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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 10, 20, 25, 500, and 510

[Docket No. FDA-2001-N-0075 (formerly Docket No. 2001N-0284)]

RIN 0910-AF78

Import Tolerances for Residues of Unapproved New Animal Drugs in Food

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA, the Agency, we) is issuing a final rule that establishes procedures by which we may establish, amend, or revoke tolerances for residues of new animal drugs in any edible portion of any animal imported into the United States (import tolerances). These import tolerances provide a basis for the legal marketing of such animal-derived food.

DATES: This rule is effective [INSERT DATE 120 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]. Submit written comments (including recommendations) on information collection issues under the Paperwork Reduction Act of 1995 (PRA) by [INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*] (see section IX, the "Paperwork Reduction Act of 1995" section of this document).

ADDRESSES: To ensure that comments on the information collection are received, the Office of Management and Budget (OMB) recommends that written comments be submitted to https://www.reginfo.gov/public/do/PRAMain. Find this particular information collection by selecting "Currently under Review--Open for Public Comments" or by using the search function. All comments should be identified with the OMB control number 0910-NEW. Also include the FDA docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT: *With regard to the final rule*: Charli Long-Medrano, Center for Veterinary Medicine (HFV-150), Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855, 240-402-0850, charli.long-medrano@fda.hhs.gov.

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I. Executive Summary

A. Purpose of the Final Rule

This rule codifies procedures and food safety criteria by which tolerances for residues of unapproved new animal drugs in any edible portion of any animal imported into the United States (import tolerances) may be established or amended. These import tolerances provide a basis for the legal marketing of such animal-derived food. The regulation also specifies procedures by which import tolerances may be revoked.

B. Summary of the Major Provisions of the Final Rule

This final rule codifies procedures and food safety criteria pertaining to the establishment, amendment, and revocation of import tolerances in new subpart C of part 510 of the Code of Federal Regulations (21 CFR part 510). Major provisions include:

- the scope and definitions;
- who may initiate proceedings to establish an import tolerance;
- contents of a submission requesting establishment of an import tolerance;
- sources of data and information supporting the safety of a proposed import tolerance;
- Agency procedures for establishment, amendment, or revocation of an import tolerance;
- public disclosure of import tolerance-related actions (actions under consideration, establishment, amendment, or revocation); and
- environmental impact assessment of import tolerance-related actions.

In addition, conforming amendments are being made in §§ 10.25, 20.100, 25.20, 500.80, 500.82, 500.88, and 500.92 (21 CFR 10.25, 20.100, 25.20, 500.80, 500.82, 500.88, and 500.92). A technical amendment is being made in § 10.25 (21 CFR 10.25) to include food additive petitions under 21 CFR 571.1 in the non-exhaustive list of petitions specified in FDA regulations.

The procedures and food safety criteria in the final rule are fundamentally the same as in the proposed rule; however, the final rule has been minimally reorganized to clarify that import tolerances established at the Commissioner's initiative follow the same procedures as those established at the request of an interested person. We have also made nonsubstantive wording changes for clarity.

C. Legal Authority

Our authority for issuing this final rule is provided by the new animal drug provisions of the Federal Food, Drug, and Cosmetic Act (FD&C Act) by which we establish tolerances for residues of new animal drugs and under provisions of the FD&C Act that give the Agency general rulemaking authority to issue regulations for the efficient enforcement of the FD&C Act.

D. Costs and Benefits

1. Costs of the Final Rule

All entities affected by this final rule will incur the one-time cost for reading and understanding this rule. Based on the small number of firms that we estimate could request an import tolerance per year, only about five firms would need to read and understand this rule over the next 10 years. The total costs for reading and understanding the rule range from around $530 to around $660. Table 1 includes a summary of these costs.

Table 1--One-time Costs for Reading and Understanding the Rule (2020 dollars)

	Low	Medium	High
Reading time (hours)	0.75	0.85	1
Wage ($ per hour)	$140.30	$140.30	$140.30
Affected entities	5	5	5
No. of people reading per entity	1	1	1
Total cost	$530	$585	$660

2. Benefits of the Final Rule

The procedures codified herein clarify the import tolerance submission process for the establishment, amendment, and revocation of these tolerances. This should result in improving the efficiency of the program for both industry and government. However, we lack data to quantify these efficiency gains.

II. Table of Abbreviations/Commonly Used Acronyms in This Document

Abbreviation	What it Means
ADAA	Animal Drug Availability Act of 1996
ADI	Acceptable Daily Intake
CFR	Code of Federal Regulations
CNADA	Application for Conditional Approval of a New Animal Drug
Codex MRL	MRL established by the Codex Alimentarius Committee
CVM	Center for Veterinary Medicine
FAO	Food and Agriculture Organization of the United Nations
FDA	U.S. Food and Drug Administration
FD&C Act	Federal Food, Drug, and Cosmetic Act
GMP	Good Manufacturing Process
GFI	Guidance for Industry
JECFA	Joint FAO/WHO Expert Committee on Food Additives
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
MRL	Maximum Residue Limit
NADA	New Animal Drug Application
US	United States
VICH	International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products
WHO	World Health Organization of the United Nations

III. Background

A. History and Scope of This Rulemaking

In 1996, the President signed into law the Animal Drug Availability Act of 1996 (ADAA) (Pub. L. 104-250), which amended the FD&C Act (21 U.S.C. 360b(a)) to authorize the establishment of import tolerances that would provide a basis for the legal marketing of imported animal-derived food containing residues of new animal drugs neither approved nor conditionally approved in the United States (unapproved new animal drugs).

Without an import tolerance, any amount of residue of an unapproved new animal drug in imported, animal-derived food would cause that food to be adulterated under section 402(a)(2)(C)(ii) of the FD&C Act (21 U.S.C. 342(a)(2)(C)(ii)) because the drug would be deemed unsafe under section 512 of the FD&C Act (21 U.S.C. 360b). Such food could be denied entry into the United States under section 801(a)(3) of the FD&C Act (21 U.S.C. 381(a)(3)). It remains unlawful to import animal-derived food containing a residue of an unapproved new animal drug, unless an import tolerance has been established for such drug and any residue of the new animal drug in the imported animal-derived food does not exceed that

import tolerance. These regulations establish procedures under which the Agency will establish, amend, or revoke import tolerances for residues of unapproved new animal drugs.

The ADAA also specified that in establishing import tolerances, FDA must rely on data sufficient to demonstrate that a proposed tolerance is safe based on similar food safety criteria used to establish a tolerance under a new animal drug application (NADA). For establishment of import tolerances, food safety data can be submitted by the drug manufacturer or be available from a relevant international organization such as the Codex Alimentarius Commission, provided such data are not inconsistent with criteria used to establish a tolerance for new animal drugs in NADAs.

The regulations make it clear that the Commissioner may start a review process to establish, amend, or revoke an import tolerance on his or her own initiative under § 10.25(b). These regulations also establish when import tolerance-related actions (actions resulting in establishment, amendment, or revocation) and their basis will be publicly disclosed.

B. General Overview of the Final Rule

In issuing this rule, the Agency finalizes the provisions in the January 2012 proposed rule (77 FR 3653, January 25, 2012). This final rule reflects revisions the Agency made after considering all comments received.

This final rule amends part 510 by adding sections to establish the scope of new subpart C (§ 510.201 (21 CFR 510.201)); to define certain relevant terms (§ 510.202 (21 CFR 510.202)); to establish who may initiate proceedings to establish or amend an import tolerance (§ 510.203 (21 CFR 510.203)); to describe the content, options for submission, and administration of a request to establish or amend an import tolerance (§ 510.205 (21 CFR 510.205)); and to describe the review of information to establish or amend an import tolerance (§ 510.206 (21 CFR 510.206)). Provisions describing when and how information relating to import tolerances will be publicly disclosed, previously in proposed § 510.205, are now described and organized in redesignated § 510.207 (21 CFR 510.207). Procedures that FDA

follows in establishment, denial of a request for establishment, and amendment of an import tolerance are described in redesignated § 510.209 (21 CFR 510.209). Procedures for revocation of an import tolerance are described in redesignated § 510.210 (21 CFR 510.210). Procedures for requesting reconsideration or administrative stay of a decision to establish, amend, or revoke an import tolerance are specified in redesignated §§ 510.212 and 510.213 (21 CFR 510.212 and 510.213), respectively.

IV. Legal Authority

We are issuing these regulations under the legal authority provided by section 512(a)(6) of the FD&C Act (21 U.S.C. 360b(a)(6)) relating to the establishment of import tolerances for unapproved new animal drugs and under section 701(a) of the FD&C Act (21 U.S.C. 371(a)), which gives FDA general rulemaking authority to issue regulations for the efficient enforcement of the FD&C Act.

V. Comments on the Proposed Rule and FDA Response

We received 17 comments on the proposed import tolerance rule by the close of the comment period, each commenting on one or more aspects of the proposed rule. We received comments from a wide array of members of the public, including trade organizations, academia, public advocacy groups, consumers, and government agencies. The comments addressed numerous provisions of the proposed rule, including our specific requests for comments set forth in the proposed rule. Some comments addressed issues that are outside of the scope of this rule. Because such comments were beyond the scope of this rule, we do not include a discussion of them here.

A. General Comments on the Proposed Rule and FDA Response

(Comment 1) Several comments expressed concern that establishment of import tolerances for unapproved new animal drugs is unfair to domestic producers who cannot legally use these drugs, thereby putting them at a competitive disadvantage.

(Response 1) The ADAA amended the FD&C Act to permit FDA to establish a tolerance for residues of a new animal drug in any edible portion of any animal imported into the United States when the intended use of the new animal drug is not approved for use in the United States. The legislative history notes there may be appropriate instances (e.g., the disease treated does not exist in the United States) in which food-producing animals in other countries are treated with animal drugs that are not approved in the United States. Thus, Congress enacted this provision to provide a legal means by which food that may contain residues of these drugs may be imported into the United States. Under the FD&C Act, lawful use of the same animal drug in the United States requires that the new animal drug be approved or conditionally approved by FDA. This requires additional information and data from the sponsor to establish, among other things, that the drug is effective for its intended use and safe for the animals receiving the drug.

(Comment 2) One comment states that establishing import tolerances would result in an increase in the volume of contaminated seafood into the United States.

(Response 2) FDA notes that one consequence of establishing an import tolerance may be an increase in imported edible tissues from food-producing animals treated with the drug that is the subject of an import tolerance. However, these imported tissues will not be permitted entry if they contain residues above the import tolerance, the maximum concentration of residues of the new animal drug in the edible tissues that is determined to be safe for human consumers.

(Comment 3) A few comments express concern that import tolerances risk exposing U.S. consumers to unsafe tissue residues.

(Response 3) Section 512(a)(6) of the FD&C Act requires that the Agency rely on human food safety criteria similar to those used to establish tolerances for approved new animal drugs when establishing import tolerances. The human food safety criteria and review processes resulting in establishment of tolerances for domestically approved new animal drugs and for import tolerances for unapproved new animal drugs are fundamentally the same. Whether the Agency is establishing an import tolerance or a tolerance in the course of approving or

conditionally approving a new animal drug, we require data and information to demonstrate that the residues of the new animal drug in the edible products of treated animals are safe for human consumers. Imported tissues will not be allowed entry into the United States if they contain residues above the import tolerance.

(Comment 4) One comment states that the rule should include a requirement that the country in which the unapproved new animal drug is legally used have an equivalent animal drug regulatory program. In addition, a few comments recommend requiring that the requester submit: a record of the foreign country's approval actions and the approved uses of the new animal drug in other countries; information on alternative treatments or competing new animal drugs and an explanation of why the use of an unapproved new animal drug is necessary in light of alternatives; and an affidavit that there are no FDA-approved new animal drugs to treat the disease or condition for which the unapproved new animal drug is indicated. The comments also recommend that the requester be required to comply with the requirement to report adverse drug events and that food containing such new animal drug residues originate from a country that has approved the drug and is actively monitoring its use.

(Response 4) We disagree. Under the FD&C Act, to establish an import tolerance, FDA only must consider information related to the human food safety of the unapproved new animal drug that is the subject of the import tolerance. The data sufficient to demonstrate that residues of the unapproved new animal drug that is the subject of a proposed import tolerance are safe is based on similar food safety criteria used to establish tolerances for new animal drugs approved in the United States. That is, the human food safety standard for domestically approved new animal drugs and new animal drugs for which an import tolerance is established is the same: reasonable certainty of no harm. The data that may be considered include data submitted to appropriate regulatory authorities in any country where the new animal drug is lawfully used and data available from an appropriate international organization, to the extent such data are not

inconsistent with the criteria used to establish a tolerance for applications for new animal drugs in the United States.

The FD&C Act does not require the Agency to consider the use of the drug in other countries (including the disease(s) for which the unapproved new animal drug is indicated and whether there are approved drugs or alternative treatments available), or that the country(ies) where the drug is approved have an equivalent regulatory program (e.g., any post-approval monitoring). In addition, the FD&C Act does not impose adverse drug event reporting requirements for the establishment of import tolerances. Once an import tolerance is established, imported animal-derived food that contains residues of the unapproved new animal drug may enter the United States if those residues are below the import tolerance. There is no requirement that the imported food originate from a country that has approved the drug.

(Comment 5) Two comments state that U.S. consumers should be informed at the point of sale or through product labeling that imported edible tissues from food-producing animals may contain residues of new animal drugs that are not approved for use in the United States.

(Response 5) FDA does not agree that such public disclosure is needed to address the safety of residues from drugs for which import tolerances are established. The purpose of the legislation was to ensure that any edible portion of any animal imported into the United States is safe so long as such residues are below the established import tolerance.

(Comment 6) One comment states that establishing import tolerances undermines the new animal drug approval process. The commenter further states that FDA's estimate that an import tolerance review will require 100 hours of a mid-level FDA employee's time is evidence that the import tolerance review will be less stringent.

(Response 6) We disagree that establishment of import tolerances undermines the new animal drug approval process. Congress recognized that there may be appropriate instances in which food-producing animals in other countries are treated with animal drugs that are not approved in the United States. For example, the disease being treated does not exist in the

United States, or the particular animal industry either may not exist in the United States or is very small, resulting in a limited or nonexistent market for the drug in the United States. Nor do we agree that our estimate that an import tolerance review will generally require 100 hours of a mid-level FDA employee's time is evidence that import tolerance review is less stringent than review of proposed tolerances as part of a new animal drug application. The human food safety standard for domestically approved drugs and drugs for which an import tolerance is established is the same: reasonable certainty of no harm. Whether a person is requesting that the Agency establish an import tolerance or approve an NADA, the requester or sponsor, respectively, is required to furnish FDA with evidence demonstrating that the residues of the new animal drug in the edible products of treated animals are safe for human consumption. In our experience, it requires about 100 hours of a mid-level FDA employee's time to review this evidence, whether submitted under a new animal drug application or a request to establish an import tolerance.

(Comment 7) One comment states that tolerances should only be considered for an unapproved animal drug that is used solely for therapeutic purposes, asserting that the ADAA was intended to establish import tolerances for situations where a drug is used for treating diseases and conditions that do not occur in the United States.

(Response 7) We disagree. The plain language of the statute does not limit the establishment of import tolerances to new animal drugs intended to be used solely for therapeutic purposes. Generally, the reason an animal drug developer does not seek approval of the new animal drug in the United States (with attendant tolerances) is because the particular animal-rearing industry may not exist in the United States at a scale to justify the expense of seeking FDA approval. In some cases, the new animal drug may be used for non-therapeutic purposes.

B. Comments on Information to Support Establishment of an Import Tolerance and FDA Response

(Comment 8) One comment notes that the phrase "some assurance that the drugs are manufactured under GMP conditions," a comment provided by a Veterinary Medicine Advisory

Committee during a public meeting held on this topic in January 2002, and discussed in the preamble to the proposed rule, seems to go beyond the scope of what is necessary to ensure public safety and should be interpreted with broad flexibility.

(Response 8) We agree. As noted previously, section 512(a)(6) of the FD&C Act provides that FDA shall rely on data sufficient to demonstrate that a proposed tolerance is safe based on similar food safety criteria used to establish tolerances for NADAs filed under section 512(b)(1) of the FD&C Act. Section 512(a)(6) of the FD&C Act does not require the Agency to consider other requirements, such as an assurance of good manufacturing processes (GMPs), applicable to the new animal drug approval process in determining whether the Agency should grant a request to establish an import tolerance.

(Comment 9) Two comments assert that conditions of use of unapproved animal drugs do not need to be considered in establishing import tolerances so long as residues in imported tissues are below the import tolerance.

(Response 9) We disagree. Information about the conditions of use of the new animal drug must be considered when deciding to establish or amend an import tolerance so that the relevance of the submitted human food safety data, particularly tissue residues that may result from the lawful dosing regimen, can be determined. The tissue residue concentration is affected by the dosing regimen, i.e., the dose level and duration for which the animal is treated. Knowing that the new animal drug tissue concentrations reported in the human food safety studies are the result of animals dosed under the same conditions of use as described in the request provides FDA with assurance that the residue data are an appropriate basis to make decisions regarding whether to establish or amend an import tolerance.

(Comment 10) One comment expressed concern that proposed § 510.205, now § 510.205(e)(5), which provides that a request for an import tolerance may include other human food safety information as deemed necessary by the Commissioner, is too broad, and that the

possibility of ad hoc requirements may serve to curtail the initiation of requests or frustrate the efforts of those who do submit import tolerance requests.

(Response 10) The Agency does not intend to use this provision to require more human food safety information than is necessary to assess whether residues of unapproved new animal drugs in edible tissues of treated animals are safe for human consumption. The Agency will use similar criteria as for the approval of NADAs in making its determinations, including any other information the Commissioner deems necessary to assure safe and effective use. See section 512(d)(1)(D) of the FD&C Act. Similarly, the Agency must ensure that a request for a particular import tolerance includes all the relevant information needed to make an appropriate human food safety determination. For example, the requester may not have submitted enough information for FDA to adequately assess the toxicity of the new animal drug or the requester may not have provided enough detail about the proposed analytical method. The information requested will not be ad hoc because it must be relevant to the criteria and review standards for human food safety, which are the same for approval of new animal drugs and establishment of import tolerances.

(Comment 11) One comment asks whether the Agency employs analysts to verify the accuracy of translations of materials submitted in a foreign language.

(Response 11) The Agency will rely on the requester's assertion that it is submitting a complete and accurate translation of any materials submitted in a foreign language. As provided for in 18 U.S.C. 1001, any person, in any matter within the jurisdiction of the Agency, who knowingly and willfully falsifies, conceals, or covers up by any trick, scheme, or device a material fact; makes any materially false, fictitious, or fraudulent statement or representation; or makes or uses any false writing or document knowing the same to contain any materially false, fictitious, or fraudulent statement or entry, may be subject to criminal fines or imprisonment.

(Comment 12) One comment requests that electronic submission of import tolerance request dossiers be an option. There should be no need for paper submissions.

(Response 12) We agree that electronic submission of import tolerance requests should be an option and are providing for electronic submission of requests in § 510.105(b) of this final rule. At present, the Center for Veterinary Medicine (CVM) Office of New Animal Drug Evaluation (ONADE) can receive and process electronic submissions for import tolerance files. Submissions to CVM can be made after first registering with FDA's Electronic Submissions Gateway (ESG) and CVM's Electronic Submission System. Additional information and a user guide on eSubmitter can be obtained at either the "CVM eSubmitter Resource Center" website or the "Getting Started with eSubmitter" website. Contact ESGHelpDEsk@fda.hhs.gov for help with the ESG or cvmesubmitter@fda.hhs.gov for help using CVM's eSubmitter tool.

(Comment 13) Several comments question how FDA will evaluate an established acceptable daily intake (ADI), especially considering different food consumption patterns of different countries. Comments also question whether FDA considers subpopulations, such as children and immune-compromised people who may be particularly sensitive to the effects of exposure to drug residues. Comments express concerns that safety standards are being loosened and unsafe residues will be allowed in foods.

(Response 13) The ADI established for residues of an unapproved new animal drug in edible tissues of food-producing animals that is used in evaluating an import tolerance request is based on the same toxicity data and information as is used to establish an ADI for a domestically approved new animal drug and is evaluated using the same standards and methodology that is used for a domestic drug approval. The toxicity data that FDA uses to determine the ADI are described in guidances available on our website (https://www.fda.gov/animal-veterinary/guidance-industry/human-food-safety-guidances). The guidances for toxicology studies are documents that are internationally harmonized through the International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH) Expert Working Groups. The ADI, expressed in a micrograms or milligrams of the new animal drug per kilogram of body weight per day (µg/kg bw/day or mg/kg bw/day), is the

amount of drug residue that can be consumed on a daily basis for up to a lifetime without adverse effects or harm to the health of a consumer.

The ADI is meant to be applied to a general population, including sensitive subpopulations. The ADI determination uses conservative procedures to ensure that the final value is protective of a general population, such as application of a safety factor to account for human variability in sensitivity to the toxicity of the new animal drug, and tests for specific subpopulations if needed (asthmatic persons, allergic persons, etc.). Additionally, the application of the ADI to safe concentrations of the drug residues in edible tissues uses a lower average human body weight (60 kg) and conservative estimates of food consumption, such as a high milk consumption factor of 1.5 liter per day. Therefore, the Agency believes using the same methodology to calculate ADI for import tolerances as U.S.-approved animal drugs is appropriate.

(Comment 14) One comment states that the rule should explicitly prohibit the setting of import tolerances for residues of new animal drugs that induce cancer when ingested by humans or animals.

(Response 14) We disagree that the rule should explicitly prohibit the Agency from considering new animal drugs of carcinogenic concern (new animal drugs that induce cancer when ingested by people or animals). Section 512(a)(6) of the FD&C Act provides FDA the authority to consider requests to establish import tolerances using food safety criteria similar to those that are applied to the approval of new animal drugs. Under section 512(d)(1)(I) of the FD&C Act, the Agency may approve NADAs for drugs of carcinogenic concern as long as the compound does not adversely affect the animals and no residue of a carcinogenic compound will be found in food produced from those animals. Pursuant to section 512(a)(6) of the FD&C Act, FDA will consider requests for import tolerances for animal drugs of carcinogenic concern using similar food safety criteria as it would for a new animal drug application for approval. Thus, if FDA determines that a new animal drug for which an import tolerance request has been

submitted is a new animal drug of carcinogenic concern, the requester will be directed to comply with the "no residue" requirements of §§ 500.80 through 500.92 (21 CFR part 500, subpart E, Regulation of Carcinogenic Compounds Used in Food-Producing Animals). Any regulatory method for ascertaining the marker residue in the target tissue will be made publicly available pursuant to § 510.207(b) of the final rule. We have revised §§ 510.205(e) and 510.207(b) of the final rule and made conforming changes to §§ 500.80, 500.82, 500.88, and 500.92 to clarify the process for evaluating a new animal drug of carcinogenic concern under these circumstances.

(Comment 15) One comment states that the rule should specifically prohibit the setting of import tolerances for antimicrobial animal drugs that are in the same classes as drugs used in human medicine.

(Response 15) We disagree. Rather than declining to establish import tolerances for residues of antimicrobial new animal drugs that are in the same classes as drugs used in human medicine, we intend to apply the same human food safety standard (reasonable certainty of no harm) as we apply to all new animal drugs, including antimicrobial new animal drugs, seeking approval under an NADA or application for conditional approval of a new animal drug (CNADA). For requests for import tolerances for antimicrobials, FDA evaluates the impacts on human health, including the potential transmission of antimicrobial resistant bacteria of human health concern through the consumption of animal-derived food products. To assess these impacts, FDA recommends conducting the qualitative risk assessment described in Guidance for Industry (GFI) #152 entitled "Evaluating the Safety of Antimicrobial New Animal Drugs with Regard to Their Microbiological Effects on Bacteria of Human Health Concern," October 23, 2003.[1] In addition, we recommend that requesters address the step-wise approach outlined in GFI #159 (VICH GL36), "Studies to Evaluate the Safety of Residues of Veterinary Drugs in

[1] Available at: https://www.fda.gov/media/69949/download.

Human Food: General Approach to Establish a Microbiological ADI," March 5, 2013,[2] to assure the Agency that any impacts of antimicrobial new animal drug residues on the intestinal flora of human consumers are minimal. By addressing these important human food safety endpoints for antimicrobial new animal drugs, requesters will be able to assure the Agency that the imported animal-derived food products are safe for human consumption.

(Comment 16) A comment stated that the rule should specifically prohibit the setting of import tolerances for veterinary drugs that have extralabel use restrictions in the United States or that are banned from use in domestic livestock enterprises (including aquaculture).

(Response 16) As noted previously, whether a person is requesting the Agency establish an import tolerance or approve an NADA, the requester or sponsor, respectively, is required to furnish FDA with evidence demonstrating that the residues of the new animal drug in the edible products of treated animals are safe for human consumption. If the requester can satisfy the human food safety requirements, the Agency may establish an import tolerance for a food-producing species for which there is no extralabel use restriction, even if an extralabel use prohibition exists for other food-producing species.

(Comment 17) One comment requests that the requirement that the unapproved animal drug be registered (lawfully used) in another country should be revised to allow a request for an import tolerance to simultaneously progress with registration of the drug in foreign countries.

(Response 17) The statute gives us discretion to "consider and rely on data submitted by the drug manufacturer, including data submitted to appropriate regulatory authorities in any country where the new animal drug is lawfully used." As we noted in the preamble to the proposed rule, the Agency has interpreted this statutory language to mean that we may establish an import tolerance for a new animal drug that is not approved or conditionally approved in the

[2] Available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/cvm-gfi-159-vich-gl36-studies-evaluate-safety-residues-veterinary-drugs-human-food-general-approach.

United States but that is lawfully used in another country. Thus, foreign lawful use in at least one country must occur before a request to establish an import tolerance is submitted to the Agency.

(Comment 18) One comment requests that FDA revise the evidentiary standard for revocation of an import tolerance to be "evidence to show a reasonable basis from which serious questions may be inferred about the ultimate safety of the unapproved new animal drug residue and any substance that may be formed as a result of the unapproved new animal drug's use." The comment raises the concern that the proposed rule appears to require consumers to bring conclusive evidence to obtain a review of the import tolerance.

(Response 18) We disagree. The standard for revoking an import tolerance is provided for in section 512(a)(6) of the FD&C Act, which states that the Agency may revoke an import tolerance "if information demonstrates that the use of the new animal drug under actual use conditions results in food being imported into the United States with residues exceeding the tolerance or if scientific evidence shows the tolerance to be unsafe." The final rule reflects this standard in § 510.210(a). An import tolerance can be revoked upon petition or by the initiative of the Commissioner.

C. Comments on Environmental Review and FDA Response

(Comment 19) In the preamble to the proposed rule, the Agency requested comments and supporting information relevant to the issue of whether import tolerances will have a significant effect on the environment in the United States or abroad. FDA received two comments indicating that available information shows that FDA's establishment of import tolerances should present no appreciable risk to the environment from either the consumption or disposal of edible tissues containing residues of animal drugs. Two comments support creation by FDA of a categorical exclusion from the requirement to prepare an environmental assessment (EA) for an import tolerance request. For example, one comment presents evidence why risks to the environment should not be significant, showing calculations and summarizing information

indicating that residues in certain media (e.g., wastewater, soil) would be below threshold criteria already established by FDA in guidance documents or in existing categorical exclusions for other actions. Thus, the basis for establishing a new categorical exclusion for import tolerances is already in place.

(Response 19) We agree with the comments' assessment of the low risk of significant environmental impacts from either the consumption or disposal of edible tissues containing residues of animal drugs. Since the 2012 proposed rule, we have reviewed EAs for several import tolerance requests for new animal drugs used in both aquatic and terrestrial environments (aquatic: azamethiphos and lufenuron in salmonids, benzocaine in Atlantic salmon and rainbow trout, and emamectin and teflubenzuron in Atlantic salmon; terrestrial: monensin and monepantel in sheep; see https://www.fda.gov/AnimalVeterinary/Products/ImportExports/ucm315830.htm). Regardless of the environment in which the drugs were used, each EA described the introduction of drug residues into the domestic environment as being through the consumption of food resulting in: (1) excreta entering sewage treatment facilities and (2) waste of edible tissues disposed of in landfills. Each EA resulted in a finding by the Agency of no significant environmental impact; thus, for each import tolerance action a finding of no significant impact was prepared.

In response to comments that FDA create a categorical exclusion from the requirement to prepare an EA for an action on an import tolerance, the Agency is considering proposing a new categorical exclusion specific to establishment, amendment, or revocation of an import tolerance. This would require review by the White House Council on Environmental Quality, as well as additional rulemaking with public notice and comment. The Agency is currently evaluating available information to determine if this category of actions would individually or cumulatively result in significant effects on the environment and will proceed as appropriate.

(Comment 20) One comment notes that establishment of an import tolerance should also have no appreciable environmental effect outside the United States. If the new animal drug is

not expected to have significant environmental impacts in the country where it is registered for use, it is hard to imagine a situation where movement of residues to another country or into the global commons, such as the open ocean, would present a significant environmental risk.

(Response 20) We agree with the comment's assessment of the low risk of significant environmental effects abroad of residues of new animal drugs appropriately registered in the country they are used based on our experience to date. An analysis of effects abroad is not currently required in the EA for establishment of an import tolerance; however, when necessary, such an analysis will be completed by the Agency.

VI. Effective Date

The rule is effective [INSERT DATE 120 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*].

VII. Economic Analysis of Impacts

We have examined the impacts of the final rule under Executive Order 12866, Executive Order 13563, the Regulatory Flexibility Act (5 U.S.C. 601-612), and the Unfunded Mandates Reform Act of 1995 (Pub. L. 104-4). Executive Orders 12866 and 13563 direct us 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). We believe that this final rule is not a significant regulatory action as defined by Executive Order 12866.

The Regulatory Flexibility Act requires us to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because the final rule will simply codify the procedures that are currently used for the import tolerance program, we certify that the final rule will not have a significant economic impact on a substantial number of small entities.

The Unfunded Mandates Reform Act of 1995 (section 202(a)) requires us to prepare a written statement, which includes an assessment of anticipated costs and benefits, before issuing "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 $158 million, using the most current (2020) Implicit Price Deflator for the Gross Domestic Product. This final rule would not result in an expenditure in any year that meets or exceeds this amount.

Summary of Cost and Benefits

Firms are currently able to request that we establish or amend an import tolerance. The final rule will not change the current procedures for these requests. Thus, we include only the incremental costs of reading and understanding the final rule on import tolerance procedures.

In table 2, FDA provides the Regulatory Information Service Center and Office of Information and Regulatory Affairs Consolidated Information Center accounting information.

Table 2.--Economic Data: Costs and Benefits Statement

Category		Primary Estimate	Low Estimate	High Estimate	Units			Notes
					Year Dollars	Discount Rate	Period Covered	
Benefits	Annualized Monetized $millions/year					7%		
						3%		
	Annualized Quantified					7%		
						3%		
	Qualitative	Codifying current practices of the import tolerance program could improve the efficiency of the program.						
Costs	Annualized Monetized $millions/year	<$0.0001	<$0.0001	<$0.0001	2020	7%	10 years	
		<$0.0001	<$0.0001	<$0.0001	2020	3%	10 years	
	Annualized Quantified					7%		
						3%		
	Qualitative							
Transfers	Federal Annualized Monetized $millions/year					7%		
						3%		
	From/ To	From:			To:			
	Other Annualized Monetized $millions/year					7%		
						3%		

	From/To	From:	To:	
Effects	State, Local or Tribal Government: No Effect Small Business: The final rule will not have a significant impact on a substantial number of small entities that manufacture unapproved drugs that are the subject of an import tolerance request. Wages: No effect Growth: No effect			

We have developed a comprehensive Economic Analysis of Impacts that assesses the impacts of the final rule. The full analysis of economic impacts is available in the docket for this final rule (FDA-2001-N-0075) and at https://www.fda.gov/about-fda/reports/economic-impact-analyses-fda-regulations.

VIII. Analysis of Environmental Impact

The Agency has 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 environmental impact statement is required.

IX. Paperwork Reduction Act of 1995

This final rule contains information collection provisions that are subject to review by OMB under the PRA (44 U.S.C. 3501-3521). The title, description, and respondent description of the information collection provisions are shown in the following paragraphs with an estimate of the annual reporting burden. Included in the estimate is the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing each collection of information.

Title: Reporting Requirements to Establish, Amend, or Revoke an Import Tolerance (21 CFR 510.205)

Description: The FD&C Act, as amended by the ADAA, authorizes the establishment and revocation of tolerances for unapproved new animal drugs where edible portions of animals imported into the United States may contain residues of such drugs (import tolerances) (section 512(a)(6) of the FD&C Act). Import tolerances provide a basis for the legal marketing of imported animal-derived food containing residues of new animal drugs neither approved nor

conditionally approved in the United States (unapproved new animal drugs). Without an import tolerance, any amount of residue of an unapproved new animal drug in imported, animal-derived food would cause that food to be adulterated under section 402(a)(2)(C)(ii) of the FD&C Act because the drug would be deemed unsafe under section 512 of the FD&C Act. Such food could be denied entry into the United States under section 801(a)(3) of the FD&C Act (21 U.S.C. 381(a)(3)). It remains unlawful to import animal-derived food containing a residue of an unapproved new animal drug, unless an import tolerance has been established for such drug and any residue of the new animal drug in the imported animal-derived food does not exceed that import tolerance.

This final rule amends our regulations in part 510 to establish new information collection provisions regarding requests to establish, amend, or revoke import tolerances for residues of unapproved new animal drugs in food. This final rule establishes procedures by which a person may make such requests, as well as procedures for reconsideration of action or an administrative stay of action to establish, amend, or revoke an import tolerance. The regulations make it clear that the Commissioner may start a review process to establish, amend, or revoke an import tolerance on his or her own initiative under § 10.25(b). These regulations also establish when import tolerance-related actions (actions resulting in establishment, amendment, or revocation) and their basis will be publicly disclosed.

The information required to be submitted in a request to establish an import tolerance is set forth in § 510.205(e). The request must identify the drug; describe the conditions of use; describe the proposed import tolerance(s) for residues of the new animal drug; provide human food safety information to support the proposed import tolerance(s); provide other human food safety information as deemed necessary by the Commissioner; describe practicable methods for determining the quantity, if any, of the new animal drug in or on food, and any substance formed in or on food because of its use; include an environmental assessment; and provide any information required under §§ 500.80 through 500.92, where applicable. The information

required to be submitted in a request to amend an import tolerance is set forth in § 510.205(f) and the information required to be submitted in a withdrawal of a request is set forth in § 510.205(g).

The information submitted to us in a request to establish, amend, or revoke import tolerances is necessary to allow us to establish import tolerances that would provide a basis for the legal marketing of imported animal-derived food containing residues of new animal drugs neither approved nor conditionally approved in the United States (unapproved new animal drugs). We will use the information collected through the import tolerances procedure to complete our evaluation.

Comments regarding the information collection topics solicited in the proposed rule are discussed in the preamble in section V. See, in particular, comments 4, 9, 10, 12, 18, and 19. None of the comments suggested we modify the estimated annual burden associated with the information collection. However, we have revised the analysis of the information collection provisions to accurately reflect the final rule. We added a row to table 3 to report the new burden of § 510.205(g) (withdrawal of a request), and we removed a row from table 3 to reflect that the collections of information in our procedural regulations at 21 CFR part 10 (in particular, 21 CFR 10.20, 10.30, 10.33, and 10.35) already are approved under OMB control number 0910-0191.

Description of Respondents: Respondents to the collection of information are: manufacturers of the unapproved new animal drug that is the subject of the request, foreign producers who use the unapproved new animal drug and their trade associations, and importers of animal-derived food bearing or containing residues of the unapproved new animal drug.

We estimate the burden of this information collection as follows:

Table 3.--Estimated Annual Reporting Burden[1]

21 CFR Section; Activity	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
510.205(e)(1) through (8); contents of request	2	1	2	1	2

510.205(a) through (e); request to establish an import tolerance based on permanent Codex MRL[2]	2	1	2	50	100
510.205(a) through (e); request to establish an import tolerance not based on permanent Codex MRL[2]	1	1	1	80	80
510.205(f), request to amend an import tolerance	1	1	1	32	32
510.205(g), withdrawal of a request	1	1	1	1	1
Total					215

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

[2] A Codex MRL is a permanent maximum residue limit (MRL) that has been established by the Codex Alimentarius Committee.

We base our estimate of the number of respondents and number of responses per respondent in table 3 on our experience since the passage of the ADAA and the number of actual requests received. We base our estimate of the average burden per response on our experience with the human food safety technical section of an NADA, as discussed previously in this document.

A request to establish or amend an import tolerance must include human food safety data and other information. The information submitted is similar to that submitted to establish a tolerance under an NADA. The collection of information required for submission of NADAs has been reviewed under the PRA. A proportion of the time estimated in that proposed extension for the paperwork associated with the human food safety technical section of an NADA was used to estimate the time (hours per response) presented in table 3 for the preparation of a request to establish or amend an import tolerance not based on a permanent Codex MRL, approximately 80 hours. We believe a request to establish or amend an import tolerance based on a permanent Codex MRL will be less burdensome, approximately 50 hours. Based on the Agency's experience with establishing tolerances for approved new animal drugs, the Agency believes that requests to revoke an import tolerance, as well as petitions for reconsideration of an action or for an administrative stay of an action, will be infrequent occurrences.

If there is a permanent Codex MRL for a new animal drug, the final rule requires the requester to provide the permanent Codex MRL and monographs and reports from the Joint FAO/World Health Organization of the United Nations (WHO) Expert Committee on Food Additives (JECFA) and/or the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) that support the development of the Codex MRL.

If there is not a permanent Codex MRL, or upon notification by FDA, the final rule requires the requester to provide full reports of investigations made with respect to the human food safety of the new animal drug including data submitted to the appropriate regulatory authority in any country in which the new animal drug is lawfully used. We may regard a request as incomplete unless it includes full reports of adequate tests by all methods reasonably applicable to show whether or not food derived from animals receiving the new animal drug will be safe for human consumption.

The information collection provisions of this final rule have been submitted to OMB for review as required by section 3507(d) of the PRA. Before the effective date of this final rule, FDA will publish a 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.

X. Federalism

We have 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, we conclude 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.

XI. Consultation and Coordination with Indian Tribal Governments

We have analyzed this rule in accordance with the principles set forth in Executive Order 13175. We have determined that the rule does not contain policies that have substantial direct effects on one or more Indian Tribes, on the relationship between the Federal Government and Indian Tribes, or on the distribution of power and responsibilities between the Federal Government and Indian Tribes. Accordingly, we conclude that the rule does not contain policies that have tribal implications as defined in the Executive Order and, consequently, a tribal summary impact statement is not required.

List of Subjects

21 CFR Part 10

Administrative practice and procedure, News media.

21 CFR Part 20

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

21 CFR Part 25

Environmental impact statements, Foreign relations, Reporting and recordkeeping requirements.

21 CFR Part 500

Animal drugs, Animal feeds, Cancer, Labeling, Packaging and containers, Polychlorinated biphenyls (PCBs).

21 CFR Part 510

Administrative practice and procedure, Animal drugs, Labeling, 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 parts 10, 20, 25, 500, and 510 are amended as follows:

PART 10--ADMINISTRATIVE PRACTICES AND PROCEDURES

1. The authority citation for part 10 continues to read as follows:

Authority: 5 U.S.C. 551-558, 701-706; 15 U.S.C. 1451-1461; 21 U.S.C. 141-149, 321-397, 467f, 679, 821, 1034; 28 U.S.C. 2112; 42 U.S.C. 201, 262, 263b, 264.

2. In § 10.25, revise paragraph (a)(1) to read as follows:

§ 10.25 Initiation of administrative proceedings.

* * * * *

(a) * * *

(1) In the form specified in other applicable FDA regulations, e.g., the form for a color additive petition in § 71.1, for a food additive petition in § 171.1 or § 571.1, for a new drug application in § 314.50, for a request to establish or amend an import tolerance in § 510.205, for a new animal drug application in § 514.1, or

* * * * *

PART 20--PUBLIC INFORMATION

3. The authority citation for 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.

4. In § 20.100, add paragraph (c)(47) to read as follows:

§ 20.100 Applicability; cross-reference to other regulations.

* * * * *

(c) * * *

(47) Requests to establish or amend import tolerances, in § 510.205 of this chapter.

PART 25--ENVIRONMENTAL IMPACT CONSIDERATIONS

5. The authority citation for part 25 continues to read as follows:

Authority: 21 U.S.C. 321-393; 42 U.S.C. 262, 263b-264; 42 U.S.C. 4321, 4332; 40 CFR parts 1500-1508; E.O. 11514, 35 FR 4247, 3 CFR, 1971 Comp., p. 531-533, as amended by E.O. 11991, 42 FR 26967, 3 CFR, 1978 Comp., p. 123-124 and E.O. 12114, 44 FR 1957, 3 CFR, 1980 Comp., p. 356-360.

6. In § 25.20, add paragraph (q) to read as follows:

§ 25.20 Actions requiring preparation of an environmental assessment.

* * * * *

(q) Establishment, amendment, or revocation of an import tolerance in accordance with subpart C of part 510 of this chapter.

PART 500--GENERAL

7. The authority citation for part 500 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 342, 343, 348, 351, 352, 353, 360b, 371, 379e.

8. In § 500.80, in paragraph (a), add a new fourth sentence; and revise paragraph (c) to read as follows:

§ 500.80 Scope of this subpart.

(a) * * * The requirements of this subpart shall also apply to a request for an import tolerance under § 510.205 of this chapter. * * *

* * * * *

(c) If FDA concludes on the basis of the threshold assessment or at a later time during the approval process or during the review of a request for an import tolerance that the data show that the sponsored compound and its metabolites should not be subject to this subpart, FDA will continue to consider the compound for approval under the general safety provisions of the Federal Food, Drug, and Cosmetic Act for risks other than cancer or continue its review of the import tolerance request under the provisions of §§ 510.201 through 510.213 of this chapter (Subpart C--Import Tolerances for Residues of Unapproved New Animal Drugs in Food).

* * * * *

9. In § 500.82(b), revise the definition of "Sponsor" to read as follows:

§ 500.82 Definitions.

* * * * *

(b) * * *

Sponsor means the person or organization proposing or holding an approval by FDA for the use of a sponsored compound or the person initiating a request for an import tolerance under § 510.205 of this chapter.

* * * * *

10. In § 500.88, add paragraph (d) to read as follows:

§ 500.88 Regulatory method.

* * * * *

(d) If the sponsor initially submitted a request for an import tolerance under § 510.205 of this chapter, FDA will make the complete regulatory method for ascertaining the marker residue in the target tissue publicly available pursuant to § 510.207(b) of this chapter.

11. In § 500.92, revise paragraph (a) to read as follows:

§ 500.92 Implementation.

(a) This subpart E applies to all new animal drug applications, food additive petitions, color additive petitions, and requests for import tolerances concerning any compound intended for use in food-producing animals (including supplemental applications and amendments to petitions).

* * * * *

PART 510--NEW ANIMAL DRUGS

12. The authority citation for part 510 continues to read as follows:

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

13. Add subpart C to read as follows:

Subpart C--Import Tolerances for Residues of Unapproved New Animal Drugs in Food

Sec.

510.201 Scope.

510.202 Definitions.

510.203 Initiation of a proceeding to establish or amend an import tolerance.

510.205 Content and administration of a request.

510.206 Review of information supporting actions to establish or amend an import tolerance.

510.207 Disclosure of information submitted in a request.

510.209 Establishment, denial, or amendment of an import tolerance.

510.210 Revocation of an import tolerance.

510.212 Administrative reconsideration of action.

510.213 Administrative stay of action.

Subpart C--Import Tolerances for Residues of Unapproved New Animal Drugs in Food

§ 510.201 Scope.

This subpart applies to tolerances for residues of new animal drugs not approved or conditionally approved for use in the United States, but lawfully used in another country and present in imported, animal-derived food and food products.

§ 510.202 Definitions.

The following definitions of terms apply when used in this subpart:

CNADA means an application for conditional approval of a new animal drug submitted under section 571 of the Federal Food, Drug, and Cosmetic Act, and includes all amendments and permissible supplements.

Import tolerance means a tolerance for a residue of a new animal drug not approved or conditionally approved for use in the United States, but present in any imported edible portion of any animal.

NADA means a new animal drug application submitted under section 512 of the Federal Food, Drug, and Cosmetic Act, including all amendments and permissible supplements, for approval of a new animal drug.

Request means a request to establish or amend an import tolerance.

§ 510.203 Initiation of a proceeding to establish or amend an import tolerance.

(a) Any interested person may request that the Commissioner establish or amend an import tolerance. Such a request must be in the form specified in § 510.205 of this chapter.

(b) The Commissioner may initiate a proceeding to establish or amend an import tolerance on his or her own initiative pursuant to § 10.25(b) of this chapter.

§ 510.205 Content and administration of a request.

(a) Pertinent information previously submitted to and currently retained in the files of the Food and Drug Administration (FDA) may be incorporated in, and will be considered as part of, a request on the basis of specific reference to such information. If the requester refers to any nonpublic information other than its own, the requester shall obtain a written right of reference to that nonpublic information and submit the right of reference with the request. Any reference to published information offered in support of a request should be accompanied by reprints or copies of such references.

(b) Requests shall be submitted and addressed to the Document Control Unit (HFV-199), Center for Veterinary Medicine, Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855. Requests may be submitted in an electronic format as authorized by FDA. See FDA′s Electronic Submissions Gateway website: https://www.fda.gov/industry/electronic-submissions-gateway.

(c) Any material submitted in a foreign language shall be accompanied by a complete and accurate English translation. Translations of literature printed in a language other than English shall be accompanied by copies of the original publication.

(d) The request must be dated and must be signed by the requester or by his or her authorized attorney, agent, or official and shall state the requester's correspondence address. If the requester or such authorized representative does not reside or have a place of business within the United States, the requester must also furnish the name and post office address of, and the request must be countersigned by, an authorized attorney, agent, or official residing or maintaining a place of business within the United States.

(e) The request must include the following information:

(1) The established name and all pertinent information concerning the new animal drug, including chemical identity and composition of the new animal drug, and its physical, chemical, and biological properties;

(2) The conditions of use for the new animal drug, including the route of administration and dosage, together with all labeling, directions, and recommendations regarding the uses in countries in which the new animal drug is lawfully used;

(3) The proposed import tolerance(s) for residues of the new animal drug;

(4) Human food safety information to support the proposed import tolerance(s) in either of the following forms:

(i) If a permanent maximum residue limit (MRL) has been established by the Codex Alimentarius Committee (Codex MRL), the requester shall provide the permanent Codex MRL and monographs and reports from the Joint Expert Committee on Food Additives (JECFA) of the Food and Agriculture Organization (FAO) and the World Health Organization (WHO) of the United Nations and/or monographs and reports from the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) that support the development of the permanent Codex MRL. FDA may request additional information as needed.

(ii) If no permanent Codex MRL has been established, or upon notification by FDA, the requester must provide full reports of investigations made with respect to the human food safety of the new animal drug. A request may be regarded as incomplete unless it includes full reports

of adequate tests by all methods reasonably applicable to show whether or not any imported edible portion of any animal receiving the new animal drug will be safe for human consumption. The reports must include detailed data derived from appropriate animal and other biological experiments in which the methods used and the results obtained are clearly set forth, including data submitted to the appropriate regulatory authority in any country where the new animal drug is lawfully used. The request must also include a statement that all such reports have been submitted or contain an explanation of why such reports were not submitted. With respect to each nonclinical laboratory study contained in the request, the requestor must submit either a statement that the study was conducted in compliance with the good laboratory practice regulations set forth in part 58 of this chapter, or, if the study was not conducted in compliance with such regulations, a brief statement of the reason for the noncompliance, and how this may have impacted the study;

(5) Other human food safety information as deemed necessary by the Commissioner;

(6) A description of practicable methods for determining the quantity, if any, of the new animal drug in or on food, and any substance formed in or on food because of its use;

(7) An environmental assessment under § 25.40 of this chapter; and

(8) Any information required under §§ 500.80 through 500.92 of this chapter (Subpart E, Regulation of Carcinogenic Compounds Used in Food-Producing Animals), where applicable.

(f) A request to amend an established import tolerance must contain information to support each proposed change. The request may omit statements made in the original request for which no change is proposed.

(g) The requester may withdraw the request at any time before the notification provided for in § 510.207(a) of this chapter has been made publicly available.

§ 510.206 Review of information supporting actions to establish or amend an import tolerance.

In establishing or amending an import tolerance, the Commissioner shall rely on data sufficient to demonstrate that a proposed tolerance is safe based on similar food safety criteria

used by the Commissioner to establish tolerances for applications for new animal drugs filed under section 512(b)(1) of the Federal Food, Drug, and Cosmetic Act. In establishing or amending an import tolerance, the Commissioner will give appropriate consideration to the anticipated residue concentrations and conditions of use of the new animal drug specified.

§ 510.207 Disclosure of information submitted in a request.

(a) When a request is determined to be complete for FDA's consideration, the Commissioner will provide public notification of the request containing the name of the requester and a brief description of the request in general terms. A copy of the notification will be sent to the requester at the time the information is made available to the public.

(b) Any notification establishing, amending, or revoking an import tolerance will be made publicly available. A summary of the basis for the decision will be publicly released in accordance with the provisions of part 20 of this chapter. If FDA determines that the new animal drug referred to in the request is a new animal drug that induces cancer when ingested by people or animals, and the requester complies with the requirements of §§ 500.80 through 500.92 of this chapter (Subpart E, Regulation of Carcinogenic Compounds Used in Food-Producing Animals), the regulatory method for ascertaining the marker residue in the target tissue will be made publicly available. All information and safety data submitted with the request, or previously submitted information incorporated in, and considered as part of, a request on the basis of specific reference to such information, shall be available for public disclosure, also in accordance with the provisions of part 20 of this chapter. Trade secrets and confidential commercial or financial information are exempted from release under § 20.61 of this chapter.

§ 510.209 Establishment, denial, or amendment of an import tolerance.

(a) If an import tolerance is established or amended, the Commissioner will provide public notification of the action, which will be effective from the date of public notification. A copy of the notification will be sent to any requestor at the time the information is made available to the public.

(b) If a request to establish or amend an import tolerance is denied, a notification of the denial will be made publicly available, and a copy of the denial letter, including the reasons for such action, will be sent to the requester.

(c) A tolerance established in an approved NADA or conditionally approved CNADA will supersede an existing import tolerance. In the event the conditionally approved CNADA is not renewed or is withdrawn, or such drug does not achieve approval under section 512 of the Federal Food, Drug, and Cosmetic Act within 5 years following the date of the conditional approval, the Agency will reinstate the import tolerance unless § 510.210(a)(1) or (a)(2) is applicable at that time.

§ 510.210 Revocation of an import tolerance.

(a) The Commissioner, on his or her own initiative or on the petition of an interested person, under § 10.25 of this chapter, may revoke an import tolerance if:

(1) Scientific evidence shows an import tolerance to be unsafe; or

(2) Information demonstrates that the use of a new animal drug under actual use conditions results in food being imported into the United States with residues exceeding the import tolerance.

(b) The Commissioner will provide public notification under § 510.207(b) that will specify the basis for the decision and will be effective at the time the information is made available to the public.

(c) A petition for revocation must be submitted in the form specified in § 10.30 of this chapter.

§ 510.212 Administrative reconsideration of action.

(a) The Commissioner may at any time, on his or her own initiative or on the petition of an interested person under part 10 of this chapter, reconsider part or all of a decision to establish, not establish, amend, or revoke an import tolerance.

(b) A petition for reconsideration must be submitted in accordance with § 10.20 of this chapter and in the form specified in § 10.33 of this chapter no later than 30 days after the date of public notification of the decision involved. The Commissioner may, for good cause, permit a petition to be filed more than 30 days after public notification of the decision. The petition for reconsideration must demonstrate that relevant information contained in the administrative record was not previously or not adequately considered by the Commissioner. No new information may be included in a petition for reconsideration.

(c) An interested person who wishes to rely on information not included in the administrative record shall submit either a petition to amend an import tolerance under § 510.205 or to revoke an import tolerance under § 510.210 and § 10.25 of this chapter.

§ 510.213 Administrative stay of action.

(a) The Commissioner may at any time, on his or her own initiative or on the request of an interested person under part 10 of this chapter, stay or extend the effective date of a decision to establish, not establish, amend, or revoke an import tolerance.

(b) A request for stay must be submitted in accordance with § 10.20 of this chapter and in the form specified in § 10.35 of this chapter no later than 30 days after public notification of the decision involved. The Commissioner may, for good cause, permit a petition to be filed more than 30 days after public notification of the decision.

Dated: September 10, 2021.

Janet Woodcock,

Acting Commissioner of Food and Drugs.

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