketing rights.

(b) If, within the time that FDA specifies, the sponsor fails to consent to the conditional approval or approval of other applications and if FDA finds that the sponsor has not shown that it can assure the availability of sufficient quantities of the MUMS-designated drug to meet the needs for which the drug was designated, FDA will issue a written order terminating designation of the MUMS drug and the associated exclusive marketing rights. This order will state FDA's findings and conclusions and will constitute final agency action. An order terminating designation and associated exclusive marketing rights may issue whether or not there are other sponsors that can assure the availability of alternative sources of supply. Such an order will not withdraw the conditional approval or approval of an application. Once terminated under this section, neither designation, nor exclusive marketing rights may be reinstated.

§ 516.52 Availability for public disclosure of data and information in requests.

(a) FDA will not publicly disclose the existence of a request for MUMS-drug designation under section 573 of the act prior to final FDA action on the request unless the existence of the request has been previously publicly disclosed or acknowledged.

(b) Whether or not the existence of a pending request for designation has been publicly disclosed or acknowledged, no data or information in the request are available for public disclosure prior to final FDA action on the request.

(c) Except as provided in paragraph (d) of this section, upon final FDA action on a request for designation, the public availability of data and information in the request will be determined in accordance with part 20 of this chapter and other applicable statutes and regulations.

(d) In accordance with § 516.28, FDA will make a cumulative list of all MUMS-drug designations available to the public and update such list periodically. In accordance with § 516.29, FDA will give public notice of the termination of all MUMS-drug designations.

Subpart C—[Reserved]

Subpart D—[Reserved]

Dated: March 12, 2007.

Jeffrey Shuren,

Assistant Commissioner for Policy.

Editorial Note: This document was received at the Office of the Federal Register on July 23, 2007.

[FR Doc. E7–14444 Filed 7–25–07; 8:45 am]

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DEPARTMENT OF THE TREASURY

Internal Revenue Service

26 CFR Part 301

[TD 9333]

RIN 1545–BG64

Application of Section 6404(g) of the Internal Revenue Code Suspension Provisions; Correction

AGENCY: Internal Revenue Service (IRS), Treasury.

ACTION: Correction to temporary regulations.

SUMMARY: This document contains corrections to temporary regulations (TD 9333) that were published in the **Federal Register** on Thursday, June 21, 2007 (72 FR 34176) on the suspension of any interest, penalty, addition to tax, or additional amount with respect to listed transactions or undisclosed reportable transactions. The temporary regulations provide guidance to individual taxpayers who have participated in listed transactions or undisclosed reportable transactions.

DATES: The correction is effective July 26, 2007.

FOR FURTHER INFORMATION CONTACT: Stuart Spielman, (202) 622–7950 (not a toll-free number).

SUPPLEMENTARY INFORMATION:

Background

The temporary regulations that are the subject of this correction are under section 6404(g) of the Internal Revenue Code.

Need for Correction

As published, temporary regulations (TD 9333) contain errors that may prove to be misleading and are in need of clarification.

Correction of Publication

Accordingly, the publication of the temporary regulations (TD 9333), which was the subject of FR Doc. E7–12081, is corrected as follows:

1. On page 34176, column 2, in the preamble, under the caption ''**SUMMARY:**'', lines 13 and 14, the language ''Opportunity Zone Act of 2005, and the Tax Relief and Health Care Act of 2006.'' is corrected to read ''Opportunity Zone Act of 2005, the Tax Relief and Health Care Act of 2006, and the Small Business and Work Opportunity Tax Act of 2007.''.

2. On page 34176, column 3, in the preamble, under the paragraph heading ''Background'', line 8 from the bottom of the paragraph, the language ''Public Law 110–28 (121 Stat. 112, 200),'' is corrected to read ''Public Law 110–28 (121 Stat. 190, 200),''.

LaNita Van Dyke,

Chief, Publications and Regulations Branch, Legal Processing Division, Associate Chief Counsel (Procedure and Administration).

[FR Doc. E7–14398 Filed 7–25–07; 8:45 am]

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